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Diagnosis and Treatment of Erectile Dysfunction

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The American College of Physicians requested and provided funding for this report. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.gov.

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Structured Abstract

Objectives: To systematically review the evidence on efficacy and harms of pharmaceutical treatments used in the management of male erectile dysfunction (ED); to explore the clinical utility of routine hormonal blood tests (e.g. testosterone, prolactin) for identifying and treating hormonal disorders and thereby affecting therapeutic outcomes for ED.

Data Sources: MEDLINE®, EMBASE, PsycINFO®, SCOPUS™, and Cochrane CENTRAL were searched up to June 2007. Reference lists of relevant studies were also searched.

Review Methods: English language primary studies reporting effects of pharmaceutical treatments used to treat men with ED were eligible for inclusion. The records were screened for relevance, abstracted, and assessed for quality by two reviewers independently. The evidence was summarized qualitatively and the results of randomized controlled trials (RCTs) were pooled using meta-analyses. Subgroup and sensitivity analyses were also conducted.

Results: The evidence needed to ascertain the clinical utility of routine hormonal blood tests was limited in terms of the amount and interpretability. Studies were heterogeneous with wide variations in the prevalence of hypogonadism or hyperprolactinemia in patients with ED. Overall phosphodiesterase type 5 (PDE-5) inhibitors were superior to placebo in treating patients with ED with clinically important and statistically significant between-group differences. Adverse events however, were more frequent in PDE-5 inhibitor-treated patients. Few trials demonstrated dose-response trends in the degree of efficacy or frequency of adverse events associated with PDE-5 inhibitors. The clinical benefits conferred by use of PDE-5 inhibitors relative to placebo were observed in patients with wide spectrum of comorbidities irrespective of the origin, duration, or severity of ED. In head-to-head trials evaluating PDE-5 inhibitors, more patients preferred tadalafil to sildenafil or vardenafil. Patients treated with intracavernosal or subcutaneous injections experienced pain and priapism. The evidence for topical, intra-urethral, and hormonal treatments for male ED was insufficient and inconclusive.

Conclusions: Evidence comparing cause-specific therapies (i.e. targeting underlying causes of ED) to symptomatic treatments (e.g. PDE-5 inhibitors, injections, hormonal treatments) for management of ED is lacking. Moreover, long-term effects of ED treatments have not been adequately explored in RCTs. Studies using comparable study populations, diagnostic criteria, and types of tests for hormonal disorders are needed to clarify the clinical utility of routine hormonal blood tests in ED patients. There is also a need for trials comparing PDE-5 inhibitors to other symptomatic treatments for ED (e.g. hormonal treatments, injections, topical applications). This review outlined current gaps in knowledge that need to be addressed in future research.

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Appendixes and Evidence Tables for this report are provided electronically at <http://www.ahrq.gov/downloads/pub/evidence/pdf/erectedys/erecdys.pdf>

Executive Summary

Introduction

Erectile dysfunction (ED) is a complex condition involving psychosocial and biological factors. It is defined as the persistent inability to achieve or maintain penile erection sufficient for satisfactory sexual performance. ED is a common disorder of male sexual function, affecting all age groups with a considerable impact on quality of life.

Oral phosphodiesterase type 5 (PDE-5) inhibitors are the first-line treatment options offered to patients with ED. This systematic review of the recent evidence on clinical benefits and harms associated with different pharmaceutical treatments used in the management of male ED is to clarify uncertainties in the field, as well as to identify existing knowledge gaps and directions for future research.

The University of Ottawa Evidence-based Practice Center (UO-EPC) reviewed and synthesized the published literature on the pharmaceutical treatment of male ED. This review addressed the following key questions (KQ):

KQ 1: What is the clinical utility of routine blood tests—testosterone, prolactin, luteinizing hormone (LH), follicle stimulating hormone (FSH)—in identifying and affecting therapeutic outcomes for treatable causes of ED?

KQ 2: What are the benefits of pharmaceutical treatments for patients with ED? How do patient-specific characteristics (e.g. specific symptoms, age, comorbid conditions) affect prognosis and treatment success for ED patients? Does likelihood of treatment success vary by underlying cause of ED?

KQ 3: What are the harms of pharmaceutical treatments for ED? What is the evidence on specific harms such as nonarteritic ischemic optic neuropathy (NAION) and penile fibrosis of pharmaceutical treatments for ED?

Methods

Literature Search

A comprehensive search was conducted in MEDLINE® (1966–2006), Cochrane CENTRAL (2006–2007), EMBASE (1980–2007), PsycINFO® (1985–2007), and SCOPUS™ (2006). The search was limited to English language reports published in 1990 or later. MEDLINE® (1966–2007) and EMBASE (1980–2007) were searched for reports of visual problems associated with the use of sildenafil, and MEDLINE® (1950–2007) and EMBASE (1980–2007) were searched for reports regarding fibrosis associated with penile injections.

Study Selection

English-language primary studies examining pharmaceutical treatments of ED were eligible for inclusion. Reviews, editorials, commentaries and letters were excluded for all questions except Q3. The reasons for exclusion were noted in the QUOROM flow diagram. Only randomized controlled trials (RCTs) were eligible for evidence on efficacy, whereas non-randomized controlled trials and observational studies were included to examine harms

associated with ED treatments. Two independent reviewers performed full-text screening; discrepancies were resolved by consensus.

Data Extraction and Assessment of Study and Reporting Quality

Two reviewers independently abstracted relevant information from included studies using a data abstraction form. One reviewer completed the primary extraction, which was then verified by a second reviewer. Abstracted data included study, population, and treatment characteristics (type, mode, dose, route of administration); efficacy outcomes such as absolute mean endpoint/change (from baseline) in scores for the International Index of Erectile Function (IIEF) “Erectile Function (EF) domain,” Sexual Encounter Profile (SEP) Q–2/3, and the proportion of patients with improved erection measured with Global Assessment Question 1 (GAQ–1)(see Appendix H). We abstracted information on any and most frequently encountered specific adverse events, withdrawals due to adverse events, and serious adverse events. Additionally, for Q1, prevalence rates of hypogonadism and hyperprolactinemia in ED populations were ascertained and abstracted. The Jadad scale and Schulz questionnaire were used to assess the study and reporting quality and the adequacy of allocation concealment in RCTs.

Synthesis of the Evidence

The outcomes for each study were summarized qualitatively. The information pertaining to sample size and demographics, setting, funding source, treatment (dose and duration), comparator characteristics, study quality, and confounders was recorded and summarized in the text and summary tables. The decision to statistically pool results of individual studies was based on clinical and methodological judgement. If relevant numerical data (e.g. arm-specific mean endpoint/change in score, standard deviation, and standard error) were not reported adequately, we attempted to calculate the needed parameters. For dichotomous and continuous effect measures, pooled estimates of relative risk (RR) and weighted mean differences (WMD) with corresponding 95 percent confidence intervals (95 percent CI) were generated using the DerSimonian and Laird random effects model. The degree of statistical heterogeneity was evaluated using a chi-square test and the I^2 statistic.

A series of subgroup analyses was also performed to explore the consistency of the results. Publication bias was assessed by means of funnel plots.

Results

KQ 1: What is the clinical utility of routine blood tests (testosterone, prolactin, LH, FSH) in identifying and affecting therapeutic outcomes for treatable causes of ED?

The prevalence of hypogonadism varied widely across the studies (12.5 to 25.32 percent). This variation reflected differences in diagnostic criteria for hypogonadism, testosterone measurement methods (e.g. serum total, bioavailable or free levels) and concurrent conditions present across the studies. The prevalence of hypogonadism was higher in men ≥ 50 years versus men < 50 years of age. The results of several studies indicated that ED patients with decreased libido, testicular damage/abnormality, arterial disease, obesity, hyperlipidemia, diabetes, or hypothalamic abnormalities were more likely to have hypogonadism than those presenting without these factors.

The prevalence of hyperprolactinemia varied from 1.42 to 14.3 percent. One Egyptian study in elderly and obese men reported a prevalence of 32 percent. In one of the 9 studies reporting abnormal levels of LH/FSH, about 44 percent of the hypogonadal men had low LH/FSH levels (<13 IU/mL). The prevalence of high LH/FSH levels across three studies varied from 1.03 to 5.79 percent.

KQ 2: What are the benefits of pharmaceutical treatments for patients with ED?

How do patient-specific characteristics (e.g. specific symptoms, comorbid conditions) affect prognosis/treatment success for ED patients?

Does likelihood of treatment success vary by underlying cause of ED?

In total, 126 RCTs evaluating clinical benefits and harms of oral PDE-5 inhibitors (i.e., sildenafil, tadalafil, and vardenafil) in ED patients were included in the review. Patients receiving PDE-5 inhibitors (regardless of dose/dosing regimen) experienced statistically significant and clinically relevant improvements in erectile functioning (mean total IIEF-“EF domain” and IIEF-Q3/Q4 scores, mean SEP-Q2/Q3 scores, improved erection measured by GAQ-Q1) and satisfaction (mean total IIEF-“Intercourse Satisfaction” and “Overall Satisfaction” domains, Erectile Dysfunction Index of Treatment Satisfaction scores) compared with those receiving placebo. The meta-analyses indicated that the use of sildenafil was associated with statistically significant improvements in penile penetration (IIEF-Q3 mean difference: 1.46, 95 percent CI: 1.26–1.65) and improved erection (RR = 2.61, 95 percent CI: 2.34–2.91) compared with placebo. The clinical benefit associated with the use of PDE-5 inhibitors relative to placebo was also observed in clinically distinct subgroups of patients (e.g. diabetes, depression, prostate cancer).

Patients with mild or moderate ED at baseline (IIEF score 11–25) achieved higher mean IIEF-“EF domain” or IIEF-Q3/Q4 scores compared with those with severe ED. The mean scores for IIEF and SEP, improvement in erection, and mean duration of penile rigidity (>60 percent) tended to increase with higher doses of sildenafil (25 mg versus 50 mg versus 100 mg) and vardenafil (5 mg versus 10 mg versus 20 mg).

Results from four head-to-head trials comparing sildenafil, vardenafil, and tadalafil for improvements in erectile function were inconclusive. The between-arm differences in the mean IIEF-EF scores were either statistically non-significant or significant but of small magnitude. In all 4 trials, higher proportion of patients preferred tadalafil to sildenafil or vardenafil. The mean time (in hours) between dosing and sexual attempt was longer for tadalafil compared with sildenafil (5.6 versus 2.7, $p < 0.001$) and a greater proportion of tadalafil-treated men had one or more successful intercourse attempt 12 or more hours post-dose versus sildenafil-treated men (55 versus 29 percent, $p < 0.001$).

The administration of intracavernosal injections (ICI) of alprostadil improved erections more often than no treatment, placebo, papaverine, or phentolamine alone, and at least as often as trimix (prostaglandin E₁ plus papaverine plus phentolamine). In three trials, the use of intraurethral suppositories containing alprostadil was shown to be more effective than placebo.

There were 18 RCTs evaluating the efficacy of hormonal treatment with testosterone (in oral, injection, gel, patch, and cream forms) predominantly in hypogonadal patients with or without

ED as a main complaint. In only one of four small trials, the intramuscular injection of testosterone improved erectile function compared with placebo. Gel testosterone (50 mg and 100 mg doses) was found to have increased sexual intercourse frequency compared with placebo or patch testosterone.

Two RCTs compared testosterone treatment (alone or combined) with PDE-5 inhibitors in hypogonadal patients with ED that was refractory to prior sildenafil therapy (this was also relevant to Question 1). In both trials, patients treated with the combination of testosterone (either patch 5 mg/d or gel 1 percent) and 100 mg sildenafil had statistically significantly greater IIEF scores compared with those treated with sildenafil alone (endpoint: 21.8 versus 14.4, $p < 0.05$ and mean change: 4.4 versus 2.1, $p = 0.029$).

KQ 3. What are the harms of pharmaceutical treatments for patients with ED?

What is the evidence on specific harms such as nonarteritic ischemic optic neuropathy (NAION) and penile fibrosis related to pharmaceutical treatments in patients with ED?

All-cause adverse events were more frequent in patients treated with PDE-5 inhibitors compared with those treated with placebo. In particular, meta-analyses demonstrated that patients receiving sildenafil (any dose) were at higher risk of any adverse (RR = 1.51, 95 percent CI: 1.32–1.72). The 12-week use of 20 mg tadalafil was also associated with an increased risk of any adverse events (RR = 1.61, 95 percent CI: 1.37–1.89). The most common adverse events in PDE-5 inhibitor-treated patients were headache, flushing, dyspepsia, and rhinitis. The use of both sildenafil and vardenafil was associated with an increased risk of headache, dyspepsia, or flushing compared with placebo. Patients treated with sildenafil had an increased risk of visual disturbances (RR = 3.66, 95 percent CI: 2.27–5.92).

Serious adverse events were not statistically different between PDE-5 inhibitor and placebo groups. For example, patients treated with vardenafil experienced a statistically non-significant 34 percent increase in risk of serious adverse events (RR = 1.34, 95 percent CI: 0.76–2.36). Although the rate of withdrawals due to adverse events was slightly increased in patients receiving vardenafil versus those on placebo, the pooled RR estimate did not reach the level of statistical significance (RR = 1.29, 95 percent CI: 0.78–2.13).

The incidence of adverse events increased with the dose of PDE-5 inhibitors. Meta-analyses demonstrated a statistically significant increase in the risk of any adverse events between patients receiving 20 mg versus 10 mg of either tadalafil (RR = 1.21, 95 percent CI: 1.05–1.38) or vardenafil (RR = 1.15, 95 percent CI: 1.06–1.25). The pooled RR estimates for specific events in sildenafil treated patients were: flushing (50 mg versus 25 mg; RR = 1.65, 95 percent CI: 1.13–2.42), headache (100 mg versus 50 mg; RR = 1.31, 95 percent CI: 0.93–1.84), and visual disturbances (100 mg versus 50 mg; RR = 4.18, 95 percent CI: 0.44–39.54). The differences in the incidence of any adverse events between treatment and placebo groups did not vary significantly among four head-to-head trials with patients treated with sildenafil, tadalafil, or vardenafil.

Penile pain or priapism was more frequent in patients treated with alprostadil injections compared with those who received placebo. Patients who received a testosterone patch had a higher rate of skin reactions at the application site compared with those who received the placebo. One trial reported prostate cancer in two patients treated with a testosterone patch. The use of gel testosterone did not show a dose-related increase in adverse events.

To ascertain the incidence of NAION in subjects using PDE-5 inhibitors, this review identified 19 case reports and one large retrospective cohort study of U.S. veterans aged 50 years or older. In almost all case reports, the minimum dose of sildenafil was 50 mg. The risk of NAION in veterans prescribed PDE-5 inhibitors for 2 years was not increased compared with those who were not prescribed PDE-5 inhibitors (RR = 1.02, 95 percent CI: 0.92–1.12). The long-term data on fibrosis amongst penile injection users (e.g. PGE₁, papaverine, and/or phentolamine) was obtained from 13 reports of non-randomized controlled trials and 7 retrospective cohort studies. In these studies, the proportion of patients with fibrosis amongst those receiving PGE₁ injections for at least one year, ranged from 4.4 to 23.3 percent. Clinical diversity (i.e., populations, intervention dose/duration/frequency, injection type, duration of followup), scarce data, confounding, and lack of appropriate comparator precluded a meaningful between-group comparison of the incidence of fibrosis.

Discussion and Future Research

The utility of routine endocrinological blood tests to identify treatable causes of ED and to improve therapeutic outcomes was unclear due to study heterogeneity. Prevalence of endocrinopathies, patient characteristics, diagnostic criteria, age distribution, laboratory methods (cut-off values, total, free, bioavailable hormonal levels), and/or study methodology varied widely. Factors such as obesity, decreased libido, testicular damage/abnormality, arterial disease, and/or insulin resistance may be predictive of hypogonadism in patients with ED. Studies to measure the prevalence of endocrinopathies and RCTs comparing the efficacy of testosterone relative to PDE-5 inhibitors would further clarify the clinical utility and cost-effectiveness of routine blood tests. The standardization of blood tests would facilitate this process. Furthermore, determination of subgroups (or risk factors) of ED patients with increased risk of hypogonadism is warranted. Additionally, clinicians would need to direct their efforts towards correctly identifying and treating underlying causes of ED, including hormonal disorders.

The efficacy of PDE-5 inhibitors was evaluated using clinically relevant and validated outcome measures. These measures are based on patient responses, and therefore are subjective in nature. Patients preferred tadalafil over sildenafil or vardenafil in four head-to-head trials in part due to the longer duration of the action of tadalafil compared with the other two agents. The evidence regarding the incidence of serious adverse events is not conclusive for several reasons, including poor reporting practices and the use of different definitions of serious adverse events. Some reports indicated only the most frequently encountered or treatment-related adverse events, the ascertainment of which may be prone to subjective judgment. In open label trials, patients or investigators may have over- or underreported the incidence of adverse events because of their knowledge of the assigned treatment. Moreover disease-specific complications in patients with comorbidities or disorders known to cause ED could have been overlooked. The exclusion criteria reported for many PDE-5 inhibitor trials mean that results may not be readily applicable to patients diagnosed with major chronic disorders (e.g. cancer, CVD, diabetes, psychiatric disorders, or hepatic or renal diseases) or those who had undergone surgery (e.g. prostatectomy).

The comparative evidence for the efficacy and harms associated with subcutaneous injections, sublingual, topical treatments, or intra-urethral suppositories was limited and inconsistent. One common limitation of the trials evaluating these therapies was that clinically relevant efficacy outcomes were not reported. Differences in patient inclusion criteria (e.g. not all trials were comprised exclusively of ED patients), methods of evaluation, interventions (e.g.

different formulations/modes of application), or outcome definitions could explain some of the discrepancies in results across the studies evaluating the efficacy of testosterone.

Future efforts are needed to improve the quality of reporting of primary studies. In the presence of comorbidities or causes underlying ED, the comparison of cause-specific therapies (i.e. targeting underlying causes of ED) to symptomatic treatments (e.g. PDE-5 inhibitors, injections, hormonal treatments) in terms of efficacy and safety profiles is warranted. New, well-designed trials are warranted to examine long-term clinically relevant treatment outcomes (6 months or longer) in both broadly defined and clinically homogeneous subgroups of ED patients. There is also a need for head-to-head trials to compare various PDE-5 inhibitors with one another as well as trials comparing PDE-5 inhibitors with other symptomatic treatments for ED (e.g. oral, injected, and topical treatments).

Viewed in perspective, this report represents a striking example of a situation that reviewers of medical effectiveness research encounter often: a field of information in which one corner is intensively cultivated and other areas lie fallow. Erectile dysfunction can be treated at present by two main classes of drugs, phosphodiesterase type-5 inhibitors and/or androgens. This review finds a dearth of credible evaluations of androgens as treatment for ED – clarifying neither short-term effectiveness nor long-term outcomes (positive or negative). In light of the growing popularity of androgen supplementation for a variety of indications in aging men, and in the context of complicated and controversial findings of the far more extensive studies of hormone replacement therapy in women, this gap in our research base is especially noteworthy. For PDE-5 inhibitors, in contrast, an impressive amount of clinical trial evidence is available, demonstrating that these drugs do have a real effect. The impetus for much of this research arose from the desire to get PDE-5 inhibitors approved by the FDA. For instance, nearly three-quarters of the PDE-5 inhibitor trials in this review were funded by pharmaceutical companies.

Even for the PDE-5 inhibitors, important aspects remain inadequately explored. The effects observed in the controlled trials mostly denote differences of small magnitude in self-reported subjective judgments of function on a standardized questionnaire (e.g., the difference between “a few times” and “sometimes,” or between “sometimes” and “most times”). Because of the randomization and the large number of subjects, the evidence is convincing that there is some therapeutic effect; the extent to which these “real” effects are great enough to be clinically meaningful is not as clear, and that is a separate question which this review does not address. Moreover, although short-term side-effects of the PDE-5 inhibitors have been investigated (as the FDA requires), very few studies have tried to investigate long-term side-effects or long-term outcomes - such as persistence or attenuation of effectiveness with continued use.

In summary, while research pertaining to short-term effects of the PGE-5 inhibitors is abundant, comparable studies on androgens and information on long-term treatment outcomes for either class are sparse. The skewed concentration of research on the effectiveness of treatments for ED reflects the short-term focus of the new-drug approval process. The value of information might be enhanced by new sources of financial support for research and/or a change in regulatory requirements that would encourage broader comparisons and a longer time horizon.

Conclusions

The evidence comparing cause-specific therapies with symptomatic treatments (e.g. PDE-5 inhibitors, injections, and hormonal treatments) for management of ED is lacking. Due to the complexity of causative and comorbid factors, more studies are needed to clarify the best treatment management options for various subgroups of patients with ED (e.g. endocrinopathies,

concurrent clinical conditions). There is also a need for trials comparing PDE-5 inhibitors with other treatments for ED (e.g. oral, injected and topical). Long-term effects of ED treatments in RCTs have not been adequately explored. To clarify and determine the clinical utility of routine hormonal blood tests in ED patients, studies are needed in representative populations, with comparable diagnostic criteria and types of tests for hormonal disorders.

Evidence Report

Chapter 1. Introduction

Objectives of the Systematic Review

The purpose of this evidence report was to review systematically the literature on the diagnosis and pharmaceutical treatments of erectile dysfunction (ED) and to address the following objectives put forth by the Agency for Healthcare Research and Quality (AHRQ) and the American College of Physicians (ACP).

The primary objectives of this evidence report were:

KQ 1. To determine the clinical utility of routine blood tests - testosterone, prolactin, luteinizing hormone (LH), follicle stimulating hormone (FSH) - in identifying and affecting therapeutic outcomes for treatable causes of ED.

KQ 2. To determine the benefits of pharmaceutical treatments for patients with ED.

KQ 3. To determine the harms of pharmaceutical treatments for patients with ED.

The secondary objectives of this evidence report were:

KQ 2a. To explore how patient-specific characteristics (e.g. specific symptoms, age, comorbid conditions) may affect prognosis and treatment success for ED patients.

KQ 2b. To determine if the likelihood of treatment success varies by underlying cause of ED.

KQ 3a. To identify specific harms, such as nonarteritic ischemic optic neuropathy (NAION) and penile fibrosis of pharmaceutical treatments in patients with ED.

The findings of this report are intended to assist the AHRQ and the ACP in identifying areas for future research and in the development of practical information for healthcare providers and consumers.

Background

Definition of Erectile Dysfunction

Erectile dysfunction (ED) is defined as the persistent inability to achieve or maintain penile erection sufficient for satisfactory sexual performance.¹ The 1992 National Institutes of Health (NIH) Consensus Development Conference recommended the use of *erectile dysfunction* as the preferred term to *impotence*, the former being more precise.¹ There is no universal consensus or agreed criteria as to how consistent the problem (i.e., inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance) has to be and for what duration it should last to fulfill this definition. A period of persistence over 3 months has been suggested as a reasonable clinical guideline.^{1,2}

Physiology of Erection

Penile erection is a complex process involving interactions between neural, psychological, vascular, and hormonal factors. The pathway of normal sexual function in males consists of four stages: sexual desire (i.e., libido), erection, ejaculation (i.e., orgasm), and detumescence (penile flaccidity).³ The erection cycle is initiated by sexual stimulation. Erection subsides at ejaculation or cessation of sexual stimulation and the subsequent flaccidity state is maintained until the next sexual stimulation or nocturnal erection occurs. Thus, both the erection and the flaccidity states of the penis exist in two phases, initiation and maintenance. Pathways responsible for penile

flaccidity are no less important than pro-erectile mechanisms, and may play critical roles in certain types of erectile dysfunction (ED).⁴ Additionally, hormones function not only at the libido level, but help maintain anatomical and physiological integrity of penile cavernosal structures; testosterone deficiency interferes not only with normal function, but can also diminish response to ED treatment.⁵

The mechanism of erection involves responses to external sensory stimuli through parasympathetic activity, which leads to release of nitric oxide (NO) from nonadrenergic-noncholinergic (NANC) cavernous (penile) nerve endings and the endothelium of the penis. The initial phase of smooth muscle relaxation results in reduced peripheral resistance of cavernosal arterioles and thereby allows blood to flow into the penis under the driving force of systemic blood pressure.⁴ Once blood rushes into the sinusoids of the corpora cavernosa, shear stress can also release NO from endothelium to augment smooth muscle relaxation and erection. In addition, oxygen tension and substances secreted by endothelium lining the sinusoidal spaces, (i.e. prostaglandins, endothelins, and angiotensin) may also be involved in penile erection and detumescence.^{6,7}

The somatic sensory nerves originate at receptors in the penis to transmit pain, temperature, touch, and vibratory sensations, and the brain modulates the spinal pathways of erection via the medial preoptic area and paraventricular nucleus of the hypothalamus, periaqueductal gray of the midbrain, and the nucleus paragigantocellularis of the medulla.³ During sexual stimulation, NO released from the penile cavernosal nerve endings and endothelium, diffuses into the trabecular and arterial smooth muscle cells to activate guanylyl cyclase, thereby catalyzing the formation of second messenger cyclic guanosine monophosphate (cGMP). The cGMP in turn activates protein kinase G, phosphorylating potassium and calcium channels; the end result is hyperpolarization, reduced intracytosolic calcium, and dissociation of the myosin head from acting as smooth muscle relaxes. Cyclic adenosine monophosphate (cAMP) is another second messenger involved in smooth muscle relaxation and is activated by cAMP-signaling molecules including adenosine, calcitonin gene-related peptides, and prostaglandins.⁴

On the other hand, norepinephrine, phenylephrine, and endothelin appear to activate phospholipase C, leading to the formation of inositol triphosphate and diacylglycerol. The net result is increased cytoplasmic calcium and subsequent smooth-muscle contraction. Detumescence occurs following degradation of cGMP and cAMP to GMP and AMP, respectively, by specific phosphodiesterases. Sympathetic discharge occurs if sexual stimulation results in ejaculation.^{8,9} Activated Rho-kinase phosphorylates, inhibits the regulatory subunit of smooth muscle myosin phosphatase, preventing dephosphorylation of myofilaments and maintaining contractile tone.¹⁰ In the flaccid state, these smooth muscles are tonically contracted due to intrinsic smooth-muscle tone, adrenergic discharge, and other signaling molecules such as endothelin.⁴

Diagnosis of Erectile Dysfunction

The diagnosis of ED involves a clinical evaluation including medical/physical examination as well as documentation of sexual and psychosocial history.^{11,12} Erectile dysfunction is one of many symptoms of sexual disorders including premature ejaculation, increased latency time associated with age, psycho-sexual relationship problems, and loss of libido. During diagnosis of ED, it is important that other sexual dysfunctions (e.g. loss of libido) be recognized and taken into account.^{13,14} A few validated instruments are used in diagnosing ED, grading its severity,

and assessing treatment satisfaction. Some examples of such instruments are the International Index of Erectile Function (IIEF),¹⁵ the modified 5-item version of IIEF (IIEF-5),¹⁶ and the Erectile Dysfunction Index of Treatment Satisfaction (EDITS).¹⁷ The IIEF is a self-administered 15-item questionnaire consisting of five distinct domains: erectile function (total score range 1–30), orgasmic function (total score range 0–10), sexual desire (total score range 2–10), intercourse satisfaction (total score range 0–15), and overall satisfaction (total score range 2–10).¹⁸

Recommendations based on biochemical investigation may consist of hormonal screening to detect hypogonadism or other underlying common diseases such as hyperprolactinemia, diabetes and dyslipidemia.^{19,20} Other methods that may be used are urine analysis, blood count, lipid levels, or prostate-specific antigen (PSA) concentration.¹ There are also specialized evaluation techniques such as duplex ultrasonography, penile tumescence studies, RigiScan, test injections, audio-visual stimulation and penile brachial index measurement.²¹

Epidemiology of Erectile Dysfunction

ED is a common disorder of male sexual function that affects all age groups and has a profound impact on quality of life.² Given the increasing trends in life expectancy across the Western world (i.e., the aging of the general population) and the high prevalence of diabetes and cardiovascular disease, the impact on lifestyle and quality of life imposed by ED in men is projected to be substantial.¹ It was estimated that, in 1995, over 152 million men worldwide experienced ED. For 2025, the prevalence of ED is predicted to be approximately 322 million worldwide.²² The severity, prevalence and incidence of ED increase with age.^{2,22,23} The Massachusetts Male Aging Study² surveyed 1,709 men aged 40–70 years between 1987 and 1989, using a self-administered questionnaire that asked participants to rate themselves as not having ED, or having minimal ED, moderate ED, or complete ED. There was a total prevalence of erectile dysfunction of 52 percent when participants with minimal (17.2 percent), moderate (25.2 percent) and complete (9.6 percent) dysfunction were combined.² Both the prevalence and severity of erectile dysfunction increased proportionally with age. When adjusted for age, patients with lower level of education, heart disease, hypertension, and diabetes had a higher probability of ED.^{2,23} In the same study, a sample of 847 men without ED at baseline (1987–1989) was followed prospectively until 1995–1997.²³ The crude incidence rate of ED in this population was estimated to be about 26 cases per 1,000 man-years (95% CI: 22.5–29.9). The annual age-specific incidence rate of ED increased with each decade of age. For example, the incidence rates (and 95% CIs) for men in two age groups of 50–59 and 60–69 years were 29.8 cases per 1,000 man-years (95% CI: 24.0–37.0) and 46.4 cases per 1,000 man-years (95% CI: 36.9–58.4), respectively.²³ In a Canadian cross-sectional survey of primary care facilities, about 50 percent of 3,921 men aged 40–88 years had ED (IIEF “EF” domain score <21).²⁴ The presence of cardiovascular diseases or diabetes was associated with an increased risk of having ED after adjustment for age and other confounders.²⁴

Classification of Erectile Dysfunction and Related Conditions

Today, ED is considered a disorder with multiple causes. The current evidence suggests that about 80 percent of ED cases are of organic origin.¹ Organic causes of ED may be vascular (e.g. cardiovascular disease, hypertension, lipid disorders, endothelial dysfunction), neurological (e.g. spinal cord injury, Parkinson’s disease, multiple sclerosis), iatrogenic (e.g. pelvic surgery,

prostatectomy, antipsychotic agents, antidepressants, beta-blockers, diuretics, antitestosterone hormonal agents), penile injury/anatomic abnormalities (e.g. Peyronie's disease, priapism), tumors (e.g. prostate cancer, colorectal cancer), various conditions (chronic renal or hepatic failure, lower urinary tract symptoms, prostatic hyperplasia), substance use and abuse (e.g. alcohol, tobacco) or endocrine disorders (e.g. diabetes, andropause, hypogonadism, hyperprolactinemia, hypothyroidism). Some of the psychogenic causes of ED may be depression, dysphoria, or anxiety states.¹ The majority of ED patients with organic causes present with vascular diseases and have decreased blood flow to the penis.^{2,21,25} In many patients the cause of ED may be a combination of psychological and organic factors.²⁶

Treatment of Erectile Dysfunction

Today, unless contraindicated, the first-line therapies offered for the treatment of ED are lifestyle and risk factor modification (e.g. exercise and weight loss)²⁷ and the use of the oral phosphodiesterase type 5 (PDE-5) inhibitors such as sildenafil, tadalafil, or vardenafil.^{13,28} Given that PDE-5 drugs may interact with nitrates with respect to vasodilatory effect, all PDE-5 drugs are contraindicated in patients taking nitrates for cardiac disease. The introduction, availability, and production of PDE-5 inhibitors have revolutionized the management of ED, allowing physicians to treat the condition in the primary care setting.

Although other types of medical treatments (e.g. intracavernosal injections, intraurethral suppositories) for erectile dysfunction have existed for years, their use has been associated with specific adverse events (e.g. local pain, priapism, fibrosis) and low compliance rates resulting from the invasive nature of these therapies. Topical therapies of agents that are approved by FDA for other indications have been explored as alternative options given their less invasive routes of administration (e.g. alprostadil, papaverine, organic nitrates). Other second-line treatment modalities for patients with refractory ED or who cannot tolerate PDE-5 therapy are hormonal treatments, vacuum constriction devices and surgical therapies (e.g. penile prosthesis implants, penile arterial bypass).¹⁴ Psychological counseling (e.g. psychotherapy) and recommended lifestyle modifications (e.g. smoking cessation, low-fat diet, physical activity, weight loss) should be offered to men with ED either alone or in combination with other treatments.

Utilization and Costs Related to Treatment of ED

Estimates from the National Health and Nutrition Examination Survey (NHANES) suggests that the cost of treatment of ED in the U.S. could reach \$15 billion if all men sought care.²⁹ Analyses by the Erectile Dysfunction subgroup for the Urologic Diseases in America Project identified that almost 1.5 percent of privately insured males between the ages of 18 and 64 had at least 1 claim related to ED in 2002; shifting forms of health care were demonstrated, as the use of diagnostic tests for underlying causes of ED markedly decreased and utilization of pharmacological therapy especially with oral PDE-5 inhibitors, increased.²⁹ National pharmacy claims data indicated an increased prevalence of sildenafil use from 1.5 percent in 1998 to 2.9 percent in 2002, with its use increasing with age. For example, in 2002, 6 percent of men aged 55 or older had one or more claims for sildenafil.³⁰ Furthermore, the Department of Veteran Affairs (VA) indicated a nine-fold increase in treatment for ED between 1999 and 2003, with 9.3 percent of men 55-64 years of age reporting filling a prescription for oral agents in 2003.²⁹ The overall use of pharmacological treatment for ED increased from 17,458/100,000 in 1999 to 56,716/100,000 in 2003.²⁹ This is reflected by data from the VA

Pharmacy Benefits Management Group, as prescriptions for specific ED drugs increased from 681/100,000 to 6,120/100,000 during this period.²⁹ According to national sales, in 2005, the pharmaceutical costs of sildenafil, tadalafil, and vardenafil were \$1.6 billion, \$747 million, and \$327 million, respectively.³¹⁻³³

Harms Observed in Clinical Trials

Headache, flushing, rhinitis, and dyspepsia are the most commonly observed adverse events related to treatment with PDE-5 drugs. There also have been concerns regarding the excess incidence of cardiovascular events and visual disturbances occurring in patients receiving PDE-5 drugs; however, the current evidence does not indicate any marked trends for increased rates of these events in ED patients taking PDE-5 drugs compared with those in the general population.^{13,34}

Measures of Efficacy in Erectile Dysfunction Therapy

From the patient's perspective, the most important measures for defining successful ED treatment are: "cure, pleasure, partner satisfaction, reproduction, and naturalness."³⁵ To address the lack of well-defined standardized guidelines for the assessment of clinical outcomes in comparative trials of ED therapies, an International Consensus Advisory Panel was convened in 2002 in Montréal, Canada, where a new conceptual framework for treatment effectiveness was adopted.³⁶

According to this framework, treatment effectiveness consists of two dimensions: *treatment response* and *treatment satisfaction*. Treatment response, in turn, consists of an integrated assessment of efficacy (i.e., ability of an agent to promote achievement and maintenance of adequate erection) and tolerability (i.e., side effects). The response was categorized as *complete responder* (e.g. consistent achievement and maintenance of full erection and ability to tolerate side effects), *partial responder* (e.g. ability to achieve full erection but not on a consistent basis over time and/or patients who experienced adequate efficacy but also had bothersome side effects of treatment), or *nonresponder* (e.g. patients who failed to respond in a clinically significant manner to the treatment and/or those who experienced intolerable effects at any dosage). Generally, the treatment efficacy in ED trials is assessed using event-log or diary-based questionnaires such as the IIEF and IIEF-5, the sexual encounter profile (SEP), and global assessment questions (GAQs).³⁶ These measures are all based on patient responses and therefore are subjective in nature.¹⁸ The other domain of treatment effectiveness—*treatment satisfaction*—is defined as the degree to which the effects of any particular treatment correspond or exceed the expectations of a patient and his partner.³⁶ This domain was categorized as *complete satisfaction* (e.g. both the patient and his partner were satisfied), *partial satisfaction* (e.g. either the patient or the partner was not satisfied), and *no satisfaction* (neither the patient nor the partner was satisfied). In summary, according to this framework, the overall measure of treatment effectiveness should ideally integrate the information on both treatment response (i.e., efficacy and tolerability) and treatment satisfaction (i.e., self-rated degree of patient-partner satisfaction).

Knowledge Gaps and Uncertainties

Currently there are several knowledge gaps in the management of ED. There is still insufficient information regarding the effectiveness and safety related to the use of different treatment modalities in various clinical subgroups of patients (e.g. diabetes, cardiovascular

disease). Furthermore, there is insufficient data with regard to long-term adverse effects of oral ED medications that have been used by millions of users for over a decade. Comparative data on the efficacy and safety profiles of PDE-5 drugs have not yet been accumulated. Safety and efficacy data from trials with head-to-head comparisons of PDE-5 drugs are needed to establish the relative superiority of one drug over the others.

Some controversy has surrounded the issue of the clinical utility of and indications for routine endocrinological blood tests (e.g. testosterone, prolactin) for all patients presenting with ED.^{19,20,37,38} Current American Urological Association Practice Guidelines Committee (AUA PGC) recommend the determination of hormone levels based on initial clinical assessment or failure of initial PDE-5 management; these tests are not mandatory for all patients.¹⁴ This is in contrast to the guidelines of the European Urological Association and the British Society for Sexual Medicine, both of which define endocrinological “screening” as a mandatory component of the initial evaluation of ED.³⁹ The purpose of this testing is to identify and treat endocrinopathies such as hypogonadism and hyperprolactinemia as underlying causes of ED. In these cases, therapeutic outcomes for hormonal disorders and resultant ED are thought to be optimized.^{20,40} The debate regarding the optimal approach still continues. One group of experts recommends basic endocrine screening to measure serum levels of testosterone and prolactin, to guide treatment of the patients with testosterone and its analogs to correct specific endocrinopathies and symptoms of ED,⁴¹⁻⁴³ as well as to detect pituitary tumors.^{38,44} Other experts do not recommend the administration of routine hormone tests to all ED patients because of the high cost of these tests and the low prevalence of endocrinopathies in the ED population.^{20,37,45} These authors suggested that the screening tests for serum hormonal levels be restricted to those patients with clinical signs of hypogonadism (e.g. decreased libido, small testes, reduced body hair) as revealed by a physical examination, or to those in whom the initial PDE-5 inhibitor therapy was ineffective.^{20,38,45} Authors of one empirical study advocated routine determination of serum testosterone levels for all ED patients older than 50 years and serum prolactin levels for only those with low testosterone levels (<4ng/mL), decreased libido, and/or gynecomastia.³⁸ Clearly, a universally accepted guideline of “standard of practice” for endocrinological testing of the ED patient is yet to be defined and established.

Chapter 2. Methods

Key Questions Addressed in This Report

The UO–EPC’s evidence report on the diagnosis and treatment of erectile dysfunction (ED) is based on a systematic review of the scientific literature. A technical expert panel was recruited to help refine key questions and provide expertise to the review team during the review process.

The finalized key questions were:

KQ 1. To determine the clinical utility of routine blood tests - testosterone, prolactin, luteinizing hormone (LH), or follicle-stimulating hormone (FSH) - in identifying and treating specific hormonal causes of ED.

KQ 2. To determine the benefits of pharmaceutical treatments for patients with ED.

KQ 3. To determine the harms of pharmaceutical treatments for patients with ED.

The secondary objectives of this evidence report were:

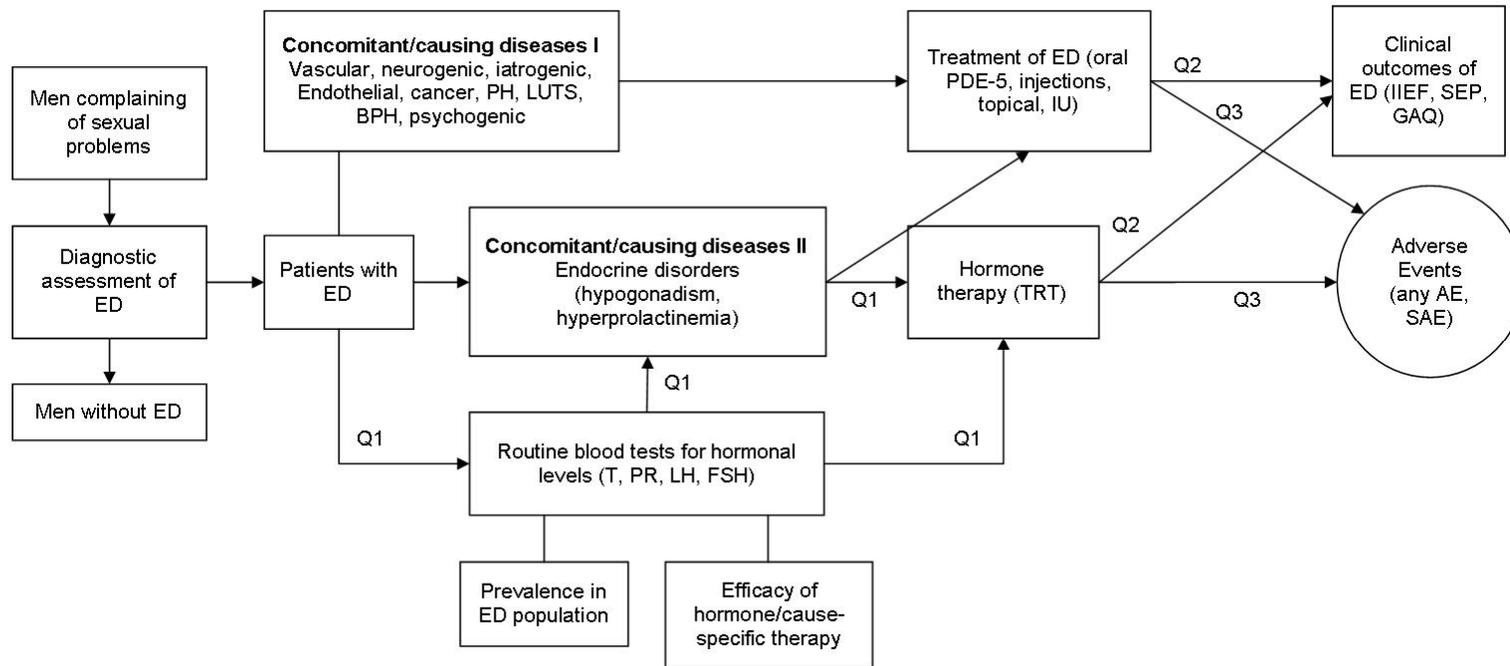
KQ 2–a. To explore how patient-specific characteristics (e.g. specific symptoms/age/comorbid conditions) may affect prognosis and treatment success for ED patients.

KQ 2–b. To determine if the likelihood of treatment success varies by underlying cause of ED.

KQ 3–a. To identify specific harms—nonarteritic ischemic optic neuropathy (NAION), penile fibrosis—of pharmaceutical treatments in patients with ED.

Analytic Framework

Figure 1. Analytic Framework for the Diagnosis and Treatment of Erectile Dysfunction



Endocrine disorders
 Hypogonadism
 Hyperprolactinemia
 Adrenal glands disease
 Diabetes

Vascular disorders
 Congestive heart failure
 Coronary artery disease
 Cerebrovascular disease
 Hypertension

Neurogenic
 Spinal cord injury
 Parkinson's disease
 Psychogenic
 Depression

Iatrogenic
 Prostatectomy
 Benign prostatic hyperplasia
 Prostate cancer

Search Strategy

A preliminary MEDLINE® (1966–January Week 3 2006) search identified systematic reviews and guidelines in erectile dysfunction published between 1990 and 2006. Searches for diagnostic and efficacy studies were undertaken in the following databases: MEDLINE® (1966–July Week 3 2006, updated to May Week 5 2007); EMBASE (1980–2006 Week 29, updated to 2007 Week 2); Cochrane CENTRAL (1st Quarter 2006 and 2nd Quarter 2007); PsycINFO® (1985–January 2006, updated to June Week 1 2007); AMED (1985–January 2006, updated to June 2007); and Scopus Feb 8 2006. All databases were searched for efficacy; MEDLINE® and EMBASE were searched for diagnostic studies. The searches were limited to English publications from 1990 and later. MEDLINE® (1966–August Week 5 2006, updated to May Week 5 2007) and EMBASE (1980–2007 Week 8, updated to 2007 Week 22) were searched for reports of visual problems and sleep apnea associated with the use of sildenafil. MEDLINE® (1950–September Week 1 2007) and EMBASE (1980–2007 Week 37) were searched for reports regarding fibrosis associated with penile injections. Search strategies are presented in Appendix A.

Study Eligibility Criteria and Selection Process

KQ 1. The clinical utility of routine blood tests—testosterone, prolactin, LH, FSH - in identifying and affecting therapeutic outcomes for treatable causes of ED was examined using reports of measurements of serum testosterone, FSH, LH, prolactin, and/or other hormone levels, (but not gonadotrophin-releasing hormone [GnRH], Inhibin, Activin, or Follistim). It was also examined in reports of the prevalence of reversible hormonal disorders in males with erectile dysfunction. The study selection criteria included the following:

Source: Primary study report published in English

Study design: Any (prevalence studies)

Population: Adults (age \geq 18 years) diagnosed with ED with or without concurrent endocrinopathy (i.e., hypogonadism, hyperprolactinemia, abnormal levels of LH/FSH)

Intervention (experimental): Hormonal blood tests (i.e., testosterone/prolactin/LH/FSH)

Outcomes: Prevalence of endocrinopathies (i.e., hypogonadism, hyperprolactinemia, abnormal levels of LH/FSH)

KQ 2. Benefits of pharmaceutical treatments (e.g. oral, injections, hormonal, topical, intra-urethral suppositories) in males with ED. To address how patient specific characteristics (e.g. specific symptoms/origin, duration, severity of ED/comorbid conditions) affect prognosis/treatment success for ED patients. Evidence on the following treatment modalities was excluded from this review: Natural health products (e.g. herbals), yohimbine, vacuum constriction devices, and sex or surgical therapies (e.g. penile prosthesis implantation, penile arterial reconstructive surgery). Study selection criteria included the following:

Source: Primary study report published in English

Study design: RCTs (comparative efficacy and harms studies)

Population: Adults (age \geq 18 years) diagnosed with ED (with or without comorbidities)

Interventions (experimental/control): Oral (PDE-5 inhibitors, sublingual) injections (IC, cream)

Outcomes: Clinically relevant efficacy measures (i.e., scores for the IIEF “EF” domain, IIEF-Q3/Q4, SEP-Q2/Q3, GAQ-Q1, EDITS)

KQ 3. Harms of pharmaceutical treatments (e.g. oral, injections, hormonal, topical, intra-urethral suppositories) in males with ED. Evidence on the following treatment modalities was excluded from this review: Natural health products (e.g. herbals), yohimbine, vacuum constriction devices, and sex or surgical therapies (e.g. penile prosthesis implantation, penile arterial reconstructive surgery). Study selection criteria included the following:

Source: Primary study report published in English

Study design: RCTs (comparative efficacy and harms studies)

Population: Adults (age \geq 18 years) diagnosed with ED (with or without comorbidities)

Interventions (experimental/control): Oral (PDE-5 inhibitors, sublingual) injections (IC, SC), hormonal (e.g. testosterone), intra-urethral suppositories, CPAP, and/or topical (e.g. patch, cream)

Outcomes: Any adverse events, serious adverse events, withdrawals due to adverse events, and specific adverse events.

KQ 3a. The incidence of specific harms such as Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) and penile fibrosis associated with use of PDE-5 inhibitor and injection therapies, respectively. The review included reports of non-RCTs or observational studies. For identification of data on fibrosis related to use of injection therapies, only studies with at least 6 months of followup were included. Study selection criteria included the following:

Source: Primary study report published in English

Study design: Non-RCTs (experimental or observational case-control and cohort studies, case reports and case-series)

Population: Adults (age \geq 18 years) diagnosed with ED (with or without comorbidities)

Interventions (experimental/control): Oral (PDE-5 inhibitors), injections (IC, SC)

Outcomes: NAION, penile fibrosis

Systematic and narrative reviews, case reports, editorials, commentaries or letters to the editor were excluded for all questions except Q3-a (specific harms). Studies evaluating interventions such as penile implant devices or natural health products used for the treatment of ED were also excluded.

The results of the literature search were uploaded to the software program TrialStat SRS version 4.0 along with screening questions developed by the review team and any supplemental instructions. A calibration exercise was undertaken to pilot and refine the screening process. One reviewer screened bibliographic records (i.e., title, authors, key words, abstract) using broad screening criteria (Appendix B). All potentially relevant records and those records that did not contain enough information to determine eligibility (e.g. no abstract was available) were retained. The reasons for exclusion are noted in the QUOROM flow diagram (Figure 2). Two reviewers independently performed full-text relevance screening. Disagreements were resolved by consensus. Reasons for exclusion were noted (Appendix E).

Relevant studies were then evaluated to determine study design and were categorized accordingly for inclusion by question. The level of eligible evidence on efficacy was limited to RCTs, since systematic bias is minimized in RCTs compared with all other study designs (e.g. cross-sectional, retrospective cohort).

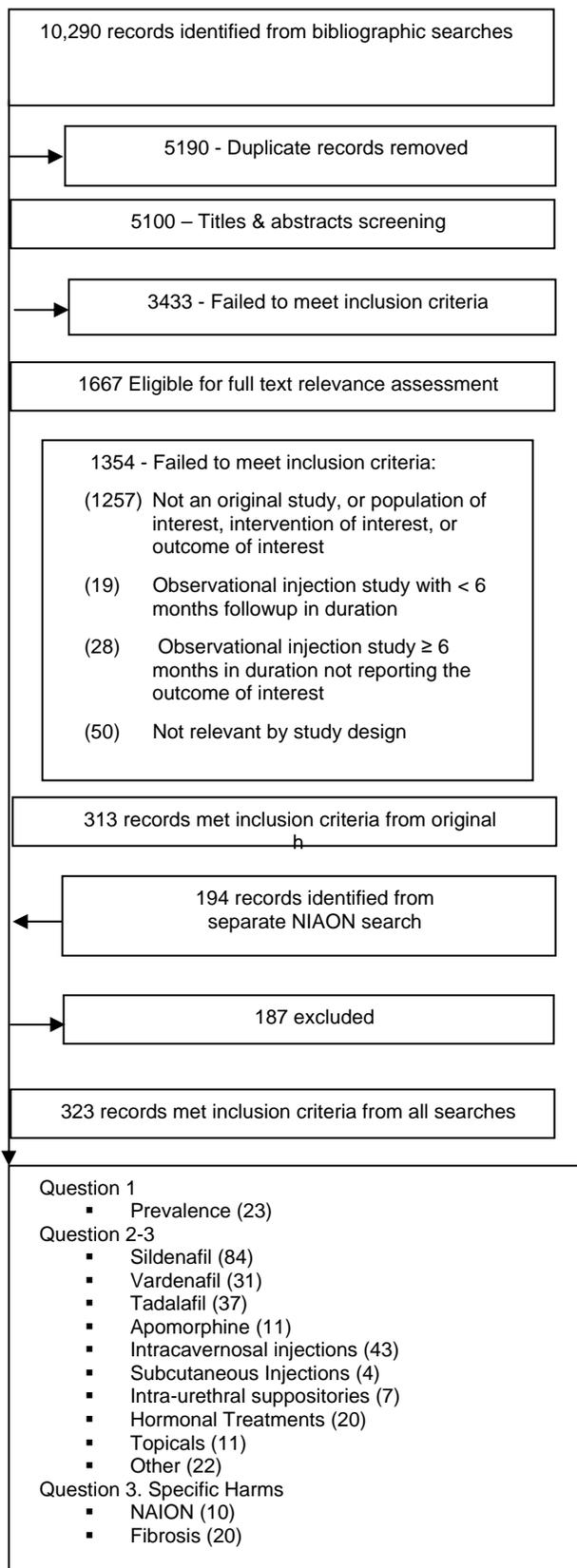
Data Abstraction

Two reviewers independently abstracted relevant information from each included study using a data abstraction form developed a priori for this review (Appendix B). One reviewer completed primary extraction, which was then verified by a second reviewer. Conflicts were discussed and

resolved by consensus. Abstracted data included study characteristics (e.g. design, sample size, country), population characteristics (e.g. age, comorbidities, severity of ED), name/type of treatment (e.g. sildenafil, testosterone), route of administration (e.g. oral, injection, topical), dose, and the duration of treatment. The following clinically relevant and validated efficacy outcomes were abstracted: absolute endpoint/change (from baseline) in scores for the International Index of Erectile Function “Erectile Function” domain (IIEF– EF), per-patient percentage on Sexual Encounter Profile for Q2 and Q3 (SEP–Q2/Q3), and the proportion of patients with improved erection measured with a Global Assessment (or Efficacy) Question (GAQ–Q1 or GEQ–Q1).(Appendix H)

For harms, reviewers abstracted information on any adverse events: i.e., number of patients who developed at least one adverse event; most frequently encountered specific adverse events; withdrawals due to adverse events; and the incidence of serious adverse events. Additionally, for Q1, prevalence estimates of hypogonadism and hyperprolactinemia in ED populations for each included study were abstracted.

Figure 2. Modified QUOROM Flow Chart



Assessment of Study and Reporting Quality

The quality of prevalence studies measuring serum hormonal levels in ED patients was assessed using a subset of QUADAS items.⁴⁶ The QUADAS tool consists of 14 items (Appendix B). QUADAS was designed to evaluate the diagnostic accuracy of a test against the reference standard. Since the included studies for this review involved measurements of serum hormone levels, no reference standards were used to assess the diagnostic accuracy of these tests (i.e., levels of testosterone, prolactin, LH and/or FSH). Therefore, the quality assessment of studies was based on a subset of 8 QUADAS items (score range 1–5) that were deemed to be relevant to the present research question.

The Jadad scale was used to assess the methodological and reporting quality of RCTs. (Appendix B).⁴⁷ This instrument is designed to assess the reporting of methods used to generate random assignments and double blinding, as well as to determine whether there is a description of dropouts and withdrawals by treatment group (i.e., number and reasons). The scoring ranges from 0 to 5, with higher scores indicating higher quality. An a priori threshold scheme was used for sensitivity analysis: a Jadad total score of ≥ 3 indicated studies of higher quality. In addition, the adequacy of allocation concealment was assessed using an approach proposed by Schulz and colleagues as: adequate, inadequate, or unclear (Appendix B).⁴⁸

Synthesis of Evidence

Qualitative data synthesis. Primary and secondary outcomes were summarized qualitatively for each study. The sample size and demographics, setting, funding source, treatment and comparator characteristics (e.g. type, dose, and duration), study quality, and methods of adjustment for confounders (where applicable) were recorded and summarized in the text, and summary tables.

To determine the clinical utility of routine hormonal blood tests in identifying and affecting therapeutic outcomes for endocrine causes of ED (KQ 1), the reviewers identified relevant studies and synthesized data for two following constructs:

1. The prevalence of hormonal abnormalities (hypogonadism, hyperprolactinemia, abnormal levels of luteinizing and/or follicle-stimulating hormones) in patients with ED
2. The efficacy of hormonal therapies in patients with the above-mentioned hormonal abnormalities for improving clinical symptoms of ED.

The two constructs (i.e., prevalence of hormonal abnormalities and efficacy of available hormonal treatments) jointly determine the clinical utility of routine hormonal blood tests. For example, the administration of routine hormonal blood tests might be justified only if the prevalence of hormonal abnormalities in patients with ED was relatively high (i.e., above a pre-specified threshold) and the available hormonal therapies in affecting symptoms of ED in this subgroup of patients were effective.

Thus, the results for KQ 1 are presented in two sub-sections: 1) the prevalence of hormonal abnormalities in ED patients and 2) the efficacy of hormonal therapy in treating ED in patients with hormonal abnormalities (see also the section for KQ 2-3, Hormonal Treatments, for more detailed description of the studies).

Quantitative synthesis. The decision whether to perform statistical pooling of individual studies was based on clinical and methodological judgment. In the case of outcomes for which meta-analysis was deemed appropriate, we extracted quantitative data (e.g. number of subjects in each group, mean, standard deviation) from reports using a standardized data extraction form

that included intervention characteristics and outcome variables at baseline and followup intervals.

If relevant data (e.g. standard deviations) were not reported adequately, we attempted to calculate the needed parameters. Trials that did not report complete numerical information for relevant efficacy/harms outcomes (i.e., arm-specific mean endpoint or change in score, standard deviation, or standard error, proportion of patients with an outcome at followup) could not be incorporated in the meta-analyses. Trial reports presenting measures of variability (e.g. standard deviation) only graphically (i.e., no numerical data were available) were not pooled. Crossover trials not reporting numerical data from the pre-crossover phase were not included in meta-analyses

We calculated standard deviations from standard errors or 95 percent confidence intervals.

For continuous outcomes (e.g. mean endpoint/change in the total score of IIEF), the absolute difference between treatment-specific means and corresponding standard deviations were ascertained for each individual study. A generic inverse variance method was used to calculate the response outcomes and corresponding 95 percent confidence intervals for the combined treatment groups.

For dichotomous outcomes (e.g. improvement in erection GAQ), studies were grouped by type of treatment and dose to minimize clinical heterogeneity. The intent-to-treat group or number enrolled at the time of study was used for analyses and, when this information was unavailable, we used the number provided in the report. Pooled relative risks with corresponding 95 percent confidence intervals were generated.

The DerSimonian and Laird random-effects model was used to obtain combined estimates across the studies.⁴⁹ The degree of statistical heterogeneity was evaluated by using a chi-square test and the I^2 statistic.⁵⁰⁻⁵² An I^2 of less than 25 percent is consistent with low heterogeneity; 25 to 50 percent with moderate heterogeneity; and over 50 percent with high heterogeneity.⁵² When statistically significant heterogeneity was identified, it was explored through subgroup and sensitivity analyses when appropriate. Sources of heterogeneity include reporting and methodological quality (e.g. methods for randomization, adequacy of allocation concealment, blinding, washout period for crossover trials, data analysis) as well as clinical heterogeneity (e.g. study population, dosing of therapeutic agent, duration of followup). Estimates from the heterogeneous groups must be interpreted with caution, especially when small numbers of trials are included.

We also performed a series of subgroup analyses to explore the consistency of the results.

The meta-analyses are presented as forest plots (Figures 3-76). Publication bias was explored through funnel plots (Figures D1-16, Appendix D) by plotting the relative measures of effect (relative risk) versus a measure of precision of the estimate (1/standard error).⁵¹ The visual asymmetry in funnel plots maybe be suggestive of publication bias, although other potential causes for asymmetry exist. The degree of funnel plot asymmetry was measured using the Egger regression test.⁵³⁻⁵⁵

The statistical analyses in this review were performed using Review Manager 4.2 (The Cochrane Collaboration, Oxford, UK, 2006).

Chapter 3. Results

Question 1. What is the Clinical Utility of Routine Blood Tests (Testosterone/Prolactin/Luteinizing Hormone/Follicle-Stimulating Hormone) in Identifying and Affecting Therapeutic Outcomes for Treatable Causes of Erectile Dysfunction (ED)?

Prevalence of Hormonal Abnormalities in ED Patients

Literature Search

A total of 22 studies (23 publications) were identified as eligible and were included in the review.^{20,38,56-76} One study was reported in two publications.^{62,76}

Overview of Trials

The prevalence of hypogonadism, hyperprolactinemia, and measurements of serum level LH/FSH were evaluated in 21^{20,38,57-75}, 10^{20,38,56,58,60,61,65,67,72,73} and 8^{20,61,63-65,67,69,73} studies, respectively.

The included studies were conducted in North America, Europe (France, Greece, Spain, Sweden, Turkey, and UK), Brazil, Australia, Egypt, Saudi Arabia, and Malaysia.

The characteristics of included studies are presented in Table 1.

Study and Reporting Quality

The quality of the 22 included studies of men with erectile dysfunction who had their serum levels of testosterone, prolactin, luteinizing hormone (LH) and/or follicle-stimulating hormone (FSH) measured was assessed using QUADAS.⁴⁶

The QUADAS scores for each study are presented in Table C-2 (Appendix C).

About 60 percent of the studies provided an adequate description of population characteristics and inclusion/exclusion criteria.

Populations (Studies Reporting on Hypogonadism)

Twenty-one of the included studies measured testosterone serum levels in men with erectile dysfunction as total testosterone (TT) serum levels.^{20,38,57-75} Two studies reported free testosterone (FT) serum levels,^{59,66} two studies reported calculated free testosterone (cFT) serum levels,^{73,74} and one study⁷³ calculated bioavailable testosterone (BT) serum levels.

Most studies recruited primary care clinic patients. In 10 studies participants were recruited from specialized clinics (urology, andrology, sexual dysfunction, and endocrinology clinics). Only 11 studies reported the use of a validated questionnaire to measure erectile dysfunction. The participants' mean age across studies ranged from 50 to 60 years. Important comorbidities such as hypertension, diabetes mellitus, and ischemic vascular disease were described in only 8 of the 22 studies.

Further details regarding the serum hormonal level measurements (e.g. time the serum was collected, cut-off values for positive/negative test results) are found in Table 1.

Prevalence of Hypogonadism (Total Serum Testosterone Levels)

The studies reporting prevalence rates of hypogonadism in ED patients are described in Table 2. All studies included men with a previous diagnosis of erectile dysfunction. The diagnosis of erectile dysfunction was given by a combination of clinical examination and validated questionnaires: the modified 5-item International Index of Erectile Function (IIEF-5) and Aging Males Symptoms (AMS).

The prevalence of hypogonadism ranged from 1.72 to 47.7 percent. In one study conducted in Japan, hypogonadism was found in 47.7 percent of the patients. Note that all participants in this study had been diagnosed with partial androgen deficiency of the aging male (PADAM) before entry in the study.⁶⁸ In one study,³⁸ which reported a prevalence of 6.6 percent, patients had been receiving androgen therapy. In Zohdy et al. 2007⁷⁵ all participants presented with obesity and other signs of metabolic syndrome.

In several studies, patients with ED and hypogonadism, who had been referred to urology clinics, were found more likely to have decreased libido,^{20,38,67,72} testicular damage/abnormality,^{20,38,70} psychological problems with their partner,⁷⁰ arterial disease,^{70,72} obesity,^{67,75} hyperlipidemia,⁶² diabetes,^{62,72} or hyperprolactinemia.⁷²

In other studies, patients with hypogonadism did not differ (p-value > 0.05) from eugonadal patients either with respect to age,^{60,64,67} ED severity,^{60,62,67} ED duration,^{60,67} the presence of chronic disease,⁶⁰ smoking,⁶⁰ loss of libido,⁶⁴ or premature ejaculation.⁶⁷ In contrast, one study⁷² demonstrated that age, ED severity, and longer duration of ED were statistically significant predictors of having hypogonadism in patients with ED.

In two primary care clinic based studies,^{57,65} hypogonadal patients were more likely to have higher levels of prolactin⁶⁵ or hypothalamic abnormalities than those with normal levels of testosterone (21.2 versus 2.9 percent).⁵⁷

Prevalence of Hypogonadism (Free Serum Testosterone Levels)

Two studies reported the prevalence of hypogonadism measured by FT (radioimmunoassay, analog method)^{66,74} and two studies reported calculated FT levels based on the TT serum levels (Table 3).^{59,73}

The prevalence of hypogonadism using FT serum levels (radioimmunoassay, analog method) across these studies varied from 12.5 to 25.32 percent. The corresponding range for the prevalence of hypogonadism using calculated-free testosterone serum levels was 15.7 to 17.58 percent.

One study,⁷⁴ found a statistically significant association between hypogonadism and insulin resistance by showing a higher proportion of patients with insulin resistance amongst hypogonadal versus eugonadal patients (92.3 versus 25.2 percent, p value= 0.02).

Prevalence of Hypogonadism (Bioavailable Serum Testosterone Levels)

Serum Bio-T levels were reported in one study.⁷³, where the prevalence of hypogonadism was 0.41 percent and the average level of Bio-T was 0.84 ± 0.28 nmol/L. (Table 4).

Populations (Studies Reporting on Hyperprolactinemia)

Ten studies measured prolactin serum levels in men with ED to detect hyperprolactinemia.^{20, 38,56,58,60,61,65,67,72,73} Patients were recruited from primary care clinics^{56,65,73} or from specialized

clinics (urology, andrology, and endocrinology).^{20,38,58,61,67,72} The mean age of participants ranged from 47 to 59 years. Only five studies reported important comorbidities, such as hypertension, diabetes mellitus, and ischemic vascular disease. Further details on these studies are provided in Table 5.

Prevalence of Hyperprolactinemia (Serum Levels of Prolactin)

The information on prevalence of hyperprolactinemia using the total level of serum prolactin was reported in 10 studies (Table 6). Erectile dysfunction was diagnosed using a combination of clinical examination and a validated questionnaire (IIEF-5 was reported in only four of the 10 included studies). Information on the cut-off used to define a positive test result was provided in all studies and ranged from 18 to 20 ng/mL. In these studies, except for one conducted in Egypt,⁷² the prevalence of hyperprolactinemia ranged from 1.42 to 14.3 percent.

The prevalence rate of hyperprolactinemia reported in the Egyptian study was 32 percent.⁷² The high prevalence observed in this study is not readily explained. Study participants were aging, obese men with ED. Of a total of 877 enrolled patients, 305 completed the study. The mean age was 53.9 (range 26–86) years; 77 percent of the patients were older than 50 years, 86 percent were overweight or obese, and 30 percent were current or former smokers.⁷²

In two other studies, the prevalence rates of hyperprolactinemia were compared between men with and without ED.^{60,73} These studies used similar cut-off points to define a positive or negative test result (Table 7). The prevalence rate of hyperprolactinemia among men with ED in the two studies ranged from 2.89 to 9.54 percent.

Prevalence of Abnormal Levels of LH/FSH

Information on the prevalence of abnormal levels of LH/FSH in men with ED was provided for eight studies.^{20,61,63-65,67,69,73} The studies were divided according to whether they measured secondary hypogonadism (low levels of LH and/or FSH) or primary hypogonadism (high levels of LH and/or FSH). All studies included men with a previous diagnosis of ED. In two studies levels of LH were measured only in patients with low levels of total testosterone.^{61,63} The diagnosis of ED was done by a combination of clinical examination and validated questionnaire (IIEF-5 or SAQ; reported in three included studies). The cut-off values used to define a positive/negative test result were provided for two studies only (Tables 8 and 9).

Secondary hypogonadism (low levels of LH and/or FSH). In Bunch et al. 2002, 66 patients with hypogonadism were screened for LH levels. Of these, 44 percent had low levels of LH (<13 IU/mL) and were diagnosed with secondary hypogonadism. Further screening with magnetic resonance imaging (MRI) or computer tomography (CT) imaging led to the identification of hypothalamic-pituitary abnormalities in 10 percent of these men.⁶³

El-Sakka 2005⁶⁷ assessed the prevalence of endocrine abnormalities in obese men with sexual dysfunction. Low levels of LH and FSH were identified only in 1.7 percent of men (Table 9).

Primary hypogonadism (high levels of LH and/or FSH). In three studies, the proportion of men with ED who had abnormally high levels of LH ranged from 1.03 to 5.79 percent.^{20,65,73} There was a prevalence of 21.7 percent in a study in which all men had been previously diagnosed with hypogonadism (i.e., low testosterone levels).⁶¹ Another study⁶⁹ investigated possible hypothalamic impotence in 21 ED patients (median age 54 years) with low testosterone and normal levels of LH or FSH by undergoing gonadotropin-releasing hormone (GnRH)

stimulation and a challenge test with clomiphene citrate. Twenty-nine percent of men presented with a reduced LH level and 5 percent with a reduced FSH level.⁶⁹

Prevalence of Hypogonadism and Hyperprolactinemia by Age

We descriptively examined patients' age distribution (mean and range) in individual studies to determine whether age could account for the between-study differences in the reported prevalence rates of hypogonadism and hyperprolactinemia. The results did not reveal any numerical trends between the age distribution and the prevalence rates.

Studies reporting age-stratified prevalence rates of hypogonadism. Buvat et al. 1997³⁸ reported the prevalence of hypogonadism in patients older than 50 years as being twice as high as that among patients younger than 50 years (9 percent versus 4 percent).³⁸ In Fahmy et al. 1999⁶⁴ the corresponding rates were 24.2 percent versus 14.3 percent, respectively. In another study, the prevalence rate in men older than 50 years was 20.25 percent (all patients were older than 50 years).⁷³ All three studies indicated higher prevalence of hypogonadism in men aged 50 years or older compared with those under 50 years of age.

Studies reporting age-stratified prevalence rates of hyperprolactinemia or abnormal levels of LH/FSH. There was no report providing evidence on prevalence of hyperprolactinemia, or on abnormal levels of LH/FSH, by age group among patients with ED.

The Efficacy of Hormonal Therapy in Treating Erectile Dysfunction in Patients with Hormonal Abnormalities

Overview of Trials

Two studies were identified and were judged to be eligible to address the present question. Both trials were randomized^{5,77} comparing the efficacy of combined treatment of testosterone (gel or patch) plus sildenafil to that of sildenafil alone in ED patients with low testosterone levels who failed to respond (score of 2–3 on IIEF–Q3/Q4) to prior treatment with sildenafil. More detailed information on trial design, patient population, and efficacy/harms results for these trials are presented in the section for Questions 2-3, Hormonal Treatments. (Evidence Table F-9, Appendix F)

Gel testosterone plus sildenafil versus sildenafil. In this double-blind trial⁵ 75 hypogonadal men (mean age: 58 years; total testosterone <400 ng/dL) with ED were randomized to 1 percent gel testosterone plus 100 mg sildenafil versus 100 mg sildenafil for 12 weeks. At the end of the study, the proportions of men with scores of 4-5 on IIEF–Q3/Q4 was statistically nonsignificantly greater in the combination therapy group than in the sildenafil only group (51.4 versus 39.4 percent; RR = 1.30, 95 percent CI 0.77–2.21). Men who received gel testosterone plus sildenafil also had greater mean change from baseline in the IIEF “EF” domain score at week 4 (4.4 versus 2.1, 95 percent CI: 0.3–4.7). One patient withdrew from the combination treatment arm due to an adverse event.

Testosterone patch plus sildenafil versus sildenafil. In this open label trial,⁷⁷ 20 hypogonadal men (mean age:56 years; total testosterone:10-13 nmol/L) with ED were randomized to receive either 5 mg patch testosterone plus 100 mg sildenafil or 100 mg sildenafil plus placebo patch. After one month of treatment, patients in the patch testosterone plus sildenafil group had either numerically or statistically significant improvements for the following outcomes: “EF domain” score (21.8 +/- 2.1 versus 14.2 +/- 0.7, WMD = 7.60, 95 percent CI:

6.23–8.97), number of sexual intercours (2.8 +/- 0.9 versus 1.5 +/- 0.5, WMD = 1.30, 95 percent CI: 0.66–1.94), intercourse satisfaction (12.1 +/- 1.6 versus 7.7 +/- 1.2, WMD = 4.40, 95 percent CI: 3.16–5.64), and reported improved erections (80 versus 10 percent, RR = 8.00, 95 percent CI: 1.21–52.69).

Questions 2-3. What is the Evidence of the Relative Clinical Benefits and Harms of Pharmaceutical Treatments (e.g. Oral Medications) for Men Diagnosed With Erectile Dysfunction?

Oral Treatments — Phosphodiesterase Type 5 (PDE–5) Inhibitors - Sildenafil

Literature Search

In total, 90 unique trials (reported in 100 publications) reporting relative efficacy and harms related to sildenafil use (mono or combined therapy) met the eligibility criteria and were included in the review.^{5,77-175}

Seventeen (reported in 16 publications) of the 90 trials are described in the following sections of the review: Question 1-3,^{5,77} Topical,¹⁴⁴ Hormonal,^{145,170} Injections,^{119,172} Tadalafil,^{103,118, 121, 163} and Sublingual (apomorphine).^{114,117,120,148,159}

This section reviews the remaining 73 unique trials (reported in 84 publications).^{78-102,104-113, 115,116,122-143,146,147,149-158,160-162,164-169,171,173-175}

In 5 publications,^{85,86,90,130,152} two separate unique trials were described (a and b). 12 unique trials were reported in two or more publications. The following list shows the reference identifications for these 12 unique trials and their corresponding publications (each row).

The first reference (author, year, citation) denotes primary publications (i.e., those reporting the most relevant and complete data for the trial), which are used throughout the Sildenafil section. (Tables F-1, in Appendices F):

1. Palmer 2000⁷⁸ and Palmer 1999¹³⁶
2. Seidman 2001⁷⁹ and Rosen 2004¹¹³
3. Goldstein 1998a,⁸⁶ Padma-Nathan 1999,¹⁵⁴ and Barry 1998a¹⁵²
4. Tan 2000⁸⁷ and Lim 2002¹²⁹
5. Meuleman 2001⁸⁸ and Hartmann 1999¹⁴⁰
6. Eardley 2002¹³⁰ and Eardley 1999¹³⁹
7. Incrocci 2001¹³¹ and Incrocci 2003⁹²
8. Cappelleri 2000¹³⁵ and Lewis 2001¹⁰⁰
9. Padma-Nathan 1998,¹⁴² Goldstein 1998b⁸⁶ and Young 1999,¹⁴¹ and Barry b,¹⁵² and Shabsigh 1999b¹⁵³
10. Glina 2001¹⁵¹, and Glina 2002¹²⁷
11. Perimenis 2007¹⁵⁵, Perimenis 2004¹¹⁶
12. Sharma 2006¹⁶⁵, and Salonia 2007¹⁷⁴

Overview of Trials

Of the 73 trials, 52 (71 percent) used a parallel-arm design,^{79-84,86-88,90,91,94-98,101,104,106, 107,109-112,115,122-126,128,133,135,138,142,143,147,151,155-158,160,162,166,167,169,171,173,175,176} while the remaining 21 used a crossover design.^{78,85,89,93,99,102,105,108,130-132,134,146,149,150,161,164,165,168}

The trials were conducted in North America,^{78,79,81,84,86,90,91,94,102,105,109,122,132,135,142,147,156,158,160,161,166,167,169,171,173,177} Australia,^{147,166} South America,^{81,83,106,123-126,143,151,166} Africa,^{83,110} Europe,^{81,85,88,89,93,95,96, 98,99,104,107,108,112,115,128,130,131,133,134,137,138,146,147,150,155,157,167} and Asia.^{80,81,81,82,87,97,101,111,149, 162,164-166,168,175}

The trials were published between 1996⁸⁵ and 2007.^{155-158,160,161,173,175}

Fifty-three trials were supported by Pfizer^{78-87,89-91,93-99,107-110,115,122,124-126,128,131,133,135, 137,138,142,143,146,147,151,156,158,160,161,164,166,167,169,171,173,175}. Two Italian trials were supported by Sigma Tau.^{104,112} The source of support was not reported for 10 trials.^{88,106,111,123,130,134, 149,150,155} Three trials had no source of support,^{101,157,162} and five other trials reported other funding sources.^{102,105,132,165,168} (Evidence Table F-1, Appendix F)

Populations

Study participants in the included trials were men diagnosed with ED. The total and mean numbers of patients randomized across the 73 trials were 11,064 and 152, respectively. The number of randomized patients across all trials ranged from 12^{85,169} to 568.¹⁴⁷

In these trials the study population inclusion criteria were: adult males aged ≥ 18 years diagnosed with ED for ≥ 3 months before study enrolment and in a heterosexual relationship with a sexual partner. The most common reported reasons for the trial exclusion were the presence or history of penile/testicular deformity, cardiovascular disease, stroke, myocardial infarction, use of nitrates, any major hepatic or renal disease, spinal cord injury, retinitis pigmentosa, diabetes, major psychiatric disorder, alcohol/drug abuse or hypotension.

In 31 (42 percent) of the 73 trials the selection of ED patients was restricted to patients with the following conditions: spina bifida,⁷⁸ depression,^{79,91,115,167} diabetes,^{81,93,94,98,101,112} stable coronary artery disease,⁸⁴ Parkinson's disease,⁹⁹ congestive/chronic heart failure,^{102,109} prostatectomy,¹⁰⁴ multiple sclerosis,¹⁰⁷ dialysis,^{108,123} obstructive sleep apnea,¹⁵⁵ colorectal cancer,¹²⁸ prostate cancer,¹³¹ cardiovascular disease,¹³³ hypertension,^{143,147} benign prostatic hyperplasia (BPH),¹⁶⁰ post-traumatic stress disorder,¹⁶⁴ renal allograft,¹⁶⁵ schizophrenia,¹⁶⁸ lower urinary tract symptoms,¹⁷³ and androgen decline.¹⁷⁵ Most patients (≥ 90 percent) included in the 31 trials were diagnosed with ED of organic and/or mixed etiology.^{78,79,81,84,91,93,94,98,99,101,102,104,107-109,112,115,123,128,131,133,143,147,155,160,164,165,167,168,173,175}

Of the remaining 42 trials,^{80,82,83,85-90,95-97,105,106,110,111,122,124-126,130,132,134,135,137,138,142,146,149-151,156-158,161,162, 166,169,171} three^{96,106,110} included participants with ED of psychogenic etiology and another three consisted mostly of participants with ED of organic/vasculogenic and mixed etiology.^{122,150,157} Participants included in the remaining 36 trials were diagnosed with ED with a broad spectrum of causes (i.e., organic, mixed, and psychogenic). The majority of these trials reported that an organic cause of ED had not been established.

The 73 trials included here enrolled participants aged 18 years or older. In one trial,⁷⁸ the participants' age ranged between 19 and 35 years, and in two trials this range was from 35 to 70 years.¹³⁰ Two trials included only participants older than 45 years.^{160,175}

Interventions

In the 73 reviewed trials, participants were randomly assigned to receive either mono and/or combined therapy of oral sildenafil citrate (as experimental or control intervention) with a dose (at randomization) ranging from 10 mg^{85,96} to 100 mg.^{101,104,122,130,134,137,146,150,155,158,161,169}

Depending on the observed efficacy and tolerability of sildenafil, the daily dose was flexible (upward or downward titrations: 50 mg – 25 mg – 100 mg) in more than half of the included trials.^{79-84,87-91,94,95,97-99,107-109,115, 124-126,128,131,133,135,138,142,143,147,150,151,156,157,160,162,164-168,171}

In eight trials, participants were randomized to receive different dosages (e.g. with respect to dose, dose escalation, fixed/on demand, time of administration) of sildenafil monotherapy.^{78,85,86,93,96,137,157,161} Of these, six trials^{78,85,86,93,96,137} assessed a dose-response effect of sildenafil given at a fixed dose (dose range 10 mg/d to 100 mg/d). In one trial,¹⁶¹ participants were randomly assigned to receive 100 mg/d of sildenafil either 1 hour before/during a meal or 30–60 minutes before sexual activity. Participants in another trial were randomly assigned to receive either fixed dosing (50 mg every night) or flexible dosing (50 mg or 100 mg, as needed) of sildenafil.¹⁵⁷

In nine trials, oral sildenafil was administered in combination with propionyl-L-carnitine (PLC),¹¹² PLC and acetyl-L-carnitine (ALC),¹⁰⁴ intranasal PT-141,¹⁰⁵ psychotherapy,¹⁰⁶ alfuzosin,¹⁷³ dihydro-ergotamine (DHE),¹⁵⁰ atorvastatin,^{158,169} quinapril,¹⁵⁸ and cabergoline.¹⁶²

In five trials, patients received either mono (or combined) therapy of sildenafil or monotherapy of another active treatment.^{106,124,132,155,173} These therapies were psychotherapy,¹⁰⁶ continuous positive air pressure (CPAP),¹⁵⁵ phentolamine,¹²⁴ Ro70–0004 (i.e., α_{1A} -adrenoceptor antagonist),¹³² or alfuzosin.¹⁷³

Of the 73 trials, 66 (91 percent) were placebo-controlled (with or without an active treatment arm),^{78-91,93-99,101,102,104,105,107-111,115,122,123,125,126,128,130-135,137,138,142,143,146,147,149,151, 156,158,160-162,164-169, 171,175} and the remaining seven trials had no placebo arm.^{106,112,124,150,155,157,173}

In most of the trials, the duration of sildenafil treatment was about 12 weeks^{79-81,83,84, 87,94,97,98, 102,107,109,115,125,126,131,133,135,137,138,142,151,155,156,158,160,166,169,171,173,175} and ranged from 1–2 weeks^{93,168} to 48 weeks.¹⁵⁷

Outcomes

Harms. The presence or absence of any all-cause adverse events (i.e., the proportion of patients with ≥ 1 adverse event) was reported in 29 trials.^{79-83,85-87,90,94,96-98,107-109,115,124-126,132,137, 142,143,147,151,160}

The presence or absence of withdrawals due to adverse events was reported in 62 trials.^{78-91,94-99,101,104,105,107-109,112,115,122-126,128,130,131,133-135,137,138,142,143,146, 147,149,151,155-157,160,162,165-168, 171,173,175}

The absence or presence of serious adverse events was reported in 52 trials.^{78,80-85,87-91, 93,95-99,101,105,107-112,123-126,128,131,133-135,138,143,146,147,149,151, 155-157,160,166-168,171,173}

Efficacy. The efficacy outcomes measuring the degree of ED reported in the 73 trials were total mean scores for the 5 IIEF domains: “Erectile Function”,^{79-84,86-88,90,91,97,98,102, 104,107-109,112,115, 122-126,128,135,137,138,142,143,147,149,155,156,160,161,164-167,169,171,173} “Intercourse Satisfaction”,^{79,80,82-84,87,88,90, 91,97,104,107-109,115,122-126,137,138,142,143,147,149,155,156,160,162,164-167,171} “Overall Satisfaction”,^{79,80,82-84,87,88, 90,91,97,104,107-109,115,122-126,137,138,142,143,147,149,155,156,160,164-167,171} “Orgasmic Function”,^{79,80,82- 84,87,88,90,91,97, 104,107-109,115,122-126,137,138,142,143,147,149,155,156, 160,164-167,171} and “Sexual Desire”,^{79,80,82- 84,87,88, 90,91,97,104,107-109,115,122-126,137,138,142,147,149,155, 156,160,164-167,171}

Other commonly reported outcomes were: mean IIEF scores for responses to Q3 and Q4 (penetration and maintenance frequency),^{79-84,86-88,90,91,94,97-99,101,107-109,112,115,123-126,131, 133,137,138, 142, 143,147,149-151,162,165,167,173} proportion of successful intercourse attempts,^{80-84,87,94,97,98,109, 112,115,124-126,}

131,137,138,142,143,147,151,155,156,161,166,167,171 and proportion of patients with improved erection (GEQ-Q1).^{79-90,93-98,107-109,112,115,124-126,128,131,133,137,138,142,143,147,149, 151,156,165,167-169,171}

Several trials reported mean IIEF scores for individual questions (e.g. Q1–Q2 and Q5–Q15)^{78,94,101,123,124,126,131,138,143,150,162,165} as well as the mean total IIEF score.^{91,106,123,128,155,164,175}

Other reported outcomes were mean severity score of ED (based on the modified 5-item IIEF),^{111,123,135,158} time to onset of erections/intercourse attempts (i.e., mean/median number of minutes),^{122,130,161} proportion of responders (erection rigidity >60 percent or erection grades 3–4),^{130,146} duration of erections (≥60 percent or ≥80 percent rigidity),^{93,105,132,146,168} mean number (per week or month) of penile erections (grade 3–4),^{85,88,89,93,95,96,138,142,168} peak systolic/end diastolic velocity (PSV/EDV) in cm/s,^{104,108,112,157} mean EDITS score,^{84,90,109,143,147,156,160,161,167} mean score of responses to Self-Esteem and Relationship questionnaire (SEAR),^{156,160,166,171} nocturnal penile tip and base tumescence/rigidity (in mean activity units),^{110,134} and endothelial function (brachial artery flow-mediated dilation).¹⁵⁸

Study and Reporting Quality

The mean of Jadad total score for the 73 trials was 3.3. The Jadad total score for the individual trials ranged from 1^{99,124,132,150,178,179} to 5.^{81,91,94,95,115,123,128,143,162,168} The method for generating the sequence of randomization was described in only 26 trials,^{81,84,89,91,94,95,99,101,104,106,107,109,112,115,123,128,143,155-157,162,164,165,167,168,171} and in four of these^{89,99,104,112} the method was determined to be inappropriate.(Table C-1, Appendix C)

Of the 73 trials, 64 (88 percent) were described as double-blind^{79-91,93-99,101,102,104,105,107-109,111,112,115,122,123,125,126,128,130,131,133-135,137,138,142,143,146,147,149,151,156,158,160-162,164-169,171,175} and nine trials as open-label.^{78,106,110,124,132,150,155,157,180} Of the 64 double-blind trials, 42 (66 percent) reported some description of the blinding methods.^{79-83,86-91,94,95,97,98,102,104,107,108,112,115,122,123,125,128, 30,133,134,137,138,142,143,151,158,162,164,168,169,173,175} The blinding methods reported for two trials^{102,146} were judged to be inappropriate.

Information on methods for allocation concealment was reported for only 11 trials.^{81,91,94,95,101,106,107,112,123,156,165} The methods reported for 10 trials were judged to be adequate,^{81,91,94,95,101,106,107,112,123,165} and for one trial inadequate.¹⁵⁶ The methods used to conceal the treatment allocation for the remaining 61 trials could not be ascertained (i.e., these were rated “unclear”).

Of the 21 crossover studies, seven (33 percent) reported the use of washout periods,^{85,130,132,146,150,165} and one study reported not to have employed a washout period.⁸⁹ For the remaining 13 trials, it was not clear whether any washout periods were applied.^{78,93,99,102,105,108,130,131,134,149, 161,164,168} The length of washout period for the seven crossover trials was 4 days,¹⁵⁰ 7 days,^{85, 130,132,146} and 2 weeks.¹⁶⁵

Qualitative Synthesis

Sildenafil (mono or combination therapy) versus placebo. In four placebo-controlled trials^{158, 161,162,169} the efficacy and safety profiles of sildenafil and placebo were not compared (see sildenafil dose/dosage one versus dose/dosage two and sildenafil mono versus sildenafil in combination sections). Thus, results provided here are based on data obtained from 62 placebo-controlled trials.^{78-91,93-99,101,102,104,105,107-111,115,122,123,125,126, 128,130-135,137,138,142,143,146,147,149,151,156,160,164-168,171,175}

Harms. In the majority of the placebo-controlled trials, the proportion of patients with at least one adverse event was greater either numerically or with statistical significance for participants taking sildenafil compared with those taking placebo. For example, in one trial of flexible dose

(titrated to 100 or 25 mg), 51.3 percent and 32.9 percent of patients experienced one or more adverse events in sildenafil and placebo arms, respectively (p values were not reported).¹²⁵ In another study, the corresponding proportions were 59.7 percent for the sildenafil treatment group versus 29.6 percent for the placebo arm, respectively (p = 0.079).¹²⁶

The most commonly observed all-cause adverse events across the trials were headache, flushing, and dyspepsia. Other adverse events were myalgia, rhinitis, cardiovascular events, flu-like symptoms, nausea, respiratory events, diarrhea, vomiting, dizziness, chest pain, urinary tract infections, depression, and anxiety. Overall, these events were less frequent for participants taking placebo compared with those taking sildenafil. These effects were usually of a mild to moderate or transient nature not requiring discontinuation of the therapy.

The occurrence of specific adverse events involving visual disturbances, including blurry vision and chromatopsia, were reported in 33 trials.^{79-84,86,88,90,91,94,95,97,98,107,109,115, 122,125,126,131,135, 137,138,142,146,147,151,156,164,165,167} The percentage of patients experiencing visual side effects across the trials ranged from 1 percent^{88,137,165} to 57 percent¹⁶⁴ for participants taking sildenafil, and from 0 percent^{80,87,88,94,95,98,101,107,109,122,125,126,135,138,147,165,167,171} to 61.9 percent¹⁶⁴ for participants taking placebo.

Cardiovascular events were reported in 18 studies.^{79,83,84,87-89,94,96,97,101,102,107,109,125,126, 137,143,166} These events were numerically more frequent in participants treated with sildenafil, ranging from 3 percent⁹⁴ to 29 percent,⁹⁷ compared with the range of 0 percent¹⁰¹ to 12 percent⁹⁷ for placebo-treated participants.

A few studies reported the need for dose reduction as a result of adverse events.^{80,84,87,115,151} The reasons for dose reduction were headache,^{80,87,151} flushing,⁸⁷ chest tightness,⁸⁷ nasal stuffiness,⁸⁷ and visual disturbance.⁸⁰

Twenty-four trials reported the absence of withdrawals due to adverse events.^{78-80,82, 85,98,104, 105,107,110,112,128,131,133,134,138,146,149,156,167,168,171} The rate of WDE (presented as the proportion of patients who withdrew) in sildenafil treatment groups was under 5 percent in 18 trials,^{81,83,84,88,90, 91,96,109,115,125,135,137,142,151,156,160,175} and up to 8 to 12.5 percent in four trials.^{96,99,101,126} In the majority of these trials, the rate for withdrawals due to adverse events in placebo-treated participants ranged between 2 and 8.5 percent. The specific events leading to withdrawals were headache,^{88,101,109,137,142,151} nausea, vomiting, gastrointestinal symptoms,^{86,88,137} visual disturbances,^{88,165} cardiovascular events,^{87,89,99,101,165,166} urinary tract infection,¹⁶⁶ chest pain,¹⁰¹ and cerebrovascular events.¹⁶⁰ These events were reported for participants treated with sildenafil, with the exception of one case of myocardial infarction⁸⁹ and one case of urinary tract infection¹⁶⁶ in placebo-treated participants.

The occurrence/absence of serious adverse events was reported in 51 trials. In 29 trials, no patient experienced any serious adverse event.^{78,80,81,85,90,91,98,99,101,105,108,110-112, 124,125,128,131,133,134, 138,146,149,156,157,167,168,173}

Thus, the occurrence of serious adverse events was reported in 22 trials (Table 10).^{82-84,87-90,93,95-97,107,109,123,126,135,143,147,151,160,166,171} In general, the quality of reporting serious adverse events was poor, and some studies did not provide a full description of events.^{82, 95,107,109,126,135,147,151,160,166} In total, 95 participants had at least one serious adverse event while taking sildenafil or placebo, of which 32 were taking sildenafil^{83,84,87,88,90,93,97,107,109, 126,135,143,147, 151,160,166} and 36 were taking placebo.^{82,84,87,89,97,107,109,123,126,135,143,147,151,160,166,171} For the remaining 27 participants in two trials,^{95,96} the treatment group designation was not reported. Cardiovascular events were the most frequent category of serious adverse events. These included myocardial infarctions, which occurred in one participant taking sildenafil,⁸³ two participants taking placebo,^{89,126} and one participant whose group designation was unknown.⁹⁶ Severe angina

pectoris occurred in a participant taking 100 mg sildenafil⁸⁷ and in another patient taking placebo.⁸⁴ Heart failure, atrial fibrillation, and arrhythmia occurred in two participants taking sildenafil.¹⁴³ Cerebrovascular events occurred in two participants taking sildenafil,^{143,160} one of which was taking 100 mg of sildenafil.¹⁶⁰ Respiratory events included pneumococcal pneumonia in one participant on placebo¹⁴³ and pulmonary edema in another participant on sildenafil.¹⁴³ Accidental injuries were reported in two participants, one severe vertebral fracture in a participant taking sildenafil,⁸³ and the other a hand injury in a participant taking placebo.⁸⁷

Six deaths during four trials,^{88,123,126,171} and one death during the open-label phase of the study⁹⁵ were reported. Four of the eight deaths occurred in placebo groups, one resulting from myocardial infarction.¹²⁶ The reasons for the other three deaths were not reported.^{123,171} Two deaths occurred in participants treated with sildenafil; one of these resulted from an accident,¹²³ and the other from cardiac arrest.⁸⁸ For more details on serious adverse events in each trial, please refer to Table 10.

Efficacy. In the trials reporting mean scores for IIEF “EF” domain and IIEF–Q3/Q4, the proportions of patients with successful intercourse attempts, and improved erection demonstrated that participants receiving sildenafil (regardless of mono/combination therapy or dosage and duration) experienced a statistically significant greater improvement in erectile function compared with those receiving placebo. These improvements were observed for the mean total “EF domain” scores (38 trials),^{79-84,86-88,90,91,97,98,102,104,107-109,115,122,123,125,126,128,135,137,142,143,147,149,156,160,164-167,171} mean IIEF Q3–Q4 scores (35 trials),^{79-84,86-88,90,91,94,97-99,101,107-109,115,123,125,126,131,133,137,138,142,143,147,149,151,165,167} the proportion of successful intercourse attempts (25 trials),^{80-84,87,94,97,98,101,109,115,125,126,131,137,138,142,143,147,151,156,166,167,171} and the proportion of patients with improved erection (based on their responses to GEQ–Q1) (all 40 trials).^{79-90,93-98,107-109,115,125,126,128,131,133,137,138,142,143,147,149,151,156,165,167,168,171}

All trials (i.e., those that reported mean scores for the five IIEF domains) except for one,¹⁶⁴ yielded statistically significant higher mean IIEF scores in participants treated with sildenafil compared with placebo-treated participants for two IIEF domains (“Intercourse Satisfaction” and “Overall Satisfaction”).^{79,80,82-84,87,88,90,91,97,104,107-109,115,122,123,125,126,137,138,142,143,147,149,156,160,165-167,171}

In general, the results for two IIEF domains of “Sexual Desire” and “Orgasmic Function” were less consistent than those for three other domains (i.e., “Erectile Function,” “Intercourse Satisfaction,” and “Overall Satisfaction”).

Specifically, in 17 trials no statistically significant difference was shown in mean IIEF scores for “Sexual Desire” between sildenafil and placebo groups.^{84,88,90,91,104,108,115,123,125,138,142,143,149,156,164,165}

In six trials,^{109,115,125,143,156,164} the between-group (sildenafil versus placebo) differences for mean scores of “Orgasmic Function” were not statistically significant.

All seven trials^{85,88,89,93,95,96,168} that assessed and reported the mean number of grade 3–4 erections per week, yielded a statistically significant increase in the mean number of erections among participants treated with sildenafil (range 1.3⁹³–6.5¹⁶⁸) compared with placebo-treated participants (range 0.6^{88,93,95}–3.32¹⁶⁸). Similarly, two other trials^{86,138} showed that participants treated with sildenafil compared with those on placebo, experienced a significantly greater mean number of erections (grade 3–4) per month. The ranges for the mean numbers of erections were 4.3–6.9 (sildenafil) and 2.4–3.1 (placebo). Five trials^{93,105,132,146,168} indicated a statistically significant longer mean duration of erections (≥60 percent rigidity) for participants treated with sildenafil compared with those who received placebo.

In nine trials, mean EDITS scores indicated that participants exhibited a statistically significant higher degree of treatment satisfaction after being treated with sildenafil compared with placebo.^{84,90,109,143,147,156,160,167}

The beneficial effect of sildenafil use found in trials of participants with psychogenic ED^{96,110} or distinct clinical subgroups (e.g. spina bifida, depression, diabetes, stable coronary artery disease, Parkinson's disease, congestive heart failure, multiple sclerosis, prostate cancer)^{78,79,81,84,91,93,94,98,99,101,102,104,107-109,115,123,128,131,133,143,147,160,164,165,167,168,175} were consistent with those of other trials conducted in patients with ED of mixed etiology or those with clinically heterogeneous conditions.

Reports of only four trials provided treatment efficacy subgroup analyses (i.e., stratification of efficacy results) with respect to baseline severity of ED.^{81,90,128} The evidence from these trials indicated that participants with mild/moderate ED (IIEF score 11–25) after taking sildenafil tended (statistically nonsignificant trends) to experience a greater degree of improvement in erectile function as measured by mean scores for responses to “EF domain” and Q3–Q4 of the IIEF questionnaire and the proportion of patients with improved erections (i.e., those who responded “yes” to GEQ–Q1) compared with those with severe ED (IIEF ≤10).

Efficacy subgroup analyses with respect to duration of ED (0–3, 3–6, and >6 years) and age (18–49, 50–64, and ≥65 years) were reported in two trials.^{94,101} In both trials sildenafil was shown to have improved erectile function (i.e., mean IIEF–Q3/Q4 scores and percentage of patients who responded “yes” to GEQ–Q1) regardless of the participants' age and the duration of ED. The results of analyses provided for these trials did not reveal any treatment effect modification by the above-mentioned factors. In another trial, younger age ($p = 0.034$) and a shorter duration of ED ($p = 0.028$) were found to be predictive of a greater baseline-to-endpoint improvement in erectile function (i.e., mean scores for the IIEF “EF” domain and “Intercourse Satisfaction” domain).¹⁵⁶

Reports of five trials provided the treatment efficacy stratification analyses by ED origin (i.e., organic, psychogenic, and mixed).^{86,88,96,134,142} The improvements in erectile function (mean scores for IIEF “EF” domain and percentage of patients who responded “yes” to GEQ–Q1) were observed regardless of the origin of ED in patients receiving sildenafil compared with those receiving placebo, without identifying the origin of ED as a treatment effect modifier or predictor.

Sildenafil dose/dosing 1 versus sildenafil dose/dosing 2. Six studies assessed the efficacy and harm profiles for different doses (i.e., 10 mg, 25 mg, 50 mg, and 100 mg) of sildenafil monotherapy.^{78,85,86,93,96,137} Additionally, two other trials^{157,161} examined and compared two different dosage regimens of sildenafil (i.e., fixed versus flexible, different timing of administration).

Harms. In one trial,¹³⁷ which reported the incidence of any adverse events, specifically, events in >5 percent of participants in one or more treatment groups, the proportions of participants experiencing at least one adverse event (due to all causes) in either the sildenafil 25 mg, 50 mg, and 100 mg treatment groups were 49, 61, and 72 percent, respectively. The corresponding dose-specific proportions observed in another trial,⁸⁶ were 32, 69, and 86 percent, respectively. Both trials indicated a numerically increasing trend in the incidence of any adverse events observed with the higher dose of sildenafil. In one trial,⁹⁶ the proportion of patients with any adverse events (i.e., events in >5 percent of patients) observed in the 25 mg and 50 mg sildenafil groups were numerically higher (59 and 45 percent, respectively) compared with the 10 mg sildenafil group (24 percent). None of these three trials^{86,96,137} reported any

statistical test results for the observed between-treatment differences. In two trials,^{85,93} the number of participants with treatment-related adverse events did not differ across the 25 mg and 50 mg sildenafil treatment groups. Of the events observed across the trials,^{78,85,86, 93,96,137} headache, myalgia, nausea, dyspepsia, and flushing were the most frequently experienced and were mild to moderate or transient in nature.

A total of four serious adverse events were reported in two studies.^{93,96} These trials compared 25 mg to 50 mg,⁹³ and 10 mg to 25 mg and 50 mg of sildenafil.⁹⁶ One participant (4.7 percent) in the 25 mg sildenafil group discontinued the treatment because of pneumococcal pneumonia (the authors did not consider this a serious adverse event).⁹³ There were three other instances of serious adverse events (myocardial infarction, renal cell carcinoma, and epileptic crisis) in one trial.⁹⁶ The group designation of the participants experiencing these events were not reported.

Withdrawals due to adverse events were reported in five trials.^{85,86,93,96,137} The rate of discontinuation ranged from 0 percent⁸⁵ to 3 percent⁹⁶ for the 10 mg dose of sildenafil, from 0 percent¹³⁷ to 4.7 percent^{93,96} for the 25 mg dose, from 0 percent⁸⁵ to 11 percent⁹⁶ for the 50 mg dose, and from 2 percent⁸⁶ to 4 percent¹³⁷ for the 100 mg dose.

Safety data was not reported for the trial that compared different timing of sildenafil (100 mg) administration in relation to food and sexual activity.¹⁶¹ In the trial¹⁵⁷ comparing “nightly” (50 mg) and “as needed” (50 mg to 100 mg) sildenafil dosing regimens, the proportion of withdrawals due to adverse events was similar across the two groups (approximately 7 percent). The authors of this trial did not report the incidence of any adverse events. Overall, more participants experienced adverse events (headache, flushing, dyspepsia, and rhinitis) in the “as needed” compared with the “nightly” group. Reportedly, none of the participants in this trial developed a serious adverse event.¹⁵⁷

Efficacy. All six trials^{78,85,86,93,96,137} assessing the efficacy of different doses of sildenafil monotherapy (10 mg, 25 mg, 50 mg, and 100 mg), demonstrated a dose-response trend for sildenafil toward improving erectile function. Although none of these trials provided a formal statistical test for the observed between-arm (sildenafil versus placebo) differences, the degree of improvement tended to increase numerically with a higher dose of sildenafil. For example, the range for the mean IIEF Q-3 and Q-4 scores for three sildenafil dose arms in two trials^{86,137} were as follows: 25 mg (Q-3: 3.18–3.20, and Q-4: 2.99–3.10), 50 mg (Q-3: 3.50–3.65, and Q-4: 3.50–3.64), and 100 mg (Q-3: 3.79–4.00 and Q-4: 3.63–3.90). The proportion of participants with an improved erection (based on GEQ-Q1) across four trials^{86,93,96,137} ranged from 50 to 79 percent for 25 mg and from 52 to 88 percent for 50 mg sildenafil arms. In two trials,^{86,137} the corresponding proportion of participants who received 100 mg sildenafil ranged from 84 to 88 percent. The authors of two trials,^{78,86} reported dose-response treatment effects associated with administration of 25 mg,^{78,86} 50 mg,^{78,86} and 100 mg⁸⁶ of sildenafil with respect to mean scores for the IIEF “EF” domain (no numerical data provided; $p < 0.001$)⁸⁶ and IIEF-Q1 (25 mg: 3.7, versus 50 mg: 4.5).⁷⁸ In two other trials^{85,93} the participants’ mean duration of penile rigidity (>80 percent and >60 percent, respectively) in minutes at the base and the tip of the penis was shown to increase numerically with higher doses of sildenafil (10 mg versus 25 mg versus 100 mg). In one trial,⁸⁵ the mean duration of penile rigidity at the base of the penis for participants receiving 10 mg sildenafil was 3.5 minutes (95 percent CI: 1.6–7.3). The ranges for the mean duration of penile rigidity (>60 percent or >80 percent) in two trials,^{85,93} were 5.0 to 8.0 minutes (in participants receiving 25 mg sildenafil) and 10.1 to 11.2 minutes (in participants receiving 50 mg sildenafil). The proportions of participants who achieved grades 3–4 erections in the 25 mg, 50 mg, and 100 mg sildenafil groups were 72, 80, and 85 percent, respectively.⁸⁶ The mean

number of erections per week (grades 3–4) was also shown to be numerically greater in two trials.^{93,96} For example, the mean number of erections per week in one trial among participants who received 10 mg, 25 mg, and 50 mg sildenafil was 2.8, 3.0, and 3.6, respectively.⁹⁶

In two trials,^{157,161} the efficacies of two different dosage regimens of sildenafil were compared. In one trial,¹⁵⁷ participants received either a fixed dose (50 mg every night) or a flexible dose (50 or 100 mg, as needed) of sildenafil for 12 months; in the other trial¹⁶¹ participants were randomly assigned to receive 100 mg/d of sildenafil either 1 hour before/during a meal or 30–60 minutes before sexual activity. In the first trial,¹⁵⁷ the effect of a fixed dose of sildenafil given every night was maintained to a greater extent compared with that achieved with a flexible dosage of sildenafil. Specifically, the proportion of patients with a normal IIEF score (i.e., mean IIEF “EF” domain score ≥ 26) at 12 months in the two treatment groups (the “fixed 50 mg nightly” arm versus the “50–100 mg, as needed” arm), was similar (66.7 versus 67.3 percent, respectively); however, the corresponding proportions for the two groups after 1 month of post-treatment followup were 60.4 percent (95 percent CI: 45.3–74.2) versus 8.2 percent (95 percent CI: 2.3–19.6) in favor of nightly dosage group. The 13-month (i.e., one month after the 12-month treatment stopped) end-point mean peak systolic velocity (PSV) values for participants in the “nightly” and “as needed” groups were 37.0 (SD = 10.4) cm/s versus 26.5 (SD = 8.9) cm/s, respectively, favoring the “nightly” group. In the other trial,¹⁶¹ the time between sildenafil administration and intercourse attempt (0–0.5 to >10 hours) had no statistically significant effect on the mean IIEF “EF” domain score and the proportion of intercourse attempts (based on SEP–Q2; $p = 0.56$), however, a longer period of time between taking sildenafil and intercourse attempt was associated with a statistically significant reduction in successful intercourse attempts (based on SEP–Q3; 92.8 percent at 1.5–2 hours versus 81.6 percent at >10 hours; $p = 0.003$). No statistically significant differences were observed for EDITS scores between the study arms ($p > 0.80$).¹⁶¹

Sildenafil monotherapy versus sildenafil in combination. This review included nine trials^{104-106,112,150,158,162,169,173} in which the efficacy and harm of mono- versus combination therapy of sildenafil were compared. In these trials, sildenafil was used in combination with PLC and acetyl-L-carnitine (ALC),¹⁰⁴ intranasal PT–141,¹⁰⁵ psychotherapy,¹⁰⁶ propionyl-L-carnitine (PLC),¹¹² dihydro-ergotamine (DHE),¹⁵⁰ cabergoline,¹⁶² atorvastatin,^{158,169} quinapril,¹⁵⁸ and alfuzosin.¹⁷³

Harms. In general, harms were poorly reported in four trials.^{106,150,158,169} The incidence of any adverse events were reported in only one¹⁶² of the nine trials.^{104-106,112, 150,158,162,169,173} This study reported a higher proportion of participants with one or more adverse events in the combination arm (cabergoline and sildenafil) compared with the sildenafil monotherapy arm (12.2 versus 2.0 percent, $p = 0.001$).¹⁶² In two trials no serious adverse events were reported during the trial period.^{112,173} The remaining seven studies did not report serious adverse events.^{104-106,150,158, 162,169}

Five studies reported information regarding withdrawals due to adverse events.^{104,105,112,162,173} There were no withdrawals due to adverse events in three of these trials in any of the compared treatment groups,^{81,105,112} and two trials^{162,173} reported higher rates of withdrawals in sildenafil combination therapy than in sildenafil monotherapy. These rates were 5.8 percent with sildenafil/cabergoline therapy compared with 1.0 percent in sildenafil monotherapy,¹⁶² and 14.5 percent with sildenafil/alfuzosin therapy compared with 9.5 percent in sildenafil monotherapy.¹⁷³

Efficacy. In all nine trials, participants who received combination therapies, in comparison with those who received sildenafil alone, were shown to have experienced numerical or statistically significant improvements for mean IIEF (or IIEF–5) scores for the “EF domain” and

individual Q1–Q15 items,^{104,106,158,162,169,173} higher frequency of penetration and maintenance of erection (mean scores for IIEF–Q3/Q4),^{112,150,162,173} improved mean duration of rigidity of the tip/base of the penis (≥ 60 percent),¹⁰⁵ and a greater proportion of participants with improved erection (positive responses to GEQ–Q1).¹¹² However, in three trials^{104,158,169} there was no statistically significant difference between the combination therapy and monotherapy groups in mean PSV values^{104,158} or the proportion of patients with improved erection (positive responses to GEQ–Q1).¹⁶⁹

Sildenafil versus other active treatment. This review included five trials in which the efficacy and harms for sildenafil and other active treatment were compared.^{106,124,132,155,173} These therapies were psychotherapy,¹⁰⁶ continuous positive air pressure (CPAP),¹⁵⁵ phentolamine,¹²⁴ Ro70–0004 (i.e., $\alpha 1A$ -adrenoceptor antagonist),¹³² and alfuzosin.¹⁷³

Harms. Among these five trials,^{106,124,132,155,173} the incidence of any adverse event was reported in only one, in which more participants were found to have experienced one or more adverse event in the 40 mg phentolamine treatment group as compared with the flexible-dose (25 mg to 100 mg) sildenafil treatment group (41.2 versus 33.3 percent).¹²⁴ More patients in the phentolamine group than in the sildenafil group experienced respiratory (17.6 versus 8.9 percent) and digestive (12.6 versus 9.8 percent) adverse events. The most frequent adverse events that occurred during the trial were headache and rhinitis.¹²⁴ In the phentolamine treatment group, three participants (2.5 percent) experienced serious adverse events, as compared with only one participant (0.8 percent) in the sildenafil treatment group. These events were flushing, chest pain, shortness of breath with tachycardia in one participant, and cerebrovascular event and worsening of existing pterygium in the other two participants. One participant in the sildenafil treatment group experienced a rupture of the Achilles tendon.¹²⁴

The rate of withdrawals due to adverse events was reported in two trials,^{124,173} in which it was higher among participants receiving phentolamine¹²⁴ or alfuzosin¹⁷³ than among those receiving sildenafil alone. The rates of withdrawals due to adverse events in participants treated with sildenafil in two trials were <1.0 percent¹²⁴ and 9.5 percent.¹⁷³ The corresponding rates for participants treated with phentolamine and alfuzosin were 3.4 percent¹²⁴ and 10 percent,¹⁷³ respectively.

Efficacy. In two trials^{124,155} sildenafil use was associated with a statistically significant increase in the proportion of successful intercourse attempts, the mean IIEF “EF” domain score, and improved erections (GEQ–Q1), in comparison with the use of CPAP¹⁵⁵ and phentolamine.¹²⁴ In two other trials,^{132,173} administration of sildenafil resulted in only numerical improvement in the mean duration of rigidity at the base/tip of the penis (>60 percent),¹³² mean IIEF scores for the “EF domain,” as well as the frequency of penetration/maintenance of the erection (mean scores for IIEF–Q3/Q4),¹⁷³ in comparison with treatment with Ro70–0004¹³² or alfuzosin.¹⁷³ In one trial,¹⁰⁶ post-treatment mean IIEF scores were lower among those treated with sildenafil in comparison with those treated with psychotherapy, but the statistical significance was marginal (52.8 versus 62.5, $p = 0.049$).

Quantitative Synthesis - Meta-analysis of Trials

Monotherapy (any dose: 10, 25, 50, 100 mg) versus placebo. In 62 trials the efficacy and harm-related effects of sildenafil compared with placebo in the treatment of ED were

investigated.^{78-91,93-99,101,102,104,105,107-111,115,122,123,125,126,128,130-135,137,138,142,143,146,147,149,151,156,160,164,168,171,175}

The quantitative analysis was considered separately for two groups of trials (n = 62), as follows:

Trials conducted in clinically heterogeneous groups of participants with ED (with no established specific organic cause) (n = 34)

Trials conducted in clinically homogenous groups of participants with ED (participants diagnosed additionally with specific clinical conditions (2a-2e) (n = 28)

The 34 clinically heterogeneous trials were potentially eligible for the meta-analyses (24 parallel-arm and 10 crossover).^{80,82,83,85-90,95-97,105,110,111,122,125,126,130,132,134,135,137,138,142,146,149,151,156,166,171}

None of the 10 crossover trials^{85,89,105,130,132,134,146,149} however, were incorporated in the meta-analyses (pre-crossover phase data were not reported), leaving 24 trials for further consideration.^{80,82,83,86-88,90,95-97,110,111,122,125,126,135,137,138,142,151,156,166,171}

Efficacy. Absolute endpoint mean IIEF “EF” domain score. The meta-analysis was based on two trials.^{88,126} The pooled estimate of mean difference was 6.39 (95 percent CI: 2.89–9.90), indicating a statistically significant improvement in the mean IIEF “EF” domain score for participants receiving sildenafil (any dose) compared with those receiving placebo (Figure 3).

Absolute endpoint mean IIEF–Q3/Q4 scores. The two meta-analyses yielded statistically significant pooled estimates of mean differences for both IIEF–Q3 (mean difference 1.46, 95 percent CI: 1.26–1.65) and IIEF–Q4 (mean difference 1.52, 95 percent CI: 1.21–1.82). Thus, the use of sildenafil was associated with statistically significant improvements with respect to penetration and erectile maintenance frequency (Figures 4–5).

Proportion of participants with improved erection (GEQ–Q1). This meta-analysis included 17 trials including two trials reported in Young et al. (2002).^{80,82,83,86-88,90,95,97,125,126,137,138,142,151,156} The pooled estimate of relative risk (RR) of 2.61 (95 percent CI: 2.34–2.91)

indicated a greater proportion of participants experiencing improved erection (i.e., those who answered “yes” to GEQ–Q1) in the sildenafil than in the placebo treatment groups (Figure 6).

Sensitivity analysis was performed with respect to the duration of sildenafil treatment. The duration of sildenafil treatment in 11 trials lasted 12 weeks.^{80,83,87,97,125,126,137,138,142,151,156} The duration of treatment in the remaining trials was 6 weeks,⁹⁰ (studies a and b) 8 weeks,⁸² 16 weeks,⁹⁵ and 26 weeks.^{86,88} The meta-analysis restricted to trials with 12-week treatment did not appreciably affect the magnitude of the effect estimate and the degree of I^2 test for heterogeneity, which decreased from 51.9 percent to 50.0 percent.

Harms. 24 trials (including trials with participants with psychogenic ED),^{96,110} were considered for the meta-analysis of adverse events.^{80,82,83,86-88,90,95-97,110,111,122,125,126,135,137,138,142,151,156,166,171} (note that “favors” in forest plots refers to increased frequency of the event for the respective treatment arm, regardless of the desirability of the event).

Proportion of participants with at least one adverse event (all cause). The pooled estimate of RR suggested that participants randomly assigned to receive sildenafil were at a higher risk of developing any all-cause adverse event than those receiving placebo (RR = 1.51, 95 percent CI: 1.32–1.72) (Figure 7).

Proportion of participants with at least one adverse event (treatment-related). This meta-analysis incorporated 11 trials.^{80,82,83,87,90,97,125,135,137,156} The meta-analysis yielded a pooled RR of 2.56 (95 percent CI: 2.17–3.03), indicating that participants randomly assigned to receive sildenafil were at a higher risk of developing any treatment-related adverse event than those receiving placebo (Figure 8).

Proportion of participants with headache (all cause). This meta-analysis was based on 16 trials.^{80,82,83,86-88,95-97,122,125,126,137,142,151,166} The pooled estimate of RR indicated that participants randomly assigned to receive sildenafil were at a higher risk of having a headache than those receiving placebo (RR = 2.57, 95 percent CI: 2.09–3.18) (Figure 9).

Proportion of participants with flushing (all cause). This meta-analysis is based on 16 trials.^{80,82,83,86-88,95-97,122,125,126,137,142,151,166} The meta-analysis yielded a pooled RR of 5.34 (95 percent CI: 3.32–8.58), indicating that participants randomly assigned to receive sildenafil were at a higher risk of having flushing than those receiving placebo (Figure 10).

Proportion of participants with visual disturbances. This meta-analysis is based on 20 trials.^{80,82,83,86-88,90,95,97,122,125,126,135,137,138,142,151,156,171} The pooled estimate of RR suggested that participants randomly assigned to receive sildenafil had a statistically significant greater risk of developing visual disturbances than those receiving placebo (RR = 3.66, 95 percent CI: 2.27–5.92) (Figure 11).

Twenty-eight trials of clinically homogenous groups compared the efficacy/safety of sildenafil to that of placebo in patients with distinct, specific clinical conditions.^{78,79,81,84,91,93,94,98,99,101,102,104,107-109,115,123,128,131,133,143,147,160,164,165,167,168,175} Of these, 13 trials were single trials per disease and were not considered further for meta-analysis. Thus, 15 trials were deemed as potentially eligible for the meta-analyses. The trials were conducted in participants diagnosed with diabetes,^{81,93,94,98,101} depression,^{79,91,115,167} congestive chronic heart failure,^{102,109} hypertension,^{143,147} or who were on dialysis.^{108,123}

Four trials with patients with diabetes could be pooled^{81,94,98,101} with respect to IIEF–Q3/Q4, GEQ–Q1, and treatment-related adverse events. The meta-analyses were based on trials involving patients with Type I and Type II diabetes combined, as well as trials involving only patients with Type II (Figures 12–17).

Efficacy. Proportion of participants with improved erection, GAQ–Q1, mean IIEF–Q3/4 score. The pooled effect estimates of meta-analyses of diabetic patients were all statistically significant, favoring the use of sildenafil over that of placebo to improve the erection (GEQ–Q1) in both Type I and II (RR = 4.25; 95 percent CI: 2.60–6.93) as well as only in Type II patients, (RR = 5.33, 95 percent CI: 3.89–7.29). The pooled effect estimates for penile penetration ability (IIEF–Q3) (WMD: 1.03, 95 percent CI: 0.34–1.73) and erectile maintenance frequency (IIEF–Q4) (WMD: 1.15, 95 percent CI: 0.74–1.55) were also statistically significant in favor of sildenafil (Figures 12–15).

Harms. Proportion of participants with at least one treatment related adverse event. In the meta-analysis of combined Type I and Type II diabetes patients, a high degree of heterogeneity was found ($I^2 = 72.2$ percent) (Figure 16). To explore the source of this heterogeneity, a sensitivity analysis was performed with respect to Type I and Type II diabetes. The meta-analysis based on Type II diabetes patients yielded a lower degree of heterogeneity ($I^2 = 24.4$ percent), and the pooled effect estimate of the meta-analysis suggested that participants receiving sildenafil had a statistically significant increased risk of having any treatment-related adverse event in comparison with those receiving placebo (RR = 9.08, 95 percent CI: 4.01–20.54) (Figure 17).

Four trials compared sildenafil to placebo in participants with depression.^{79,91,115,167} Of these, three trials^{91,115,167} involved participants with major depressive disorder (MDD) in remission. In two of these trials,^{91,167} participants had ED associated with the use of antidepressants, namely, selective serotonin reuptake inhibitors (SSRIs). In the third trial,¹¹⁵ about 28 percent of the participants used SSRIs. The three trials^{91,115,167} were deemed to be potentially combinable.

Given that the fourth trial⁷⁹ looked at ED patients who had depression but were not being treated with antidepressants at the time of their enrollment (this being one of the exclusion criteria), SSRI use could not be considered the cause of the ED, and the trial was therefore not combined with the other three for meta-analysis.^{91,115,167}

The results for the following efficacy outcomes (i.e., numerical effect estimates and standard deviations [SDs]) were ascertained from the three trials: percentage of successful intercourse attempts,^{115,167} patients with improved erection (GEQ-Q1),^{115,167} and mean IIEF-Q3/Q4 score.^{91,115} The mean IIEF-Q3/Q4 scores and the corresponding SDs were ascertained graphically from one trial.¹¹⁵ Separate meta-analyses for these efficacy outcomes are presented (see Figures 16–19). No meta-analysis for adverse events could be performed, due to a lack of sufficient detail for the adverse events definitions provided in the trials. Note that one trial⁹¹ included younger patients (mean: 45, range 18–55 years) compared with the other trial (mean: 53, range 24–75 years).¹¹⁵

Efficacy. Percentage of successful intercourse attempts, proportion of patients with improved erection, mean IIEF-Q3/Q4 score.

The pooled effect estimates of meta-analyses based on participants with depression were statistically significant, favoring the use of sildenafil over placebo with respect to: increasing the percentage of successful intercourse attempts (RR = 2.44, 95 percent CI: 1.87–3.18); improving erection, GEQ-Q1 (RR = 2.40, 95 percent CI: 1.87–3.06); improving penile penetration ability, IIEF-Q3 (mean difference 1.26, 95 percent CI: 0.82–1.70); and improving erectile maintenance frequency, as assessed by IIEF-Q4 (mean difference 1.48, 95 percent CI: 0.96–1.99) (Figures 18–21).

Two sildenafil versus placebo trials conducted in participants with chronic congestive heart failure (CHF) were potentially combinable.^{102,109} However, no meta-analysis was performed in view of the fact that the only common outcome reported in both trials was the mean IIEF “EF” domain score, for which numerical values of the measures of variability—SD or standard error (SE) could not be ascertained. One of the trials¹⁰² used a crossover design; it reported pre-crossover results graphically, without presenting numeric measures of the variability. In the same trial, no participant had any adverse events; therefore, no meta-analysis for adverse events was performed.

There were two trials that looked at patients with chronic renal failure on peritoneal dialysis. Although they were both eligible for meta-analysis (with respect to the mean IIEF “EF” domain score),^{108,123} they could not be pooled in view of a lack of complete numerical data (i.e., a SD or SE) in one of the trials.¹⁰⁸ A meta-analysis for adverse events was also not feasible, since in one of the trials¹⁰⁸ only one event was observed.

Meta-analysis was possible for sildenafil versus placebo trials involving hypertensive patients using multiple antihypertensive drugs (i.e., two or more different classes).^{143,147} The meta-analyses were performed for efficacy outcomes (i.e., mean IIEF-Q3/Q4, GEQ-Q1, percentage of successful intercourse attempts) as well as all-cause and treatment-related specific adverse events (headache, flushing, and dyspepsia) (Figures 22–29).

Efficacy. Mean IIEF-Q3/Q4, GEQ-Q1, percentage of successful intercourse attempts.

The mean IIEF-Q3/Q4 scores with respective SDs were ascertained from the reports of both trials, as well as for GEQ-Q1, along with the percentage of successful intercourse attempts (see Figures 20–23). The pooled effect estimates indicate a statistically significant improvement in patients receiving sildenafil in comparison with those receiving placebo with respect to: improving penile penetration ability, IIEF-Q3 (mean difference 1.09, 95 percent CI: 0.59–1.58);

erectile maintenance frequency, IIEF–Q4 (mean difference 1.34, 95 percent CI: 0.75–1.93); erection, as assessed by GEQ–Q1 (RR = 3.07, 95 percent CI: 1.81–5.19); and percentage of successful intercourse attempts (RR = 2.41, 95 percent CI: 1.99–2.92) (Figures 22–25).

A high degree of heterogeneity with respect to the proportion of patients with improved erection (GEQ–Q1) was present across the two trials ($I^2 = 83.2$ percent) (Figure 24). Although the effect size for the two estimates of the RR was in the same direction, the magnitude of this effect differed between the two trials (2.33¹⁴³ versus 3.94¹⁴⁷). One explanation of this finding could be the disparate rates of improvement on GEQ observed in the placebo arms of these trials (29 percent¹⁴³ versus 18 percent¹⁴⁷). Note that the respective rates in the sildenafil arms were quite similar (73 percent versus 71 percent). The higher rate of improvement on GEQ for the placebo arm in the first trial¹⁴³ resulted in the smaller effect size (RR = 2.33). This could be explained by a higher proportion of participants with a mild to moderate form of ED, which may have resulted from the difference between the two trials in with respect to the use of inclusion criteria based on IIEF scores (≤ 25 ¹⁴³ versus ≤ 21 ¹⁴⁷). Moreover, other contributing factors for the observed differences for the improvement rates between the two placebo arms could have been due to the fewer patients with organic ED (18 percent¹⁴³ versus 51 percent¹⁴⁷) and a shorter mean duration of ED in the first trial (2.2 years¹⁴³ versus 4.5 years¹⁴⁷). The two trials employed similar dosing regimens (from 50 mg to 25 mg or 100 mg) and duration of sildenafil treatment (6–8 weeks).^{143,147}

Harms. Incidence of any adverse event: headache, dyspepsia, flushing.

The pooled RR estimates showed a statistically significant increase in risk among participants treated with sildenafil compared with those receiving placebo for all-cause adverse events (RR = 1.72, 95 percent CI: 1.33–2.24) and for the treatment-related specific events such as headaches (RR = 6.32, 95 percent CI: 1.92–20.85), dyspepsia (RR = 8.31, 95 percent CI: 1.54–44.86), and flushing (RR = 7.10, 95 percent CI: 1.58–31.95) (Figures 26–29).

Meta-analysis of trials comparing different doses of sildenafil (dose-response effect).

The dose-response efficacy/harm effect of sildenafil given at a fixed dose (10 mg, 25 mg, 50 mg, and 100 mg) was assessed in six trials.^{78,85,86,93,96,137} Of these, two trials were conducted in clinically distinct groups of participants (those with spina bifida⁷⁸ and diabetes⁹³) and therefore were not included in the meta-analysis. Therefore, the meta-analysis exploring the dose-response effect of sildenafil was based on three trials.^{86,96,137}

The following two pair-wise comparisons were made:

- 1) Sildenafil 25 mg versus sildenafil 50 mg
- 2) Sildenafil 50 mg versus sildenafil 100 mg

The efficacy and harm outcomes examined in the meta-analysis (i.e., those assessed and reported in sufficient detail in all three trial reports) were the proportions of participants with improved erection (GEQ–Q1) and the proportions of participants who experienced a specific all-cause adverse event (i.e., headache, flushing, or visual disturbances) (Figures 30–37).

Sildenafil 25 mg versus sildenafil 50 mg – Efficacy. Proportion of participants with improved erection (GEQ–Q1). A statistically significant greater proportion of participants in the 50 mg sildenafil treatment group reported improved erection (GEQ–Q1) in comparison with the 25 mg group (RR = 1.19, 95 percent CI: 1.06–1.34) (Figure 30).

Sildenafil 25 mg versus sildenafil 50 mg – Harms. Proportion of participants with headache, flushing, or visual disturbances.

The pooled estimates for the observed between-group (50 mg sildenafil versus 25 mg sildenafil) differences with respect to proportions of participants experiencing all-cause

headaches (RR = 1.02, 95 percent CI: 0.69–1.50) and visual disturbances (RR = 2.87, 95 percent CI: 0.70–11.80) were not statistically significant (Figures 31 and 33). The latter result may have been due to the small sample of the meta-analysis (Figure 31). The incidence of all-cause flushing was significantly greater among participants receiving the higher 50 mg dose of sildenafil (RR = 1.65, 95 percent CI: 1.13–2.42) (Figure 32).

Sildenafil 50 mg versus sildenafil 100 mg – Efficacy. Proportion of patients with improved erection.

The difference in the proportion of participants with improved erection (i.e., those who answered “yes” to GEQ–Q1) between the 50 mg and 100 mg sildenafil treatment groups was not statistically significant (RR = 1.10, 95 percent CI: 1.00–1.20) (Figure 34).

Sildenafil 50 mg versus sildenafil 100 mg - Harms.

Proportion of patients with all-cause headache, flushing, or visual disturbances. There was no statistically significant difference between the 100 mg and 50 mg sildenafil treatment groups in the incidence of all-cause headaches (RR = 1.31, 95 percent CI: 0.93–1.84), flushing (RR = 0.87, 95 percent CI: 0.61–1.23), and visual disturbances (RR = 4.18, 95 percent CI: 0.44– 39.54) (Figures 35–37).

Assessment of Publication Bias

Funnel plots were generated to assess the extent of asymmetry for each meta-analysis. Visual inspection of these plots did not reveal any substantial asymmetry.⁵³ (Figures D-1-8, Appendix D).

Oral Treatments — Phosphodiesterase Type 5 (PDE–5) Inhibitors – Vardenafil

Literature Search

In total, 22 unique randomized controlled trials (RCTs) (31 publications) met the eligibility criteria and were included in the review.¹⁸⁰⁻²¹⁰ (see also summary Evidence Table F-2, Appendix F) Seven unique trials were reported in more than one publication. The following list shows the reference identifications for these trials and corresponding publications (each row).

The first reference (author, year, citation) denotes the primary publication (i.e., reporting the most relevant and complete data for the trial), which is used to designate the trial throughout the Vardenafil section.

1. Valiquette 2005¹⁸² and Valiquette 2006²⁰²
2. Nehra 2005¹⁸³ and Brock 2003¹⁸⁷
3. Carson 2005¹⁸⁴ and Hatzichristou 2005¹⁸⁸
4. Hatzichristou 2004¹⁹¹ and Hatzichristou 2005²⁰⁷
5. Porst 2001¹⁹⁴ and Porst 2003¹⁸⁵
6. Goldstein 2005¹⁹⁷ and Fisher 2005¹⁸⁶
7. Hellstrom 2002,¹⁹² Hellstrom 2003,²⁰⁸ Hellstrom 2005,²⁰⁹ and Donatucci 2004²¹⁰

Overview of Trials

The trials were conducted in North America,^{181-184,190,190,192,192,197,197-199,199,203} Europe,^{184,190,191,193-201,203,204} South America,^{182,190,203} and Asia.^{180,182,184,189,203,203,205,206}

Of the 22 trials, two were of crossover design^{193,195} and the remaining 20 trials used parallel-arm design. All but one (active arm-controlled)¹⁹⁰ were placebo-controlled trials.

The trials were supported by Bayer^{181,183,189,190,192-195,197,198,200,201,203,205} Bayer and GlaxoSmithKline,^{182,184,191,196,199} and GlaxoSmithKline.²⁰⁴ Funding sources could not be ascertained for two trials.^{180,206}

Populations

The included trials involved participants diagnosed with ED. The total and mean numbers of patients randomly assigned to an intervention or placebo across the 22 trials were 8,621 and 392, respectively, while the number of randomly assigned patients in each trial ranged from 21¹⁹³ to 1020.¹⁹⁰

The inclusion criteria across most of the included trials were: adult males aged ≥ 18 years, diagnosed with ED for ≥ 6 months in a stable monogamous heterosexual relationship.^{180-184,189-195,197-201,203,204} In one trial,²⁰⁵ the inclusion criteria for the patients' age and duration of ED were slightly different (≥ 20 and ≥ 5 years, respectively). In the report of one trial²⁰⁶ the patient inclusion criteria for age and duration of ED were not clear.

The additional inclusion criteria in seven trials were diagnoses for the following conditions: diabetes types I or II,^{181,205} diabetes type I,²⁰⁴ nerve-sparing retropubic prostatectomy,¹⁸³ history of renal transplant,²⁰⁶ untreated mild major depressive disorder,¹⁹⁹ or arterial hypertension.¹⁹⁶ One trial included ED patients who had not responded to previous sildenafil therapy.¹⁸⁴ In three trials, the included patients were sildenafil-naïve.^{180,201,204} In one of these trials,¹⁸⁰ patients had not received any previous treatment for ED.

In most trials, patients had ED with a broad spectrum of causes (i.e., organic, psychogenic, and mixed).^{180,182,184,189-195,197,198,200,201,203} The mean age across the 22 trials ranged from 34 years¹⁹⁵ to 60 years.^{183,184}

Exclusion criteria were not reported for two trials.^{180,200} Patients with the following conditions were excluded from the trials: primary hypoactive sexual desire^{181-184,190-193,196-199,201,203-205} penile/genital anatomical deformity,^{182,184,189-192,195-199,201,203,204,206} any medical psychiatric or substance abuse disorder affecting the ability to complete the study,^{182,184,189,199,201,205} ED resulting from spinal cord injury,^{181-184,189-199,201,203-205} cardiovascular conditions (e.g. coronary artery disease, myocardial infarction, electrocardiographic ischemia, life-threatening arrhythmia, stroke, uncontrolled atrial tachyarrhythmia, unstable angina pectoris, uncontrolled atrial fibrillation),^{181-184,189-193,195-198,201,203-206} hyper/hypotension (resting),^{181-184,189-193,195,196,201,203-206} postural hypotension,^{182,183,189,192,196,201,204,205} liver disease,^{181,183,189,191,192,196,198,201,204-206} radical prostatectomy,^{190-199,201,203-205} bleeding or hematological disorder,^{181,183,189,191,192,198,201,203,204,206} retinitis pigmentosa,^{181-183,190,192,193,195-199,203-205} poorly controlled diabetes mellitus,^{182,183,189-195,198,203} hepatitis B,^{189,192,194,195,198,203} hepatitis C,^{189,192,194,196,201,204} peptic ulceration,^{183,189,192,201,205,206} major psychiatric disorders,^{193,195,199} endocrine diseases,^{193,195} autonomic neuropathy,¹⁸¹ or prostate cancer.¹⁸³

The following concomitant medications were not allowed: nitrates or nitric oxide donors,^{181-184,189,191-198,201,203-206} cimetidine, erythromycin, ketoconazole or trazodone, current use of digoxin derivatives or digitoxin antiarrhythmics,^{189,192,194,196-198,201,204} anticoagulants,^{181-183,192,194,196-198,201,204} androgens,^{192,196-198,201,203,204} ketoconazole,^{194,196,197,204} alpha blockers,^{196-198,201} or rifampicin.^{189,194}

Patients with abnormal hormone profiles such as low serum total testosterone,^{182-184,189,192,194,201,203} elevated serum creatinine,^{184,189,192,196,201,203,204} serum free thyroxine (T4) out of the normal range,¹⁸⁹ or thyroid-stimulating hormone (TSH) below the normal range were also excluded.^{189,194}

Also excluded were sildenafil nonresponders^{189-194,198,199,203} and patients who had discontinued previous sildenafil treatment because of side effects.^{181,183,189-191,198}

Interventions

The patients in all 22 included trials were randomly assigned to receive monotherapy of oral vardenafil at either a fixed or a flexible dose. In 12 trials,^{180-183,189,190,192-195,198,205} vardenafil was administered at a fixed dose ranging from 5 mg/d^{189,192,194} to 40 mg/d,¹⁹³ whereas in the remaining 10 trials a flexible dose with upward and downward titration was used, depending on the observed response in terms of efficacy and tolerability (i.e., 10 mg/d, 5 mg/d, 20 mg/d).^{184,191,196,197,199-201,203,204,206}

The patients were randomly assigned to receive placebo in all but one trial,¹⁹⁰ in which two doses (10 mg/d and 20 mg/d) of vardenafil were compared. In one trial the study medication (i.e., vardenafil) was coadministered with visual sexual stimulation.¹⁹⁵

In 10 trials patients were randomly assigned to receive two or more different fixed doses of vardenafil in each arm: 10 mg/d versus 20 mg/d,^{181,183,190,195,198,205} 5 mg/d versus 10 mg/d versus 20 mg/d,^{189,192,194} and 20 mg versus 40 mg.¹⁹³

In the majority of included trials, the duration of treatment with vardenafil was about 12 weeks.^{181-184,189,194,211} The treatment duration across the trials ranged from 4 weeks^{198,206} to 24 months.¹⁹⁰

Patients were instructed to take the study medication one hour before their sexual activity^{182-184,189-192,194,196,204-206} or as needed^{181,198} for maximum of one dose per day. In one trial patients were instructed to take the dose 8 hours before sexual activity for up to one dose a day.²⁰³ Five trials did not report the dosage instructions clearly.^{180,197,199-201}

Outcomes

Harms. The presence or absence of any adverse events was reported in eight trials.^{182-184,189,191,193,200,203} The presence or absence of serious adverse events was reported in 18 trials.^{181-184,190-198,200,201,203-205} The presence or absence of withdrawals due to adverse events was reported in 19 trials.^{181-184,189-199,201,203-205}

Efficacy. The most commonly reported outcomes that measured the degree of ED were: the mean IIEF scores for the “Erectile Function” domain (endpoint or mean change from baseline);^{181-184,189-192,194,196-201,203-206} the mean endpoint score/mean score changes on questions two and three of the Sexual Encounter Profile (SEP–Q2: “*Were you able to insert your penis into your partner’s vagina?*”) and SEP–Q3: “*Did your erection last long enough for you to have successful intercourse?*”)^{181-184,190-192,196-201,203-205} and a Global Assessment Question (GAQ–Q1: “*Has the treatment you are taking improved your erection?*”).^{181-184,189-192,196,199-201,203}

Other commonly reported outcomes were total mean scores for the following IIEF domains: “Intercourse Satisfaction,”^{183,194,198,204} “Overall Satisfaction,”^{183,194,198,204} “Orgasmic Function,”^{183,194,204} “Sexual Desire,”^{194,204} and the mean scores for individual IIEF questions Q3/Q4 (i.e., penetration and maintenance frequency).^{183,189,194,200,205}

Other less frequently reported outcomes were measured using the following instruments: Center for Epidemiologic Studies Depression Scale (CES-D),^{183,190,199} the quality of life (QoL) Fugl-Meyer assessment,^{189,190,194} the Rosenberg Self-Esteem Scale,^{199,200} tip and base rigidity activity unit (RAU) and tumescence activity units (TAU),^{193,195} the duration of erection with rigidity of >60 percent (or >80 percent),^{193,195} patient’s diary of satisfaction with erection/ejaculation,¹⁹¹ ED severity,²⁰⁶ endothelial function of cavernous and brachial arteries (flow mediated dilation: FMD),¹⁸⁰ and sexual quality of life domain from the modified Sexual Life Quality Questionnaire (mSLQQ).¹⁹⁷

Study and Reporting Quality

The mean total Jadad score for the 22 trials was 3.3 (Appendix C, Table C-1). The Jadad total score for the individual trials ranged from one²⁰⁶ to five.^{191,197} The methods for generating the sequence of random assignment were described for four studies^{183,191,192,197} and were judged to be appropriate. All trials except for one²⁰⁶ were described as double-blind. For all trials except for one¹⁸⁹ the methods for treatment allocation concealment were judged to be “unclear.” The method of allocation concealment reported in the above-mentioned trial was deemed to be appropriate.¹⁸⁹ Both crossover trials^{193,195} employed a washout period of five days.

Qualitative Synthesis

Vardenafil (any dose, fixed dose, flexible dose) versus placebo. This section presents results derived from 21 placebo-controlled trials that compared the efficacy and harms profile of vardenafil (any dose) to that of placebo.^{180-184,189,191-201,203-206} One trial¹⁹⁰ that explored a dose-response effect of vardenafil, without using a placebo arm, is reviewed in a later section (vardenafil dose 1 versus vardenafil dose 2).

Harms. Of the 21 trials, harms-related data were reported in all but one.¹⁸⁰ Therefore, this section describes harms reported in 20 trials.^{181-184,189,191-201,203-206}

Any all-cause adverse events. This outcome was reported in eight trials, where it was shown that the incidence of any adverse events (number of patients with one or more adverse event),^{182-184,189,191,193,200,203} was higher (either numerically or with statistical significance) in vardenafil groups (regardless of vardenafil dose or dose regimen) than in placebo groups. The proportions of patients with one or more adverse event in vardenafil groups across the trials ranged from about 27 percent (10 mg dose)¹⁸² to 74 percent (20 mg dose).¹⁸⁹ The corresponding proportion for the placebo groups ranged from about 17 percent²⁰⁰ to 52 percent.¹⁸⁹

Specific adverse events. In general, vardenafil was described as well tolerated. Most adverse events were reported as mild or moderate in nature and followed a profile similar to that seen in other medications of the PDE-5 class (e.g. sildenafil, tadalafil). Most commonly, patients in the vardenafil arms experienced headache, flushing, rhinitis, and dyspepsia.

Withdrawals due to adverse events. Two^{200,206} of the 20 trials^{181-184,189,191-201,203-206} did not report the proportion of withdrawals due to adverse events. Overall, the rate of withdrawals due to adverse events (i.e., the proportion of patients) in vardenafil and placebo-treated groups of patients were numerically similar. The withdrawal rate in vardenafil groups across the 18 trials^{181-184,189,191-199,201,203-205} ranged from 0 percent^{193,195,198} to 5 percent.¹⁹² The corresponding rate for the placebo-treated patients ranged from 0 percent^{193,195,203} to 6 percent.¹⁸⁹ Some of the reported specific events leading to the withdrawals were myocardial infarction, proctalgia, aortic bifurcation graft,²¹² abnormal liver enzyme levels,^{182,192} myalgia, flushing,^{181,182} nausea,¹⁹² headache,^{181,191,192} kidney calculus,¹⁹² abnormal vision, and rhinitis.¹⁸¹

Serious adverse events. The absence or occurrence of serious adverse events could not be ascertained for three trials.^{189,199,206} The specific serious adverse events observed across the trials in patients after random assignment to vardenafil therapy were: skin ulcer,¹⁹⁸ reflux disease,¹⁹⁸ unstable angina,¹⁹⁷ myocardial infarction,^{198,201} syncope and encephalitis¹⁹⁸ aortic bifurcation,²⁰¹ facial palsy, and appendicitis.¹⁸² Serious adverse events that occurred in 10 trials were not specified.^{181,183,184,191,192,194,196,203-205} In three trials^{193,195,200} reportedly no serious adverse events occurred. In general, judging from the results of these trials, there were no obvious numerical or statistical differences in the occurrence of serious adverse events between patients randomly assigned to receive vardenafil and those assigned to placebo.

Vardenafil (fixed dose: 5 mg, 10 mg, 20 mg, 40 mg) versus placebo. In 11 trials vardenafil was administered at a fixed dose (5 mg, 10 mg, 20 mg, and/or 40 mg).^{180-183,189,192-195,198,205}

The results of all trials demonstrated statistically significant improvements for patients who received vardenafil (5 mg, 10 mg or 20 mg) compared with those treated with placebo after 12 weeks of treatment (or longer followup) with respect to the mean IIEF scores for the “EF domain,”^{181-183,189,192,194,198,205} IIEF-Q3/Q4,^{189,194} SEP-Q2/Q3,^{181,182,192,198,205} GAQ-Q1,^{181,182,189,192,194} and the mean IIEF scores for the domains of “Intercourse Satisfaction,” “Overall Satisfaction,” “Sexual Desire,” and “Orgasmic Function.”^{183,194}

Results obtained from two trials^{193,195} showed a statistically significant increase in the mean duration (in minutes) of penile tip/base rigidity (>60 percent) in patients randomly assigned to receive vardenafil at a dose of 10 mg,¹⁹⁵ 20 mg,^{193,195} or 40 mg,¹⁹³ as compared with those randomly assigned to receive placebo.

In one trial,¹⁸⁰ patients treated with vardenafil (20 mg), in comparison with those treated with placebo, experienced a statistically significant improvement in endothelial function measured by the degree of brachial artery flow-mediated dilation (13.0 percent versus 10.7 percent).

The beneficial effects of vardenafil use relative to that of placebo observed in trials of homogeneous clinical groups such as diabetes,^{181,205} nerve-sparing retropubic prostatectomy,¹⁸³ and no previous ED treatment¹⁸⁰ were consistent with those of other trials conducted in participants with ED and a wide spectrum of diseases.^{182,189,192-195,198}

Treatment efficacy subgroup analyses (i.e., stratified efficacy results) were reported for five trials with respect to the origin of ED,^{180,194} baseline severity of ED,^{182,192,194} age groups,¹⁹⁴ and previous sildenafil use.^{194,198} The results of these analyses indicated numerically greater improvements associated with milder forms of ED,^{192,194} no previous use of sildenafil (i.e., sildenafil-naïve patients),¹⁹⁸ and arteriogenic ED (versus organic nonarterial or psychogenic ED).¹⁸⁰ In one of these trials,¹⁹⁴ the degree of improvement in IIEF “EF” domain scores was not modified by age, previous sildenafil use or the origin of ED (organic, mixed, or psychogenic).

Vardenafil (flexible dose: 5 mg- 10 mg- 20 mg) versus placebo. Ten trials administered vardenafil with a flexible daily dose (5 mg, 10 mg, 20 mg).^{184,191,196,197,199-201,203,204,206} The results of all trials demonstrated statistically significant improvements for patients receiving a flexible dose of vardenafil compared with those treated with placebo after 12 weeks of treatment (or longer followup) with respect to the mean IIEF scores for “EF domain,”^{184,191,197,199-201,203, 204, 206} IIEF-Q3/Q4,^{200,206} SEP-Q2/Q3,^{184,191,196,197,199-201,203,204} and GAQ-Q1.^{184,191,196,199-201,203} Statistically significant improvements in vardenafil-treated patients, relative to those on placebo, were also observed with respect to mean scores for the following IIEF domains: “Intercourse Satisfaction,” “Overall Satisfaction,” “Orgasmic Function”^{199,200} and/or “Sexual Desire.”^{199,204}

In four trials,^{184,201,203,204} at followup after 12 weeks of treatment, a statistically significant greater proportion of patients with an IIEF “EF” domain score ≥ 26 was found in groups treated with vardenafil compared with those who received placebo.

The relative beneficial effects of vardenafil use with respect to the above-mentioned outcomes observed in trials of homogeneous clinical groups, such as patients with diabetes,²⁰⁴ renal transplant,²⁰⁶ untreated mild major depressive disorder,¹⁹⁹ or arterial hypertension,¹⁹⁶ as well as sildenafil nonresponders¹⁸⁴ and sildenafil-naïve patients^{201,204} were consistent with those of other trials conducted in participants with ED and a wide spectrum of diseases.^{191,197,200,203}

Treatment efficacy subgroup analysis (i.e., stratified efficacy results) was reported for only one trial¹⁹¹ with respect to dose-sequence, in which patients who received a stable dose of 10 mg vardenafil over 12 weeks experienced greater improvements on the mean scores for IIEF “EF domain,” SEP-Q2/Q3, and the proportion for GAQ-Q1 compared with those who gradually increased their vardenafil dose to 20 mg over the followup of 8 weeks.

Vardenafil dose 1 versus vardenafil dose 2. There were 10 trials with two or more dose-specific arms of vardenafil.^{181,183,189,190,192-195,198,205} None of the trials were designed to compare flexible and fixed dosage regimens of vardenafil.

Harms. Any all-cause adverse events.

In seven^{183,189,190,192,193,195,205} of the 10 dose-response studies,^{181,183,189,190,192-195,198,205} the incidence of any adverse events was shown to be numerically dose-dependent, increasing with a

higher dose. In one multicenter North American study, for example, after 26 weeks of treatment with 5 mg, 10 mg, or 20 mg of vardenafil or placebo 19, 33, 42 and 7 percent of patients, respectively, experienced at least one adverse event.¹⁹² In a trial of similar design of 12 weeks' duration, these proportions were 57, 63, 74, and 52 percent, respectively.¹⁸⁹ The similar trend was observed in a trial that compared 20 mg and 40 mg doses of vardenafil (47.6 versus 60.9 percent, respectively).¹⁹³ Statistical test results for these differences were not reported.

Specific adverse events. The most frequently observed adverse events in the 10 trials were headache, flushing, dyspepsia, or rhinitis. In one trial,¹⁹⁰ eight and 13 patients developed visual disturbance(s) in the 10 mg and 20 mg groups, respectively. In another trial,¹⁸⁹ two patients (one patient in each 5 mg and 20 mg groups) were observed to have visual disturbances (sensory, abnormal vision, and brightening).

Withdrawals due to adverse events. In three trials,^{193,195,198} none of the patients treated with vardenafil withdrew because of adverse events. For the remaining seven trials,^{181,183,189,190,192,194,205} the rate of withdrawals was numerically similar between treatment arms using 10 mg versus 20 mg of vardenafil.^{181,183,189,190,192,194,205}

Serious adverse events. There was no apparent numerical or statistically significant difference in the occurrence of serious adverse events across the treatment arms of various doses of vardenafil. For example, one trial reported 4, 1, and 1.4 percent of patients with at least one serious adverse event in 5 mg, 10 mg, and 20 mg vardenafil groups, respectively.¹⁹⁴ In another study, the corresponding proportions of patients with at least one serious adverse event were 5, 3, and 4 percent.¹⁹² Four deaths were reported during one trial;¹⁹⁰ one death resulted from suicide (10 mg group), while the other three (in the 20 mg group) occurred after myocardial infarction, coronary angioplasty, and ischemic cardiomyopathy. None of the deaths was attributed to the effects of vardenafil.

Efficacy. In three trials,^{189,192,194} at 12 weeks after randomization, a dose-related effect of vardenafil with respect to the mean IIEF "EF" domain score was observed. Specifically, patients in either 10 mg or 20 mg vardenafil groups had statistically significant higher mean IIEF "EF" domain scores compared with those in the 5 mg vardenafil groups. Although for five trials^{189,190,192,194,198} the differences in the mean IIEF "EF" domain scores observed between the 10 mg and 20 mg were not statistically significant, patients receiving 20 mg of vardenafil had numerically greater scores than those receiving 10 mg vardenafil.

In two trials,^{181,205} patients treated with 20 mg had statistically significantly higher mean IIEF "EF" domain scores compared with those treated with 10 mg vardenafil: 19.0 versus 17.1¹⁸¹ and 22.9 versus 21.8.²⁰⁵ In another trial,¹⁸³ the mean IIEF "EF" domain score was similar for patients receiving 10 mg and 20 mg of vardenafil (7.7 versus 7.2, respectively).

After 12 weeks of treatment, there was a numerical increase (a statistically nonsignificant improvement) in the mean scores of IIEF-Q3/Q4^{189,194} and SEP-Q2/Q3^{181,190,192} across the three doses of vardenafil (5 mg versus 10 mg versus 20 mg), the highest being observed in the 20 mg group. For the mean SEP-Q2/Q3, one trial²⁰⁵ demonstrated a statistically significant difference between the two doses of vardenafil (10 mg and 20 mg) in favor of the 20 mg dose.

In one trial,¹⁹⁴ the proportion of participants with improved erections (i.e., who answered "yes" to GAQ-Q1) was shown to be statistically significantly greater in the 20 mg versus 5 mg (80 versus 66 percent, $p < 0.01$). Results from two other trials^{189,192} demonstrated trends of a numerical increase in the rate of improved erections across 5 mg, 10 mg, and 20 mg doses of vardenafil. The highest proportion of patients with improved erections was observed in the 20 mg groups (range 80.7–86.4 percent).^{189,192} In another trial,¹⁸¹ the proportion of participants with

improved erections was higher in participants who received 20 mg compared with those who received 10 mg of vardenafil (72 versus 57 percent, $p < 0.03$).

In one trial,¹⁹³ the difference in the mean change of the duration of penile rigidity (>60 percent) between the 20 mg and 40 mg doses of vardenafil was not statistically significant (42.9 versus 49.3).

Quantitative Synthesis - Meta-Analysis of Trials

Series of meta-analyses were performed using efficacy and harms data obtained from the reports of 21 trials^{180-184,189,191-201,203-206} that were conducted in:

- 1) Clinically heterogeneous groups of patients
- 2) Clinically homogenous groups of patients

Clinically heterogeneous groups of patients - vardenafil (any dose: 5 mg, 10 mg, 20 mg, 40 mg) versus placebo. The analyses presented in this section did not include 10 trials for the following reasons: distinct clinical groups of patients (e.g. those with diabetes, prostatectomy, renal transplant, depression, hypertension);^{181,183,196,199,204-206} crossover design in which no pre-crossover data were reported);^{193,195} and lack of measurement or reporting of relevant clinical outcomes.^{180,195} Thus, there remained 11 trials that were potentially eligible for meta-analysis.^{182,184,189,191,192, 194,197,198,200,201,203}

Efficacy. Mean IIEF “EF” domain score.

This meta-analysis incorporated three trials^{182,194,200} in which the pooled estimate of mean difference at 12 weeks after randomization was 7.35 (95 percent CI: 6.43–8.27), indicating a statistically significant improvement in the mean IIEF “EF” domain score in participants on vardenafil (any dose) compared with those on placebo. (Figure 38)

Mean per-patient proportion of successful intercourse attempts (SEP–Q2). This meta-analysis was based on two trials of flexible vardenafil dose.^{184,200} The estimated mean difference between vardenafil- and placebo-treated participants after 12 weeks of treatment was statistically significant in favor of vardenafil (WMD = 27.59, 95 percent CI: 17.06–38.11). One of the trials¹⁸⁴ was restricted to patients who were nonresponders to previous treatment with sildenafil. This difference between the populations of the two trials might have led to the high degree of statistical heterogeneity that was found ($I^2 = 61$ percent) (Figure 39).

Mean per-patient proportion of successful intercourse attempts (SEP–Q3). This meta-analysis was based on two trials^{184,200} and yielded a statistically significant pooled estimate of mean difference for erectile maintenance (SEP–Q3) (WMD = 33.19, 95 percent CI: 26.04–40.33), indicating that the treatment with vardenafil was associated with greater improvements in erectile maintenance frequency compared with placebo. (Figure 40)

Proportion of patients with improved erection (GAQ–Q1). Two separate meta-analyses were performed (Figures 41–42). The first incorporated results of 9 trials (Figure 41).^{182,184,189,191,192, 194,200,201,203} There was a statistically significantly higher rate of improvement at week 12 in erection among participants who received vardenafil compared with those who received placebo (RR = 2.50, 95 percent CI: 2.19–2.86). The trial that included only participants who did not respond to sildenafil¹⁸⁴ had an outlying value of larger effect estimate size (RR = 4.1), leading to a high degree of statistical heterogeneity across the trials ($I^2 = 51.5$). The second meta-analysis, which did not incorporate the trial of sildenafil nonresponders¹⁸⁴ (see Figure 42), yielded a substantially lower degree of heterogeneity ($I^2 = 3.7$) and a pooled RR of 2.38 (95 percent CI: 2.16–2.61). The vardenafil effect size may have been modified by the previous response to

sildenafil; specifically, this effect might be greater in sildenafil nonresponders compared with responders or participants naïve to sildenafil or other PDE-5 treatments.

Proportion of patients with IIEF-*EF* ≥ 26 . This outcome was reported for three trials.^{184,201,203} The pooled estimate of relative risk in the meta-analysis based on the results of these three trials indicated that a higher proportion of participants reached at least 26 on the IIEF score in the vardenafil group compared with the placebo group (RR = 4.05, 95 percent CI: 2.74–6.01) (Figure 43).

Harms.

Proportion of patients with any adverse events (all-cause). The result of this meta-analysis, based on six trials,^{182,184,189,191,200,203} showed a statistically significantly higher incidence of adverse events from any cause among participants who received vardenafil compared with those who received placebo (RR = 1.61, 95 percent CI: 1.40–1.87) (Figure 44). (Note: “favors” in forest plots refers to increased frequency of the event for the respective treatment arm, regardless of desirability of the event)

Patients who withdrew due to adverse events. This meta-analysis incorporated data from 10 trials.^{182,184,189,191,192,194,197,198,201,203} Although the pooled effect estimate of RR indicated a 29 percent increase in the rate of withdrawal due to adverse events for patients treated with vardenafil relative to those treated with placebo, the observed difference in rates between the two treatment groups was not statistically significant (RR = 1.29, 95 percent CI: 0.78–2.13) (Figure 45).

Patients with serious adverse events (all-cause). This meta-analysis incorporated 9 trials.^{182,184,191,192,197,198,200,201,203} Although the pooled effect estimate of RR indicated a 34 percent increase in the risk of experiencing at least one serious adverse event among patients treated with vardenafil relative to those treated with placebo, the observed difference in the rates between the two treatment groups was not statistically significant (RR = 1.34, 95 percent CI: 0.76–2.36) (Figure 46).

Patients with headache (all-cause). This meta-analysis incorporated the results of nine trials.^{182,191,192,194,197,198,200,203,213} According to the pooled estimate, the use of vardenafil was associated with a significantly increased risk of headache relative to the use of placebo (RR = 4.10, 95 percent CI: 2.56–6.57) (Figure 47).

Proportion of patients with flushing (all-cause). This meta-analysis included nine trials.^{182,191,192,194,197,198,200,201,203} Patients treated with vardenafil patients were at a statistically significant increased risk of flushing compared with patients treated with placebo (RR = 10.22, 95 percent CI: 5.26–19.87). The magnitude of the pooled RR may have been an overestimate of the true RR because low counts observed in the placebo arms which would cause some instability and inflation of individual estimates of RR (Figure 48).

Proportion of patients with dyspepsia (all-cause). This meta-analysis included six trials,^{182,191,192,194,197,198} the outcome of dyspepsia was not ascertainable for five trials.^{184,189,200,201,203} Patients who received vardenafil were at a statistically significantly higher risk of dyspepsia compared with those who received placebo (RR = 6.58, 95 percent CI: 2.61–16.60) (Figure 49).

Clinically homogenous groups of patients. Seven trials included ED patients who additionally presented with diabetes Types I and II,^{181,204,205} nerve-sparing retropubic prostatectomy,¹⁸³ renal transplantation,²⁰⁶ untreated mild major depression,¹⁹⁹ or arterial hypertension.¹⁹⁶ Only three trials^{181,204,205} including diabetic patients were potentially suitable for meta-analysis.

Efficacy. Meta-analyses for efficacy outcomes in diabetes patients were not performed in view of missing qualitative or quantitative information (i.e., the outcome was not reported at all or no numerical data were given on measures of variability).

Harms.

Patients with serious adverse events (all-cause). This meta-analysis included results from three trials.^{181,204,205} There was a statistically nonsignificant finding of a 40 percent increased risk of a serious adverse event in patients who received vardenafil versus those who received placebo (RR = 1.40, 95 percent CI: 0.59–3.29) (Figure 50).

Patients who withdrew due to adverse events. This meta-analysis included results from three trials of patients with diabetes.^{181,204,205} The difference in the withdrawal rates resulting from adverse events between these patients in vardenafil and placebo groups was not statistically significant (RR = 1.80, 95 percent CI: 0.66–4.91) (Figure 51).

Dose-response effect of vardenafil (20 mg versus 10 mg). There were 10 trials with two or more dose-specific arms of vardenafil.^{181,183,189,190,192-195,198,205} The analysis in this section excluded trials of distinct clinical groups of patients^{181,183,205} and crossover trials.^{193,195} Therefore, five potentially eligible trials remained for the analyses.^{189,190,192,194,198} Meta-analysis could be performed with respect to only one efficacy outcome, the IIEF “EF” domain endpoint score. For other efficacy outcomes (IIEF–Q3/Q4, SEP–Q2/Q3) quantitative data necessary for meta-analysis were missing.^{189,190,192,198}

Efficacy.

Mean IIEF “EF” domain score. This meta-analysis incorporated two trials.^{190,194} The estimate of pooled mean difference for the IIEF “EF” domain score observed between the two groups of patients at weeks 12–104 was not statistically significant (WMD = 0.92, 95 percent CI: -0.03 to 1.87) (Figure 52).

Proportion of patients with improved erection (GAQ–Q1). This meta-analysis incorporated results of four trials.^{189,190,192,194} The proportion of patients with improved erection at week 12 was similar in the 20 mg and 10 mg vardenafil treatment groups (RR = 1.03, 95 percent CI: 0.99–1.08) (Figure 53).

Harms.

Proportion of patients with any adverse events (all cause). The result of this meta-analysis, incorporating two trials,^{189,190} indicated a marginally statistically significant increase in risk for any adverse event for patients treated with 20 mg vardenafil compared with those treated with 10 mg vardenafil (RR = 1.15, 95 percent CI: 1.06–1.25) (Figure 54).

Proportion of patients with serious adverse events (all cause). This meta-analysis was based on results of three trials.^{190,192,198} The occurrence of serious adverse events could not be ascertained for two trials.^{189,194} The pooled estimate of relative risk indicated that the risk of developing any serious adverse event did not differ between the groups of patients receiving 20 mg and 10 mg doses of vardenafil (RR = 1.02, 95 percent CI: 0.37–2.82) (Figure 55).

Patients who withdrew due to adverse events. This meta-analysis included five trials.^{189,190,192,194,198} The difference in withdrawal rates resulting from adverse events observed

between patients treated with 20 mg and 10 mg doses of vardenafil was not statistically significant (RR = 1.60, 95 percent CI: 0.85–3.00) (Figure 56).

Patients with headache, flushing, or dyspepsia (all cause). Three meta-analyses, each incorporating results from three trials,^{192,194,198} were performed separately for the incidence of headache, flushing, and dyspepsia (Figures 57–59). The occurrence of these events could not be ascertained for two trials.^{189,190}

Although the pooled effect estimates indicated an increased risk ranging from 25 percent (RR = 1.25, 95 percent CI: 0.87–1.79) to 56 percent (RR = 1.56, 95 percent CI: 0.83–2.91) for the occurrence of any of these events in patients treated with 20 mg vardenafil versus 10 mg vardenafil, none of these estimates reached statistical significance.

Assessment of Publication Bias

Funnel plots were generated and examined to graphically assess the extent of asymmetry (i.e., possible publication bias) present in each meta-analysis. Visual inspection of these plots did not reveal any substantial asymmetry.⁵³ (Figures D-9-11, Appendix D)

Oral Treatments — Phosphodiesterase Type 5 (PDE–5) Inhibitors – Tadalafil

Literature Search

In total, 30 RCTs (in 37 publications) met the eligibility criteria and were included in the review.^{103,118,121,163,214-247}

One additional trial,²³¹ which employed the combination of topical testosterone and tadalafil is described in the section on hormonal treatments.

Results of four unique trials were presented in multiple publications. The following list shows the reference identifications for these trials and corresponding publications (each row).

The first reference (author, year, citation) denotes primary publications (i.e., those reporting the most relevant and complete data for the trial), which are used throughout the Tadalafil section. (Table F-3, Appendix F)

1. Eardley 2005¹⁰³ and Dean 2006²⁴¹
2. Mirone 2005,²¹⁴ Moncada 2005,²⁴⁴ Costa 2006,²⁴⁵ Wespes 2007,²⁴⁶ Buvat 2006²⁴⁷
3. McMahon 2005²¹⁶ and McMahon 2006²⁴²
4. Carson 2005²¹⁷ and Carson 2005²⁴³

Overview of Trials

The trials were conducted in the US,^{118,121,215,217,222,224,225,230,233,235} Canada,^{221,222,227} Europe/UK,^{103,118,121,163,214,218-220,222,223,225,226,232,234,239} East and Southeast Asia,^{229,236,237,240} Japan,²³⁸ and Australia.^{216,228,242} The trials were published between 2002²²⁶ and 2007^{232,233,235} inclusively. The authors of all trials but three^{163,218,219} stated that the trials were funded by Lilly ICOS LLC. Of the two Italian trials,^{218,219} one was funded by Pfizer;²¹⁸ the other²¹⁹ did not report the funding source.

Of the 30 trials, 22 were parallel-arm^{215-227,229,230,233-238,240} and eight were^{103,118,121,163,214,228,232,239} crossover trials. Of the 22 parallel-arm trials, 13 had two arms^{216-220,222-225,233,234,236,240} and nine trials had three or more arms.^{215,221,226,227,229,230,235,237,238} Of the 30 trials, 23 were placebo controlled^{215-227,229,230,233-240} and seven were active-arm (e.g. sildenafil, tadalafil, vardenafil) controlled trials.^{103,118,121,163,214,228,232} Further information on trial characteristics is provided in Table F-3 (Appendix F).

Populations

The included trials involved men diagnosed with ED. The total and mean numbers of patients randomly assigned to study interventions or placebo across the 30 trials were 10,718 and 358, respectively. The number of patients randomly assigned across the trials ranged from 20²³² to 4,262.²¹⁴

The inclusion criteria in all trials except five^{218,222,226,233,239} were: adult males aged ≥ 18 years, diagnosed with ED for ≥ 3 months, and in a stable monogamous heterosexual relationship. The inclusion criteria in two studies^{222,226} were restricted to patients who either additionally had diabetes (Type I or II)²²⁶ or who had undergone bilateral nerve-sparing retropubic prostatectomy 1–4 years before their enrolment into the trial.²²² In one trial,²¹⁸ the study population consisted of mostly older men, aged 59–71 years, who had two or more risk factors for coronary artery disease (CAD) (e.g. total cholesterol level >5.20 mmol/L, diabetes Type II, hypertension $>135/85$ mmHg, tobacco smoking, family history). Only 50 percent of these patients had ED. In

two other trials^{233,239} the patient populations comprised those with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH)²³³ and patients with ED undergoing three-dimensional conformal external-beam radiotherapy (3DCRT) for prostatic carcinoma.²³⁹ In the former trial,²³³ only 65 percent (183,281) of the patients had ED. In one trial,¹⁶³ only PDE-5 naïve patients were enrolled.

The exclusion criteria in the majority of included trials were pelvic surgery,^{103,118,121,215,216,219-223,225,229,233,235-240} penile/testicular deformity,^{103,215,216,219,221-225, 227,228,230,234-236,238} unstable angina/myocardial infarction,^{103,118,121,163,215-218,220-222,224,225,227-229,232-240} prostatectomy,^{103,216,217, 220,221,223-225,227-230,233-238,240} HIV-positivity/AIDS,^{103,118, 121,221-223,227,229,230,235-238,240} use of nitrates,^{103,118,121,163,214,215,217,219,220,222,227,229,230,232-235,237-240} any major hepatic/renal disease,^{103,216, 219-224,227,228,233,234,236-238,240} previous ineffective treatment with sildenafil,^{216,217,221,223, 224,227,229,230, 234,235,238} stroke,^{103,118,121,214,215,217,219,224,225,228,233-235,238,239} endocrine disease,^{103,118,216,221,223,230,234-236, 238} retinitis pigmentosa,^{103,118,121,163,228} or a history of cancer.^{214,215,219,227,229,230,233,239,240} Other exclusion criteria were cancer chemotherapy^{232-235,237-240} premature ejaculation,^{234-236,238} spinal cord injury^{215,219,233-235,239} uncontrolled hypertension,^{103,217,233,235,236,238} use of alpha-blockers/androgens,^{163,238} and diabetes.^{216,221-223,233,234,236} One trial additionally excluded patients with prostate-specific antigen levels >10 ng/mL.²³³ None of the trials failed to report exclusion criteria.

The mean age of the study participants across the included trials ranged from 46²¹⁹ to 69²³⁹ years. The patients' race was not reported in eight trials.^{217-219,223,228,229,232,239} Three trials included Southeast Asian,^{236,237,240} one trial Japanese,²³⁸ and one trial Turkish and Egyptian patients.²³⁴ The approximate proportion of Caucasians in the remaining 17 trials ranged from 73 percent²²⁴ to 100 percent.^{163,220} The duration of ED of patients was not reported in four trials.^{218, 219,221,222} In 24 of the remaining 26 trials,^{103,118,121,214-217,220,223-230, 232-238,240} eligible patients had to have been diagnosed with ED for at least 3 months before their enrolment into the trial. In two trials, patients had been diagnosed with ED for at least 6¹⁶³ and 12 months²³⁹ before trial enrolment. In 22 trials, the majority of patients (≥70 percent) had been diagnosed with ED for at least 1 year before trial entry.^{103,118,121,214-217,220,223-227,229,230,234-240}

The most commonly reported comorbidities among study participants were diabetes,^{103,118,163, 214-217,220,221,223,224,226-230,232,234-238,240} hypertension,^{103,118,163,214-217,220,223, 224,226-230,232,234-240} coronary artery disease (CAD),^{103,118,163,214,215,217,221,224,228,229,235} hyperlipidemia,^{163,214,216,217,223,224,226,227,229, 230,232,234,235,237,238,240} BPH,^{223,224,233,234,236-238,240} and depression.^{103,118,214,224,230,235} The presence or absence of comorbidities could not be ascertained for six trials.^{121,218,219,222,225,233} In three trials,^{103,215,239} the proportion of ED patients with diabetes was below 10 percent; in five trials,^{216,220, 223,235,237} this proportion ranged from 11 percent²²⁰ to 14 percent;²³⁵ in four trials^{118,214,224,240} it ranged from 17 percent^{118,224} to 18 percent;^{214,244-247} and in 10 trials^{217,221,227-230,232,234,236,238} the proportion ranged from 20 percent^{217,227,232} to 31 percent.²³⁶ In two trials^{234,240} the proportion of ED patients with hypertension ranged from 14 percent²⁴⁰ to 17 percent.²³⁴ In other 12 trials^{103,118, 214,218,220,227-229,232,237-239} this proportion ranged from 20 percent²³² to 29 percent,²²⁸ and in eight trials^{215-217,223,224,230,235,236} from 30 percent^{216,236} to 43 percent.²³⁵ The remaining eight trials^{121,163, 219,221,222,225,226,233} failed to report the proportion of hypertensive patients. The proportion of ED patients with CAD in six trials^{103,118,214,215,224,229,241} was below 10 percent, and in three trials^{217, 228,235} it ranged around 10–11 percent. The proportion of patients with CAD could not be ascertained from the remaining 21 trials.

The approximate proportion of smokers was ascertained for 17 trials,^{103,118,121,214,215,217-221,225,227-229,232,234,238} and ranged from 15–16 percent^{215,217} to 37–40 percent.^{229,238} The authors of 13 trials^{163,216,222-224,226,230,233,235-237,239,240} did not report the proportion of smokers.

The majority of the trials included patients with ED of all three etiologic groups (i.e., organic, psychogenic, and mixed).^{103,118,121,163,214-217,219,220,223-225,227-229,232,234-238,240} In eight trials^{118,215-217,227,229,234,235} the proportion of patients with ED of psychogenic origin was below 10 percent, whereas in 13 other trials^{103,121,214,219,220,223-225,228,236-238,240} this proportion ranged from about 10 percent²²⁴ to 29 percent.²³⁸

The approximate proportion of patients with severe ED (IIEF “EF” domain score: 1–10) across 24 trials^{103,118,121,214-217,219-225,227-230,234-238,240} ranged from 18–23 percent^{223,228,240} to 50–52 percent.^{217,222} In 14 trials,^{103,214-216,219-221,224,225,227,230,235,237,238} the approximate proportion of patients with severe ED ranged from 30–32 percent^{103,237,241} to 40–42 percent.^{220,224,235} In seven trials,^{118,121,223,228,229,234,236} this proportion was from 20 to 30 percent. The proportion of patients by ED severity groups was not reported in six trials.^{163,218,226,232,233,239}

Interventions

Patients across the 30 trials that were reviewed received oral tadalafil monotherapy in either experimental or active control arms. In most of the trials, tadalafil was given in 10 mg^{215,221,226-230,237,238} and 20 mg doses.^{118,121,163,214-220,222-230,232,234,236-240} One trial²²¹ included three additional randomized arms in which patients received 2 mg, 5 mg or 25 mg of tadalafil. In another trial,²³⁸ one additional arm of randomly assigned patients received 5 mg of tadalafil. In one placebo-controlled trial,²³⁵ patients were randomly assigned to receive either 2.5 mg or 5 mg of tadalafil. Dose escalations were used in two trials: 10–20 mg¹⁰³ and 5–20 mg.²³³

In three trials,^{214,228,232} 20 mg tadalafil on demand was compared with 20 mg three times per week,²¹⁴ 20 mg on alternate days,²³² or 10 mg daily.²²⁸ In addition to these three trials,^{214,228,232} a fixed dose of tadalafil was used in nine others.^{118,121,163,217-220,225,235} “On demand” (i.e., “as needed”) dosing of tadalafil was used in 17 trials.^{103,215,216,221-224,226,229,230,234,236-240}

The duration of tadalafil treatment across the trials ranged from about 4–6 weeks^{214,215,218,230,232,233,239} to 24–26 weeks.²¹⁶ In half of the trials, tadalafil was administered for about 12 weeks.^{103,118,217,219,220,222-224,226-229,234,236-238}

Tadalafil was compared with placebo,^{215-227,229,230,233-240} sildenafil^{103,118,121,163}, tadalafil (control dose/dosing regimen),^{214,215,221,226-230,232,235,237,238} and vardenafil.¹⁶³

Outcomes

In total, all 30 trials reported some information on the absence and/or occurrence of either total or serious adverse events. In four trials, the incidence of any adverse events was not reported.^{121,217,221,224,232} Authors of 14 trials failed to report the absence or occurrence of serious adverse events.^{118,121,163,216,218,219,221,225-227,229,230,232,237} The number of patients who withdrew as a result of adverse events was reported in all but two trials.^{221,232}

Efficacy. The efficacy outcomes measured in the 30 included trials varied to some degree. The most commonly measured and reported outcomes across the trials were the mean or median endpoint score/mean score change on IIEF domains and/or individual questions,^{103,163,214,216,217,219,220,222-224,226-229,233,234,236-240,242,243} the mean endpoint/ mean change in the per-patient proportion of “yes” answers to the Sexual Encounter Profile questions 2 and 3 (i.e., SEP–2/3, “*Were you able to insert your penis into your partner’s vagina?*” and “*Did your erection last long enough for you to have successful intercourse?*”),^{103,214-217,219,220,222-230,234,236-240,243} and the proportion of

patients who answered “yes” to the Global Assessment Question 1 or 2 (i.e. GAQ–Q1: “*Has the treatment you have been taking improved your erections?*” and GAQ–Q2: “*If yes, has the treatment improved your ability to engage in sexual activity?*”).^{216,217,220,222-224,226-229,234, 236-240} Of the 16 trials that reported outcomes based on GAQs, nine trials^{216,217,224,226-229, 237,238} evaluated the proportion of patients who answered “yes” to GAQ–Q1 only, whereas the remaining seven trials^{220,222,223,234,236,239,240} evaluated this parameter for both GAQ–Q1 and GAQ–Q2.

Eight trials additionally evaluated the efficacy (i.e., the mean per-patient percentage of successful intercourse attempts based on “yes” responses to SEP Q3) for different time-periods after dosing of tadalafil.^{216,217,219,220,224,225,227,230}

The authors of one trial,²²¹ derived logistic regression models based on the patient data obtained from a randomized placebo-controlled trial. These dose-response models assessed the relationship between the dose of tadalafil (2, 5, 10, or 25 mg) and the probability of getting an outcome (SEP questions 2 and 3 and/or on IIEF questions 3 and 4). The models included such covariates as baseline severity of ED and IIEF–EF domain score.

In five trials,^{103,163,217,222,223,241,243} treatment satisfaction was measured using the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire.

The patients’ treatment preference (e.g. percentage of patients who preferred the use of tadalafil to that of sildenafil) was evaluated and reported in six trials, all of which were of a crossover design in which the patients received both tadalafil and sildenafil^{103,118,121, 163,241} or alternating dosing regimens of tadalafil (i.e., on demand versus fixed).^{214,228,244-247}

Endothelial function using percentage change (compared with baseline) in the mean flow mediated dilation (FMD) of brachial and cavernous arteries was measured in two trials.^{218,232}

Study Quality and Reporting

The mean Jadad total score for the 30 included trials was 3.2. The individual Jadad total score for 30 trials ranged from 1¹⁶³ to 5.^{216,222,225} All 30 trials but six^{103,163,214, 219,228, 232} were double-blind. Three trials could not have been double blinded because patients received either on-demand or fixed dosing regimens of tadalafil.^{214,228,232} Of the 24 double-blind trials, only nine trials^{118,216,218,221,222,224,225,227,239} reported some description of the blinding method(s) used. Only three trials^{219,238,239} reported some information on the allocation concealment, which was deemed to be adequate. The adequacy of allocation concealment for the remaining 27 trials could not be ascertained (i.e., was unclear).

Of the eight crossover trials,^{103,118,121,163,214,228,232,239} only one²³⁹ failed to report whether a washout period had been applied between the treatment periods. The length of washout period for the seven remaining crossover trials ranged from 4 days¹¹⁸ to 14 days.^{121,228,232}

Qualitative Synthesis

Tadalafil (any dose: fixed or flexible) versus placebo.

Harms. The occurrence of total and serious adverse events across the 23 placebo-controlled trials was reported poorly.^{215-227,229,230,233-240}

In the majority of these trials, the frequency of any adverse events (i.e., the proportion of patients with at least one adverse event) was greater either numerically or with statistical significance in the tadalafil arms than in the placebo arms.^{215,220,222,223,225-227,229, 230,236-240}

For example, in one trial, the proportion of patients who experienced at least one adverse event in the tadalafil and placebo arms were 51.7 versus 26.5 percent, respectively ($p < 0.001$).²²² In another trial,²²⁵ the corresponding numbers were 40 (22.5 percent) versus two (1.3 percent) (p

value was not reported). Even though the proportion of patients in one trial²²⁶ was numerically greater in the tadalafil arms (39.7–44.4 percent) than in the placebo arm (31.0 percent), this difference was not statistically significant ($p = 0.247$). Most common adverse events reported across all trials were headache, back pain, dyspepsia, dizziness, nasal congestion, flushing, and myalgia. In general, the occurrence of these events tended to be numerically more frequent in tadalafil arms than in placebo arms. Moreover, a statistically significant higher incidence of these events was reported across several trials in tadalafil versus placebo arms.^{215,220,222,223,225,226,239} The majority of the trials reported that tadalafil was well tolerated and that patients had had adverse events mostly of mild or moderate severity.

Eleven of the 23 trials did not report whether there had been any occurrence of serious adverse events.^{216,218,219,221,225-227,229,230,237,239}

In the remaining 12 trials,^{215,217,220,222-224,233-236,238,240} the incidence of serious adverse events (i.e., the proportion of patients with at least one serious adverse event) was reported to have been about 5.0 percent²²² or less, or 0,²³⁸ and to have been similar in tadalafil and placebo arms.^{215,217,220,222-224,233,235,240} In one trial,^{217,243} three patients who received tadalafil developed carotid artery bruit, esophageal spasm, and brain neoplasm (one case of each event).²¹⁷ Other specific serious adverse events that were reported were single cases of pulmonary embolism and subarachnoid hemorrhage,²²³ two cases of chest pain requiring hospital admission,²²⁴ and one case of worsening CAD.²³⁶ In one trial,²³⁵ five patients experienced at least one of the following serious adverse events in the tadalafil arm: acute myocardial infarction (AMI), benign lung neoplasm, back pain, road traffic accident, and pancreatitis. Two trials^{215,234} reported one death each which had occurred due to AMI²¹⁵ and cardiac arrest.²³⁴ Of the 12 trials that reported any occurrence of serious adverse events, three trials^{215,220,222} did not specify what these events were.

The proportion of patients who withdrew due to adverse events across trials was five–six percent^{217,222,224} or less and similar across the tadalafil and placebo arms.^{215-220,222-227,229,230,233-240}

Efficacy. In general, the results of the 23 placebo-controlled trials showed that patients who received tadalafil (10 or 20 mg) experienced greater improvement in erectile functioning (e.g. outcomes based on responses to IIEF, SEP, and GAQ) compared with those who received placebo. The observed between- or within-arm differences in the mean endpoint scores/mean score changes for the IIEF “EF” domain^{216,217,219,220,222-224,226,227,229,234,236-240} and for the per-patient proportion of “yes” answers to the SEP questions 2–3, were statistically significant (p value < 0.05).^{215-217,219,220,222-227,229,230,234,236-240} Similarly, the proportion of patients who answered “yes” to the GAQ–Q1/2 was statistically significantly greater in tadalafil than in placebo arms.^{216,217,220,222-224,226,227,229,234,236-240}

For example, the mean within-arm IIEF “EF” domain absolute score change observed in tadalafil arms (10 or 20 mg dose) across trials^{216,217,219,220,222-224,226,227,229,234,236-240} ranged from 5.2²²² to 12.0,²¹⁹ whereas the corresponding treatment response observed in placebo arms ranged from –1.6^{216,242} to 2.9.²¹⁹ The mean change in the proportion who responded “yes” to SEP Q3 (i.e., per-patient percentage of successful intercourse attempts) in tadalafil arms (10 or 20 mg dose) ranged from 23.0 percent²²² to 56.5 percent.^{220,237} The corresponding mean treatment response change in placebo arms ranged from 0.9 percent²¹⁶ to 18.3 percent.²³⁷ The proportion of patients who responded “yes” to GAQ–Q1 in tadalafil arms (10 or 20 mg) across trials^{216,217,220,222-224,226,227,229,234,236-240} ranged from 62.0 percent²²² to 92.3 percent.²²⁹ For placebo arms this proportion across the same trials ranged from 12.8 percent²¹⁶ to 54.5 percent.²²⁹

In a parallel-arm trial of patients with LUTS (65 percent ED patients),²³³ 138 patients ($n = 99$ ED patients) received the dose-escalated tadalafil (5 mg for 6 weeks and the 5–20 mg dose-

escalation for another 6 weeks) and, compared with those receiving placebo, had a statistically significant greater mean change in the IIEF “EF” domain score at 6 and 12 weeks of treatment (12 weeks: 7.7 versus 1.4, $p < 0.001$). Furthermore, results of two trials^{235,238} indicated that patients receiving even lower doses of tadalafil (2.5 mg and 5 mg) compared with those in the placebo group had greater statistically significant improvements in erectile functioning with respect to the mean score changes in the IIEF “EF” domain (19.1–20.8 versus 14.6, $p < 0.001$) and the per-patient proportion of “yes” answer to SEP Q2–3 (for Q2: 65.3–70.7 versus 51.1, $p < 0.001$ and for Q3: 50.0–57.0 versus 31.3, $p < 0.001$).²³⁵ Compared with the placebo group, in both tadalafil dose-groups there was a significantly greater proportion of patients who answered “yes” to GAQ1–2 (5 mg: 70.7–72.8 percent, versus 2.5 mg: 58.5–62.8 percent, versus placebo: 23.9–26.1 percent).²³⁵

Furthermore, patients who received tadalafil compared with those who received placebo had statistically significant greater improvements in erectile function as measured by the mean IIEF score change from baseline to endpoint for the IIEF “Intercourse Satisfaction” and “Overall Satisfaction” domains.^{216,217,223,224,226,227,229,234-240,243}

In several trials, there was a statistically significant greater mean per-patient percentage of successful intercourse attempts measured at different intervals after dosing in tadalafil arms compared with placebo arms.^{217,219,220,224,225,230}

The mean overall EDITS score in patients who received tadalafil showed a statistically significant improvement compared with that in patients who received placebo.^{217,222,223} The mean overall EDITS score values in tadalafil arms across the trials were 66.8,^{217,243} 58.0,²²² and 77.²²³ The corresponding values for placebo arms in these trials were 35.6, 34.0, and 46.0, respectively. In one of these trials,²²³ patients treated with tadalafil had a median EDITS score of 84 (95 percent CI: 80–86) as opposed to those treated with placebo, who had a median EDITS score of 41 (95 percent CI: 32–59). The difference between the two median scores was statistically significant ($p < 0.001$).

The mean change measured on individual IIEF Q3–4 scores (Q3, penetration ability; Q4, maintenance ability) was reported in 8 trials (out of the 23 placebo-controlled trials),^{217,220,226,234-237,240} all of which showed highly statistically significant improvements for patients treated with tadalafil patients compared with those treated with placebo ($p < 0.001$).

The authors of one trial²¹⁸ showed that after a 4-week therapy, patients treated with tadalafil experienced greater improvements in endothelial function as measured by brachial artery flow-mediated dilation (FMD) than patients treated with placebo. For example, in the tadalafil arm, the mean change in FMD from baseline to the end point was statistically significant (9.3 versus 4.2 percent, $p < 0.01$), whereas in the placebo arm the mean FMD did not change (4.1 versus 4.3, $p > 0.05$).

Four studies examined the efficacy according to severity of ED.^{216,235,237,238} The number of patients achieving normal scores in IIEF–EF were higher in mild ED compared with moderate or severe ED.^{216,235,237,238} Similarly higher end scores of IIEF–EF were achieved in patients with mild compared with moderate or severe ED.^{216,235,237,238} (Table 11)

Tadalafil (20 mg) versus tadalafil (10 mg) versus tadalafil (5 mg). The effects of both tadalafil doses 20 mg and 10 mg were evaluated in eight trials.^{215,226-230,237,238} In one of these trials,²³⁸ there was an additional randomized arm in which patients received 5 mg tadalafil. Another trial²²¹ evaluated dose-response models for different doses of tadalafil (e.g. 5, 10, 25 mg).

Harms. The incidence of most reported adverse events (e.g. myalgia, nausea, back pain, diarrhea, headache, dizziness, dyspepsia, nasal congestion, facial flushing, infection, flu syndrome) across the eight trials was numerically comparable in patients receiving 20 mg versus 10 mg of tadalafil. In three trials,^{228,230,238} the incidence of headache was slightly higher in patients receiving 20 mg tadalafil as compared with those receiving 10 mg (or 5 mg) of tadalafil. For example, in the first trial,²²⁸ the proportions of patients with headache in 20 mg and 10 mg tadalafil arms were 17.1 and 8.1 percent, respectively, with a statistically significant between-arm difference ($p < 0.001$).

In the same trial the incidence of serious adverse events (i.e., two cases of myocardial infarction) was numerically similar in the 20 mg and 10 mg tadalafil groups (two patients in each arm). In the second trial,²³⁰ numerically more patients who received 20 mg tadalafil had headache compared with those who received a 10 mg dose (8.0 versus 4.1 percent). In one trial,²²⁷ compared with those who received 10 mg of tadalafil, patients receiving a 20 mg dose experienced numerically higher rates of dyspepsia (22.0 versus 9.7 percent), vasodilation (6.0 versus 3.9 percent), and accidental injury (5.0 versus 1.0 percent). The incidence of back pain was numerically slightly higher in patients receiving 20 mg versus those receiving 10 mg of tadalafil in one trial (4.0 versus 0.8 percent, respectively).²³⁷ In another trial,²¹⁵ one patient died from an AMI after being randomly assigned to receive 20 mg tadalafil. Of the eight trials comparing the efficacy/safety profiles of 20 mg and 10 mg tadalafil, the absence or presence of serious adverse events could not be ascertained for six trials.^{221,226,227,229,230,237}

Efficacy. In five trials,^{226,227,229,237,238} the degree of improvement in the mean change for IIEF “EF” domain and per-patient proportion of “yes” to SEP Q2–Q3 from baseline was numerically similar between 20 mg, 10 mg, and 5 mg tadalafil arms. The proportions of patients with improved erection (i.e., those who answered “yes” to GAQ) were also similar between the 10 mg and 20 mg tadalafil dose arms.^{226,227,229,237,238} In one trial,²¹⁵ the magnitude of improvement with respect to the mean change in per-patient proportion of “yes” responses to SEP–Q3 from baseline was numerically greater in the 20 mg than the 10 mg tadalafil arm 24 hours post-dose (46.3 versus 25.5 percent). Similarly, in another trial,²³⁰ the cumulative proportion of patients with at least one successful intercourse attempt (“yes” to SEP–Q3) attempt 30 minutes post-dose was numerically improved in patients who received 20 mg relative to those who received 10 mg of tadalafil (34.0 versus 25.0 percent). In the same trial, patients on 20 mg tadalafil had a faster erectogenic response (starting 16 minutes post-dose) than those on 10 mg of tadalafil (starting 26 minutes post-dose).²³⁰

The results of one trial²²⁸ were slightly inconsistent with those of others.^{215,226,227,229, 230} More specifically, patients on 10 mg (daily) of tadalafil experienced greater improvement in erectile function (based on responses to SEP–Q3, IIEF, GAQ–Q1) compared with those receiving 20 mg (on demand) of tadalafil. For example, there was a statistically significant higher mean per-patient proportion of successful intercourse attempts (i.e., based on “yes” answers to SEP–Q3) among patients receiving 10 mg tadalafil compared with those receiving 20 mg tadalafil (80 versus 67 percent, $p < 0.05$). Similarly, the proportion of patients who answered “yes” to GAQ Q1 was higher in the 10 mg arm compared with the 20 mg arm of tadalafil (88.0 versus 73

percent, $p < 0.05$). Furthermore, patients in the 10 mg tadalafil arm had a higher mean IIEF “EF” domain score than those in the 20 mg tadalafil arm (26.4 percent versus 23.3 percent, $p < 0.05$).

In one study,²²¹ authors who employed logistic regression models based on patient data obtained from a randomized placebo-controlled trial, showed a statistically significant dose-dependent effect of tadalafil on the patients’ outcomes as defined by responses to SEP–Q2/3 and the IIEF “EF” domain questions; more specifically, the magnitude of response increased between the 10 mg and 25 mg doses of tadalafil. Furthermore, the baseline ED severity was an important covariate in these models, indicating that patients with severe ED at baseline experienced greater incremental improvement in erectile function compared with those with moderate or mild ED at baseline.

Tadalafil (20 mg; on-demand therapy) versus tadalafil (20 mg; scheduled therapy). Two trials^{214,232} compared the efficacy/safety of two dosing regimens of 20 mg tadalafil (on demand therapy versus scheduled therapy).

Harms. In the first trial,²¹⁴ the rate of any adverse events (percentage of patients with at least one adverse event) did not differ between groups who were given tadalafil either on demand or 3 times per week (21.7 versus 25.3 percent, respectively). The most frequent events in both tadalafil arms were headache (7.5 percent), dyspepsia (6.5 percent), back pain (2.7 percent), flushing (2.6 percent), and myalgia (2.5 percent). The proportion of patients who withdrew from the on-demand and the 3 times per week dosing regimens were 4.0 percent and 5.1 percent, respectively. No deaths or serious adverse events occurred during the trial. In the second trial,²³² the most frequent adverse events were dyspepsia, headache, back pain and myalgia, observed in two of the 20 patients.

Efficacy. One crossover trial²¹⁴ evaluated the relative effects of alternative dosing regimens of tadalafil (on demand versus 3 times per week) on the outcomes of ED (e.g. patient preference, mean change in IIEF “EF” domain scores and the per-patient proportion of successful intercourse attempts). The 3861 patients’ responses to the treatment preference question (TPQ) showed that the on-demand regimen was preferred more frequently than the 3 times per week scheduled regimen, regardless of the sequence of the treatment regimens (57.8 versus 42.2 percent, $p < 0.001$). The on-demand and the scheduled 3 times per week dosing regimens were shown to be similarly efficacious with respect to the mean IIEF “EF” domain scores (24.6 versus 24.8, respectively). Similarly, the mean per-patient proportion of successful intercourse attempts (“yes” to SEP–Q3) did not differ between the on-demand and scheduled 3 times per week tadalafil groups (72.6 versus 74.4 percent).

The other trial evaluated whether 20 mg tadalafil dosing regimens (on demand versus scheduled on alternate days) differed in improving endothelium-dependent vasodilation of cavernous arteries (e.g. peak systolic velocity and flow-mediated dilation) and in producing morning erections in men diagnosed with ED as ascertained by one of the items of the SIEDY questionnaire (question: “*In the last four weeks, did it ever occur that you wake up with an erection?*”).²³² After 4 weeks of therapy, the mean increase in flow-mediated dilation (FMD) from baseline in patients treated with scheduled dosing regimen on alternate days was statistically significant (1.2 versus 8.3 percent, $p < 0.05$), whereas the corresponding parameter for patients treated with the on-demand therapy schedule did not change (3.3 versus 2.1 percent, $p \geq 0.05$). The improvement in FMD observed in patients who had received scheduled therapy was maintained 2 weeks after the discontinuation of the therapy. There was also a statistically significant improvement in regard to morning erections observed in patients treated with the

scheduled dosing regimen (90 percent of the patients; $p < 0.0001$), but not in those treated with the on-demand dosing regimen.

Tadalafil versus sildenafil versus vardenafil. Four crossover trials compared efficacy/safety of tadalafil (20 mg) and sildenafil (25-100 mg, 50 mg, or 100 mg) in treating patients with ED.^{103,118,121,163} One of these¹⁶³ additionally evaluated the efficacy/safety profile of vardenafil (20 mg).

Harms. In general, in these trials, all three therapies were well tolerated and had similar safety profiles. There were no statistically significant differences in the incidence of any adverse events between tadalafil- and sildenafil-treated groups of patients. In the tadalafil arms the proportion of patients with at least one adverse event across the four trials ranged from 27.7 percent¹⁶³ to 34.9 percent.¹⁰³ The corresponding proportion in the sildenafil arms ranged from 23.8 percent¹²¹ to 34.1 percent.¹⁰³ In the vardenafil group, about 26.6 percent patients had at least one adverse event.¹⁶³ Most common events in the three therapy groups were: headache (7.8–12.2 percent), dyspepsia (3.0–6.4 percent), flushing (2.5–7.4 percent), back pain (1.8–4.8 percent), and nasal congestion (1.1–4.7 percent).

In one trial,¹⁰³ the incidence of serious adverse events did not differ between the tadalafil (5 patients had prostate cancer, purpura, pulmonary edema, gastric cancer) and sildenafil groups (4 patients had cardiac biopsy, chest pain, perianal abscess). Three remaining trials^{118,121,163} did not report the occurrence or absence of serious adverse events.

The total number of withdrawals due to adverse events across the four trials ranged from two¹²¹ to 12 patients.^{103,163} The proportion of patients who withdrew from tadalafil groups ranged from one¹²¹ to seven.^{103,241} The respective proportion of patients who withdrew from the sildenafil arms ranged from one¹²¹ to five.^{103,163} Two patients withdrew due to adverse events in the vardenafil group.¹⁶³

Efficacy. In one trial,¹⁰³ the IIEF mean changes from baseline to endpoint were greater in the tadalafil than in the sildenafil arm for the domains of “Orgasmic Function” (difference between the mean changes: 0.28, 95 percent CI: 0.02–0.53) and “Sexual Desire” (difference between the mean changes: 0.19, 95 percent CI: 0.02–0.35).

In general, results of the four trials^{103,118,121,163} regarding the measures of erectile function (i.e., mean IIEF-“EF domain” scores) were not consistent.

For example, in one trial the difference between the mean changes for IIEF “EF” domain scores did not reach statistical significance (0.51, 95 percent CI: -0.07 to 1.09).¹⁰³ In another trial,¹⁶³ there was a statistically significant higher median (percentile range 10–90) IIEF score in the tadalafil group in comparison with the vardenafil group: 30 (25–30) versus 28 (23.1–30.0), $p = 0.00022$. In the same trial, the differences in the mean IIEF score between the sildenafil/tadalafil and sildenafil/vardenafil groups were not statistically significant.¹⁶³

In one trial,¹¹⁸ the proportion of men who had at least one successful intercourse attempt 12 or more hours post-dose was greater among patients receiving 20 mg tadalafil than in patients receiving 50 mg sildenafil (55.0 versus 29.0 percent, $p < 0.001$). In another trial,¹⁰³ the mean change in per-patient proportion of successful intercourse attempts (“yes” to SEP Q3) was slightly greater in patients receiving tadalafil compared with those receiving sildenafil (difference between the mean changes: 5.2 percent, 95 percent CI: 1.8–8.6). The mean time (in hours) between dosing and sexual attempt was found to be longer for tadalafil than for sildenafil (5.6 versus 2.7, $p < 0.001$).^{118,121}

In the four trials, the proportion of patients preferring tadalafil (range 52.2 to 73.0 percent) was statistically significantly greater than the proportion of patients preferring sildenafil (27.0–

33.7 percent) or vardenafil (20.0 percent). In one trial,¹¹⁸ 73 percent of the patients preferred tadalafil and 27 percent preferred sildenafil ($p < 0.001$). Similarly, the results from the two other trials^{121,163} also indicated that more patients preferred tadalafil (66.3 and 52.2 percent, respectively) compared with those preferring sildenafil (33.7 and 27.7 percent, respectively) or vardenafil (20 percent). In one trial,¹⁶³ the reason for 25 percent of men preferring tadalafil to sildenafil was that they could have intercourse again the next day post-dose.

Quantitative Synthesis - Meta-analysis of Trials

A series of meta-analyses was conducted to address the safety and efficacy of tadalafil.^{103,118,121,163,214-230,232-240} Of the 30 eligible trials, five were excluded as potentially ineligible given the following distinct clinical features of the patients studied: patients with increased cardiovascular risk of whom 50 percent were patients with ED,²¹⁸ patients with radical prostatectomy,²²² diabetic patients,²²⁶ patients with benign prostatic hypertrophy (BPH),²³³ and patients with radical prostatic carcinoma.²³⁹ In addition, two more trials were excluded because relevant numerical data needed for meta-analysis was lacking²²¹ and an inappropriate dose of tadalafil was used (2.5 mg and 5 mg).²³⁵

Of the remaining 23 trials,^{103,118,121,163,214-217,219,220,223-225,227-230,232,234,236-238,240} 16 were placebo-controlled,^{215-217,219,220,223-225,227,229,230,234,236-238,240} and seven were active-treatment trials.^{103,118,121,163,214,228,232} All 16 placebo-controlled randomized trials had parallel-group design and compared the efficacy and safety of tadalafil (10 mg or 20 mg or both) to placebo.

Tadalafil (any dose: 20 mg or 10 mg) versus placebo.

Efficacy.

Absolute mean change from baseline in IIEF–EF score. This meta-analysis included eight trials.^{216,217,220,223,224,227,229,234} The estimate of the pooled mean difference was 8.10 (95 percent CI: 6.98–9.22), favoring the use of tadalafil (any dose: 10 mg or 20 mg) compared with placebo in increasing the mean IIEF “EF” domain total score relative to baseline (Figure 60).

Mean per-patient percentage absolute change (from baseline) in SEP–Q2. This meta-analysis included seven trials.^{216,217,220,224,227,229,234} The estimate of the pooled mean difference was 29.34 (95 percent CI: 25.06–33.62), favoring the use of tadalafil (any dose: 10 mg or 20 mg) compared with placebo in increasing the mean per-patient percentage of SEP–Q2 relative to baseline (Figure 61).

Proportion of patients with improved erection (GAQ–Q1). This meta-analysis included eight trials.^{220,223,227,234,236-238,240} The pooled estimate of the relative proportion of patients (i.e., RR) with improved erection (i.e., those answered “yes” to GAQ–Q1) was 2.40 (95 percent CI: 2.03–2.83), indicating a statistically significantly higher rate of improvement for patients who received any dose of tadalafil (20 mg or 10 mg) relative to the placebo-treated patients (Figure 62).

Tadalafil (20 mg) versus placebo.

Efficacy.

Absolute mean change from baseline in IIEF–EF score. This meta-analysis included eight trials.^{216,217,220,223,224,227,229,234} The estimate of the pooled mean difference was 8.21 (95 percent CI: 7.10–9.32), favoring the use of tadalafil (20 mg) compared with placebo in increasing the mean IIEF “EF” domain total score relative to baseline (Figure 63).

Mean per-patient percentage absolute change (from baseline) on SEP–Q2. This meta-analysis included 7 trials.^{216,217,220,224,227,229,234} The estimate of the pooled mean difference was 29.60 (95 percent CI: 25.15–34.04), favoring the use of tadalafil (20 mg) versus placebo in increasing the mean per-patient percentage of SEP–Q2 relative to baseline. (Figure 64).

Proportion of patients with improved erection (GAQ–Q1). This meta-analysis included eight trials.^{220,223,227,234,236-238,240} The pooled estimate of the relative proportion of patients with improved erection (i.e., those who answered “yes” to GAQ–Q1) was 2.43 (95 percent CI: 2.06–2.87), indicating a statistically significantly higher rate of improvement for patients who received tadalafil (20 mg) relative to the placebo-treated patients (Figure 65).

Harms.

Proportion of patients with any adverse event (all- cause). This meta-analysis included five trials^{215,227,229,238,240} and yielded a RR of 1.95 (95 percent CI: 1.40–2.71) with a statistically significant heterogeneity across trials ($\text{Chi}^2_{df=4} = 15.60$, $p = 0.004$; $I^2 = 74.4$ percent) (Figure 66).

We explored potential sources of this heterogeneity by examining other trial characteristics (e.g. populations, severity of ED, duration of ED, length of followup). Figure 67 presents the results based on 4 trials^{227,229,238,240} with a 12-week followup that yielded similar effect estimates (RR range 1.45–2.08), whereas one trial²¹⁵ whose length of follow up was 6 weeks yielded a more inflated estimate of RR (i.e., $\text{RR} = 4$). After excluding this trial, the pooled estimate of RR was 1.61 (95 percent CI 1.37–1.89), indicating a statistically significantly greater rate of any adverse events in patients who received tadalafil (20 mg) relative to placebo-treated patients. There was no significant heterogeneity between the trials ($\text{Chi}^2_{df=3} = 2.88$, $p = 0.41$; $I^2 = 0$ percent) (Figure 67). (Note that “favors” in forest plots refers to increased frequency of the event for the respective treatment arm, regardless of the desirability of the event).

Tadalafil (20 mg) versus tadalafil (10 mg).

Efficacy.

Mean change from baseline in IIEF–EF score. Two trials^{227,229} compared 10 mg and 20 mg doses of tadalafil and also reported mean change in IIEF “EF” domain total score. The pooled estimate of these trials indicated that the mean increase in IIEF “EF” domain total score was not statistically different between the two dose-arms (mean difference 0.60, 95 percent CI: -0.92 to 2.11) (Figure 68)

Mean per-patient percentage absolute change (from baseline) on SEP–Q2. Two trials^{227,229} compared 10 mg and 20 mg of tadalafil and also reported the mean per-patient percentage of SEP–Q2. The meta-analysis of these trials indicated that the mean increase in per-patient percentage of SEP–Q2 was not statistically different between the two dose-arms (mean difference 0.32, 95 percent CI: 7.53–8.18) (Figure 69).

Proportion of patients with improved erection (GAQ–Q1). Four trials^{227,229,237,238} compared 10 mg and 20 mg of tadalafil and also reported the proportion of patients with improved erections as measured by GAQ–Q1. The meta-analysis incorporated three of these trials^{227,237,238} and indicated that the difference observed between the rates of improvement in erection for patients who received 10 mg and 20 mg of tadalafil was not statistically significant ($\text{RR} = 1.07$, 95 percent CI: 0.99–1.16) (Figure 70).

Harms.

Proportion of patients with any adverse events (all- cause). This meta-analysis included six trials,^{215,227,229,230,237,238} which compared 10 mg and 20 mg doses of tadalafil and also reported the proportion of patients who developed at least one adverse event. The pooled summary estimate of RR indicated a statistically significant higher incidence of adverse events in patients treated with 20 mg tadalafil compared with those treated with 10 mg tadalafil ($\text{RR} = 1.21$, 95 percent CI: 1.05–1.38). There was no statistically significant heterogeneity across the trials ($\text{Chi}^2_{df=5} = 6.60$, $p = 0.25$; $I^2 = 24.3$ percent) (Figure 71).

Tadalafil (10 mg) versus placebo.

Efficacy. No meta-analysis was performed.

Harms.

Proportion of patients with any adverse events (all-cause). This meta-analysis included four trials,^{215,227,229,238} which compared 10 mg of tadalafil to placebo and also reported the proportion of patients who experienced at least one adverse event. The pooled summary estimate of RR indicated a statistically significant higher incidence of adverse events in patients treated with 10 mg tadalafil as compared with those treated with placebo (RR = 1.53, 95 percent CI: 1.11–2.11). The test of heterogeneity was statistically significant (Chi2df=3 = 8.99, p = 0.03; I2 = 66.6 percent) (Figure 72).

After excluding a trial with a 6 week followup,²¹⁵ the pooled estimate of RR for the remaining three trials with 12 weeks of followup^{227,229,238} was RR = 1.31 (95 percent CI: 1.10–1.57). The result indicated a statistically significant higher incidence of adverse events in patients treated with 10 mg tadalafil compared with those treated with placebo. There was no statistically significant heterogeneity present across the trials (Chi2df=2 = 0.01, p = 0.99; I2 = 0 percent) (Figure 73).

Tadalafil versus sildenafil. No meta-analysis of the four crossover trials^{103,118,121,163} that compared tadalafil with sildenafil was performed because the sildenafil dose/dosage varied,^{103,118,121,163} and there was a lack of relevant efficacy outcome data such as the mean absolute change in IIEF “EF” domain total score,^{118,121,163} per-patient percentage of successful attempts on SEP-Q2,^{118,121,163} and the proportion of patients with improved erection on GAQ-Q1).^{118,121,163}

Assessment of Publication Bias

Funnel plots were used to assess the extent of asymmetry (i.e., possible publication bias) present in each meta-analysis. Visual inspection of these plots did not reveal any substantial asymmetry.⁵³ (Funnel plots, Appendix G.)

Sublingual Treatments - Apomorphine

Literature Search

In total, 12 unique randomized controlled trials (RCTs) (11 publications) met the eligibility criteria and were included in the review.^{114,117,120,148,159,248-253} One report²⁵² described two distinct trials (a and b).

Overview of Trials

The trials were published between 2000²⁵³ and 2007¹⁵⁹ inclusively, and were conducted in the US,²⁵¹⁻²⁵³ Europe,^{114,120,148,159,248-250} the United Kingdom,¹¹⁷ and Mexico.²⁵¹ The trials were supported by funds from Abbot Laboratories,^{248,250,252} Takeda,^{248,252} Pfizer UK,^{117,159} and Zonagen Inc.²⁵¹ Funding sources were not reported for four trials.^{114,120,148,249} The duration of followup of eight trials^{114,117,120,248,249,252,253} ranged from 4 weeks^{249,252} to 8 weeks.^{117,148,159,248,253} The duration of followup for two trials could not be ascertained.^{250,251} Of the 12 trials, four were parallel-group^{248-250,253} and eight were crossover studies.^{114,117,120,148,159,251,252} Of the four parallel-group RCTs, three were two-armed²⁴⁸⁻²⁵⁰ and one was a four-armed trial.²⁵³ Further information on trial characteristics is provided in (Table F-4, Appendix F).

Populations

The included trials involved men diagnosed with erectile dysfunction (ED). The total and mean (range) numbers of patients randomly assigned to trial arms were 1975 and 179 (12–569), respectively. The inclusion criteria across the trials were adult men (age ≥ 18 years) diagnosed with ED in a stable heterosexual relationship of at least 6 months of duration. The inclusion criteria in two studies^{114,120} were restricted either to patients with arteriogenic¹²⁰ or nonarteriogenic ED.¹¹⁴ In one trial,²⁴⁹ the inclusion criteria were restricted to patients with ED and a history of diabetes (type I or II) who had been naïve to any ED-related treatment. The enrolled patients in one trial¹⁵⁹ had to be naïve to ED drug therapy and had to have an IIEF–5 score ≤ 21.

The exclusion criteria in the majority of the included trials were spinal cord injury^{114,120,248,253} and penile/testicular deformity.^{114,120,148,159,248,249,251-254} Other frequently reported exclusion criteria were uncontrolled hypertension,^{114,148,251-253} diabetes,^{148,248,252,253} endocrine disease,^{114,248,251-253} any major hepatic/renal disease,^{117,148,251} prostatectomy,^{148,248,251,253} peptic ulcers,¹⁵⁹ HIV-positivity/AIDS,^{248,252,253} the use of nitrates,^{114,117,120,148,159,251} a history of cancer,^{248,252,253} and serious cardiovascular diseases (e.g. angina pectoris).^{148,159} Only one trial failed to report exclusion criteria.²⁵⁰

The mean age of the study participants across the included trials ranged from 35²⁵⁰ to 59 years.¹²⁰ The race of the study participants was reported in six trials.^{117,159,248,252,253} The proportion of Caucasians across these trials ranged from 85 percent²⁵² to 99 percent.²⁴⁸ The duration of ED was at least 3 months at study entry in all trials. The longest mean duration of ED (3.5–4.2 years) was reported in the trial by Porst et al 2007.¹⁵⁹ Most commonly reported comorbidities among the study participants were diabetes,^{114,120,148,159,248,252,253} hypertension,^{114,120,148,159,248,249,252,253} ischemic heart disease,^{114,249} and coronary artery disease.^{120,159,248,252,253} The presence or absence of comorbidities could not be ascertained from three trials.^{117,250,251} The underlying cause of ED (i.e., etiology) in the patients was specified in three trials to be nonarteriogenic (all patients),¹¹⁴ arteriogenic (all patients),¹²⁰ and various causes (patients with

organic, psychogenic or mixed origin ED).¹⁵⁹ In four trials,^{114,120,249,250} the proportion of smokers ranged from 35 percent²⁴⁹ to 95 percent.^{114,120} In the remaining trials this proportion could not be ascertained.^{117,148,159,248,251-253}

In seven trials^{117,159,248,249,252,253} the authors provided baseline arm-specific distributions of the patients' sociodemographic and clinical characteristics (e.g. age, race, duration/severity of ED, comorbidities) and explicitly stated that the distribution of these characteristics between the randomized arms was generally similar. The authors of the remaining five trials^{114,120,148,250,251} did not report this information.

Interventions

Patients in all reviewed 12 trials^{114,117,120,148,159,248-253} received apomorphine sublingually with a dose ranging from 2 mg^{159,248} to 6 mg.^{251,253} In all trials except one,²⁵¹ patients received apomorphine monotherapy. In this one trial,²⁵¹ two groups of patients received the combination of apomorphine either with phentolamine (40 mg) or with phentolamine (40 mg) plus papaverine (150 mg). One trial did not report the dose of apomorphine.¹¹⁷

In six trials^{148,249-252} apomorphine was given only at a fixed dose. A flexible-dose-only regimen was used in other five trials.^{114,117,120,158,248} In one trial,²⁵³ patients were randomly assigned to receive either a fixed (5 mg or 6 mg) or flexible dose (2 mg–6 mg) of apomorphine.

The duration of apomorphine treatment across the trials ranged from 4 weeks^{249,252} to 8 weeks.^{117,148,159,248,253} Patients in the control arms received placebo in five trials,^{248-250,252,253} sildenafil (50-100 mg/d) in six trials,^{114,117,120,148,159,251} and apomorphine (control dose) in two trials.^{252,253} An additional comparison group of patients in one trial²⁵¹ received a combination of phentolamine (40 mg) and papaverine (150 mg).

Outcomes

Harms. All trials but one¹¹⁴ reported some information on the absence and/or occurrence of adverse events: any adverse events,^{117,159,248,250,251} serious adverse events (including death),^{117,159,248,250,251} withdrawals due to adverse events,^{117,120,159,248,249,253} and frequently reported (≥ 5 percent) specific adverse events.^{120,148,159,248-253}

Efficacy. The efficacy outcomes measured in the 11 trials varied to some degree. The most commonly measured and reported outcome across the trials was the percentage of successful intercourse attempts.^{114,117,120,148,159,248,252,253} In four trials, the percentage of attempts resulting in erections firm enough for intercourse was also measured^{148,252,253}. Similarly, in one trial,²⁵¹ the proportions of successful vaginal penetration and vaginal intercourse leading to orgasm were estimated. The above-mentioned outcomes were calculated based on the patients' and/or their partners' responses to pre-specified questions provided in home-use diaries.

In five trials, the mean IIEF score (domains of "erectile function," "orgasmic function," "sexual desire," "intercourse satisfaction," "overall satisfaction") was used to assess the relative efficacy of apomorphine.^{117,148,159,249,253} For example, in one trial¹¹⁷ the primary endpoint was the mean difference in IIEF score for the "erectile function" domain, whereas secondary endpoints were mean difference IIEF scores for other domains (e.g. "orgasmic function," "sexual desire," "intercourse satisfaction," and "overall satisfaction"). In another trial,²⁵³ the authors provided differences between treatment-arm specific mean IIEF scores for the "erectile function," "intercourse satisfaction," and "overall satisfaction" domains as secondary efficacy endpoints. In this trial,²⁴⁹ primary efficacy endpoint was a response rate defined as the proportion of patients who answered "yes" to a Global Efficacy Question (GEQ) (i.e., "*Has the treatment you have*

been taking over the past two or four weeks improved your erections?") combined with an improvement of ≥ 5 points in the "erectile function" domain of the IIEF.

Global Assessment Questions (GAQs) were evaluated and reported in three trials,^{117,159,251} as a secondary response endpoint. In one trial¹¹⁷ the endpoint was defined as the proportion of patients who answered "yes" to two GAQ questions, and in the other trial²⁵¹ the corresponding endpoint was treated as a continuous variable whereby responses to one GAQ were given on an ordinal scale (1 = very satisfied, 5 = very dissatisfied).

The treatment preference/satisfaction was measured and reported in three trials.^{117,120,251} In one trial the treatment satisfaction was measured as a proportion of patients satisfied with one drug only, alternative drug only, both drugs, or none of the drugs.¹²⁰ In two trials,^{117,159} the treatment-arm specific differences in IIEF "Overall Satisfaction" domain and the Erectile Dysfunction Index of Treatment Satisfaction (EDITS) questionnaire-based mean scores were used to evaluate the patient's satisfaction with treatment regimens. In their trial, Lammers et al.,²⁵¹ employed the Visual Analogue Scale (VAS; range 0–100) to assess patients' treatment satisfaction. The endpoint was the post-treatment mean VAS satisfaction score calculated for patients in each treatment arm.

The authors of one trial²⁵¹ measured and reported the mean Sexual Encounter Profile (SEP) questionnaire-based overall score.

Penile rigidity was reported in two trials.^{250,251} In one trial,²⁵¹ it was measured on VAS as the mean VAS rigidity (range 0–100), and in the other trial,²⁵⁰ it was measured using a RigiScan and expressed as the percentage rigidity (i.e., percent of linear displacement of the loops due to the constant force). A post-treatment rigidity of at least 40 percent was considered a positive treatment response.

Study Quality and Reporting

The mean (range) of Jadad's total score for the 12 included trials was 2.36 (1¹¹⁴ – 5²⁴⁹). Six of the 12 trials were reported to be double-blind.^{248,249,251-253} Of these, only two trials^{249,253} provided some description of blinding method(s) used. Only one trial reported some information on the adequacy of allocation concealment.²⁴⁹ The adequacy of allocation concealment for the 11 remaining trials was unclear.

Of the eight crossover trials,^{114,117,120,148,159,251,252} only one²⁵¹ failed to report whether a washout period was applied between the treatment periods. The length of the washout period for six trials^{114,117,120,159,252} ranged from 24–96 hours²⁵² to 2 weeks,^{117,159} and for one trial this duration was 4 weeks.¹⁴⁸

Qualitative Synthesis

Apomorphine versus placebo. In total, there were five placebo-controlled trials.^{248-250,252,253}

Harms. The occurrence of any adverse events across the trials was reported poorly. In one trial,²⁴⁸ the rate of any adverse events was numerically slightly higher in patients receiving apomorphine than in those receiving placebo (37.8 versus 24.5 percent, respectively). Another trial²⁵⁰ reported only two patients who had experienced headaches after receiving placebo. Only one trial²⁴⁸ explicitly stated that none of the patients died during the trial. In two trials,^{248,250} the rate of serious adverse events did not differ between patients receiving apomorphine and placebo. In the first trial,²⁴⁸ four patients had one or more serious adverse events. Specifically, of the two patients in the apomorphine arms (2–3 mg), one had chest infection/severe cough/cough syncope and the other one had moderate unstable angina pectoris. In the placebo arm, two

patients had angina pectoris. In the second trial,²⁵⁰ no serious adverse events had occurred. The other three trials did not report whether or not patients had experienced any serious adverse events.^{249, 252, 253} In two trials,^{248, 253} the proportion of patients who withdrew due to adverse events was numerically higher in the apomorphine arms compared with placebo arms (5–10 percent versus 1 percent); in the other trial,²⁴⁹ none of the patients withdrew due to adverse events. Other trials^{250, 252} failed to report whether any patients withdrew due to adverse events. The most common adverse event reported across trials was nausea^{148, 248, 249, 252, 253} ranging from 7.0 percent²⁵² to 44 percent²⁵³ in the apomorphine arms and from 0.4 percent²⁴⁸ to 5.0 percent²⁴⁹ in the placebo arms. Other commonly reported adverse events were headache, dizziness, and yawning. In general, these events had occurred numerically more frequently in apomorphine arms than in placebo arms.^{248, 252, 253}

Efficacy. The three trials^{248, 252, 253} that measured the mean percentage of successful intercourse attempts found that this parameter was higher among patients who received apomorphine compared with those who received placebo; this finding was statistically significant. The mean percentage of successful intercourse attempts observed in apomorphine groups in these trials ranged from 38 percent²⁴⁸ to 51 percent,²⁵³ whereas the corresponding treatment response observed in the placebo groups ranged from 28 percent²⁴⁸ to 34 percent.²⁵² The difference for each comparison between apomorphine and placebo groups in the three trials was statistically significant ($p \leq 0.01$). The results for the above-mentioned endpoint, whether based on responses obtained from patients or from their partners, did not differ.^{252, 253}

Two trials^{252, 253} showed that patients who received apomorphine had a statistically significant higher percentage of attempts resulting in erections firm enough for intercourse than those in placebo group. For example, in one trial²⁵² the percentages of attempts resulting in erections firm enough for intercourse in the apomorphine (3 mg) and placebo groups were 46.9 percent and 32.3 percent respectively ($p < 0.001$). In the other trial,²⁵³ the corresponding percentages were 53.1 (apomorphine 5 mg) and 34.5 (placebo), respectively ($p \leq 0.01$).

The mean IIEF score for the “Erectile Function (EF) domain” obtained from two trials^{249, 253} were not consistent. For example, in the first trial,²⁴⁹ differences in mean IIEF “EF” domain scores between patients receiving apomorphine and placebo were not statistically significant (13.81 versus 13.24; $p = 0.52$). In contrast, the authors of the other trial²⁵³ observed a statistically significantly greater mean IIEF score (“erectile function” domain) in the apomorphine group compared with placebo (actual mean IIEF values were not provided; $p \leq 0.01$).

There was no statistically significant difference between apomorphine and placebo groups in the proportion of patients who answered “yes” to the GEQ (“*Has the treatment you have been taking over the past two or four weeks improved your erections?*”) combined with an improvement of ≥ 5 points in the IIEF “EF” domain (22.92 percent versus 17.31 percent, $p = 0.48$).²⁴⁹

The proportion of patients with positive response on rigidity (≥ 40 percent) was numerically greater in the apomorphine compared with the placebo group (4/6 versus 0/6).²⁵⁰

Apomorphine mono (dose/dosing 1) versus apomorphine mono (dose/dosing 2). In total, two trials compared different doses/dosing of apomorphine in patients with ED.^{252, 253}

Harms. The incidence of several adverse events such as nausea, yawning, and dizziness across trials was numerically greater in patients receiving higher doses (4–6 mg) than lower doses of apomorphine (2–3 mg).^{252, 253} In one trial,²⁵³ a dose-optimization schedule (2–6 mg) was associated with fewer events of nausea (30 percent of patients) than the fixed doses of

apomorphine (5 and 6 mg: 38 and 49 percent of patients, respectively). Statistical test results for significance were not reported.

Efficacy. Neither of the two trials^{252,253} identified a dose-response effect on the percentages of successful intercourse attempts and attempts resulting in erections firm enough for intercourse. For example, in one trial²⁵² the percentage of successful intercourse attempts was similar in patients who received 3 and 4 mg doses of apomorphine (48.4 versus 49.6 percent, respectively; $p > 0.4$). In the other trial,²⁵³ the percentage of successful intercourse attempts was numerically similar for patients in two dose-escalation (2–4 mg and 2–4 mg to 5–6 mg) and two fixed-dose (5 mg and 6 mg) apomorphine groups, ranging from 45.1 percent (2–4 mg) to 50.9 percent (5 mg).

Apomorphine mono versus sildenafil mono. Five trials compared the efficacy/safety of apomorphine monotherapy to that of sildenafil monotherapy^{114,117,120,148,159}

Harms. In two trials,^{117,159} the number of patients who experienced any adverse event(s) was numerically greater in the sildenafil groups (94.0 and 35.7 percent, respectively) in comparison with the apomorphine groups (64.0 versus 21.8 percent, respectively). In another trial,¹²⁰ the proportions of patients with any adverse events in sildenafil and apomorphine groups were 7 percent (3/43) and 14 percent (6/43), respectively. One trial¹¹⁷ explicitly stated that none of the patients had died during the trial and reported that five patients had had at least one serious adverse event; of these patients, three were receiving sildenafil (deterioration of arthritic shoulder in one patient and myocardial infarction/atrial fibrillation in two patients) and two were receiving apomorphine (myocardial infarction and deterioration in Dupuytren's contracture). In another trial,¹⁵⁹ serious adverse events occurred in two patients from the sildenafil group (exacerbation of chronic bursitis and stroke) and in two patients from the apomorphine group (stricture of the urethra and sudden cardiac death). The number of patients with vasodilation was numerically higher in the 50 mg sildenafil than in the 3 mg apomorphine group (6 versus 0)¹⁴⁸

In three trials,^{117,120,159} the number of patients who withdrew due to adverse events ranged from one¹⁵⁹ to three¹¹⁷ for the apomorphine arms and from zero^{120,159} to two¹¹⁷ for the sildenafil arms.

Some specific adverse events that occurred in one trial in sildenafil versus apomorphine groups were headache (16 versus 5 percent) and nausea (3.2 versus 5.6 percent).¹¹⁷ In another trial,¹⁵⁹ the proportions of patients with headache in the sildenafil versus apomorphine groups were 10.3 versus 3.2 percent, respectively.

Efficacy. All five trials^{114,117,120,148,159} measuring the number of successful intercourse attempts showed that the mean percentage of successful intercourse attempts was higher in patients who had received sildenafil (range 62.7–81.0 percent) compared with those receiving apomorphine (range 28.3–62.7 percent). The observed differences were statistically significant. In fact, in three trials,^{117,120,159} the percentage of successful intercourse attempts in the sildenafil groups was about twice as that in the apomorphine groups. For example, in one trial,¹¹⁷ the percentages of successful intercourse attempts in sildenafil and apomorphine groups were 75.1 percent (95 percent CI: 69.2–81.0) and 35.3 percent (95 percent CI: 29.4–41.3) respectively, with a mean difference of 39.7 percent (95 percent CI: 33.0–46.5) between the two groups. In the other trial,¹²⁰ the corresponding values of the mean percentage of successful intercourse attempts in the sildenafil (50–100 mg) and apomorphine (2–3 mg) groups, regardless the dose, were 63.7 and 32.1 percent, respectively ($p < 0.01$). Similarly, in another trial,¹¹⁴ overall, patients receiving sildenafil (50–100 mg) had a statistically significantly greater mean percent of successful intercourse attempts than those receiving apomorphine (2–3 mg) (73.1 versus 62.7 percent, $p = 0.0004$).

The use of sildenafil was shown to be more efficacious than apomorphine in improving (i.e., increasing) IIEF scores for “erectile function” as well as for other domains (e.g. “intercourse satisfaction,” “overall satisfaction”).^{117,148,159} For example, the mean IIEF score values for the “EF” domain in patients who received sildenafil and apomorphine were 25.2 (95 percent CI: 23.7–26.7) and 15.9 (95 percent CI: 14.4–17.3), respectively, with a mean difference of 9.3 (95 percent CI: 7.6–11.1) between the two groups.¹¹⁷ In the other trial,¹⁵⁹ the corresponding least square mean values for the IIEF “EF” domain were 23.1 (95 percent CI: 21.8–24.4) and 15.7 (14.5–17.0), with a mean difference of 7.2 (95 percent CI: 5.5–8.8).

The proportions of patients who answered “yes” to questions 1 and 2 of GAQ (Question 1: “Compared with having no treatment at all for your erection problem, has the medication you have been taking over the past 4 weeks improved your erections?”; Question 2: “Compared with having no treatment at all for your erection problem, has the medication you have been taking over the past 4 weeks improved your ability to have sexual intercourse?”) were numerically higher in the sildenafil group than in the apomorphine group (94.8 and 93.9 percent versus 51.7 percent and 48.7 percent, respectively).¹¹⁷ Similarly, in the other trial,¹⁵⁹ statistically significant differences were observed between patients receiving sildenafil and apomorphine with respect to GAQ–Q1 (88.7 percent versus 43.1 percent, $p < 0.0001$).

In the same trials,^{117,159} the mean EDITS scores for patient satisfaction were higher in patients receiving sildenafil (82.5 and 74.0, respectively) compared with those receiving apomorphine (46.8 and 47.0, respectively).

According to results obtained from two trials,^{117,120} more patients preferred sildenafil than apomorphine. The percent of patients who preferred sildenafil over apomorphine across these trials ranged from 65.1 percent¹²⁰ to 96.6 percent.¹¹⁷ In contrast, the percentage of patients who preferred apomorphine over sildenafil ranged from 2.3 percent¹²⁰ to 3.4 percent.¹¹⁷

Apomorphine (combined with phentolamine and/or papaverine) versus sildenafil.

Harms. In this trial,²⁵¹ the overall rates of adverse events in apomorphine combined with papaverine and phentolamine (APP), a combination of phentolamine and papaverine, and a combination of apomorphine and phentolamine, and sildenafil were 25.0, 19.1, 17.1, and 15.0 percent, respectively. Only one patient developed a serious adverse event (i.e., right nephrectomy) in the APP arm. The most frequently reported adverse events in this trial were rhinitis (4.8–15 percent) and headache (2.4–5.0 percent), the highest percentages observed in the APP arm. The authors of this trial did not report the proportion of patients in each arm that withdrew due to adverse events.

Efficacy. One trial,²⁵¹ found no significant differences (one-tailed $p > 0.05$) between the combined apomorphine (either with phentolamine or phentolamine and papaverine) and sildenafil arms for most of the outcomes (e.g. mean SEP VAS rigidity, duration, and satisfaction scores, proportion of successful vaginal penetration, and mean satisfaction score based on GAQ scale).

Quantitative Synthesis - Meta-analysis of Trials

Apomorphine mono versus placebo. Five trials^{248-250,252,253} were considered to be eligible for meta-analysis. However, no meta-analysis could be performed because numerical information was lacking such as standard deviations (or standard errors)²⁴⁸⁻²⁵³, pre-crossover data²⁵², mean values²⁵³ for percent successful intercourse attempts and the IIEF-EF domain.

Apomorphine versus sildenafil. Trials (all crossover design) comparing the efficacy and safety profiles of apomorphine and sildenafil were not meta-analyzed because of clinical

heterogeneity with respect to populations and outcomes.^{114,117,120,148,159} For example, in two trials the patient populations were nonarteriogenic¹¹⁴ and arteriogenic.¹²⁰ Types of patients studied in the third trial could not be ascertained.¹¹⁷ The patient population of the one remaining trial¹⁵⁹ was comprised of those with ED of “mostly psychogenic,” “mostly organic,” and “mixed” etiology. Apomorphine dose(s) administered in one of the trials¹¹⁷ were not reported.

Injection Treatments - Intracavernosal Injection

Literature Search

Forty-two trials (in 43 publications) met eligibility criteria as randomized trials of intracavernosal injection (IC) therapy for treatment of men diagnosed with ED.^{119,172,255-280,280-294} One trial was reported in two publications^{261,276} and one publication described two trials (Aversa et al. 1996; studies: a and b).²⁶⁷

Overview of Trials

Among the 42 unique trials, 32 used a crossover design (n = 1957; range: 7 to 240 subjects) and 10 a parallel design (n = 1074, range: 30 to 296 subjects).

Populations

ED was primarily of physiologic origin (58 percent). Amongst ED patients, vascular disease and diabetes were the most commonly reported underlying conditions. Three trials exclusively enrolled men with previous radical prostatectomy or cystectomy (n = 159 subjects). Only eight trials reported smoking status, two trials ethnicity, and none reported body weight (e.g. body mass index).

Interventions

IC alprostadil (PGE₁) was evaluated alone or in combination with numerous other pharmacologic agents. One specific alprostadil combination (alprostadil plus papaverine plus phentolamine) was also tested alone or in combination with other pharmacologic agents. Other types of evaluated IC were papaverine; papaverine plus phentolamine, with or without additional sexual counseling; moxisylate; sodium nitroprusside; linsidomine; linsidomine plus urapidil; papaverine plus sildenafil; and vasoactive intestinal peptide plus phentolamine. For a full description of treatment interventions in these individual trials refer to Evidence Table F-5 (Appendix F).

Study Quality and Reporting

Information on pharmaceutical funding was provided for nine trials. Only three studies specifically reported the use of an intention-to-treat analysis. None of the trials reported methods of allocation concealment. Study withdrawals, drop-outs or lost to followup were reported in 33 trials and were 13 percent (16 percent in crossover studies and 6 percent for parallel studies). The majority of the trials were considered to be of low quality with total Jadad score < 3. Only six of the 43 trials received a score of four, and none received a score of five. Twenty-nine trials received a score of two or less. In addition, many studies reported physiologic (e.g. degree or duration of penile rigidity) rather than clinically validated outcomes (IIEF, SEP, GAQ-Q1). No study assessed therapies beyond 12 weeks.

Outcomes

Many of the 42 trials measured only physiologic efficacy outcomes (e.g. penile rigidity). Of the clinically relevant outcomes, more commonly reported were quality of erections achieved at home, without regard to whether the patient was able to achieve successful sexual intercourse, (e.g. “improvement” in erections, “full response,” full erection,” or “grade 4 or 5 erections”).

Finally, two studies reported on whether erections were “valid for intromission,” and one on whether patients were “satisfied with treatment.” Trials that reported clinically relevant efficacy outcomes or harms are emphasized in the Outcomes section below.

Qualitative Synthesis

Tables 12–14 illustrate the results.

PGE₁ versus no treatment. One trial, involving men who had undergone nerve-sparing radical retropubic prostatectomy, compared efficacy and harms of PGE₁ to those of no treatment.²⁶⁵

Harms. In total, 6.7 percent and 13.3 percent of participants treated with PGE₁ reported prolonged erection and hematoma, respectively. No untreated participants reported these adverse events.

Efficacy. In total, 66.7 percent of participants receiving PGE₁ had improved erections versus 20 percent of those who did not receive any treatment. The absolute risk difference (RD) between the two groups was 47 percent (95 percent CI: 13–80).

PGE₁ versus placebo. Six trials compared efficacy and/or harms of PGE₁ versus placebo.^{266,268,274,281,282,292}

Harms. Penile pain was reported in four trials and occurred numerically more commonly in participants treated with PGE₁. In one trial, penile pain was reported by 22.7 percent of the participants treated with PGE₁²⁷¹ and in another in 13.3 percent of the participants.²⁸² Neither study reported data on pain for the placebo groups. A third trial reported pain to have occurred in 35 percent of the participants who received PGE₁ versus 0 percent of the placebo-treated participants.²⁶⁶ The fourth trial observed similar proportions of patients with pain between the treatment groups (PGE₁: 11.7 percent versus placebo: 10.9 percent).²⁷⁴ Prolonged erection or priapism was reported by 15 percent²⁶⁶ and 2.5 percent²⁷¹ of the PGE₁–treated participants. In placebo-treated subjects, none of the participants had priapism in the first trial, and no priapism-related data were reported for the second trial. In a single trial, hematoma was reported for 1.5 percent of injections with PGE₁, with no data reported for the placebo group.²⁸²

Efficacy. In four crossover trials, between 28.9 and 66 percent of participants reported improved erections in the PGE₁ treatment groups. In two of these trials, placebo-treated participants did not experience improved erections^{266,268} The other two trials did not report any outcomes data for the placebo groups.^{281,292}

In one parallel trial, none of the placebo-treated participants reported improved erections, as compared with 35 percent of the participants treated with PGE₁. The observed pattern conformed a dose-response trend (17 percent with 2.5μg PGE₁, 27 percent with 5μg, 45 percent with 10μg, and 50 percent with 20μg).²⁷¹

PGE₁ versus PGE₁ (comparison of timing of treatment initiation or dose delivery). One trial compared the harms related to fast versus slow PGE₁ injection (i.e., 5-second injection versus 60-second injection).²⁷⁰ A second trial, involving men who had undergone non–nerve-sparing radical prostatectomy, compared the efficacy and harms of early versus late post-prostatectomy PGE₁ treatment (i.e., 1–3 months post-operatively versus 4–12 months post-operatively).²⁵⁶

Harms. In the first trial, 54.5 percent of those receiving fast PGE₁ injections reported pain during injection versus 18.2 percent of those receiving slow injections.²⁷⁰ In the second trial, 8.3 percent of participants who received early PGE₁ treatment reported prolonged erections versus 0 percent of those who received late PGE₁ treatment.²⁵⁶

Efficacy. In total 72.2 percent of participants receiving early PGE₁ treatment reported improved erections versus 43.2 percent of those receiving late PGE₁ treatment.²⁵⁶

PGE₁ versus papaverine. Four trials compared the efficacy and/or harms of PGE₁ versus papaverine,^{287,288,291,293} Only one trial of intracavernosal injection evaluated the outcome of sexual intercourse success.²⁹¹

Harms. In three trials that reported penile pain, two^{288,291} showed statistically nonsignificant differences between PGE₁ and papaverine (8.5 percent versus 4.7 percent, and 46 versus 44 percent, respectively).^{288,291} The third trial reported more frequent occurrence of pain in the papaverine participants (32.7 percent versus 11.5 percent, RD 21 percent, 95 percent CI: 6.0–37.0).²⁸⁷ All four trials reported the incidence of priapism. In one trial, this occurred in 10 percent of the participants treated with PGE₁ versus 6.7 percent of those treated with papaverine.²⁹³ In two trials no cases of priapism occurred in either treatment group.^{287,288} In the fourth trial, no priapism occurred among PGE₁-treated subjects versus 0.8 percent of the participants among papaverine-treated subjects.²⁹¹

Efficacy. In one trial²⁹¹, the proportions of PGE₁- and papaverine-treated patients achieving at least one successful intercourse attempt over 4 weeks of treatment were similar (31 percent versus 33 percent).

In four trials, from 26.4 to 80.8 percent of the PGE₁-treated participants reported improved erections, as compared with 10 to 63.5 percent of papaverine-treated subjects. The estimates of RR favouring PGE₁ over papaverine were statistically significant in three trials^{288,291,293} and marginally significant in the fourth trial.²⁸⁷

PGE₁ plus papaverine versus phentolamine plus papaverine. One trial compared efficacy and harms of papaverine plus PGE₁ versus papaverine plus phentolamine.²⁸⁹

Harms. In total, 16.3 percent of the papaverine plus PGE₁ participants reported pain versus 0 percent of the papaverine plus phentolamine participants. Approximately 8 percent of the participants in each treatment group reported prolonged erection.

Efficacy. In total, 77.6 percent of participants allocated to papaverine plus PGE₁ reported improved erections versus 57.1 percent of participants allocated to papaverine plus phentolamine.

PGE₁ versus papaverine plus phentolamine. One trial compared the efficacy and harms of PGE₁ versus papaverine plus phentolamine.²⁶⁶

Harms. In total, 35 percent of PGE₁ participants reported pain versus 15 percent of papaverine plus phentolamine participants. There was no difference in prolonged erections between the two treatments (15.0 percent versus 18.3 percent; RD -3.0 percent, 95 percent CI: -17.0 to 10.0)

Efficacy. In total, 50 percent of participants treated with PGE₁ reported improved erections versus 56.7 percent of those treated with papaverine plus phentolamine.

PGE₁ versus trimix. (see papaverine plus phentolamine plus PGE₁ versus PGE₁ below)

PGE₁ versus moxisylate. Two trials compared the efficacy and harms of PGE₁ to moxisylate.^{262,293} In both trials, PGE₁ was shown to be more effective than moxisylate.

Harms. In the first study, compared with participants in the moxisylate group, those in the PGE₁ group experienced the following events more frequently: pain during injection (14.8 versus 25 percent), pain during erection (4.9 versus 23.5 percent), pain after erection (4.9 versus 19.1 percent), prolonged erection (1.6 versus 4.4 percent), and bleeding (4.9 versus 14.7 percent), whereas, the occurrence of dizziness/hypotension was numerically more common in moxisylate-treated participants (8.2 versus 1.5 percent). Not all differences were statistically significant. In

the second study, prolonged erection appeared more common in the participants treated with PGE₁ (3.3 versus 10 percent)

Efficacy. In the first trial, 85.3 percent of the participants treated with PGE₁ reported improved erections versus 60.7 percent of the moxisylylate-treated participants.²⁶² In the second trial, the rates of improved erection in PGE₁ and moxisylylate groups were 40 percent and 6.7 percent, respectively.²⁹³

PGE₁ versus sodium nitroprusside. One trial compared the efficacy and harms of PGE₁ with three different doses of nitroprusside (100µg, 300µg, or 400µg).²⁷⁸

Harms. In total, 6.7 percent of the participants in PGE₁ group reported pain during injection versus 0 percent of those in each of the nitroprusside group. About 4.0 percent of the participants treated with PGE₁ reported dizziness versus 10, 8 and 3 percent for each of the nitroprusside groups (100µg, 300µg, and 400µg, respectively).

Efficacy. In total, 20 percent of the participants treated with PGE₁ reported full rigidity. Nitroprusside 100µg was reported to be ineffective in producing erections. In the 300µg and 400µg nitroprusside groups, 15 percent and 14.3 percent of the participants, respectively had full rigidity.

PGE₁ versus linsidomine. Three trials compared the efficacy and harms of PGE₁ to linsidomine.^{273,279,284}

Harms. In one trial, 17.5 percent of participants receiving PGE₁ reported penile pain. Similar data for the linsidomine-treated subjects was not provided. In the linsidomine group, moderate to severe headache was reported by 7.5 percent of the subjects.²⁸⁴ In a second trial, 7.5 percent of PGE₁ participants reported pain during injection versus 2.5 percent of linsidomine subjects.²⁷³

Efficacy. Between 30 and 65 percent of the participants treated with PGE₁ had improved erections compared with 7.5–12.5 percent of those treated with linsidomine.

PGE₁ versus linsidomine plus urapidil. One trial compared the efficacy and harms of PGE₁ to linsidomine plus urapidil.²⁷³

Efficacy. In total, 40 percent of participants randomly assigned to PGE₁ therapy reported improved erections versus 25 percent of those randomly assigned to linsidomine plus urapidil therapy.

Harms. In total, 7.5 percent of participants in each treatment group reported pain during injection, while 0 percent of those receiving PGE₁ and 12.5 percent of those receiving linsidomine plus urapidil reported severe hypotension.

PGE₁ versus PGE₁ plus lidocaine. One trial compared the efficacy and harms of PGE₁ injections with or without lidocaine.

Harms. The proportions of participants reporting pain in PGE₁ plus lidocaine versus PGE₁ only groups were 45.4 percent and 86.4 percent, respectively.

Efficacy. In total 63.6 percent of the participants allocated to PGE₁ plus lidocaine reported improved erections versus 27.3 percent of those allocated to PGE₁ alone.

PGE₁ versus PGE₁ plus procaine. One trial compared the efficacy and harms of PGE₁ injections with and without procaine (10mg or 20mg).²⁸⁰

Harms. Of participants allocated to PGE₁ plus procaine, 62.5 percent reported moderate to severe pain compared with 83.3 percent of those allocated to treatment with PGE₁ only. The occurrence of severe pain was reported by 16.6 percent versus 45.8 percent of the participants, respectively.

Efficacy. In total, 66.7 percent of those assigned to receive PGE₁ plus procaine reported improved erections versus 66.7 percent of those assigned to receive PGE₁ only.

PGE₁ versus PGE₁ plus sodium bicarbonate. One trial compared the harms of PGE₁ injections with or without sodium bicarbonate.²⁶⁹

Harms. In total, 70 percent of participants assigned to the PGE₁ plus sodium bicarbonate group reported pain versus 80 percent of those assigned to the PGE₁ group. The incidence of pain in PGE₁ plus sodium bicarbonate group was reduced compared with PGE₁ alone group but the between-group difference was not statistically significant (70 percent versus 80 percent, RD - 10 percent, 95 percent CI: -48.0-28.0).

Efficacy. The efficacy was not reported

PGE₁ plus sexual counseling plus sildenafil versus PGE₁ plus sildenafil. One trial compared the efficacy and harms of PGE₁ plus sexual counseling plus adjunctive open label oral sildenafil versus PGE₁ plus adjunctive open label sildenafil in men who had undergone non-nerve sparing radical retropubic prostatectomy or radical cystectomy.²⁹⁴

Harms. The frequency of adverse events was similar for PGE₁ plus counseling plus sildenafil versus PGE₁ plus sildenafil groups, including moderate pain (34.4 percent versus 42.8 percent), severe pain (13.7 percent versus 10.7 percent), prolonged erection (17.2 percent versus 17.8 percent), and hematomas (6.9 percent versus 10.7 percent). There were no withdrawals among the participants allocated to PGE₁ plus counseling plus sildenafil. In contrast, 29 percent of those treated with PGE₁ plus sildenafil withdrew (3 of 8 withdrawals were due to prolonged pain after injections).

Efficacy. Mean score on the IIEF “EF domain” after 18 months of treatment was significantly higher in men allocated to PGE₁ plus counseling plus sildenafil versus those allocated to PGE₁ plus sildenafil (26.5 versus 24.3, $p < 0.05$).

Papaverine versus placebo. None of the identified studies compared papaverine monotherapy to placebo. One trial reported the efficacy and harms of papaverine plus PGE₁ versus PGE₁ alone.²⁸⁹ Papaverine plus PGE₁ was not shown to be more effective and it was associated with more frequent pain than PGE₁ alone.

Harms. In total 34.2 percent of participants allocated to papaverine plus PGE₁ reported pain versus 18.4 percent of those allocated to PGE₁ alone. The incidence of prolonged erection was reported by 15 percent and 18.3 percent of the participants in each group, respectively.

Efficacy. In total, 73.7 percent of participants allocated to papaverine plus PGE₁ reported improved erections versus 60.5 percent of those allocated to PGE₁ alone.

Papaverine versus PGE₁ (see PGE₁ versus papaverine, above).

Papaverine versus moxisylate. One trial compared the efficacy and harms associated with the use of papaverine versus moxisylate.²⁹³

Harms. In total, 6.7 percent of the papaverine-treated participants reported prolonged erection versus 3.3 percent of the moxisylate-treated participants ($p \geq 0.05$).

Efficacy. In total, 10 percent of the papaverine-treated participants reported improved erections versus 7 percent of the moxisylate-treated participants ($p \geq 0.05$).

Papaverine followed by sildenafil versus sildenafil followed by papaverine. One trial compared the efficacy and harms for a single 30 mg dose of papaverine followed by a single 50 mg dose of sildenafil versus a single 50 mg sildenafil dose followed by 30 mg papaverine.¹⁷²

Harms. Adverse events were reported for both treatment groups combined, including priapism (10 percent), headache (4 percent), blurred vision (2 percent), and dyspepsia (2 percent).

Efficacy. Data on clinically relevant outcomes were not reported.

Moxisylate versus placebo. One trial compared the efficacy and harms for moxisylate versus placebo.²⁸⁵

Harms. Participants receiving moxisylate reported prolonged erection (1.6 percent), pain (3.3 percent), faintness (3.3 percent), hypotension/nausea/bradycardia (1.6 percent) and hot flushes (1.6 percent). Though no participants receiving placebo experienced any of these side effects, these differences were not statistically significant.

Efficacy. In total, 86.9 versus 27.9 percent of moxisylate and placebo participants, respectively, reported improved erections (RR = 3.12, 95 percent CI: 2.06-4.72).

Moxisylate versus PGE₁ (see PGE₁ versus moxisylate, above).

Moxisylate versus papaverine (see papaverine versus moxisylate, above).

Phentolamine plus PGE₁ versus PGE₁. Two trials compared phentolamine plus PGE₁ versus PGE₁ alone for efficacy and/or harms (Aversa 1996; studies: a and b).²⁶⁷

Harms. In the single trial that reported prolonged erection,²⁶⁷ 4.2 percent of participants in each treatment group reported this adverse effect.

Efficacy. In the first trial, 54.2 percent of participants randomized to phentolamine plus PGE₁ reported improved erections versus 20.8 percent of those randomized to PGE₁.²⁶⁷ The corresponding proportions reported for the other study were 60 versus 30 percent, respectively.²⁶⁷

Papaverine plus phentolamine versus placebo. One trial compared the efficacy and harms of papaverine plus phentolamine versus placebo.²⁶⁶

Harms. In total, 15 and 18.3 percent of the participants randomized to papaverine plus phentolamine reported the occurrence of pain and prolonged erection, respectively. None of the participants in placebo group experienced these adverse events.

Efficacy. In total, 56.7 percent of participants randomized to papaverine plus phentolamine reported improved erections versus 0 percent of those randomized to placebo.

Papaverine plus phentolamine versus papaverine plus phentolamine plus sexual counseling. One trial compared the efficacy and harms of papaverine plus phentolamine versus papaverine plus phentolamine plus sexual counseling.²⁵⁷

Harms. Results for harms in this study were pooled for the two treatment groups. 12 percent of the men discontinued the treatment due to prolonged erection. Priapism was reported in three (4.3 percent), hematoma in four (5.7 percent), and curvature of the penis in one participant (1.4 percent).

Efficacy. The mean values on a self-rated erections score (scale 0–100) for papaverine plus phentolamine versus papaverine plus phentolamine plus sexual counseling groups were 79 versus 84 percent, respectively.

Trimix versus PGE₁. Two trials compared the efficacy and harms of trimix versus PGE₁ alone.^{255,272} In the first trial, 32 men (mean age: 61 years) with ED of at least 6 months of duration (etiology not reported) refractory to in-clinic injection of papaverine plus phentolamine, were randomized in a crossover fashion to 40µg of PGE₁ versus 17.64 mg papaverine plus 0.58 mg phentolamine plus 5.8µg PGE₁.²⁷² Another trial enrolled 180 men (mean age: 51 years) with ED at least 6 months' duration, predominately of organic cause, of whom 20 percent had complete ED.²⁵⁵ Men in this trial were randomized in a crossover fashion to 20µg of PGE₁ alone versus one of nine different dose combinations of papaverine (range 5mg–20mg) plus phentolamine (1 mg) plus PGE₁ (2.5–10µg).

Harms. In the first trial, 12.5 percent of participants randomized to trimix reported pain versus 40.6 percent of those allocated to PGE₁.²⁷² In the second trial, corresponding proportions

were 14.4 percent (for trimix) versus 17.3 percent (for PGE₁).²⁵⁵ Only the second trial reported data on priapism, which occurred in 5.0 percent of participants allocated to trimix versus 0.6 percent of those allocated to PGE₁.²⁵⁵

Efficacy. About half (50 percent) of the participants randomized to trimix reported grade 4 or 5 erections versus 21.9 percent of those randomized to PGE₁ alone.²⁷²

There was no difference between trimix and PGE₁ for erections of either grade 4 or 5 (trimix: 66.7 percent versus PGE₁: 67.8 percent), or for improvement in self-rated erection compared with home (trimix: 83.2 percent versus PGE₁: 84.9 percent, $p = 0.85$). There was no statistically significant difference in efficacy outcomes between PGE₁ and any individual trimix dose combination.²⁵⁵

Trimix plus atropine versus trimix. One trial compared the efficacy and harms of trimix versus trimix plus atropine.²⁶⁴ Addition of atropine to trimix did not reduce pain or improve erections compared with trimix alone.

Harms. In total 55.3 percent of participants allocated to trimix plus atropine reported pain versus 50 percent of those allocated to trimix alone.

Efficacy. Each treatment group reported improved erections in 45.6 percent of the participants.

Trimix plus sodium bicarbonate versus trimix. One trial compared the efficacy and harms of trimix injections with and without sodium bicarbonate.²⁸³

Harms. In total pain was reported by 5.3 percent of the participants receiving trimix plus sodium bicarbonate compared with 57.9 percent of those in the group treated with trimix alone.

Efficacy. The difference between the rates of improved erection in participants allocated to trimix plus sodium bicarbonate versus trimix alone was not statistically significant (78.9 percent versus 68.4 percent; RD 11 percent, 95 percent CI:-17.0–38.0).²⁸³

Vasoactive intestinal peptide (VIP) plus phentolamine versus placebo. Two trials compared the efficacy and harms of vasoactive intestinal peptide (VIP) plus phentolamine versus placebo.²⁶⁰

Harms. Compared with participants receiving placebo, those randomized to VIP plus phentolamine reported more frequent bruising (12.3 percent versus 43.1 percent), bleeding at injection site (5.1 percent versus 20.5 percent) urethral bleeding (2.6 percent versus 12.3 percent), flushing (13.3 percent versus 74.4 percent), palpitation (0 percent versus 7.7 percent), and tachycardia (0.5 percent versus 5.1 percent).

The participants in the placebo group reported bleeding at the injection site. There was no statistically significant difference between the treatment groups with respect to pain during injection (4.6 percent versus 8.2 percent), priapism (0.5 percent versus 0 percent), or headache (3.6 percent versus 1.5 percent).

Efficacy. Three hundred and four men with ED were screened for response to in-clinic or home administration of 25µg VIP plus either 1mg or 2 mg of phentolamine.

Based on the phentolamine dose to which responses were observed, 240 participants were randomized in a crossover design to active treatment versus placebo. Efficacy results were reported only for the 172 men who received at least one dose of active drug and placebo.

Seventy-two percent of injections in men allocated to VIP plus 1 mg phentolamine produced grade 3 erections (suitable for sexual intercourse) versus 13 percent in men allocated to placebo ($p < 0.001$). The proportions of participants with grade three erections in VIP plus 2 mg phentolamine and placebo groups were 65 and 16 percent, respectively ($p < 0.001$)

Tables 13–15 illustrate the results presented in this section.

Quantitative Synthesis

There was a large degree of clinical heterogeneity in the potentially eligible IC trials with regard to patient characteristics (e.g. proportion with psychogenic versus physiologic ED, exclusion of nonresponders during screening phase), interventions (e.g. number, dose, and duration of treatment), and assessed outcomes (see Outcomes section above). Therefore, meta-analyses were not performed.

Injection Treatments - Subcutaneous Injections

Literature Search

Three trials (four publications)²⁹⁵⁻²⁹⁸ were identified and included in the review. One trial was reported in two publications.^{295,296}

Overview of Trials

All three studies used a crossover design. (Evidence Table F-7, Appendix F)

Populations

In these studies, ED etiology was primarily of psychogenic (69 percent) origin. Obesity, hypertension, and hypercholesterolemia were the most commonly reported underlying diseases. Mean duration of ED in one trial was 8 years.

Interventions

The evaluated SC injection treatments were Melanotan II,²⁹⁵ PT-141 (cyclic heptapeptide melanocortin analog) (n=25),²⁹⁸ and apomorphine (n=12).²⁹⁷ In all studies, SC therapy was administered in a clinic and subjects were monitored or kept under observation from 30 minutes up to 24 hours.

Study Quality and Reporting

None of the studies reported the source of pharmaceutical funding. None of the trials reported methods of allocation concealment. Study withdrawals, drop-outs or participants lost to followup were reported in all trials. All trials were double-blind. All trials received a Jadad score of 3 (Evidence Table F-6, Appendix F).

Outcomes

Three eligible studies assessed clinical efficacy (e.g. improvement in erections) and harms. (Tables 15 and 16)

Qualitative Synthesis

Melanotan II versus placebo. One small trial enrolling 20 subjects, 10 men with psychogenic ED and 10 men with organic ED, compared the efficacy and harms of Melanotan II (SC) to placebo²⁹⁵. Melanotan II was administered by the investigator in doses between 0.025 mg/kg and 0.157 mg/kg in a double blind, placebo-controlled fashion. Subjects were monitored by RigiScan in the clinic and at home for a total of 6 hours.

Harms. Men administered Melanotan II reported an increased frequency of nausea (38.5 percent versus 9.8 percent), yawning and stretching (56.4 percent versus 12.2 percent).²⁹⁵

Efficacy. 17 of the 20 subjects administered Melanotan II reported a “subjectively apparent erection” on at least one of two injections of Melanotan II. The number of subjects with improved erections following administration of placebo was not reported. Overall, erectile activity (based on RigiScan activity) was reported in 69 percent (27/39) of Melanotan II injections compared with 2 percent (1/41) of placebo injections. In a subgroup analysis of the 10 subjects with organic ED, nine men treated with Melanotan II reported a “subjectively apparent

erection” versus one placebo treated subject²⁹⁶. Erectile activity was reported in 63 percent (12/19) of Melanotan II injections compared with 2 percent (1/21) of placebo injections.

PT-141 versus placebo. One small trial that enrolled 25 subjects with moderate to severe ED who had an inadequate response to sildenafil compared the efficacy and harms of PT-141 (SC) to placebo²⁹⁸. PT-141 was administered in doses of 4 or 6 mg, utilizing a placebo-controlled three-way crossover design²⁹⁸. Patients were kept under observation until 24 hours after the dose administration.

Harms. Men who were administered PT-141 reported an increased frequency of nausea (4 mg: 24 percent versus 6 mg: 36 percent versus placebo: 0 percent) and headache (4 mg: 36 percent versus 6 mg: 27 percent versus placebo: 0 percent) compared with placebo.

Efficacy. Clinically and statistically significant erectile response (assessed by RigiScan) in the presence of visual sexual stimulation was observed following the administration of single dose of 4 or 6 mg PT-141, relative to placebo. A greater than two-fold increase in the duration of base rigidity ≥ 60 percent, compared with placebo, was reported in 82 percent of subjects receiving the 4 mg dose and 84 percent of patients receiving the 6 mg dose.

Apomorphine versus placebo. One small trial enrolling 12 subjects with coital erectile failure of at least 6 months compared apomorphine (SC) to placebo.²⁹⁷

Harms. Eight subjects reported side effects, including yawning, drowsiness and nausea. Two participants experienced extreme nausea and hypotension, with one transiently losing consciousness after the 1.0 mg apomorphine dose.

Efficacy. Eleven out of the 12 subjects exceeded a change of 1cm in circumference after injection).

Quantitative Synthesis

No meta-analysis was performed due to the clinical heterogeneity with regard to intervention types.

Intra-urethral Suppositories

Literature Search

Seven RCTs (in seven publications) were eligible and were included in the review.²⁹⁹⁻³⁰⁵

Overview of Trials

Of the seven trials,²⁹⁹⁻³⁰⁵ one reported only physiologic outcomes (timing and degree of penile rigidity as measured by RigiScan) and no harms data.³⁰⁵ Therefore, the remaining six trials are described in more detail in this section. Of five studies, four assessed clinically relevant efficacy outcome such as home sexual intercourse success^{299,300,302,304} and one trial reported on whether in-clinic erections were judged sufficient for intercourse. Of these six trials,²⁹⁹⁻³⁰⁴ two were cross-over design (n=345; range: 111-234 participants) and four were parallel design (n=1726, range: 60-996 participants). No studies assessed therapies beyond 12 weeks. (Evidence Table F-7, Appendix F)

Populations

Among the six trials reporting clinical efficacy and/or harms data, the mean age of the subjects was 60.4 years (n=6 trials reporting). Racial characteristics were reported in only one trial. ED etiology was of physiologic origin in the four studies reporting. Vascular disease and diabetes were the most commonly reported underlying diseases. Mean duration of ED was approximately 4 years. In four trials reporting, 56 percent of men reported previous treatment for ED. No trials reported smoking status and body weight (e.g. body mass index), both risk factors of ED.

Interventions

IU treatment interventions evaluated in eligible trials were alprostadil, prazosin, and the combination of the two agents.

Among alprostadil interventions, one 3 month trial of IU alprostadil utilized a fixed dose of 1000µg.³⁰¹ Three trials utilized fixed doses of alprostadil from 125 to 1000µg administered at home based on each subject's response to various doses or a dose titration.^{300,302,304} The home treatment phases of these trials were 3 weeks and 3 months,^{302,304} respectively. In another trial, subjects received single in-clinic administrations of two of four alprostadil doses (125, 250, 500 and 1000µg) over a 2 to 4 week period.³⁰³ In a sixth trial, subjects started at either 250 or 500µg alprostadil for 4 weeks with subsequent dose titration so that final dose at 12 weeks ranged from 125 to 1000µg.²⁹⁹ Pubic bands were allowed as optional adjunct therapies in two trials.^{299,300}

In one trial that evaluated a prazosin intervention, subjects received single in-clinic administrations of two of four prazosin doses (250, 500, 1000 and 2000µg) over 2 - 4 week period.³⁰³

Finally, in the single trial that evaluated a combined alprostadil/prazosin intervention, subjects received single in-clinic administrations of two of nine possible IU alprostadil/prazosin dose combinations over a 2 to 4 week period.³⁰³

Study Quality and Reporting

Information on pharmaceutical funding was reported to have been provided for five^{299,300,302-304} of the six trials. One trial³⁰¹ did not report a funding source. None of the trials reported

methods of allocation concealment. Participant withdrawals, drop-outs or lost to followup were reported in all trials and ranged from 7 percent to 42 percent. The majority of the trials were considered to be of low quality as assessed by the Jadad scale. Only one of the six trials received a Jadad score of 3. The remaining trials received a score of 2 or less. (Table C-1, Appendix C)

Outcomes

Both clinical efficacy (e.g. sexual intercourse success, improvement in erections) and harms (e.g. penile pain) outcomes were assessed in all six trials.²⁹⁹⁻³⁰⁴ More commonly reported were quality of erections achieved at home, without regard to whether the patient was able to achieve successful sexual intercourse (“improvement” in erections, “full response,” full erection,” or “grade 4 or 5 erections”). All six trials reported data on penile or urogenital pain and three trials reported results on prolonged erections or priapism/fibrosis.

Qualitative Synthesis

Summary of qualitative synthesis for this section is presented also in Tables 17-19.

Alprostadil versus placebo. Three trials compared the efficacy and harms of IU alprostadil to placebo.³⁰²⁻³⁰⁴

Harms. In the first trial, compared with men in placebo group, alprostadil-treated men had an increased frequency of penile pain (3.3 percent versus 32.8 percent) and minor urethral trauma (1.0 percent versus 5.2 percent).³⁰⁴ Urinary tract infection occurred in fewer than 1 percent of participants in both groups. No cases of prolonged erection, priapism or fibrosis were observed in either treatment group.

In the second trial, men randomized to IU alprostadil reported an increased frequency of urogenital burning (6.4 percent versus 0 percent), but statistically nonsignificant increase in risk of penile pain (5.1 percent versus 1.2 percent), dizziness (2.6 percent versus 0 percent), prolonged erection (1.3 percent versus 0 percent), and testicular pain (2.6 percent versus 0 percent).³⁰²

Minor urethral trauma was reported by 1.3 and 1.2 percent of men allocated to IU alprostadil and placebo, respectively.

There were no cases of priapism or fibrosis, or urinary tract infection in either treatment group.

In the third trial, penile pain was reported by 1.7, 23.6, 20.5, 20.9 and 17.0 percent of men allocated to placebo, 1000µg, 500µg, 250µg, and 125µg IU alprostadil, respectively.³⁰³ The corresponding proportions for reporting testicular pain were: 0.4, 1.8, 4.4, 4.4, and 2.0 percent.

Urethral pain was reported by 1.7, 9.1, 8.0, 5.1, and 1.0 percent of the men allocated to placebo, 1000µg, 500µg, 250µg, and 125µg IU alprostadil, respectively.

Efficacy. Men randomized to IU alprostadil reported that 50.4 percent of their sexual intercourse attempts during the 3 month treatment period were successful versus 10.1 percent for men allocated to placebo. Sixty-two percent of men allocated to IU alprostadil reported at least one successful sexual intercourse attempt during the study period versus 18.2 percent of men allocated to placebo.

In the second trial, men randomized to IU alprostadil reported that 51.1 percent of their sexual intercourse attempts during the 3 month treatment period were successful versus 7.5 percent for men allocated to placebo. In the third trial,³⁰³ 31 percent of men reported erections sufficient for intercourse (grade 4 or 5) with 500µg IU alprostadil versus 14.1 percent of the men

treated with 125µg IU alprostadil. Results were not provided for 250µg and 1000µg alprostadil doses.

Alprostadil (250µg) versus alprostadil (starting dose: 500µg). One trial²⁹⁹ compared the efficacy and harms of initiating IU alprostadil treatment at doses of 250µg and 500µg.

Harms. In the 4 weeks prior to IU alprostadil dose titration, 14.5 percent of men allocated to an initial dose of 250µg reported penile pain versus 27.7 percent of those allocated to an initial dose of 500µg ($p < 0.05$). During this period, there was no difference between treatment groups for urethral pain (250µg: 1.2 percent versus 500µg: 2.4 percent) or hypotension/dizziness (250µg: 2.4 percent versus 500µg : 3.6 percent).

Efficacy. Seventy-seven percent of men allocated to an initial dose of 250µg versus 69 percent of those allocated to an initial dose of 500µg elected to increase their dose at 4 weeks. Pooled clinical efficacy results were presented for treatment groups, namely the proportion of men during the study period with at least one successful sexual intercourse attempt (68.1 percent) and the proportion with erections sufficient for intercourse (grade 4 or 5) (73.5 percent).²⁹⁹

Alprostadil (IU) versus alprostadil (IC). Two trials compared the efficacy and harms of IU alprostadil versus IC alprostadil.^{300,301}

Harms. In the first trial, men allocated to IU alprostadil were less likely to report urogenital pain than those allocated to IC alprostadil (6.7 percent versus 46.7 percent) with statistically nonsignificant differences between the treatment groups for urethral bleeding (3.3 percent versus 0 percent) or dizziness (6.7 percent versus 0 percent).³⁰¹ In the second trial, there was no statistically significant difference between the two treatment groups with regard to penile pain (25.0 percent versus 33.8 percent), prolonged erections (0 versus 2.9 percent), or local bleeding (2.9 versus 1.5 percent).³⁰⁰

Efficacy. In one trial, men randomized to IU alprostadil reported 55.0 percent successful intercourse attempts versus 85.1 percent for those allocated to IC alprostadil.³⁰¹ Furthermore, 53.3 percent of men allocated to IU alprostadil reported at least one successful sexual intercourse attempt during the study period versus 86.7 percent of men allocated to IC alprostadil. In the second 3-week trial, 61.8 percent of men randomized to IU alprostadil reported at least one erection sufficient for intercourse during at home use versus 92.6 percent of those allocated to IC alprostadil.³⁰⁰

Alprostadil (IU) versus prazosin (IU). One trial compared the efficacy and harms of IU alprostadil versus IU prazosin.³⁰³

Harms. Penile pain was reported by 23.6, 20.5, 20.9 and 17.0 percent of men allocated to 1000µg, 500µg, 250µg, and 125µg IU alprostadil, respectively versus 5.5, 0.7, 1.4 and 1.1 percent of men allocated to 2000µg, 1000µg, 500µg, and 250µg IU prazosin, respectively.³⁰³ Urethral pain was reported by 9.1, 8.0, 5.1, and 1.0 percent of men allocated to 1000µg, 500µg, 250µg, and 125µg IU alprostadil, respectively versus 0, 2.0, 2.0, and 2.1 percent of men allocated to 2000µg, 1000µg, 500µg, and 250µg IU prazosin, respectively.

Efficacy. In this trial, each of 234 participants received single administrations of two of four potential alprostadil doses (125, 250, 500 and 1000µg) and two of four potential prazosin doses (250, 500, 1000 and 2000µg). Thirty-one percent of men with 500µg IU alprostadil reported erections sufficient for intercourse (grade 4 or 5) versus 14.1 percent with 125µg IU alprostadil versus 3 percent of men with 2000µg prazosin. Results were not provided for the 250µg and 1000 µg alprostadil doses or for the 250µg, 500µg, and 1000µg prazosin doses.

Prazosin (IU) versus placebo. One trial compared the efficacy and harms of prazosin versus placebo.³⁰³

Harms. Penile pain was reported by 5.5, 0.7, 1.4 and 1.1 percent of men allocated to 2000, 1000, 500, and 250µg IU prazosin, respectively, versus 1.7 percent of those allocated to placebo. Urethral pain was reported by 0, 2.0, 2.0, and 2.1 percent of men allocated to 2000, 1000, 500, and 250µg IU prazosin, respectively, versus 1.7 percent of those allocated to placebo.

Efficacy. In this trial, 3 percent of men assigned to 2000µg IU prazosin reported erections sufficient for intercourse versus 0.4 percent of those assigned to treatment with placebo. Results were not provided for the 250, 500, and 1000µg prazosin doses, though it was stated that 2000µg was the most efficacious prazosin dose.

Alprostadil (IU) plus IU prazosin versus IU alprostadil versus IU prazosin versus placebo. One trial compared the efficacy and harms of IU alprostadil plus IU prazosin versus IU alprostadil versus IU prazosin versus placebo.³⁰³ All combinations of IU alprostadil plus IU prazosin appeared to improve erections more than IU prazosin or placebo.

Harms. The proportions of patients with penile pain among those allocated to various alprostadil/prazosin combinations were: 23.9(125µg/250µg), 23.4 (125µg/500µg), 23.4 (250µg/250µg), 17.0 (250µg /500µg), 27.3 (250µg /1000µg), 23.2 (500µg /500µg), 23.1 (500µg/1000µg), 31.6 (500µg /2000µg), and 26.9 percent (1000µg /1000µg). The proportions of patients with penile pain who were allocated to various doses of IU alprostadil were: 23.6 (1000µg), 20.5 (500µg), 20.9 (250µg), and 17.0 percent (125µg). The corresponding proportions for various doses of IU prazosin were: 5.5 (2000µg), 0.7 (1000µg), 1.4 (500µg) and 1.1 percent (250µg). Of the placebo-treated patients, 1.7 percent experienced penile pain.

The corresponding proportions of patients with urethral pain with respect to various alprostadil/prazosin combinations were: 6.5, 10.6, 8.5, 8.5, 11.4, 7.1, 1.9, 5.3, and 13.5 percent respectively. The corresponding proportions of men with urethral pain for various doses of IU alprostadil were: 9.1, 8.0, 5.1, and 1.0 percent, respectively. The proportions for various doses of IU prazosin were: 0, 2.0, 2.0, and 2.1 percent respectively. Urethral pain was experienced by 1.7 percent of the placebo-treated patients.

Efficacy. Erections sufficient for intercourse were reported by 30.4 percent of men assigned to 125/500µg alprostadil/prazosin versus 31.9 percent with 250/500µg alprostadil/prazosin, 35.7 percent with 500/2000µg alprostadil/prazosin, 31.1 percent with 500µg alprostadil, 14.1 percent with 125µg alprostadil, 3 percent with 2000µg prazosin, and 0.4 percent with placebo. Results were not provided for the other six alprostadil/prazosin combinations tested, for the 250 and 1000µg alprostadil doses, or for the 250, 500, and 1000µg prazosin doses. However, it was stated that 500/2000µg was the most efficacious alprostadil/prazosin dose, 500µg was most efficacious alprostadil dose, and 2000µg was the most efficacious prazosin dose.

Quantitative Synthesis

There was a large degree of clinical heterogeneity among the eligible IU trials with regard to patient characteristics (e.g. inclusion/exclusion criteria), interventions (e.g. fixed or flexible dosing, dose titration, treatment duration per individual ranging from single administration to 3 months), and assessed outcomes (see Outcomes section above). Therefore, meta-analyses on these studies were not performed.

Topical Treatments

Literature Search

Twelve unique trials (11 publications) were identified as eligible for evaluating topical treatments in ED patients and were included in the review.^{144,306-315} One publication³⁰⁶ described and reported two distinct trials in patients with mid to moderate (trial a) and severe ED (trial b). Additional studies of topical testosterone are described in the Hormonal Treatment section.

Overview of Trials

Of the 12 trials, five reported only physiologic efficacy outcomes, such as in-clinic assessment of degree or duration of penile rigidity.³⁰⁷⁻³¹¹ The remainder of this section emphasizes results from the seven trials that assessed validated and clinically relevant efficacy outcomes such as sexual intercourse success or improvement in erections at home.^{144,306,312-315} Of these seven trials, three used crossover and four used parallel design. None of these studies assessed therapies beyond 6 months. (Evidence Table F-8, Appendix F)

Populations

Patient characteristics presented are based on data from all 12 unique trials. The mean age of the subjects was 59 years. Racial characteristics were reported in only three trials. The majority of the subjects were Caucasians (86 percent). ED etiology was primarily of physiologic origin (59.7 percent). Vascular disease and diabetes were the most commonly reported underlying causes of ED. Mean duration of ED was approximately 2.7 years, (three trials reporting). Only two trials reported smoking status and none of the trials reported data on obesity.

Interventions

Topical treatments evaluated in the seven trials that reported clinical efficacy outcomes were alprostadil³⁰⁶, nitroglycerine;^{313,315} aminophylline plus isosorbide dinitrate plus co-dergocrine;^{312,314} minoxidil;³¹³ and sildenafil.¹⁴⁴

In the first two trials (studies a and b)³⁰⁶, the administered alprostadil doses were 50µg, 100µg, 200µg or 300µg. In one trial, 2.5 gm of 10 percent nitroglycerine ointment was applied twice daily to the penile shaft for 2 months.³¹³ In another, subjects applied a plaster to the penile shaft one hour prior to anticipated sexual activity that released 10 mg nitroglycerine per 24 hours.³¹⁵

In two trials, subjects received 2 gm doses of 3 percent aminophylline plus 0.25 percent isosorbide dinitrate plus 0.05 percent co-dergocrine cream, to be applied to the penile shaft and glans penis 15 minutes before anticipated sexual activity.^{312,314}

In one trial, subjects applied 1 mL of 2 percent minoxidil solution twice daily on the glans penis.³¹³

Finally, in one trial, subjects applied 0.5 gm of 1 percent sildenafil gel applied to the glans penis five minutes before expected sexual activity. Participants were followed for up to 2 weeks, though it was not clear whether or not they received more than one dose.¹⁴⁴

Study Quality and Reporting

Sources of pharmaceutical funding was provided for four trials. The remainder of trials did not report a funding source. Treatment allocation concealment was usually unclear. One trial

reported adequate allocation concealment during randomization.³¹² Only one trial received a total Jadad score of 4 and none received a score of 5. The remaining trials received scores of 3 or 2. (Table C-1, Appendix C)

Outcomes

Only the seven studies^{144,306,312-315} that assessed clinical efficacy outcomes (e.g. IIEF-EF domain scores, sexual intercourse success, improvement in erections) are described here. Of the trials reporting the clinical efficacy outcomes, only four reported results for sexual intercourse success. More commonly reported outcomes were quality of erections achieved at home.

Qualitative Synthesis

Summary of the results presented in this section is also available in Tables 20–22

Topical Alprostadil versus Placebo.

Harms. According to data reported from one trial (study a),³⁰⁶ in patients with mild to moderate ED, any adverse events were more frequent in those allocated to alprostadil given at 50µg (66.7 percent), 100µg (66.7 percent) or 200µg (77.5 percent) versus placebo (52.5 percent) the corresponding proportions in the second trial with patients with severe ED (study b) for alprostadil given at 100µg, 200µg, 300µg versus placebo were 30, 60, and 51 versus 11 percent respectively. The incidence of adverse events and withdrawals due to adverse events in both patient populations conformed a dose-response trend and that urogenital pain and hypotension occurred numerically more frequently with alprostadil than with placebo.

Efficacy. The success rate of vaginal penetration was assessed in two trials of mild to moderate (study a) and severe patients (study b).³⁰⁶ Within men with severe ED (study b), compared with those allocated to placebo, who reported a 15.6 percent success rate of vaginal penetration at study end, success rates for men allocated to alprostadil were 32.3 percent for 100µg, 36.2 percent for 200µg, and 38.6 percent for 300µg, with none of the between group differences reaching statistical significance. In men with mild to moderate ED (study a), men allocated to placebo reported a 55.3 percent success rate, while the success rates in alprostadil groups were 69.4 percent for 50µg ($p > 0.05$ versus placebo), 69.1 percent for 100µg ($p > 0.05$ versus placebo), and 82.9 percent for 200µg ($p = 0.01$ versus placebo).

Topical Nitroglycerine versus Placebo. Two trials compared the efficacy and harms of nitroglycerine to placebo.^{313,315}

Harms. In the first trial, men allocated to nitroglycerine ointment compared with placebo reported more adverse events (frequent burning at the application site: 12.6 versus 0 percent; hypotension: 10.3 versus 0 percent).³¹³ In the second trial, men allocated to nitroglycerine plaster had more frequent headache (35.4 versus 1.1 percent) and smarting pain (23.2 versus 1.1 percent) compared with placebo.³¹⁵ In addition, 6 percent of men allocated to nitroglycerine withdrew from therapy due to adverse events (severe pain) versus 0 percent of placebo subjects.

Efficacy. In one trial of men with physiologic ED ($n=132$ randomized), 20.7 percent of those allocated to 2.5 g nitroglycerine ointment twice daily over 2 months reported improved erections versus 1.7 percent of those allocated to placebo.³¹³ In a second trial, men with predominately psychogenic ED and at least partial in-clinic erectile response to intracavernosal papaverine ($n=19$) were allocated to 10 mg nitroglycerine plaster administered at least one hour prior to anticipated sexual activity for up to 6 doses not more often than once daily versus placebo plaster. Among those in the nitroglycerine plaster group, 16.7 percent reported improved erections versus 11.1 percent of those in the placebo plaster group.³¹⁵

Topical Nitroglycerine versus Minoxidil. One trial (n=132 participants) compared the efficacy and harms of nitroglycerine ointment to minoxidil.³¹³

Harms. Men assigned to received nitroglycerine ointment group reported more frequent side effects than did men in the minoxidil group, including more frequent burning at the application site (12.6 versus 6 percent) and hypotension (10.3 versus 0 percent).³¹³

Efficacy. Among men in the nitroglycerine ointment group, 20.7 percent reported improved erections versus 44.0 percent of those in the minoxidil group.

Topical Aminophylline plus Isosorbide dinitrate plus Co-dergocrine versus Placebo.

Two crossover trials compared the efficacy and harms of Aminophylline plus Isosorbide dinitrate plus Co-dergocrine versus placebo.^{312,314} In the first trial (n=36), men with predominately physiologic ED were assigned to receive 2 gm of 3 percent aminophylline plus 0.25 percent isosorbide dinitrate plus 0.05 percent co-dergocrine mesylate taken once during a 7 day period versus placebo.³¹⁴ In the second trial (n=14), men with predominately psychogenic ED who previously responded to IC injections were allocated to 2 ml doses of 3 percent aminophylline plus 0.25 percent isosorbide dinitrate plus 0.05 percent co-dergocrine mesylate or placebo.³¹²

Harms. None of the patients had prolonged erection or priapism, clinically significant cardiovascular adverse events (such as postural dizziness), headache, or pain at site of application.³¹⁴ The other trial did not report any data on harms.³¹²

Efficacy. In the first trial, among men assigned to active treatment, 58.3 percent reported erection sufficient for successful intercourse versus 8.3 percent of those allocated to placebo.³¹⁴ In the second trial, men assigned to the active treatment reported that they experienced erections adequate for intercourse after 3.9 percent of treatment applications versus after 5.3 percent of placebo applications. All successful applications for both the active treatment and placebo groups occurred in a single participant.³¹²

Minoxidil versus Placebo. One crossover trial (n=132) compared the efficacy and harms of minoxidil to placebo.³¹³

Harms. Compared with placebo, men allocated to minoxidil reported more frequent burning at the application site (6 versus 0 percent). No hypotension was reported by either the minoxidil or placebo-treated participants.

Efficacy. Among men allocated to minoxidil, 44.0 percent reported improved erections versus 1.7 percent of those allocated to placebo.

Topical Sildenafil versus Oral Sildenafil. One trial (n=80) compared the efficacy and harms of topical sildenafil to oral sildenafil.¹⁴⁴

Harms. In men assigned to receive topical sildenafil, four (10 percent) reported mild headache. In those assigned to receive oral sildenafil, two participants (5 percent) developed severe headache, one participant (3 percent) reported disturbed visual function, and one participant (3 percent) experienced severe dyspepsia.

Efficacy. Among men assigned to the topical sildenafil plus oral placebo group, 12.5 percent reported improved erections versus 70.0 percent for men assigned to the oral sildenafil plus topical placebo group.

Quantitative Synthesis

No meta-analysis could be performed because of substantial degree of clinical heterogeneity across the trials with regard to patient characteristics, interventions, and the assessed outcomes.

Hormonal Treatments

Literature Search

There were 20 unique studies (in 20 publications) that met eligibility criteria.^{5,77,145,170,231,316-330} One study was reported in two publications^{317,318} and will be referred as Seftel et al. 2004.³¹⁷ Two distinct trials were reported in one publication (studies: a and b).¹⁴⁵ The summary of results for efficacy and harms of two trials^{5,77} comparing combination of PDE-5 inhibitors versus PDE-5 inhibitors alone (and placebo) are presented also in the section for Question 1.

Overview of Trials

Three trials used crossover,^{322,323,326} and the remaining 17 used parallel design. Treatment duration in several trials was 6 months^{319,321,323,330} and in one trial 12 months.³¹⁶ (Evidence Table F-9, Appendix 9)

Populations

The mean age of the subjects in the trials was approximately 57 years. Racial characteristics were reported in only three trials with the majority of the subjects being Caucasians. ED etiology was physiologic in 89 percent of men, psychogenic in 4 percent, and mixed in 7 percent. Not all trials were comprised of exclusively patients with ED.^{5,77,145,231,322,326,329} Several trials required a minimum duration of ED for study entry, of 3 months,⁵ 5 months,³²⁹ or 6 months.^{77,145,231,326} Few trials were comprised of special populations: HIV positive men (n=74),³²⁵ men with major depressive disorder (n=32),³²⁸ obese men with type 2 diabetes (n=48),³²⁴ and men with hypopituitarism (n=9).³²³

While trials generally enrolled men with hypogonadism and/or andropause, the specific sexual dysfunction and testosterone entrance criteria across trials varied widely. With respect to testosterone, all but three trials^{145,323,326} mandated that participants have levels below a specified threshold. Specific entrance criteria regarding total serum testosterone levels varied: 200-350 ng/dL,³²² ≤ 300 ng/dL,^{317,318,320,327,329} ≤ 340 -350 ng/dL,^{231,328} < 400 ng/dL,⁵ < 436 ng/dL,³²⁴ and < 500 ng/dL.³²⁵ Additional trials required that participants have a low total testosterone (range of thresholds from 232 to 434 ng/dL) in combination with a low free testosterone,⁷⁷ low free androgen index,³³⁰ a high SHBG,³²¹ or a free testosterone index between 0.3 and 0.5.³¹⁶ (Tables 23-26)

Interventions

Of the 21 trials involving testosterone therapy for treatment of male ED, most assessed testosterone monotherapy including oral,^{145,316,319,324} intramuscular (IM),^{325,326,328} gel,^{231,317,320,327} patch,^{317,320,327,330} and cream forms.^{322,329} Five trials studied testosterone in combination with a phosphodiesterase inhibitor.^{5,77,145,231} Two other trials studied a cream combining testosterone, isosorbide dinitrate and co-dergocrine.^{322,329} Finally, one trial compared dihydrotestosterone gel versus placebo.³²¹

Study Quality and Reporting

Information on pharmaceutical funding was provided for seven trials.^{5,316,317,320,321,327,330} Only three studies reported using an intention to treat analysis.^{5,316,317} Three of the trials reported

adequate allocation concealment^{319,322,325} and six trials an appropriate double-blinding method.^{5,316,321,322,325,329} There was adequate description of study withdrawals, drop-outs by treatment group in eight trials.^{5,231,321,324,325,327,328,330} Three trials received a total Jadad score of 5,^{5,321,325} two trials received a score of 2,^{316,330} and four received a score of 3.^{322,327,329,331} The remainder received a score of 2 or less.

Outcomes

The eighteen eligible trials utilized diverse efficacy outcome measures. Seven trials reported data on frequency of successful sexual intercourse attempts.^{5,77,231,317,322,326,329} Three other trials reported data on the frequency of full erection during intercourse or the ability to maintain erection during sexual intercourse,^{321,326,328} and three trials reported intercourse satisfaction.^{77,231,319} Other reported outcomes were IIEF-EF^{5,77,145,319,324} and the Male Erectile Dysfunction Quality of Life questionnaire.³³⁰ Two trials reported data for sexual performance defined as the frequency of days with either orgasm, erection, masturbation, ejaculation and/or intercourse in the past week.^{320,327}

Finally, several trials reported data on erections (e.g. frequency of erections,³²³ improvement in erections,^{77,316,325} satisfaction with erections,³²⁷ and full erections with sexual interest).³²² With respect to harms outcomes, five trials reported no adverse effects data.^{5,316,323,324,326} Several trials reported that adverse effects were absent²³¹ or were negligible and without a difference in frequency between treatment groups.^{77,145,319} Data on specific adverse events were reported in only a minority of trials, including skin irritation,^{329,332} increased PSA,^{77,317,322,329,330} headache,^{145,319,321,322,329} and worsening of lower urinary tract symptoms.³¹⁷

Qualitative Synthesis

Oral testosterone versus no treatment. In one open label trial outcomes for efficacy and harms were compared between oral testosterone and no treatment.³²⁴ In this study, 48 diabetic men aged 45-65 years, with ED, increased abdominal girth, and symptoms of mild androgen deficiency, (total testosterone <15.1 nmol/L) were randomized to either 120 mg oral testosterone undecanoate taken daily for 3 months or no treatment. Subjects were excluded from the trial if they had prostate abnormality or any illness considered likely to impair sexual function.

Harms. No adverse events were reported for this trial.

Efficacy. There was a statistically significant improvement in mean IIEF-5 scores (1=absent, 2=mild, 3 = mild to moderate, 4 = moderate, and 5 = severe) at 3 months in testosterone-treated patients compared with those with no treatment assigned (1.06 versus 2.25, $p < 0.05$).

Oral testosterone versus placebo. The outcomes for efficacy and harms associated with the use of oral testosterone versus placebo were compared in two trials.^{316,319} In the first trial, 150 men aged 60–74 years, with symptoms attributed to androgen decline, including decreased libido and erectile quality, and free testosterone <6 pg/ml, were randomized to either 160 mg oral testosterone undecanoate taken daily for 6 months, or 2 gm propionyl-L-carnitine plus 2 gm acetyl-L-carnitine daily or placebo.³¹⁹ Exclusion criteria were prostate enlargement, elevated PSA, and significant LUTS. In the second trial, 76 men aged 60-86 years, with at least two symptoms on the ADAM questionnaire, total testosterone <8 nmol/L, and a free testosterone index (FTI) between 0.3 and 0.5, were randomized either to 80 mg oral testosterone undecanoate taken twice daily for 12 months or placebo.³¹⁶ Patients with a history of prostate cancer, elevated PSA, and significant LUTS were excluded.

Harms. In the first trial, the difference in the occurrence of adverse events between the two treatment groups was not statistically significant. Epigastralgia was reported in 2.5 percent of testosterone-treated versus 2.2 percent of placebo-treated subjects. In the second trial, the occurrence of adverse events was not reported.

Efficacy. In the first trial³¹⁹, men assigned to receive testosterone had median IIEF sexual intercourse satisfaction scores (range 0–15) of 5 (range 3–10) at 6 months ($p < 0.01$). The corresponding median score for patients receiving placebo was 4 (range 3–5). The median IIEF–“EF domain” scores at 6 months of followup for men assigned to receive testosterone and placebo were 16 (range 6–29) and 8 (range 5–21), respectively.³¹⁹ In the second trial, 86 percent and 93 percent of men in the testosterone and placebo group, respectively, reported that their erections were “less strong” at 12 weeks of the followup.³¹⁶

Oral testosterone versus oral testosterone plus sildenafil. One trial evaluated and compared the efficacy and harms between oral testosterone alone and oral testosterone combined with sildenafil.¹⁴⁵ This study enrolled 20 men (mean age: 56 years) with ED of >6 months duration and symptoms of partial androgen deficiency (mean baseline total testosterone 7.3 nmol/L) who failed to respond to 50–100 mg sildenafil given twice weekly for 2 weeks. These men were randomized to 2 months of treatment with either oral testosterone undecanoate alone (120 mg/d) or oral testosterone undecanoate (120 mg/d) plus sildenafil (50–100 mg). Patients with prostate hypertrophy, prostate cancer, and mammary carcinoma were excluded.

Harms. The study reported that apart from mild headache occurring in three patients taking sildenafil 100 mg, no serious adverse events were observed.¹⁴⁵

Efficacy. Men in the oral testosterone group reported no significant change in their IIEF–5 scores from 9.9 (SD 1.4) at baseline to 11.1 (1.5) at 2 months ($p = 0.27$), whereas men in the oral testosterone plus sildenafil group scored 10.1 (1.3) at baseline and 15.0 (1.4) at 2 month followup ($p < 0.01$).

Oral testosterone versus propionyl-L-carnitine plus acetyl-L-carnitine. One trial evaluated and compared the efficacy and harms for oral testosterone versus propionyl-L-carnitine plus acetyl-L-carnitine.³¹⁹ In this study, 150 men aged 60–74 years, with symptoms of androgen decline, and free testosterone below 6 pg/mL, were randomized to receive either 160 mg oral testosterone undecanoate daily for 6 months or 2 gm propionyl-L-carnitine plus 2 gm acetyl-L-carnitine daily or placebo.³¹⁹ Exclusion criteria were prostate enlargement, elevated PSA, and significant LUTS. Results comparing testosterone and propionyl-L-carnitine plus acetyl-L-carnitine are reported here.

Harms. The occurrence of adverse events was not statistically significantly different between the two treatment groups. Epigastralgia was reported in 2.5 percent of the testosterone-treated versus 0 percent of propionyl-L-carnitine plus acetyl-L-carnitine-treated subjects. Mild headache was reported for 2.2 percent of the propionyl-L-carnitine plus acetyl-L-carnitine-treated subjects versus 0 percent for testosterone-treated subjects.

Efficacy. At 6 months, in men assigned to receive testosterone, the median IIEF–“EF domain” score changed from 8 (range 5–19) at baseline to 16 (range 6–29) (within-group difference: $p < 0.01$). The corresponding median score in those assigned to the propionyl-L-carnitine plus acetyl-L-carnitine group changed from 8 (range 5–22) to 24 (range 8–29) (within-group difference: $p < 0.01$).

Oral testosterone plus sildenafil versus sildenafil. One trial evaluated and compared the efficacy and harms outcomes of oral testosterone plus sildenafil compared with sildenafil

alone.¹⁴⁵ This study enrolled 20 men (mean age: 56 years) with ED of > 6 months and symptoms of partial androgen deficiency (mean baseline total testosterone 7.3 nmol/L) who partially responded to previous sildenafil therapy (50-100 mg twice weekly for 2 weeks). The men were randomized to receive a 2-month treatment with either oral testosterone undecanoate (120 mg daily) plus sildenafil (50-100 mg) or sildenafil alone. Patients with prostate hypertrophy, prostate cancer, and mammary carcinoma were excluded.

Harms. Apart from mild headaches occurring in three patients taking sildenafil 100 mg, no serious adverse events were observed.

Efficacy. At 2 months of followup, the difference in mean IIEF-5 scores between patients who received the oral testosterone plus sildenafil versus the sildenafil monotherapy groups was not statistically significant (17.5 versus 15.9, $p \geq 0.05$).

Intramuscular Testosterone (IM) versus placebo. Four trials compared the efficacy and harms of IM testosterone and placebo.^{323,325,326,328}

In the first trial,³²³ nine gonadotropin-deficient males aged 15 years or older (range 16-20) and currently being treated for hypopituitarism, only 3 of whom had partners, were randomized to 1 cc IM testosterone enanthate every 2 weeks versus 2000 units human chorionic gonadotropin three times weekly versus placebo. The active treatment arms each lasted for at least 6 months, while the placebo treatment lasted for 2 months.

In the second trial,³²⁶ 18 men, aged 45-74 years, with ED) were randomized either to IM testosterone enanthate 200 mg given twice weekly for 6 weeks or IM placebo. Patients with major disorders, a history of substance abuse, obesity, or major psychopathology were excluded from the trial.

In the third trial,³²⁵ 74 HIV-positive men (CD4 <400), with ED or substantial loss of sexual desire, with low-to-normal levels of total testosterone (<22.6 nmol/L if the patient had AIDS plus wasting or fatigue, or otherwise <17.4 nmol/L) and at least one mood symptom of hypogonadism, were randomized either to IM testosterone cypionate 400 mg given twice daily for 6 weeks or placebo.

In the fourth trial,³²⁸ 32 men ≥ 35 years (mean age: 52 years) with depression and total testosterone ≤ 350 ng/dL were randomized either to IM testosterone enanthate 200 mg given once weekly for 6 weeks or IM placebo. Patients with psychiatric disorders or abnormal prostate exam result (men aged > 50 years) were excluded.

Harms. In two trials,^{323,326} no adverse events were reported. In the third trial,³²⁵ men who received testosterone were more likely to report acne (testosterone: 20.5 percent versus placebo: 0 percent). Differences between men in the testosterone and placebo groups with respect to the occurrence of irritability (17.9 versus 17.1 percent) and testicular atrophy (5.1 versus 0 percent), were not statistically significant. In the fourth trial,³²⁸ it was reported that no adverse events occurred except that one placebo-treated subject had a MI.

Efficacy. In the first trial,³²³ weekly frequency of erections in the testosterone and placebo treatment groups were 7.9 (SD 6.1) and 4.9 (SD 3.3), respectively. The between-group difference was not statistically significant.

In the second trial,³²⁶ results were based on 12 (67 percent) men who completed all assessments. At week 6, men in the IM testosterone group reported a median number of "sex with partner" of 1.25 times per week versus 0.54 times per week for men in the placebo group (between-group difference: $p \geq 0.05$). There was no difference in the degree of erection during

sex with partner (scale 1–6, with 1 = “none” and 6 = “full”), with a mean score of 5.5 for each group, or in the degree of erection during masturbation.

In the third trial,³²⁵ results were reported for the 52 men (70 percent) who completed the treatment schedule. Within this group, 62.5 percent of men who received testosterone versus 20 percent of those who received placebo reported that their erectile function was much or very much improved (RR = 3.12, 95 percent CI: 1.25–7.82).

In the fourth trial,³²⁸ the difference in frequency (1 = less than 1 per month” and 2 = 1–2 per month”) of full erections during one month between men in the IM testosterone and IM placebo groups was not statistically significant (1.77 versus 1.53)

Testosterone (IM) versus human chorionic gonadotropin (IM). One trial compared the efficacy and harms of IM testosterone versus IM human chorionic gonadotropin.³²³ In this trial, 9 gonadotropin-deficient men aged 15 years or older (range 16–20) being treated for hypopituitarism, were randomized to 1 cc IM testosterone enanthate given every 2 weeks versus 2000 units of human chorionic gonadotropin 3 times weekly versus placebo. The active treatment arms each lasted for at least 6 months, while the placebo treatment lasted for 2 months.

Harms. No adverse event data were reported.

Efficacy. The weekly frequency of erection was not different between the two groups of testosterone and human chorionic gonadotropin treatment (7.9 versus 8.2).

Gel testosterone versus placebo. The efficacy and harms of gel testosterone versus placebo were compared in one trial.³¹⁷ In this trial, 406 hypogonadal men (total T <300 ng/dL) aged 20–80 years (mean age: 58 years) reporting one or more symptoms of low testosterone deficiency (i.e. fatigue, decreased muscle mass, reduced libido), were randomized to 50 mg gel testosterone (Testim) daily versus 100 mg gel testosterone (Testim) daily versus 24.4 mg patch testosterone (Androderm) versus placebo.

Harms. In total, 29.3 percent of men receiving 50 mg gel testosterone; 36.8 percent receiving 100 mg gel testosterone and 40.4 percent receiving placebo reported at least one treatment-related adverse event (including application site reactions, BPH, increase in blood pressure, increase in hematocrit, gynecomastia, headache, hot flashes, insomnia, mood swings, or spontaneous erections). These differences were not statistically significant. One participant from the group treated with 50 mg gel testosterone, five in the group treated with 100 mg gel testosterone, and none treated with placebo withdrew due to an adverse event.

Efficacy. At day 30, among men with sexual partners (63 percent of randomized men), 24 percent of placebo-treated men reported an increase from baseline in the number of days in the past week with sexual intercourse, compared with 31 percent of 50 mg gel testosterone-treated men (p <0.05 versus placebo) and 39 percent of 100 mg gel testosterone men (p = 0.0096 versus placebo).

Gel testosterone versus patch testosterone. The efficacy and harms of gel testosterone versus patch testosterone was compared in three trials.^{317,320,327} In the first trial,³²⁷ 227 men aged 19–68 years (mean age: 58 years) with total testosterone levels <10.4 nmol/L (300 ng/dL) were randomized to 50 mg gel testosterone (Androgel) given daily versus 100 mg gel testosterone (Androgel) given daily versus 5 mg patch testosterone (Androderm) given daily. Patients with increased PSA, significant skin disease, and substantial under- or overweight were excluded.

The other two trials^{317,320} had similar protocols. The inclusion criteria were low total testosterone (≤ 10.4 nmol/L³²⁰ and ≤ 300 ng/dL³¹⁷) and/or symptoms of hypogonadism (i.e. fatigue, decreased muscle mass, reduced libido, or “reduced sexual functioning” of nonmechanical

origin). Both trials randomized men to 50 mg gel testosterone (Testim) daily versus 100 mg gel testosterone (Testim) daily (deliver a daily dose of 5 and 10 mg testosterone, respectively). The first of these trials included an additional group randomized to 5 mg patch testosterone (Andropatch),³²⁰ and the second trial randomized two additional groups to 24.4 mg patch testosterone and placebo.³¹⁷

In the first of these trials,³²⁰ men were to remain on their initially assigned treatment dose throughout the 90 day study, but in the second trial,³¹⁷ titration from the initial gel testosterone dose was possible at 60 days.

Harms. In the first trial,³²⁷ skin irritation was reported by 5.7 percent of men who received 50 mg gel testosterone, 5.3 percent of those who received 100 mg gel testosterone, and 65.8 percent of those who received patch testosterone. Urogenital adverse events (e.g. prostate enlargement, increased PSA) were reported by 9.6 percent of men who received 50 mg gel testosterone, 5.1 percent of those who received 100 mg gel testosterone, and 0 percent of those who received patch testosterone.

In the other two trials,^{317,320} approximately 30–35 percent of men who received either of the gel testosterone groups versus 60 percent of those who received patch testosterone reported at least one treatment-related adverse event. Most common adverse events were skin application site reactions and less frequent events were BPH, increase in blood pressure, increase in hematocrit, gynecomastia, headache, hot flashes, insomnia, mood swings, or spontaneous erections. The second of these trials³¹⁷ reported that withdrawals due to adverse events occurred in one 50 mg gel testosterone subject, five 100 mg gel testosterone subjects, and 15 patch testosterone subjects. In the same trial, two patients in the patch testosterone arm were diagnosed with prostate cancer.³¹⁷

Efficacy. In the first trial,³²⁷ patients in the gel testosterone group experienced slightly greater sexual enjoyment compared with those receiving the testosterone patch ($p = 0.0113$).

In the second trial,³²⁰ compared with baseline, men in the 50 mg gel testosterone, 100 mg gel testosterone, and patch testosterone groups experienced 38, 50 and 33 percent improvement in “sexual performance” (within-group comparison: $p < 0.05$; between-group comparisons: $p \geq 0.05$). Similarly, all three groups significantly improved from baseline, but without between-group differences for the domains of sexual motivation and sexual desire. Although spontaneous erections were significantly increased in frequency compared with baseline in both gel testosterone groups, and not in the patch testosterone group, there were no significant between-treatment group differences.

In the third trial,³¹⁷ at baseline approximately 20 percent of men reported having no sexual partner available, and approximately 45 percent reported no sexual intercourse during the past week. At day 30, among men with sexual partners for whom these data were reported (61 percent of randomized men), 31 percent of 50 mg gel testosterone men reported an increase from baseline in the number of days in the past week with sexual intercourse versus 39 percent of 100 mg gel testosterone men (versus 50 mg, $p \geq 0.05$, and versus patch, $p = 0.03$) and 21 percent of patch testosterone men (versus 50 mg group, $p \geq 0.05$).

Gel testosterone versus gel testosterone plus tadalafil. One trial compared the efficacy and harms of gel testosterone versus gel testosterone plus tadalafil.²³¹ This trial enrolled 69 hypogonadal men (total testosterone < 3.4 ng/ml) aged 34–78 years (mean: 59 years), who had > 6 months of ED and a history of nonresponse (i.e. poor IIEF score or persistent patient/partner dissatisfaction) to 20 mg tadalafil. Men were randomized to 50 mg gel testosterone (Testogel)

daily for 4 weeks followed by concurrent treatment with tadalafil 20 mg twice weekly for 9 weeks versus 50 mg gel testosterone (Testogel) daily for 10 weeks followed by concurrent treatment with tadalafil 20 mg twice weekly for 3 weeks. All treatments were open label.

Harms. No adverse events were observed.

Efficacy. At 10 weeks, there was no difference between treatment groups in mean IIEF intercourse satisfaction score (13.1 +/- 0.8 versus 12.8 +/- 0.9, WMD = 0.30, 95 percent CI: -0.10 to 0.70). After 13 weeks, 66.7 percent of patients were rated sufficient to good for successful intercourse completion in group one versus 63.6 percent in group two (RR = 1.05, 95 percent CI: 0.68– 1.62), and 47.6 percent of patients were rated sufficient to good for intercourse frequency in group one versus 59.1 percent in group two (RR = 0.81, 95 percent CI: 0.46–1.42).

Gel testosterone plus sildenafil versus sildenafil. This double-blind trial⁵ studied 75 men aged 26–79 years (mean age: 58 years) with ED of >3 months, and total testosterone <400 ng/dL. The men, refractory to prior sildenafil therapy were randomized to 1 percent gel testosterone daily plus 100 mg sildenafil once daily for each day with sexual activity as needed for 12 weeks versus 100 mg sildenafil as needed. Exclusion criteria were: history of prostate cancer, prostate disease with diminished urine flow rate, neurologic ED, substance abuse, or significant or uncontrolled medical or psychiatric conditions.

Harms. One subject in gel testosterone plus sildenafil arm withdrew due to adverse events. There were no withdrawals due to adverse events among patients receiving sildenafil alone.

Efficacy. In men receiving gel testosterone plus sildenafil, the mean number of successful sexual attempts (per week) ranged from 1.7 to 2.1. The corresponding range for those receiving sildenafil was 1.5–2.4 per week. At the end of the study, the proportions of men with scores of 4–5 on IIEF–Q3/Q4 was statistically nonsignificantly greater in the combination therapy group than in the sildenafil only group (51.4 versus 39.4 percent; RR = 1.30, 95 percent CI: 0.77–2.21). Men who received gel testosterone plus sildenafil had greater mean change from baseline in the IIEF “EF” domain score compared with those receiving sildenafil and placebo. The between-group differences were statistically significant at week 4 (4.4 versus 2.1, 95 percent CI: 0.3–4.7).

Cream testosterone versus cream testosterone plus isosorbide dinitrate plus co-dergocrine. One trial compared the efficacy and harms of cream testosterone versus cream testosterone plus isosorbide dinitrate plus co-dergocrine.³²² In this two phase crossover trial, 42 men aged 41–67 years (mean: 54 years) with ED, decreased libido and total testosterone 200–350 ng/dl were randomized to 0.8 percent cream testosterone versus 0.8 percent cream testosterone plus 0.5 percent isosorbide dinitrate plus 0.06 percent co-dergocrine. Each treatment was to be applied daily at bedtime to the penile shaft and glans; if intercourse was going to occur then the cream was applied 15 minutes before intercourse. Each arm of the crossover lasted 30 days.

Harms. Five men who received combination therapy reported a mild transient headache versus none who received cream testosterone alone. No significant increase in PSA occurred.

Efficacy. In total 67 percent of men who received cream testosterone plus isosorbide dinitrate plus co-dergocrine reported a complete response to treatment (full erection and sexual interest compared with 31 percent of men who received cream testosterone alone (RR = 2.15, 95 percent CI: 1.31–3.55). Among men with psychogenic ED (n = 19), 84.2 percent of those who received combination therapy reported a complete response versus 57.9 percent of those who received cream testosterone alone (RR = 1.45, 95 percent CI: 0.95–2.24). Among men with vascular ED (n=18), 55.6 percent of those who received combination therapy reported a complete response versus 11.1 percent of those who received cream testosterone alone (RR = 5.00, 95 percent CI:

1.27–19.68). Among men with neurogenic ED (n = 5), two who received combination therapy reported a complete response versus none who received cream testosterone alone. Among all men with complete responses, those who received cream testosterone plus isosorbide dinitrate plus co-dergocrine reported a mean of 6.46 (SD 2.7) full erections with satisfactory intercourse per month versus 4.05 (SD 1.8) for men who received cream testosterone only (WMD = 2.41, 95 percent CI: 1.43 to -3.39).

Cream testosterone plus isosorbide dinitrate plus co-dergocrine versus placebo. One trial compared the efficacy and harms of cream testosterone plus isosorbide dinitrate plus co-dergocrine versus placebo.³²⁹ In this trial, 89 men aged 35-65 years (mean: 54 years) with more than 5 months of decreased libido and of decreased frequency and quality of sexual erections, and total testosterone <300 ng/dL, were randomized to 0.8 percent cream testosterone plus 0.5 percent isosorbide dinitrate plus 0.06 percent co-dergocrine versus placebo. Each treatment was applied twice daily to the shoulder for two months. Patients with abnormal rectal exam results, PSA >4 ng/ml, and urine flow rate <12 ml/second were excluded.

Harms. Among men who received combination treatment, 11.1 percent reported headaches, 2.2 percent reported skin irritation (versus 0 percent for placebo subjects). Neither treatment group reported priapism.

Efficacy. Of men who received combination therapy, 40 percent reported at least one full erection with successful intercourse during followup versus 0 percent of those who received placebo. No men who received placebo reported full erections after two months of treatment in any ED etiology subgroup, whereas among men who received combination treatment, full erections were reported by 68.8 percent of men with psychogenic ED (n = 11/16), 11.1 percent of men with vascular ED (n = 1/9), 37.5 percent of men with neurogenic ED (n = 3/8), and 25 percent of men with mixed ED (n = 3/12). Men who received combination therapy also reported improved enjoyment with partner and satisfaction with intercourse.

Patch testosterone versus placebo. The efficacy and harms of patch testosterone versus placebo were evaluated and reported in two trials.^{317,330} The design and study population of the first trial³¹⁷ are described elsewhere in two other sections: Gel Testosterone versus Placebo and Gel Testosterone versus Patch Testosterone. In the second trial,³³⁰ 39 “borderline” hypogonadal men (total testosterone <10 nmol/l or a free androgen index <30 percent) aged 40–77 years (mean: 62 years) were randomized to 6 months of treatment either with 5 mg patch testosterone (Testoderm) once daily or placebo.

Harms. In the first trial,³¹⁷ 62.7 percent of men assigned to the patch testosterone group versus 40.4 percent of those in the placebo group had at least one treatment-related adverse event. Withdrawals due to a skin reaction occurred in 15 percent of patch testosterone subjects, but not in placebo subjects.

In the second trial,³³⁰ 15 percent of patch testosterone subjects and 5.3 percent of placebo subjects had an increased hematocrit. One subject assigned to the placebo group developed angina.

Efficacy. In the first trial,³¹⁷ among men with sexual partners (62 percent of randomized men), 24 percent of men receiving placebo reported an increase from baseline in the number of days in the past week with sexual intercourse, compared with 21 percent of men receiving patch testosterone (p ≥ 0.05, versus placebo).

In the second trial,³³⁰ men who received placebo had a statistically significantly greater decline from baseline in their Male Erectile Dysfunction Quality of Life questionnaire

(MEDQoL) score (range 0-100) compared with men who received patch testosterone (from 61.4 at baseline to 61.8 at followup for patch testosterone versus from 54.2 at baseline to 43.6 at followup for placebo) ($p = 0.017$).

Patch testosterone plus sildenafil versus sildenafil. One open label trial compared the efficacy and harms of patch testosterone plus sildenafil versus sildenafil.⁷⁷ This trial enrolled 20 men aged 48-66 years (mean age: 56 years), with arteriogenic ED of ≥ 6 months duration, and refractory to prior sildenafil therapy, The inclusion criteria were: total testosterone 10-13 nmol/L and free testosterone 200-300 pmol/L, no response to previous treatment with 100 mg patch testosterone, and an IIEF erectile function score of less than 24 in response to 100 mg sildenafil. Men with a history of hematological disorders or prostate disease were excluded. Men were randomized to 5 mg patch testosterone daily plus 100 mg sildenafil, as needed for one month versus placebo patch daily plus 100 mg sildenafil, as needed.

Harms. Data on adverse events was not reported.

Efficacy. Men who received placebo patch plus sildenafil did not improve in erectile function compared with baseline on any IIEF question or domain reported. Those in the combination group (patch testosterone plus sildenafil) had a greater endpoint percentage of successful intercourse attempts (data not provided), higher “EF domain” scores (21.8 +/- 2.1 versus 14.2 +/- 0.7, WMD = 7.60, 95 percent CI 6.23–8.97), an increased number of sexual intercourses (2.8 +/- 0.9 versus 1.5 +/- 0.5, WMD = 1.30, 95 percent CI 0.66–1.94), greater intercourse satisfaction (12.1 +/- 1.6 versus 7.7 +/- 1.2, WMD = 4.40, 95 percent CI 3.16–5.64), and more frequently reported that treatment had improved their erections (80 versus 10 percent, RR = 8.00, 95 percent CI: 1.21–52.69).

Dihydrotestosterone gel versus placebo. One trial compared the efficacy and harms of dihydrotestosterone gel versus placebo.³²¹ This trial enrolled 120 men with nocturnal penile tumescence no more than once weekly, at least one symptom of andropause (decreased libido, ED, “urinary disorder,” asthenia, or depressed mood), and total serum testosterone <15 nmol/L and/or SHBG >30 nmol/L. Men were randomized to daily dihydrotestosterone gel versus placebo for 6 months. Dihydrotestosterone gel was initiated at 125 mg daily and could be titrated to 250 mg daily after 30 days according to DHT levels.

Harms. Of men who received dihydrotestosterone gel, 5 percent reported mild headache (versus 3.3 percent for placebo) and 3.3 percent reported mild depression (versus 3.3 percent for placebo).

Efficacy. At baseline and 6-month followup, participants rated their ability to maintain erection during intercourse on a scale of 1–6, in which 2 = “75 percent of intercourses” and 3 = “50 percent of intercourses. Mean scores reported for participants who received dihydrotestosterone were 2.26 at baseline and 3.24 at 6 months, whereas those for the participants in the placebo group were 2.53 at baseline and 2.81 at followup ($p = 0.04$ for mean change from baseline between treatment groups).

Quantitative Synthesis

There was a large degree of clinical heterogeneity in the eligible testosterone trials with regard to patient characteristics (e.g. characterization of sexual dysfunction, testosterone level), interventions (e.g. specific testosterone formulation, dose and duration of treatment, use of testosterone monotherapy or combination), and outcomes assessed (e.g. various definitions of sexual intercourse success, and of erection improvement). Therefore, no MA was performed.

Other Treatments (Off Label)

Literature Search

There were 21 (in 22 publications) unique studies reporting on different off label oral treatments that met the eligibility criteria of this review.^{265,333-353}

Note: Korenman et al. (1994)³⁴⁹ is a reprint of Korenman et al. (1993).³⁴⁵

Overview of Trials

The trials evaluated the following treatments: phentolamine (one additional trial of phentolamine is described in the Sildenafil section¹²⁴),^{333,338} trazodone,^{336,337,339,341,344} cabergoline,^{162,350} pentoxifyling (in 4 reports),^{340,343,345,349} and miscellaneous medications. The latter consisted of treatments with moclobemide,³³⁴ isoxsuprine,³³⁵ opiate antag,³⁴² ACE,³⁴⁶ moxonidine,³⁴⁷ dehydropiand,³⁴⁸ tetrahydrobiopterin (BH4),³⁵³ Myoinositol,³⁵¹ and Tianeptine.³⁵² (Table F-10, Appendix F)

Phentolamine. Two trials investigated the effect of phentolamine in comparison to placebo.^{333,338} One of the trials was used a crossover design (n = 5)³³³ and the other a parallel design (n = 44).³³⁸ Subjects in these trials were generally older than 18 years, with ED of at least 3 months of duration and various etiologies (the majority with organic causes). Total Jadad score was 3 for both trials.^{333,338} The allocation concealment was unclear for both trials. The trial outcomes were patient diary³³⁸ and RigiScan measures on nocturnal erectile activity.³³³

Harms. One trial reported one adverse event occurring in a patient taking 60 mg dose.³³⁸ In another trial, no adverse events occurred.³³³ No serious adverse events were reported in any of these trials.

Efficacy. Forty to 50 percent of patients improved their erections with higher doses of phentolamine (40 and 60 mg) compared with 30 and 20 percent with lower dose (20 mg) or placebo respectively.³³⁸

Oral phentolamine (40 mg, 3 consecutive nights) administered before sleep increased the number of erectile events with rigidity of at least 60 percent lasting at least 10 minutes (p = 0.02), and the rigidity activity unit (RAU) per hour of sleep both at the base (p = 0.023) and the tip of the penis (p = 0.019), which were not different from changes after administration of placebo.³³³

Trazodone versus other active treatment versus placebo. Five trials reported on the effect of treatment with trazodone (n = 333, range: 34-100 participants).^{336,337,339,341,344} The trials were conducted in Belgium,³³⁶ Turkey,^{341,344} the Netherlands,³³⁹ and US.³³⁷ Total Jadad score ranged from 1³⁴¹ to 4³³⁹ with a mean of 2.8.

Four studies used a parallel^{336,339,341,344}, and one crossover design.³³⁷ Trazodone was administered at doses of 50 mg,^{337,344} 150 mg,^{339,341} or 200 mg³³⁶ per day. Aydin et al. (1995)³⁴¹ compared the effect of trazodone to oral testosterone (120 mg/d), hypnosis or placebo. Kurt et al. (1994) compared trazodone to ketanserin and mianserin (antiserotonergic agents).³⁴⁴ Subjective measures such as self reported questionnaires to address improvement in erection with treatment were used in four trials.^{336,337,341,344} The outcomes based on RigiScan measurements (i.e. NTP, rigidity) were reported in two trials.^{336,339}

Harms. In one trial, numerically more patients in the trazodone group reported dry mouth (25.0 percent), drowsiness (18.8 percent), and fatigue (14.6 percent) compared with the placebo

group (16.7, 12.5, and 8.3 percent, respectively).³³⁷ Another study reported 50 percent more withdrawals due to adverse events in trazodone group versus the placebo group.³³⁹ In the trazodone arm of one trial, five patients experienced sedations; no information on adverse events for other groups (i.e., testosterone, hypnosis, and placebo) was reported.³³⁹ In a trial comparing the efficacy and harms of trazodone to mianserin,³⁴⁴ two patients (8 percent) withdrew due to adverse events from the mianserin treatment group and two patients (8 percent) in the trazodone group developed serious adverse events (priapism and sedation).

Efficacy. Improvement in erection measured by Index of Sexual Satisfaction was 19 and 24 percent in trazodone and placebo groups, respectively.³³⁷ One study reported minor improvement from baseline in trazodone group but the between-group (versus placebo) difference for base rigidity (> 60 percent), nocturnal erection, or morning erection, was not statistically significant.³³⁶ For one trial, improved erections were observed in 66, 60, 80, and 39 percent of the patients treated with trazodone, testosterone, hypnosis, and placebo, respectively.³⁴¹

The proportions of patients with positive response (3 or more successful intercourse attempts during 30 days and rigidity \geq 30 minutes) at the end of 30 days of treatment with 50 mg trazodone, 20 mg ketanserin, 10 mg mianserin, and placebo were 65.2, 19.1, 31.6, 13.6 percent, respectively.³⁴⁴

Cabergoline versus placebo. Two trials were identified with a total of 452 participants randomly assigned to treatment with cabergoline (n = 225) or placebo (n = 222).^{162,350} The trials were conducted in Germany³⁵⁰ and Iran.¹⁶² The German study recruited patients with no organic cause of ED. The Iranian study recruited non-responders to previous sildenafil therapy. The mean age of participants was approximately 40 years. Total Jadad scores for the two trials were 3³⁵⁰ and 5.¹⁶² The allocation concealment was unclear in one³⁵⁰ and adequate in the other.¹⁶² Both studies were parallel design and placebo controlled. The dose of cabergoline was 0.5 mg per day³⁵⁰ or 0.5–1 mg.¹⁶² In both trials, the IIEF was used to measure baseline severity and treatment effect.

Harms. The number of patients with any adverse events was greater in cabergoline group (12.2 percent versus 2.0 percent, p = 0.001).¹⁶² Withdrawals due to adverse events were higher in the active arm versus placebo in the study which reported this information (5.9 versus 1.01 percent).¹⁶² No information on serious adverse events was reported in any of these trials.

Efficacy. Both trials reported numerically or statistically significant improvements in the results with cabergoline 0.5 mg versus placebo. The German study reported a change of 11.7 in mean scores of erectile domain of IIEF from baseline in comparison to a change of 6.9 in the placebo group. In the Iranian trial, patients improved by 5 points in the Intercourse Satisfaction domain of the IIEF.¹⁶² The improvement in Q3 (frequency of penetration), and Q4 (ability to maintain the erection after sexual penetration) was 45.5 and 51.4 percent in the cabergoline arm versus 15 and 20 percent in the placebo arm, respectively.¹⁶²

Pentoxifylline. Three parallel design studies were included (n = 114, range 18–60).^{340,343,345} Mean age of participants was approximately 60.6 years. The trials were conducted in Turkey³⁴⁰ and US.^{343,345} The trial duration ranged from 2 to 3 months.

Total Jadad score ranged from 1³⁴⁰ to 2.^{343,345} Allocation concealment methods were unclear in all three studies.

All three trials were placebo controlled administering 1.2 g/day of pentoxifylline and evaluating subjective measures of improvement in erection. One study also included RigiScan outcomes (i.e., NPT, penile rigidity).³⁴³

Pentoxifylline versus Placebo.

Harms. The adverse events including nausea and headaches were transient and mild.³⁴⁰ Harms data was not presented in the other two trials.^{343,345}

Efficacy. Full erection (sufficient for penetration) was achieved in 10 versus 0 percent³⁴⁰, and in 78 versus 0 percent³⁴⁵. One trial³⁴³ reported a slight decrease in average percent rigidity after 3 months of treatment with pentoxifylline.

Miscellaneous treatments of ED. Nine trials were identified (n = 449, range: 11–176 participants) that evaluated miscellaneous off label medications for treatment of ED.^{334,335,342,346-348,351-353} Information on the participants' characteristics, intervention and outcomes is presented in Table 32.

These were five parallel-arm^{334,346,348,351,353} and four crossover trials.^{335,342,347,352} Eight trials were placebo controlled^{334,335,342,346,348,351-353} and one trial used active medication as comparator.³⁴⁷

Funding sources were reported for only three trials.^{334,347,352} One trial had no source of support.³³⁵

Total Jadad scores ranged from 2^{335,346,353} to 4.³⁴⁸ The methods for allocation concealment were unclear in all studies.

The mean IIEF scores were measured in four trials.^{346-348,351} Other self-reported outcomes related to erection were assessed in four trials^{334,335,342,352} One trial assessed and reported only rigidity measures (RigiScan).³⁵³

Harms. see Table 27.

Efficacy. see Table 27.

Question 3a. What Are the harms of Pharmaceutical Treatments for Male Patients with ED?

Specific Adverse Events Oral Medications: PDE-5 inhibitors

Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

In total, 194 records were identified that discussed incidence of NAION in men treated with sildenafil. Of these, 10 records reporting on cases of nonarteritic anterior ischemic optic neuropathy (NAION) were included in this review.³⁵⁴⁻³⁶³ These records were seven case reports^{354-359,363}, two case series^{361,362}, and one retrospective cohort study.³⁶⁰ The remaining records not reporting NAION were excluded.

This review identified 19 cases of NAION reported between 1999 and 2007. Findings of the retrospective cohort study, of 4,157,357 veterans 50 years of age or older indicated that men who were prescribed PDE-5 inhibitors over the period of 2 years were not at increased risk of being diagnosed with NAION compared with those who were not prescribed PDE-5 inhibitors (RR = 1.02, 95 percent CI: 0.92–1.12).³⁶⁰ Note that for possible NAION, the corresponding relative risk was statistically significant (RR = 1.34, 95 percent CI: 1.17–1.55). In all cases except for one,³⁶² the administered minimum dose of sildenafil was 50 mg. Overdose of sildenafil was reported in two case reports.^{354,363} Further details can be found in Table 28.

Injection Treatments

Penile Fibrosis (Non-randomized studies: observational studies and clinical trials)

In total, 20 non-randomized studies (retrospective observational cohort, and clinical trials) reporting the absence or presence of penile fibrosis in long-term followup (at least 6 months) met the eligibility criteria for inclusion in the review (in 20 publications).³⁶⁴⁻³⁸³ Of these, 13 were clinical trials of prospective design^{364-366,368-371,376-378,380,381,383} and seven were retrospective cohort studies.^{367,372-375,379,382}

The number of subjects included in the 20 studies ranged from 10³⁷⁰ to 1089.³⁷⁴ The majority of the study subjects were middle aged (mean age range: 50-62 years). Four trials included special population subgroups such as patients diagnosed with diabetes,^{366,369} multiple sclerosis,³⁸¹ and prostate cancer followed by prostatectomy.³⁶⁷ One study evaluated ICI therapy in geriatric men (age >65 years).³⁸²

Prostaglandin (PGE₁) alone or in combination with other vasoactive agents (papaverine and/or phentolamine) was evaluated in 15 studies.³⁶⁴⁻³⁷⁸ Papaverine alone or in combination with phentolamine (or verapamil) was evaluated in 13 studies.^{366,367,369,371,373,374,376,377,379-383} The duration of treatment ranged from 3 months³⁶⁸ to 10 years.³⁶⁶ In the majority of studies, the approximate frequency of PGE₁ injections was up to twice per week with a mean dose of 20 µg or lower.^{365,370,372,375,378}

Of the 20 studies, five explicitly reported the absence of new cases of fibrosis.^{367,368,370,371,378} and six studies reported the incidence of fibrosis to be under 5 percent.^{373,376,377,379-382}

The proportion of patients with fibrosis in studies that used PGE₁ alone after at least one year of followup ranged from 4.4 percent³⁶⁵ to 23.3 percent.³⁷² In two of these studies no cases of fibrosis were observed.^{370,378} For example, one retrospective cohort study in Australian men³⁷² reported an incidence of fibrosis in 57 of the 245 patients (23.3 percent) who had been treated with PGE₁ 2–60µg (mean 13µg) for 2 years on average. The total amount of PGE₁ (p = 0.0062) and the total number of injections (p = 0.0032) over the whole treatment period were statistically significantly greater in the men with fibrosis. However, there were no significant differences between the men who developed fibrosis and men who did not with regard to duration of followup, injection frequency, or dose per injection.³⁷² In contrast, in another prospective trial,³⁶⁵ only three (4.4 percent) of the 68 PGE₁-treated patients (the mean PGE₁ dose: 11.6µg) developed fibrosis after at least one year of followup. Of these three patients, only one patient injected PGE₁ more frequently and at a higher dose (20-60µg every 2-3 days) than it was prescribed (one injection 10-20µg per 5-7 days).

The largest study that evaluated and compared adverse events in patients receiving ICI injections with different medications was a retrospective U.S. study of 1089 patients who had received either 5-10µg PGE₁, trimix (1.47µg PGE₁ plus 4.41 mg papaverine plus 0.5 mg phentolamine), papaverine plus phentolamine, or 10µg PGE₁ plus 30 mg papaverine for up to 80 months. This study investigated reasons for attrition in each treatment group. Of the subjects discontinuing the treatment, penile scarring/nodules was the reason for study withdrawal in 23 percent (6/26), 11 percent (4/36), and 10 percent (8/75) of the subjects receiving triple therapy (PGE₁/papaverine/ phentolamine), combination papaverine and phentolamine therapy, and PGE₁ monotherapy, respectively. None of the patients receiving the combination of PGE₁ with papaverine developed penile scarring/nodules.³⁷⁴ In a controlled trial conducted in Taiwan,³⁷⁷ 51 patients with ED (mean age: 58 years) received self-injections either with 20µg PGE₁ or 30 mg papaverine for about 12 months (range: 1.5-30.5 months). Two patients (3.9 percent) developed fibrosis after 60 mg papaverine injections. No cases of fibrosis were observed in patients after PGE₁ injections.³⁷⁷ Similarly, in a trial conducted in Turkey,³⁷⁶ 69 patients with ED (mean age: 52.6 years) were divided to receive injections either with 10µg PGE₁ (n = 13 patients) or 15-30 mg papaverine (n = 56 patients) for approximately 12 months. Two patients (3.6 percent) in the papaverine group developed fibrosis versus none in the PGE₁ group. In a retrospective North American cohort study,³⁷³ 108 ED patients received self-injections with either 30 mg papaverine (n = 21 patients), the combination of 25 mg papaverine with 0.83 mg phentolamine (n = 77), or PGE₁ (n = 2 patients) were followed-up for 5 years. Only one of the 108 subjects developed fibrosis (the assigned intervention not reported). (Table 29)

Chapter 4. Discussion

This evidence report summarized, critically appraised, and compared the evidence on clinical benefits and harms associated with the administration of different types of pharmaceutical agents in the treatment of erectile dysfunction (ED).

Strength of the Evidence

Erectile dysfunction is a complex condition related to psychosocial and biological factors. It is difficult to reliably document and measure the degree of treatment success in patients diagnosed with this condition. Most of the validated and clinically relevant efficacy outcomes assessed in clinical trials of ED patients are subjective.

The strength of evidence regarding the utility of routine endocrinological blood tests found in this review was limited in terms of the both amount and quality of data. The studies were heterogeneous with respect to patient population characteristics, diagnostic methods, estimates of prevalence, and laboratory methods used (e.g. cut-off values, total, free, or bioavailable hormonal levels).

The placebo-controlled randomized trials that evaluated the efficacy and harms of PDE-5 inhibitors provided large amount of evidence and consistently indicated that patients who received PDE-5 inhibitors experienced greater improvements in erectile dysfunction compared with placebo-treated patients. The magnitude of benefit was clinically relevant and statistically significant. The methodological and reporting quality of the evidence provided by these trials was better than that for other studies (e.g. trials with active control arms or trials evaluating sublingual apomorphine, injections, topical, hormonal, or off-label therapies). Most of these trials enrolled ED patient populations with a broad spectrum of etiologies or comorbidities and assessed the same set of clinically relevant and validated outcome measures. Given the reported exclusion criteria for these trials, their results may not be readily applicable to ED patients with major chronic disorders (e.g. cancer, CVD, diabetes, psychiatric disorders, hepatic or renal diseases) or post-surgery patients, because the magnitude of clinical benefit conferred by PDE-5 inhibitors in such patients is relatively modest.³⁸⁴⁻³⁸⁶ Furthermore, vardenafil trials may have been comprised of more responsive patients due to the fact that about half of these trials excluded patients refractory to prior sildenafil therapy, thereby limiting the applicability of the results to a broader population of ED patients. On average, trials that evaluated injected (e.g. intracavernosal, subcutaneous), intra-urethral, topical, or other treatments were of relatively lower methodological and reporting quality.

A common limitation of these trials was a failure to assess and/or report clinically relevant treatment efficacy outcomes used for the measurement of the degree of erectile dysfunction (e.g. mean scores for International Index of Erectile Function, Sexual Encounter Profile, Global Assessment Question regarding improved erection). The most commonly assessed efficacy outcomes in these trials were penile rigidity (using RigiScan) and the quality of erections achieved at home. The trials did not report information on the methods used for randomization, blinding, and allocation concealment. Many study results may have been biased in favor of active treatment, because the analyzed samples predominantly included responders and excluded many randomized participants from their efficacy analyses. There was substantial heterogeneity across the hormonal treatment trials with respect to the diversity of patient populations (variations in inclusion/exclusion criteria; not

Appendixes and Evidence Tables for this report are provided electronically at <http://www.ahrq.gov/downloads/pub/evidence/pdf/erectedvs/erecdvs.pdf>

all patients had ED), treatment interventions (type of intervention, mode of administration, dose, dosing regimen, duration), and the assessed outcomes.

In general, the reporting of harms was less consistent and detailed than that of efficacy outcomes. For example, the occurrence of any or serious adverse events was not reported in many trials. The definition of a serious adverse event may have varied across the trials. Some trials reported only most frequently encountered or treatment-related adverse events, the ascertainment of which may be prone to subjective judgment. In some instances, it was not explicitly defined whether the number and percentage referred to the actual number of adverse events or to the number of patients with at least one adverse event. In open label trials, patients or investigators may have over- or under-reported the incidence of adverse events because of their knowledge of the assigned treatment. Moreover disease-specific complications in patients with comorbidities and/or disorders known to cause ED could have been overlooked. In many cases, the statistical test results for between-group differences in adverse events were not reported, thereby limiting the interpretability of the data.

The reviewed evidence indicated that there is a lack of long-term efficacy and harms data associated with treatments for ED. This is especially important in the case of oral PDE-5 inhibitors and associated harms, given their prevalent use by men in the Western world (e.g. 7 percent of American men aged 56-65 years in 2002).³⁰ Overall, duration of followup for the majority of reviewed trials was not sufficient to permit the reliable assessment of long-term (>6 months) treatment-related outcomes in patients with ED. The duration of followup for many of the PDE-5 inhibitor trials did not exceed 12 weeks. The long-term safety data obtained from retrospective observational studies is not as conclusive as that obtained from well-conducted long-term large randomized trials, which have fewer methodological limitations.

The reviewed evidence consisted of randomized trials using either parallel-arm or crossover design. Although crossover trials are efficient in terms of resources and study power, they require additional caution and careful interpretation of results. For example, one problem inherent in all crossover trials is a potential for a carryover effect, which could be minimized by employing an adequate washout period between alternative treatment periods.³⁸⁷ Although most of the authors reported the duration of washout periods (about 1-2 weeks), it is not clear what minimum length of time would be sufficient to avert or minimize carryover effects from the different types of treatment in patients with ED.

Question 1: What is the Clinical Utility of Routine Blood Tests—Testosterone, Prolactin, Luteinizing Hormone, Follicle-stimulating Hormone—in Identifying and Affecting Therapeutic Outcomes for Treatable Causes of ED?

The current evidence does not clarify the role of routine hormonal blood tests in all men who present with ED, nor does it clarify whether testing should occur before initiation of a first-line PDE-5 inhibitor treatment versus a more selective approach guided by elevated clinical suspicion for endocrinopathies. The signs and symptoms indicative of hypogonadism may include decreased testes size, alteration in secondary sexual characteristics, decreased libido, changes in mood, a chronic fatigued state or reduced physical performance, as well as altered hematocrit, high- and low-density lipoproteins, or cholesterol.³⁸⁸ Also, it remains unclear whether testing for prolactin, LH, and FSH endocrinopathies is justified as a stand-alone diagnostic strategy if testosterone levels are within the normal limits.

In total, 21 unique studies were reviewed to summarize information needed for determining the clinical utility of routine testosterone, prolactin, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) testing in ED patients. Overall, the heterogeneous nature of the data precludes the reliable evaluation of the utility and limitations of endocrinological testing in the ED population.

Prevalence of Endocrinological Abnormalities

In the reviewed studies, the prevalence of hypogonadism in the ED population varied widely, with reported rates ranging from 1.72 to 24.1 percent. The total, free and calculated testosterone levels were used as primary measures inconsistently, limiting the ability to meaningfully pool data across studies. The effect of age on the prevalence rates of hypogonadism may not be readily determined. For example, the descriptive analysis did not reveal the patients' age to be an important factor in explaining the observed variation in the prevalence rates of hypogonadism across studies. In contrast, within-study age-stratified results reported for three trials demonstrated that the prevalence rates of hypogonadism (i.e., low free serum testosterone) among men aged 50 years or older were almost doubled compared with the corresponding rates among men below age 50.^{38,64,73} Similarly, there was a wide variation in the prevalence rates of hyperprolactinemia (1.42–14.3 percent). In general, the evidence is inconsistent in indicating what subgroups of ED patients are more likely to have hypogonadism. Very few studies consistently indicated that patients referred to urology clinics for ED who had had decreased libido, testicular damage/abnormality, arterial disease, insulin resistance, or diabetes were more likely to have hypogonadism. The evidence is less consistent with respect to such factors as severity of ED, duration of ED, or sexual disorders (e.g. premature ejaculation).

The wide variation in the prevalence rates of hypogonadism and hyperprolactinemia could be explained by between-study differences in age distribution, types of tests (e.g. measurements of total, free, or bioavailable hormone levels), diagnostic criteria, and many other concurrent conditions that can influence blood testosterone levels.

Efficacy of Hormonal Treatments

Both studies^{5,77} that evaluated efficacy of hormonal treatment compared a combination hormonal treatment (i.e., testosterone gel or patch plus PDE-5 inhibitor) to monotherapy with a PDE-5 inhibitor, and were conducted exclusively in hypogonadal patients refractory to prior PDE-5 treatment. Results from these trials indicated greater improvements in erectile outcomes based on International Index of Erectile Function–Erectile Function domain scores (i.e., erection frequency, erection firmness, penetration ability, and erection confidence), favoring patients who received a combination of testosterone and PDE-5 inhibitors versus those who received PDE-5 inhibitors alone.^{5,77} These results warrant a cautious interpretation. For example, one of these trials⁷⁷ used an open-label design and had low quality methodology and reporting (total Jadad score of 1), thereby limiting the interpretability of the results. These studies were conducted only in ED patients refractory to PDE-5 inhibitor treatments, so the results may not be readily applicable to patients with a partial response or to those naïve to PDE-5 inhibitor treatments. Studies that are more methodologically sound are needed to determine definitively the efficacy of hormonal treatments relative to PDE-5 inhibitors (or any other first-line treatment) in patients with ED and concurrent endocrinological abnormalities.

Clinical Practice

Evidence regarding accurate identification of men who would benefit from testosterone replacement therapy is scarce. Thus, there is no universally accepted method of identifying men with clinically relevant hypogonadism affecting erectile function and the implications of androgen status for erectile dysfunction and its treatments remains controversial.³⁸⁹ Given the current gaps in knowledge, the most adequate and cost-effective laboratory test for hormonal evaluation is unclear. This problem is reflected in two differing guideline statements.^{14,39} The American Urological Association recommends testosterone testing based on initial clinical assessment results or failure of prior management with PDE-5 inhibitors,¹⁴ while the European Urological Association mandates testosterone measures (bioavailable or calculated-free testosterone begin preferred over total levels) for all men with ED.³⁹ These two groups have similar guidelines, which suggest that further endocrinological laboratory investigations including prolactin, LH, and FSH testing are indicated when low testosterone levels are detected. Optimal approaches from a clinical and resource-allocation standpoint remain to be determined. Regardless of the results, clinicians need to direct their initial efforts towards correctly identifying and treating, if possible, an underlying cause of ED, whether it is an endocrine or non-endocrine cause.

Questions 2–3: What are the Benefits and Harms of Pharmaceutical Treatments for ED? Oral Medications - PDE–5 Inhibitors

PDE–5 Inhibitors Versus Placebo

Efficacy. Overall, the evidence consistently indicated that patients with ED who received these agents (i.e., sildenafil, vardenafil, or tadalafil), compared with those on placebo, experienced greater improvements in the clinical measures of erectile function such as the mean scores for the International Index of Erectile Function (IIEF) “Erectile Function domain” (i.e., erection frequency, erection firmness, penetration ability, and erection confidence), IIEF–Q3/Q4 (i.e., penetration ability and maintenance frequency), and Sexual Encounter Profile (SEP)–Q2/Q3 (i.e., the per-patient proportion of successful intercourse attempts). The evidence was also consistent in favor of PDE–5 inhibitors over placebo in showing the clinical benefit with respect to the proportion of patients with improved erection (GAQ–Q1). Sildenafil, vardenafil, and tadalafil also demonstrated consistent statistically significant clinical benefits over placebo with regard to mean total scores for the specific IIEF domains such as “Intercourse Satisfaction” (i.e., intercourse frequency, satisfaction, and enjoyment) and “Overall Satisfaction” (i.e., overall satisfaction and relationship satisfaction). Results obtained from the same trials suggested that the effects of sildenafil and tadalafil did not differ from that of placebo for the IIEF domains of “Sexual Desire” (i.e., desire frequency and desire level) and “Orgasmic Function” (ejaculation and orgasm frequency). In a few trials, patients treated with vardenafil had improved in the domains of “Sexual Desire” and/or “Orgasmic Function” compared with placebo-treated patients.^{183,194,199,204} Furthermore, all trials that reported patient satisfaction with a medication (i.e., mean Erectile Dysfunction Index of Treatment Satisfaction scores) showed statistically significant improved scores for patients who received sildenafil or tadalafil compared with those who received placebo. None of the vardenafil trials reported scores for the Erectile Dysfunction Index of Treatment Satisfaction (EDITS). The results of meta-analyses conducted in this review were consistent with those of qualitative assessments in that they indicate statistically significant improvements in PDE–5 inhibitor-treated (regardless of dose/dosing regimen) patients versus placebo-treated patients with respect to the mean change/endpoint scores of IIEF “EF domain,” IIEF–Q3/Q4, SEP–Q2/Q3, as well as with respect to the proportion of patients with improved erection (GAQ–Q1).

Harms. In general, all three PDE–5 inhibitors were described as well-tolerated drugs whose use was associated with adverse events mainly of a mild or moderate nature. Overall, the occurrence of any all-cause adverse events tended to be higher either numerically or with a statistical significance in patients treated with PDE–5 inhibitors as compared with those treated with placebo. The most commonly observed all-cause adverse events for all three PDE–5 inhibitors were headache, flushing, dyspepsia, and rhinitis. The incidence of serious adverse events was poorly reported. Numerically, there was no obvious imbalance with respect to the occurrence of serious adverse events between patients who received PDE–5 inhibitors and those who received placebo. The result of meta-analysis agreed with those for the qualitative assessment of harms in their indication of an increased risk of any adverse events in patients who received PDE–5 inhibitors (regardless of dose/dosing regimen) compared with those who received placebo.

Two meta-analyses also showed that there were no statistically significant differences with respect to the occurrence of serious adverse events or withdrawals due to adverse events between vardenafil- and placebo-treated groups. Compared with placebo, the use of either sildenafil or vardenafil was associated with an increased risk of either headache or flushing. In addition, patients treated with vardenafil or sildenafil, in comparison with those treated with placebo, were at increased risk of dyspepsia and visual disturbances, respectively.

Dose-response Effect of PDE–5 Inhibitors

Efficacy. In general, the degree of efficacy in improving erectile function (e.g. scores for the IIEF “EF domain” or individual item scores, SEP–Q2/Q3 scores, percentage of patients who responded “yes” to GAQ–Q1) tended to increase with the doses of PDE–5 inhibitors. The observed trends were either numerical or statistically significant. Formal statistical test results for differences in efficacy between dose-specific arms for PDE–5 inhibitors were not provided in many trial reports, which complicated the interpretation. The observed dose-response trends in efficacy were less obvious for tadalafil trials, in which the degree of improvement in erectile function was numerically similar in patients who received three doses of tadalafil (20 mg, 10 mg, and 5 mg). According to our meta-analyses, in sildenafil trials the proportion of patients with improved erection (GAQ–Q1) was greater for men who received 50 mg compared with those who used a 25 mg dose. The difference for the corresponding proportions between 50 mg and 100 mg groups favored the higher 100 mg dose but was not statistically significant. Although the mean IIEF “EF” domain score and the proportion of “yes” responses to GAQ–Q1 among patients treated with vardenafil favored the 20 mg dose over the 10 mg dose, the differences did not reach the statistical significance.

Harms. The incidence of any all-cause adverse events in sildenafil (25 mg versus 50 mg versus 100 mg) and vardenafil (5 mg versus 10 mg versus 20 mg) trials had a numerical pattern of dose-dependence, indicating that adverse events occurred more frequently at the higher doses. The dose-response pattern for the effect of tadalafil (10 mg versus 20 mg) was not obvious. The meta-analyses conducted on vardenafil trials showed an increased risk of any adverse events in patients treated with the 20 mg versus the 10 mg dose. The difference for the proportion of patients with serious adverse events between the two doses of vardenafil was not statistically significant. Neither the rate of withdrawal resulting from adverse events nor specific adverse events (i.e., headache, flushing, dyspepsia) differed between the two doses. The meta-analyses of sildenafil trials revealed no statistically significant differences in the incidence of specific adverse events (i.e., headache, flushing, or visual disturbances) between the 25 mg, 50 mg, and 100 mg sildenafil groups. The meta-analysis of tadalafil trials found a statistically significant increase in the risk of any adverse events for patients in the 20 mg group relative to those in 10 mg group.

Dosing Regimens of PDE–5 Inhibitors

Efficacy. Different dosing regimens of PDE–5 inhibitors were evaluated in sildenafil (fixed dose of 50 mg versus flexible dose of 50 mg or 100 mg)¹⁵⁷ and tadalafil (20 mg “on demand” versus 20 mg “scheduled”)^{214,232} trials. The results of both sildenafil and tadalafil trials indicated no difference in the degree of clinical benefit experienced by patients randomly assigned to different dosing regimens (fixed versus flexible, or “on demand” versus “scheduled”). The benefits were observed for the IIEF “EF” domain or individual item scores, SEP–Q2/Q3 scores, and the percentage who responded “yes” to GAQ–Q1.

Harms. There were no obvious differences in the occurrence of adverse events between “on demand” versus “scheduled” intakes of tadalafil.

PDE-5 Inhibitors – Mono versus PDE-5 Inhibitors – Combined Therapy

Efficacy. The results suggest that sildenafil used in combination with other therapies may be clinically more beneficial than sildenafil used as monotherapy. In these trials, the administration of sildenafil combination therapies was associated with statistically significant improvements in IIEF “EF” domain and individual IIEF (Q1–Q15) scores as well as in the mean duration of rigidity (≥ 60 percent) of the penis and the proportion of patients with improved erection (GAQ–Q1), relative to sildenafil monotherapy.

Harms. Based on the limited data from only one trial,¹⁶² there was a statistically significant greater proportion of patients with at least one any adverse event (all-cause) in the sildenafil combination therapy (with cabergoline) group compared with the sildenafil monotherapy group. In two trials,^{162,173} more patients withdrew due to adverse events in the combined (with either cabergoline or alfuzosin) treatment groups than in the monotherapy groups.

PDE-5 Inhibitors Versus Other Treatments

Efficacy. Improvements in erectile function (IIEF-“EF domain” scores) observed in 4 head-to-head trials comparing sildenafil, vardenafil, and tadalafil were inconclusive. In these trials, more patients preferred tadalafil over sildenafil or vardenafil. The mean duration from dosing to attempted sexual intercourse was also longer for tadalafil. The patients’ preference in favor of tadalafil could partially be explained by a longer acting duration of tadalafil compared with sildenafil or vardenafil observed in these trials. The half-life for tadalafil, sildenafil, and vardenafil is about 17.5 hours, 4 hours, and 4-5 hours, respectively. Furthermore, unlike sildenafil, the absorption of tadalafil is not influenced by food, making it more convenient.^{390,391}

Compared with other treatments (i.e., continuous positive air pressure [CPAP], phentolamine, alfuzosin, Ro70–0004), sildenafil was shown to be associated with either statistically significant or numerically greater improvements in the mean IIEF “EF” domain and IIEF–Q3/Q4 scores, the rate of improved erections (GAQ–Q1), and the mean duration of rigidity (>60 percent).^{124,132,155,173} The four trials comparing sildenafil to apomorphine^{114,117,120,159} suggest that sildenafil is more effective in improving several outcomes including mean percentage of successful intercourse attempts, mean IIEF scores, and patient satisfaction. Sildenafil had a beneficial clinical effect similar to that of apomorphine in combination with either phentolamine or with phentolamine plus papaverine.²⁵¹ One explanation for this observed pattern could be that the effect of apomorphine might have been optimized by combining apomorphine with phentolamine alone or also with papaverine.

Harms. The incidence of any adverse events showed no statistically significant difference between patients treated with sildenafil, tadalafil, and vardenafil.^{103,121,163} The limited amount of evidence obtained from one trial¹⁰³ suggested that groups treated with sildenafil or tadalafil did not differ in the proportion of patients with serious adverse events. In another trial,¹²⁴ limited data indicated that fewer patients treated with sildenafil had any adverse events (all-cause) or serious adverse events compared with patients treated with

phentolamine. Rates of withdrawal due to adverse events were also numerically lower in the sildenafil groups than in either the phentolamine¹²⁴ or the alfuzosin group.¹⁷³ The incidence of any adverse events in three trials^{114,117,120} was poorly reported and was numerically greater in patients treated with sildenafil than in those treated with apomorphine. In one trial,²⁵¹ the proportion of patients with any adverse events was numerically lower in the sildenafil arm compared with the apomorphine combination arms (with phentolamine).

Sublingual Agents – Apomorphine

Apomorphine Versus Placebo

Efficacy. Overall, results from the five placebo-controlled trials indicated statistically significant improvements with respect to measures of erectile function (e.g. mean percentage of successful intercourse attempts, percentage of attempts resulting in erections firm enough for intercourse, rigidity ≥ 40 percent, and the mean IIEF “Erectile Function” domain score) in patients treated with apomorphine compared with those who received placebo. Clinically significant differences were seen in the mean percentage of improved erectile function with apomorphine compared with placebo arms.

Harms. There was insufficient information on the occurrence of any adverse events in these trials to allow comparison of incidence of harms across apomorphine and placebo groups. Adverse events such as nausea, headache, dizziness, and yawning occurred more frequently among patients who received apomorphine than among those who received placebo. The results from two trials suggested that the use of apomorphine was not associated with an increased incidence of any serious adverse events compared with the use of placebo.^{248,250}

Dose-response Effect of Apomorphine

Efficacy. Limited evidence from two trials indicated that the mean percentage of successful intercourse attempts did not differ across groups who received various doses of apomorphine treatment (e.g. 3mg, 4 mg, 5 mg, 6 mg, 2–6 mg). This observation suggests that the efficacy of apomorphine may not be dose-related.

Harms. In multiple-dose trials, the occurrence of nausea, yawning, dizziness, vomiting, and glossitis was numerically greater in patients who received higher doses of apomorphine.^{248,252,253}

Intracavernosal Injections

Prostaglandin E1 (PGE1)

Efficacy. The administration of PGE₁ was shown to have improved erections more frequently relative to no treatment, placebo, papaverine, moxisylate, linsidomine, sodium nitroprusside, or the combination of linsidomine and urapidil. The rates of improvement in erection for patients receiving PGE₁, sexual therapy, or the combination of papaverine plus phentolamine were found to be similar. Patients who received PGE₁ alone experienced rates of improved erection similar to those among patients who received papaverine combined with phentolamine, while improved erection was less frequent after treatment with PGE₁ plus papaverine. Limited detailed evidence suggests that trimix was at least as effective as PGE₁

alone. Compared with trimix alone, the combination of trimix and sodium bicarbonate improved erections, while trimix combined with atropine did not produce such benefit. The interpretation of results from trials using trimix is complicated, because concentrations of the three constituents varied from study to study.³⁹²

Harms. Penile pain occurred more frequently in patients treated with PGE₁ than among those treated with placebo, moxisylyate, or the combination of papaverine and phentolamine. The pain associated with the treatment was significantly less frequent when the PGE₁ was injected slowly, or in combination with either lidocaine or procaine, but not when injected in combination with sodium bicarbonate. The combination of papaverine and phentolamine was less frequently associated with pain in comparison with either PGE₁ alone or PGE₁ plus papaverine. The treatment with trimix was associated with priapism more frequently relative to treatment with PGE₁. The variation in rates of priapism may additionally depend on proper testing of the agent in the office setting, dose adjustment process for use at home, teaching sessions during which the patient administers his own injection under supervision, patient compliance, instruction handouts, and/or missed injections.

Subcutaneous Injections

Melanotan II, PT-141 (cyclic heptapeptide melanocortin analog), Apomorphine

Efficacy. The trial results indicated greater improvements on RigiScan in patients who received either melanotan II²⁹⁵ or PT-141²⁹⁸ compared with those who received placebo.

Harms. Although adverse events were generally mild, subcutaneous treatments were associated with an increased risk of nausea and headache in comparison with placebo.

Intraurethral Suppositories

Alprostadil

Efficacy. The use of IU alprostadil was shown to be associated with a higher sexual intercourse success rate compared with placebo.

Harms. Patients receiving IU alprostadil had an increased risk of local pain compared with those who received placebo. The followup period of the trials did not exceed 3 months, so the relative benefits and harms of long-term treatment with IU suppositories remain unclear.

Topical Treatments

Alprostadil, Nitroglycerine, Aminophylline, Isosorbide Dinitrate, and Co-dergocrine

Efficacy. Although the use of topical alprostadil was associated with improvements in erection and a higher sexual intercourse success rate relative to placebo, the magnitude of this improvement might be small (about 10 percent) and limited to men with mild to moderate ED. Patients who used nitroglycerine plaster before planned intercourse did not have improved erections in comparison with those who used placebo. Nitroglycerine

ointment produced only a small improvement in erections. Fewer patients who used nitroglycerine ointment or placebo improved compared with those who took minoxidil. Results for topical aminophylline plus isosorbide dinitrate and co-dergocrine were contradictory, improved erections being found in only one of two trials.

Harms. Adverse events, including local pain, was statistically significantly more frequently in patients treated with topical alprostadil compared with those treated with placebo. Patients who used nitroglycerine plaster before planned intercourse experienced a higher frequency of pain and headaches than those who used placebo. The use of nitroglycerine ointment was associated with increased pain and hypotension.

Hormonal Treatments

Testosterone

Efficacy. The effectiveness of testosterone regarding to improve erectile function and sexual intercourse satisfaction was inconsistent compared with placebo. Differences in patient inclusion criteria (e.g. not all trials were comprised of exclusively of ED patients), methods of evaluation, interventions (e.g. mono versus combination treatment, cream, patch, gel, injections), outcome definitions, and use of subjective measures (e.g. IIEF, SEP), could explain some of the discrepancies in results across the studies evaluating the efficacy of testosterone. The intramuscular administration of testosterone was shown to have improved erectile function compared with placebo in only one of four small trials. The “patch” testosterone did not improve sexual function compared with placebo. However, in men with poor response to previous use of sildenafil, testosterone patch plus sildenafil significantly improved the sexual intercourse success rate and satisfaction compared with placebo and sildenafil alone. Gel testosterone (50 mg and 100 mg doses) was found to have increased sexual intercourse frequency compared with placebo. The 100 mg dose of gel testosterone also significantly improved sexual intercourse frequency versus patch testosterone. The use of combination cream of testosterone, isosorbide dinitrate, and co-dergocrine was associated with an increased rate of successful sexual intercourse and improved erections compared with placebo or cream testosterone alone. The application of dihydrotestosterone gel was related to an increased rate of successful sexual intercourse compared with that of placebo.

Although there is insufficient head-to-head data, the gel formulation of testosterone may be a more effective treatment compared with other formulations of testosterone.

Harms. Patients receiving testosterone patch had a higher rate of having application site skin reactions than those with placebo. The use of gel testosterone did not show a dose-related increase in adverse events. The use of combination cream containing testosterone, isosorbide dinitrate, and co-dergocrine was associated with an increased risk of mild headaches compared with placebo or cream testosterone alone. The short-term followup precluded ascertainment of the incidence of prostate cancer. In one trial,³¹⁷ two patients who had been treated with patch testosterone, developed prostate cancer.

Other Treatments (Off-label use)

For summary of trials refer to Evidence Table F-10 (Appendix F).

Phentolamine

Efficacy. The results indicated either numerical or statistically significant improvements in erectile function (i.e., percent of successful intercourse attempts, base/tip rigidity >60 percent for ≥ 10 minutes) were associated with the use of phentolamine relative to placebo. There was no between-group difference for tumescence activity units.³³³ With insufficient data, statistical test results, and a small number of studies, the trial results are inconclusive regarding the efficacy of phentolamine relative to placebo.

Harms. Due to the lack of sufficient amount of harms data it is not clear if patients taking oral phentolamine are at higher risk of developing adverse events.

Trazodone

Efficacy. Evidence regarding efficacy of trazodone relative to placebo to treat ED was insufficient (i.e., only 5 smaller-scale trials) and inconsistent. In general, the use of trazodone was not associated with improved erectile function compared with placebo.^{336,337,339,341} Note that in one trial,³⁴⁴ patients on trazodone experienced statistically significant improvement in erectile response (i.e., at least 3 successful intercourses within 30 days of treatment) compared with those on placebo, ketanserin, or mianserin. Since this trial was not double blind, it is hard to judge if the observed differences were truly due to the treatment administered or to other extraneous factors. The current American Urological Association Practice Guidelines Committee (AUA PGC) does not recommend the use of trazodone in the treatment of ED.¹⁴

Harms. Limited evidence suggests that the use of trazodone may be associated with an increased risk of adverse events (priapism, sedation, headache) and higher rates of withdrawal due to adverse events compared with placebo.

Cabergoline

Efficacy. The limited amount of evidence suggests that the use of cabergoline was associated with numerically or statistically significantly improved mean scores of IIEF “EF” domain and IIEF–Q3/Q4 compared with placebo. Additional evidence from trials using different doses is needed to corroborate or disprove these findings.

Harms. In general, treatment with cabergoline was well tolerated. Nevertheless, there were higher frequencies of adverse events and withdrawals due to adverse events in the active treatment groups than in the placebo groups.

Pentoxifylline

Efficacy. The results of the trials were inconsistent, one³⁴⁰ indicated statistically significant improvements in peak systolic velocity; and the other trial³⁴³ yielded no difference in the frequency of morning erections, nocturnal penile tumescence, or penile rigidity in patients receiving pentoxifylline compared with those on placebo. Another trial³⁴⁵ demonstrated an increased number of successful coital episodes for the active treatment group of patients. However no formal statistical test results were presented to substantiate the findings. Given the above-mentioned limitations, more evidence is needed to draw more definitive conclusions regarding the relative efficacy of pentoxifylline.

Harms. No harms data were reported for two trials.^{343,345} Some of the reported treatment-related adverse events in one trial³⁴⁰ were nausea and headache. The harms profile of pentoxifylline in treating ED remains unclear.

Miscellaneous Agents

Efficacy. Overall, the limited amount of evidence suggested that naltrexone, tianeptine, tetrahydrobiopterin, and dehydroepiandrosterone may be more efficacious than placebo in improving early morning erections, proportion of patients with successful intercourse attempts, duration of rigidity (>60 percent), and mean total IIEF domain-specific scores, respectively.^{342,348,352,353} The evidence regarding the efficacy of moclobemide, isoxsuprine, angiotensin-converting enzyme (ACE), and myoinositol/folic acid was less conclusive.^{334,335,346,351} The degree of erectile response was not statistically significantly different for isoxsuprine or ACE relative to placebo.^{335,346} Although moxonidine was shown to be more effective in increasing deep penile diameter and artery velocities compared with metoprolol, this result may have been biased because this trial did not employ double blind techniques to adequately mask the treatment modality.³⁴⁷ More trials using a double-blind design are needed to corroborate these findings.

Harms. The limited amount of evidence suggested that the number of patients with adverse events was greater in the treatment groups than in the placebo groups. No definitive conclusions can be made at this time.

Question 2a-b: Do Specific Patient Characteristics (e.g. Origin, Severity, or Duration of ED, and Comorbid Conditions) Affect Prognosis or Treatment Success for ED Patients?

Origin of ED

There was a consistent clinical benefit (i.e., IIEF “EF” domain and GAQ–Q1) in patients receiving sildenafil, tadalafil, or vardenafil compared with placebo regardless of their origin of ED (i.e., organic, psychogenic, and mixed). This suggests that quite a broad etiologic spectrum of ED patients could potentially benefit from using these agents to improve the clinical symptoms of ED. This review of evidence did not reveal the presence of any obvious treatment effect modification by the origin of ED. However, these results were obtained from only a few trials, so the evidence warrants a cautious interpretation. Additional trials conducted in these subgroups using uniformly defined clinical outcomes would help to draw more definitive conclusions.

Baseline Severity of ED

The use of PDE–5 appeared to elicit a better improvement in erectile function (i.e., higher endpoint scores on IIEF “EF domain,” IIEF–Q3/Q4, GAQ–Q1) for patients with mild or moderate baseline severity of ED (IIEF score: 11–25) than for those with severe forms of ED (IIEF score ≤ 10).

Duration of ED

There is a paucity of evidence on the relative efficacy of PDE–5 inhibitors according to the duration of ED. Only a few trials (i.e., sildenafil versus placebo) reported the efficacy analysis stratified according to the duration of ED with consistent clinical benefits for all patients irrespective of the duration of ED. Furthermore, the two trials in diabetic men with ED^{94,101} did not reveal any trends in efficacy (IIEF–Q3/Q4 and GAQ–Q1) across the ED duration strata. The evidence is still inconclusive whether or not the duration of ED is an important prognostic factor for the degree of treatment success (e.g. endpoint IIEF “EF” domain scores, proportion of patients with IIEF >25 at followup).

Distinct Clinical Subgroups

Evidence on incremental therapeutic benefits associated with the use of PDE–5 inhibitors was consistent across a broad spectrum of patients with ED. The obvious clinical benefit of PDE–5 inhibitors relative to placebo in treating ED was observed not only in the trials that included a broad spectrum of patient population with ED but also in the trials restricted to specific clinically defined homogenous groups of patients with ED (e.g. diabetes, depression, prostate cancer, spina bifida, stable CAD, Parkinson’s disease, CHF, LUTS, MS, renal transplants, arterial hypertension, prostatectomy, and no prior treatment for ED). The results of meta-analyses conducted for this review also showed that the use of sildenafil in patients with diabetes, depression, or hypertension led to improvements with respect to IIEF–Q3/Q4, GAQ–Q1, and percentage of successful intercourse attempts.

Questions 3a: Specific Harms of Pharmaceutical Treatments in Male Patients With ED

Non-arteritic Anterior Ischemic Optic Neuropathy (NAION) in Men Treated With PDE-5 Inhibitors

This review aimed to search and identify studies reporting the occurrence of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in men treated with sildenafil. Reports included case reports and case series but the absence of denominators precluded the calculation of rates of NAION for sildenafil-exposed versus nonexposed populations. The incidence rates and their ratios (i.e., RRs and 95 percent CIs) for NAION calculated and reported in one cohort study provided inconclusive evidence. Most cases of NAION reported in the reviewed case reports and case series had been treated with 50 mg or higher doses of sildenafil. Moreover, the occurrence of overdose (200 mg) was reported for two NAION cases. The observed trend may suggest potential for an increased risk of NAION in men receiving high doses of sildenafil. Overall, given the insufficient amount and low methodological quality of the identified evidence, it is not clear whether or not men receiving long-term treatment with sildenafil are at increased risk of developing NAION relative to those not receiving this treatment.

Fibrosis in Men Treated With Injection Treatments

Penile fibrosis, scarring, and indurated nodularity have been reported to be associated with long-term use of ICI with papaverine. There is less data regarding the effect of PGE₁ on the incidence of penile fibrosis. Penile fibrosis and scarring can lead to abnormal penile curvature with erections and subsequent discontinuation of therapy.³⁷² Since RCTs are of insufficient duration to adequately assess the risk of penile fibrosis, this review evaluated the evidence from 20 retrospective observational studies and clinical trials that reported the incidence of penile fibrosis. The incidence of fibrosis varied widely and was not consistent across studies of treatments with papaverine, triple therapy (Trimix) and PGE₁. The design of the identified studies and many confounding factors precluded a comparison of the rates of fibrosis between patients receiving injections of PGE₁ versus papaverine alone or in combination. The rates of fibrosis may depend on the type and dose of medication, frequency of injections, at home versus office injections, and presence of priapism.^{393,394} Evidence regarding the relative incidence of penile fibrosis amongst patients treated with different types of injection therapies is inconclusive. The conduct of well-designed trials is needed to determine the incidence, severity, and health impact of penile fibrosis in long-term ICI users. Moreover, it is important to determine whether there is a medication-, dose- or frequency-response effect of injections. Further evidence is required on whether different injection strategies (e.g. alternating sites) would help to further reduce risk of fibrosis. Penile fibrosis is a complication of ICI and all ED patients receiving this treatment need to be warned of the risk of fibrosis and be examined periodically for fibrotic changes in the penis.

Methodological and Logistic Limitations of the Systematic Review

This review had methodological and logistic limitations. Some of the important limitations are listed here.

In many cases, the methodological and/or reporting quality of the primary studies was poor, as judged by the Jadad scale and the Schulz allocation concealment component. For example, the adequacy of methods used for randomization, treatment allocation concealment, or blinding could not be ascertained for majority of the reviewed studies. In turn, the absence of this information compromised the valid interpretation of the study results.

There was substantial heterogeneity with respect to efficacy/harms outcomes, types of interventions, diverse concurrent clinical conditions, and reporting quality across the reviewed studies. Clinical and/or methodological heterogeneity limited the extent of statistical pooling of the efficacy- and harms-related data.

In crossover trials, pre-crossover quantitative data was usually not reported making it difficult to incorporate the results into the meta-analyses.

Primary studies did not always provide sufficient quantitative information (e.g. standard deviations, mean endpoint estimates of treatment efficacy, statistical test results) needed to pool the individual trial results and to judge the treatment-related between-group differences in the outcomes. Due to limited resources and the timelines of this review, the authors of individual studies could not be contacted for additional information that was not provided in the reports.

Empirical evidence has shown that harms occurring during a trial are generally underreported. Overall, the occurrence and details of adverse events was poorly reported in the primary studies. Many trial reports did not provide the data on the incidence of any all-cause adverse events and serious adverse events. Moreover, the types of adverse events across the trials, as well as the definition of adverse events and in particular serious adverse events were not reported consistently from study to study. The authors often did not provide statistical test results for the between-group differences in adverse events. Thus, the reviewers resorted solely to qualitative judgment.

This review did not investigate the effectiveness and harms of interventions such as natural health products, vacuum constriction devices, penile prosthesis implants, surgery, or lifestyle modifications. This review also did not include trials in ED patients with spinal cord injury.

The interpretation of the study results was complicated by the lack of well accepted guideline(s) regarding the magnitude of clinically important (or meaningful) difference for a given validated outcome. It is well recognized that the interpretation based solely on the statistical test results may be misleading. The clinically important difference for a valid and relevant outcome may or may not be statistically significant and the opposite also holds true. In many cases, study authors did not report whether the study power to detect a pre-specified minimally relevant clinical difference was estimated.

The evidence needed to evaluate the utility of routine endocrinological testing administered to the ED population is sparse and inconclusive.

Future Research Recommendations

Efforts are needed to improve the quality of reporting primary studies (i.e., randomized trials). The CONSORT Statement could be considered as a reporting guide for authors reporting trials and journals that publish ED-related research.³⁹⁵

Future studies should focus on both short- and long-term (6 months or longer) clinically relevant valid treatment outcomes. Such studies could clarify important unanswered questions involving both realms of efficacy and harms as well as evaluate relative sustainability of the clinical benefit conferred by different treatment modalities. Additional research should evaluate patient preferences, satisfaction, and compliance with different treatments, including PDE-5 inhibitors. Well designed longer-term RCTs evaluating the effects of PDE-5 inhibitors or other therapies will allow better documentation of the incidence of specific adverse events (e.g. mortality, cardiovascular events, visual disturbances, NAION, penile fibrosis). In light of the presence of comorbidities or causes underlying ED, the comparison of cause-specific therapies (administered alone or in combination) with the first-line treatment(s) in terms of efficacy and safety profiles is warranted. The trials should be more population-based to maximize the degree of external validity of their results.

More trials in clinically homogenous subgroups of ED patients presenting with concomitant conditions (e.g. diabetes, cardiovascular disease, prostate cancer, high blood pressure) are needed to better explore and characterize potential treatment effect modification. Additional investigations of treatment effects in patient subgroups defined by severity, duration, and etiology of ED are also warranted as are therapeutic trials in different ethnic groups of patients with ED.

More efforts are needed to elucidate the minimum clinically important difference (MCID) for the validated and clinically relevant outcomes (e.g. mean scores on IIEF, SEP, proportion of patients with improved erection) for various situations (e.g. patient subgroups, instruments used to measure change in the outcome, self-, partner- or investigator-reported).

Further research is warranted to determine the utility of routine endocrinological blood tests (e.g. serum testosterone, prolactin levels). This would involve studies with large and representative samples of ED patients to estimate precisely the age-stratified prevalence rates for endocrinological abnormalities (e.g. hypogonadism, hyperprolactinemia) and to determine subgroups (or risk factors) of patients with ED who have increased risk of hypogonadism. Ultimately, routine endocrinological blood tests (e.g. total, free, bioavailable) need to be standardized.³⁹⁶

Ideally, studies of testosterone used for the treatment of ED should enroll men with testosterone deficiency. If men with higher testosterone levels are to be included in these trials, stratified analyses should be conducted based on baseline testosterone levels. More data from large trials regarding the safety of long-term use of testosterone therapy is needed for more definitive conclusions.

Future trials of intracavernosal injection treatments should focus on clinically relevant efficacy and harm-related outcomes such as the degree of ED/treatment satisfaction (e.g. scores for International Index of Erectile Function, Erectile Dysfunction Index of Treatment Satisfaction), sexual intercourse success rate (Sexual Encounter Profile scores), penile pain, fibrosis, and priapism. The analyses should include all randomized participants in order to reduce the potential for selection bias (i.e. intention-to-treat analysis).

Tables and Figures.

Summary Tables

Table 1: Population Characteristics of Studies Measuring Hypogonadism in Men with Erectile Dysfunction

Study details ¹	Study Design	Setting	ED Scale	Age		Comorbidity	Serum Levels	Test time	Cut-off (T)	Normal range (T)	Assay
				Mean (SD)	Range						
Jaffe 1996	Prospective	Clinic	NR	55.3		hypertension	TT, BT, PRL, LH, FSH	morning	TT: <3ng/mL BT: <1 ng/ml	NR	RIA
Citron 1996	Prospective	Endocrinology	NR	61.2 ±8.9	27–79	Secondary hypogonadism	TT, FT, BT, LH	NR	<2.3 ng/ml	2.3–9.9 ng/ml	RIA
Hatzichristou 2002	Prospective	Andrology outpatient clinic	NR	56 ± 14		DM, cardiovascular disease, urinary tract pathology, neurological disease, endocrine pathology	TT, PRL	NR	NR	NR	NR
Martinez-Jabaloyas 2006	Prospective	Urology clinic	IIEF-EF	55 ± 10		DM, dyslipidemia, hypertension, ischemic cardiopathy	TT, FT, LH, FSH, PRL	morning 8–10 a.m	TT: <2.8 ng/ml FT: <0.228 ng/ml	2.8–8 ng/mL	NR
Acar 2004	Prospective	NR	IIEF-5	47±10.1		chronic disease	TT, PRL, FSH, LH	morning after 8 hours fasting	<3ng/ml (2x)	NS	ECLA

¹Baseline serum levels: TT = total testosterone; FT = free testosterone; BT: bioavailable testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulant hormone
SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (cmi); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA)

* calculated free testosterone

Scales: Sex Health Inventory for Men (SHIM); Sexual Functioning Questionnaire (SFQ); International Index of Erectile Function (IIEF-5) and Aging Males Symptoms (AMS)

Study details ¹	Study Design	Setting	ED Scale	Age		Comorbidity	Serum Levels	Test time	Cut-off (T)	Normal range (T)	Assay
				Mean (SD)	Range						
Earle 2003	Prospective	Department of Endocrinology and Diabetes	NR	54.9	16–82	NR	TT, PRL LH and FSH if low TT	1 st test NR 2 nd test if TT low in first test, taken in the morning	NR	11–37 nmol/L	RIA
Rhoden 2002	Prospective	Department of urology, andrology division	IIEF–5	60	40–60	NR	TT	morning 08:00–10:00	<2.4 ng/mL	2.4–8.3 ng/mL	RIA
Bunch 2002	Retrospective	Outpatients	NR	64.6 ± 10.8	51–85	DM, IHD, hypertension, hyperlipidemia, depression, sleep apnea, CVA, AF, hypothyroidism, prostate cancer, CRF, head tumors, compression fractures	TT, LH	NR	<3 ng/ml	<60: 3–8.9; >60: 2–7.2 ng/ml	RIA
Fahmy 1999	Prospective	ED clinic	sexual activity questionnaire	NR		NR	TT, FSH, PRL	morning (9–11 am)	10 nmol/L	NR	NR
Buvat 1997	Retrospective	NR	NR	NR		NR	TT, PRL	morning post 20 min rest	3 ng/ml (low 2–3; lowest <2)	NR	RIA
Akpunonu 1994	Prospective	Primary care clinics	NR	55.4±10	24–76	Renal Failure, DM	TT, PRL, LH, FSH	ns	<10 nmol/L	10–34.7 no/L	NR
Drinka 1993	Prospective	Outpatient department	NR	71.7 ± 6		NR	FT	morning (fasting)	<9 pg/mL	9–25 pg/ml	RIA

Study details ¹	Study Design	Setting	ED Scale	Age		Comorbidity	Serum Levels	Test time	Cut-off (T)	Normal range (T)	Assay
				Mean (SD)	Range						
Johnson 1992	Prospective	Urology clinic	NR	NR		NR	TT, PRL, LH	NR	<3 ng/dl	2.2–7.7 ng/dl	RIA
El-Sakka 2005	Prospective	Endocrinology clinic	IIEF	Endocrinopathy (297) -51.9 ± 12.2 No endocrinopathy (951) -52.3 ± 11.7		Obesity, diabetes, hypertension, ischemic heart disease, dyslipidemia, Cerebrovascular stroke	TT, PRL, LH, FSH	morning	<2.8 ng/mL (3x)	2.8–8.8 ng/mL	ECLA
Tsujimura 2005	Prospective	Sexual function clinic	AMS, IIEF-5	56 (median)	50–79	NR	TT, LH, FSH, PRL	Morning 09:00–11:00	<3.7 ng/mL (11nmol/L)	2.7–10.7 ng/ml	RIA
Guay 1991	Prospective	Endocrinology clinic	–	NR		NR	TT, LH, FSH	morning	NR	TT >3 ng/mL FT 50–200 pg/mL	RIA
Forsberg 1990	Prospective	Department of urology and clinic for sexual therapy	NR	47 (median)		Vascular disease, DM	TT, LH, FSH, PRL	same time of day	Low <10 nmol/L Borderline 10–15 nmol/L	NR	NR
Reyes-Vallejo 2006	Prospective	NR	NR	55.2	30–79	Hypercholesterolemia, DM, hypertension, CAD, depression	TT, FT, FSH, LH, PRL	NR	<3 ng/mL	NR	ECLA
El-Sakka 2006	Prospective	Andrology clinic	IIEF	53.9 ± 8.5	26–86	overweight, DM, hypertension, IHD, dyslipidemia,	TT, PRL	morning	<2.8 ng/mL (3x)	2.8–8.8 ng/mL	ECLA

Study details ¹	Study Design	Setting	ED Scale	Age Mean (SD) Range		Comorbidity	Serum Levels	Test time	Cut-off (T)	Normal range (T)	Assay
						psych. Dis.					
Hwang 2007	Prospective	Community	IIEF-5	NR		smoking	cFT, TT, BT, FSH, LH, PRL	9-12 in the morning	≤11nmol/l	>11nmol/l	NR
Low 2006	Prospective	Community	IIEF-5	59.3 ± 7.38		depression	cFT, TT, BT, PRL, LH	before 11 AM	TT: ≤11nmol/l FT: <0.02 nmol/dl BT: <0.2 nmol/dl	NR	direct CMI
Guay 2007	Retrospective	clinic	SHIM	NR		DM, metabolic syn., IHD, hyperlipidemia, neurological dys., pelvic surgery	FT	NS	<10 pg/mL	NS	RIA
Zohdy 2007	Retrospective	NR	IIEF-5	40.3 ± 8.9	20- 56	NR	TT	morning	<2.8 ng/ml	2.8-8 ng/mL	ECLA

Table 2: Prevalence of Hypogonadism in Men with Erectile Dysfunction (serum total testosterone)

Study Details ²	Study Design	Setting	T Mean (SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hypogonadism			Test time	Cut-off (TT)	Normal Range	Assay
							n	N	%				
Studies performed in North America													
Akpunonu 1994 (USA)	Prospective	Primary care clinics	14±5.1 nmol/L	6.3 ± 6.5 mcg/L	10.6±5.8 IU/L	14.7±8.6 IU/L	51	212	24.1	NR	<10 nmol/L	10–34.7	-
Johnson 1992 (USA)	Prospective	Urology clinic	NR	NR	NR	NR	7	330	2.12	NR	<3 ng/ml	2.2–7.7 ng/ml	RIA
Citron 1996 (USA)	Prospective*	Endocrinology	173 ± 44 ng/dl	NR	5.3±2.8ml U/ml	NR	11 [‡]	167	6.59	NR	<2.3 ng/dl	2.3–9.9	RIA
Bunch 2002 (USA)	Retrospective*	Out-patients	177.73 ± 78.36 ng/dL	NR	6.8±9.1 mIU/ml	NR	29 [‡]	201	14.42	NR	<3 ng/dl	3–8.9	RIA
Study performed in South America													
Rhoden 2002 (Brazil)	Prospective	Department of urology, andrology division	530 ± 201 ng/ml	NR	NR	NR	27	520	5.19	morning	<2.4 ng/dl	2.4–8.3 ng/dl	RIA
Studies performed in Europe													
Buvat 1997 (France)	Retrospective	Urology clinic	NR	NR	NR	NR	68	1022	6.65	morning	<3 ng/ml	–	RIA

²Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone

SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (CMI); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA)

* All patients in those studies were diagnosed with ED and hypogonadism at baseline; [‡]secondary hypogonadism caused by hypothalamic-pituitary structural abnormalities;

[‡]approximately 2/3 of men on this study were using testosterone gel

Study Details ²	Study Design	Setting	T Mean (SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hypogonadism			Test time	Cut-off (TT)	Normal Range	Assay
							n	N	%				
Hatzichristou 2002 (Greece)	Prospective	Andrology clinic	NR	NR	NR	NR	22	1276	1.72	NR	–	–	-
Martinez-Jabaloyas 2006 (Spain)	Prospective	Urology clinic	19.6±7.1	NR	NR	NR	8	165	4.85	08:00 – 10:00 in the morning	<2.8 ng/ml	2.8–8 ng/mL	CMI
Forsberg 1990 (Sweden)	Prospective	Department of urology and clinic for sexual therapy	NR	NR	NR	NR	13	100	13.0	NR	<10 nmol/L	–	-
Fahmy 1999 (UK)	Prospective	ED clinic	NR	NR	NR	NR	19	90	21.1	morning	<10 nmol/L	–	-
Acar 2004 (Turkey)	Prospective	NR	4.9±1.7	10.6 ± 6.4	5±3.9	6.9±7.7	29	262	11.1	morning	<3 ng/ml	–	ECLA
Studies performed in Asia and Australia													
Earle 2003 (Australia)	Prospective	Department of endocrinology and diabetes	7.8 (1–10) [101 men with low TT]	48–7800 µg/L [7 men with high PRL]	20 (10–56) U/L [18 men with high LH]	NR	83	1455	5.70	1 st test NR 2 nd test if TT low in first test, taken in the morning	<11 nmol/l	12–37 nmol/l	RIA
Tsujimura 2005 (Japan)	Prospective	Sexual function clinic	Low TT (43): 2.2±0.5 Normal TT (47): 4.5 ±	13.7 ± 15.4 ng/mL	10.7±9.5 ng/ml	4.0±2.4 ng/ml	43	90	47.7	morning	<3.17 ng/ml	2.7–10.7	RIA

Study Details ²	Study Design	Setting	T Mean (SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hypogonadism			Test time	Cut-off (TT)	Normal Range	Assay
							n	N	%				
			1.1										
Low 2006 (Malaysia)	Prospective	Primary care	17.4±6.5	NR	NR	NR	49	242	20.2	NR	<11 nmol/l	–	CMI
Studies performed in the Middle East													
El-Sakka 2005 (Egypt)	Prospective	Andrology clinic	1.8±0.9 ng/mL	34 ± 13.9 ng/mL	NR	NR	187	1248	15.0	morning	<2.8 ng/ml	2.8–8.8	ECLA
El-Sakka 2006 (Egypt)	Prospective	Andrology clinic	Baseline: 5.1±1.3 Final visit: 3.5±1.3	NS	NR	NR	16	305	5.25	morning	<2.8 ng/ml	2.8–8.8	ECLA
Low 2006 (Malaysia)	Prospective	Primary care	17.37±6.49 nmol/L	NR	NR	NR	49	242	20.2	before 11 AM	≤11 nmol/l	NR	direct chemiluminescent
Zohdy 2007 (Saudi-Arabia)	Retrospective	NR	3.9±1.7 ng/ml	NR	NR	NR	54	158	34.2	morning	<2.8 ng/ml	2.8–8.0	ECLA

Table 3: Prevalence of Hypogonadism in Men with Erectile Dysfunction (serum free or calculated testosterone)

Study Details ³	Study Design	Setting	T Mean(SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hypogonadism			Test Time	Cut-off (FT)	Normal Range	Assay
							n	N	%				
Drinka 1993 (USA)	Prospective	Outpatient department	NR	NR	NR	NR	6	48	12.50	morning (fasting)	<9 pg/mL*	9–25 pg/ml	RIA (analog)
Guay 2007 (USA)	Prospective	Primary care	With IR – 13 pg/mL No IR – 15.5 pg/mL	NR	NR	NR	39	154	25.32	NR	<10 pg/mL*	–	RIA (analog)
Low 2006 (Malaysia)	Prospective	Community	0.035 ± 0.012 nmol/L	NR	NR	NR	38	242	15.70	morning (fasting)	<0.0225 nmol/dl*	–	direct CMI
Martinez-Jabaloyas 2006 (Spain)	Prospective	Urology clinic	0.34± .1 nmol/L	NR	NR	NR	29	165	17.58	morning 8–10 a.m	0.228 ng/ml*	–	CMI

³Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone
SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (cmi); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA)

* calculated free testosterone

Table 4: Prevalence of Hypogonadism in Men with Erectile Dysfunction (serum bioavailable testosterone)

Study Details ⁴	Study Design	Setting	T Mean(SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hypogonadism			Test time	Cut-off (FT)	Normal Range	Assay
							n	N	%				
Low 2006 (Malaysia)	Prospective	Community	0.84 ± 0.28 nmol/L	NR	NR	NR	1	242	0.41	morning (fasting)	<0.2 nmol/dl	–	direct CMI

Table 5: Population Characteristics of Studies Measuring Hyperprolactinemia in Men with Erectile Dysfunction

Study Details ⁵	Study Design	Setting	ED Scale	Age Mean (SD) Range		Comorbidity	Serum levels	Test time	Cut-off (PRL)	Normal Range (PRL)	Assay
Jaffe 1996 (Israel)	Prospective	Outpatient clinic	NR	55.3		hypertension	TT, BT, PRL, LH, FSH	at least 2hrs post awakening	>20 ng/ml	NR	EIA
Netto 1993 (Brazil)	Prospective	Outpatient clinic	NR	55	31–69	NR	PRL	morning	20 ng/ml	NR	RIA
Hatzichristou 2002	Prospective	Andrology outpatient	NR	56 ± 14		DM, cardiovascular	TT, PRL	NR	NR	NR	NR

⁴Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone
SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (cmi); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA)

* calculated free testosterone

⁵Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone
SD = standard deviation; n = number of events; N = total number of participants; % = prevalence; 2X: test was performed twice

Assay: chemiluminescent microparticle immunoassay (cmi); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA), enzyme immunoassay (EIA)

Scales: Sex Health Inventory for Men (SHIM); sexual functioning questionnaire (SFQ);

* calculated free testosterone, ‡if 1st test elevated, serial measurements in a rested state at 0, 30, 60, and 90 minutes

Study Details ⁵	Study Design	Setting	ED Scale	Age Mean (SD) Range		Comorbidity	Serum levels	Test time	Cut-off (PRL)	Normal Range (PRL)	Assay
(Greece)		clinic				disease, urinary tract pathology, neurological disease, endocrine pathology					
Acar 2004 Turkey)	Prospective	NR	IIEF-5	47±10.1		chronic disease	TT, PRL, LH, FSH	morning after 8 hours fasting	>18ng/ml (2x)	NR	ECLA
Earle 2003 (Australia)	Prospective	Department of endocrinology and diabetes	NR	54.9	16–82	NR	TT, PRL LH and FSH if low TT	morning [†]	≥25 mcg/L	<25 mcg/L	RIA
Buvat 1997 (France)	Prospective	Urology clinic	NR	NR		NR	TT, PRL	morning post 20 min rest	20 ng/ml (high 20–35; highest >35)	NR	RIA
Akpononu 1994 (USA)	Prospective	Primary care clinic	NR	55.4±10	24–76	Renal failure, DM	TT, PRL, LH, FSH	NR	>20 mcg/l	0–20 mcg/l	NS
Johnson 1992 (USA)	Prospective	Urology clinic	NR	NR		NR	TT, PRL, LH	NR	≥18 ng/ml	NR	NR
El-Sakka 2005 (Egypt)	Prospective	Andrology clinic	IIEF	Endocrinopathy (297) – 51.9 ± 12.2 No endocrinopathy (951) – 52.3 ± 11.7		Obesity, diabetes, hypertension, ischemic heart disease, dyslipidemia, cerebrovascular stroke	TT, PRL, LH, FSH	morning	>20 ng/ml	4.1–20 ng/ml	ECLA

Study Details ⁵	Study Design	Setting	ED Scale	Age Mean (SD) Range		Comorbidity	Serum levels	Test time	Cut-off (PRL)	Normal Range (PRL)	Assay
El-Sakka 2006 (Egypt)	Prospective	Andrology clinic	IIEF	53.9 ± 8.5	26–86	overweight, DM, hypertension, IHD, dyslipidemia, psych. Dis.	TT, PRL	NR	>20 ng/ml	4.1–20 ng/mL	ECLA
Low 2006 (Malaysia)	Prospective	Community	IIEF–5	59.3 ± 7.38		depression	cFT, TT, PRL, LH	before 11 AM	>18.8 mcg/l	NR	direct CMI

Table 6: Prevalence of Hyperprolactinemia in Men with Erectile Dysfunction (serum prolactin levels)

Study Details ⁶	Study Design	Setting	T Mean(SD)	Prolactin Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hyperprolactinemia			Test time	Cut-off (PRL)	Normal Range	Assay
							n	N	%				
Studies performed in North America													
Akpononu 1994 (USA)	Prospective	Primary care clinics	14±5.1	6.3 ± 6.5 mcg/L	10.6±5.8 IU/L	14.7±8.6 IU/L	3	212	1.42	–	>20 mcg/l	0–20	NR
Johnson 1992 (USA)	Prospective	Urology clinic	NR	NR	NR	NR	1	7	14.29	–	≥18 ng/ml	NR	NR
Studies performed in Europe													
Buvat 1997 (France)	Prospective	Urology clinic	NR	NR	NR	NR	3	451	0.67	Morning	20 ng/ml (high 20–35;	NR	RIA

⁶Baseline serum levels: T = total testosterone; LH = luteinizing hormone; FSH = follicle-stimulating hormone

SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (CMI); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA); automated enzyme immunoassay system (AEIA)

[‡] if 1st test elevated, serial measurements in a rested state at 0, 30, 60, and 90 minutes

Study Details ⁶	Study Design	Setting	T Mean(SD)	Prolactin Mean(SD)	LH Mean(SD)	FSH Mean(SD)	Hyperprolactinemia			Test time	Cut-off (PRL)	Normal Range	Assay
							n	N	%				
											highest >35)		
Hatzichristou 2002 (Greece)	Prospective	Andrology clinic	NR	NR	NR	NR	8	1276	0.63	–	NR	NR	NR
Acar 2004 (Turkey)	Prospective	NR	4.9±1.7	10.6 ± 6.4	5±3.9	6.9±7.7	25	262	9.54	Morning	>18ng/ml (2x)	NR	ECLA
Other countries													
Earle 2003 (Australia)	Prospective	Department of endocrinology and diabetes	7.8 (1–10) [101 men with low TT]	48–7800 µg/L [7 men with high PRL]	20 (10–56) U/L [18 men with high LH]	NR	7	1455	0.48	Morning [†]	NR	NR	RIA
Netto 1993 (Brazil)	Prospective	Primary care	NR	NR	NR	NR	23	600	3.83	Morning	20 ng/ml	NR	RIA
Low 2006 (Malaysia)	Prospective	Community	17.4±6.5	8.9±7.99 mcg/L	NR	NR	7	242	2.89	Before 11 AM	> 18.8 mcg/l	NR	direct CMI
El-Sakka 2005 (Egypt)	Prospective	Andrology clinic	1.8±0.9	34 ± 13.9 ng/mL	NR	NR	171	1248	13.7	NR	>20 ng/ml	4.1–20	ECLA
El-Sakka 2006 (Egypt)	Prospective	Andrology clinic	Baseline – 5.1±1.3 Final visit – 3.5 ±1.3	NS	NR	NR	97	305	32	NR	>20 ng/ml	4.1–20	ECLA

Table 7: Prevalence of Hyperprolactinemia in Men with and without Erectile Dysfunction (serum prolactin levels)

Study Details ⁷	Study Design	Setting	Hyperprolactinemia			Hyperprolactinemia			Test time	Cut-off (PRL)	Normal Range	Assay
			n	N	%	n	N	%				
Acar 2004 (Turkey)	Prospective	NR	25	262	9.54	2	53	3.77	Morning	>18ng/ml (2x)	NR	ECLA
Low 2006 (Malaysia)	Prospective	Primary care	7	242	2.89	1	109	12.5	before 11 AM	>18.8 mcg/l	NR	direct CMI

Table 8: Population Characteristics of Studies Measuring Serum LH/FSH Levels in Men with Erectile Dysfunction

Study Details ⁸	Study Design	Setting	ED Scale	Age Mean (SD) Range		Comorbidity	Serum Levels	Test time	Cut-off (LH/FSH)	Normal Range (LH/FSH)	Assay
Jaffe 1996 (Israel)	Prospective	clinic	-	55.3		Hypertension	TT, BT, PRL, LH, FSH	Morning	LH: >15 mIU/mL ⁹ ; FSH: NR	NR	EIA
Earle 2003 (Australia)	Prospective	Department of Endocrinology and Diabetes	NR	54.9	16-82	Prostate cancer, secondary hypogonadism	TT, PRL, LH, FSH	NR	>10U/L	LH: 2-9 U/L	RIA
Bunch 2002 (USA)	Retrospective	outpatients	NR	64.6 ± 10.8	51-85	DM, IHD, hypertension, hyperlipidemia, depression, sleep	TT, LH	NR	LH: <13nIU/ml	NR	RIA

⁸Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone

SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (CMI); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA), enzyme immunoassay (EIA)

* calculated free testosterone;⁸ the cut for LH > 15mIU/ml was used to define primary hypogonadism

Scales: Sex Health Inventory for Men (SHIM); sexual functioning questionnaire (SFQ);

Study Details ⁸	Study Design	Setting	ED Scale	Age		Comorbidity	Serum Levels	Test time	Cut-off (LH/FSH)	Normal Range (LH/FSH)	Assay
				Mean (SD)	Range						
						apnea, CVA, AF, hypothyroidism, prostate cancer, CRF, head tumors, compression fractures					
Fahmy 1999 (UK)	Prospective	ED clinic	sexual activity questionnaire	NR	NR	NR	TT, FSH, PRL	morning (9–11 am)	NR	NR	NR
Akpunonu 1994 (USA)	Prospective	Primary care clinic	NR	55.4±10	24–76	Renal failure, DM	TT, PRL, LH, FSH	NR	NR	LH: 5–20 IU/L; FSH: 5–20 IU/L	NR
Johnson 1992 (USA)	Prospective	Urology clinic	NR	NR		NR	TT, PRL, LH	NR	NR	NR	NR
El-Sakka 2005 (Egypt)	Prospective	Andrology clinic	IIEF	Endocrinopathy (297) -51.9 ± 12.2 No endocrinopathy (951) -52.3 ± 11.7		Obesity, diabetes, hypertension, ischemic heart disease, dyslipidemia, cerebrovascular stroke	TT, PRL, LH, FSH	NR	LH <1.3 mIU/mL; FSH <0.9 mIU/mL	NR	ECLA
Guay 1991 (USA)	Prospective	Endocrinology clinic	–	53.2 ± 9.1		NR	TT, LH, FSH	Morning	NR	LH: 2–20 mIU/L; FSH: 2–10 mIU/L	RIA
Low 2006 (Malaysia)	Prospective	Community	IIEF-5	59.3 ± 7.38		Depression	cFT, TT, PRL, LH	Morning	>12 IU/l	NR	direct CMI

Study Details ⁸	Study Design	Setting	ED Scale	Age Mean (SD) Range	Comorbidity	Serum Levels	Test time	Cut-off (LH/FSH)	Normal Range (LH/FSH)	Assay
							(before 11am)			

Table 9: Prevalence of Primary or Secondary Hypogonadism in Men with Erectile Dysfunction (total serum levels of LH and FSH)

Study details ¹⁰	Study design	Setting	T Mean(SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean (SD)	LH/FSH			Test time	Cut-off (TT)	Normal range	Assay
							n	N	%				
Secondary hypogonadism (Low levels of LH and/or FSH)													
Bunch 2002 (USA)	Retrospective*	Outpatients	177.73 ± 78.36 ng/dL	NR	6.8±9.1 mIU/ml	NR	↓LH: 29 [‡]	66	43.9	NR	<13 mIU/ml	NR	RIA
El-Sakka 2005 (Egypt)	Prospective	Andrology clinic	1.8±0.9 ng/mL	34 ± 13.9 ng/mL	NR	NR	↓LH/FSH: 21	1248	1.68	morning	NR	NR	ECLA
Primary hypogonadism (High levels of LH and/or FSH)													
Akpunonu 1994 (USA)	Prospective	Primary care clinics	14±5.1 nmol/L	6.3 ± 6.5 mcg/L	10.6±5.8 IU/L	14.7±8.6 IU/L	↑LH: 2	194	1.03	NR	NR	5–20 IU/L	-
							↑FSH: 0	194	0				

¹⁰Baseline serum levels: T = total testosterone; Pr = prolactin; LH = luteinizing hormone; FSH = follicle-stimulating hormone

SD = standard deviation; n = number of events; N = total number of participants; % = prevalence

Assay: chemiluminescent microparticle immunoassay (CMI); electrochemiluminescence immunoassay (ECLA), radioimmunoassay (RIA)

* All patients in those studies were diagnosed with ED and hypogonadism at baseline; [‡]secondary hypogonadism caused by hypothalamic-pituitary structural abnormalities; [§]approximately 2/3 of men on this study were using testosterone gel

Study details ¹⁰	Study design	Setting	T Mean(SD)	PRL Mean(SD)	LH Mean(SD)	FSH Mean (SD)	LH/FSH			Test time	Cut-off (TT)	Normal range	Assay
							n	N	%				
Johnson 1992 (USA)	Prospective	Urology clinic	NR	NR	NR	NR	↑LH: 5	330	1.52	NR	NR	NR	RIA
Earle 2003 (Australia)	Prospective	Departme nt of Endocrin ology and Diabetes	7.8 (1– 10) [101 men With ↓TT]	48–7800 µg/L [7 men with ↑PRL]	20 (10– 56) U/L [18 men with ↑LH]	NR	↑LH: 18	83 (all ↓TT)	21.7	morning	NR	2–9 U/L	RIA
Fahmy 1999 (UK)	Prospective	ED clinic	NR	NR	NR	NR	↓FSH: 1	90	1.11	morning	NR	NR	NR
Guay 1991 (USA)	Prospective	Endocrin ology	NR	NR	NR	NR	↓LH: 6	21	28.6	NR	Gonadot ropin reserve (≥20mIU/ mL ↑ in LH, FSH)	NR	RIA
							↓FSH: 1	21	4.76				
Low 2006 (Malaysia)	Prospective	primary care	17.4±6.5	NR	NR	NR	↓LH: 14	242	5.79	NR	NR	NR	CMI

Table 10: Serious Adverse Events in Sildenafil vs. Placebo (data from RCTs)

Author year	ED Population Country/Ethnicity	Serious Adverse Events n/N (%)		Active dose	Description of Adverse Events (study arm)
		Sildenafil	Placebo		
Choi (2003)	All causes Asia-NR	0/66	2/67 (3%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> NR (CG)
Levinson (2003)	All etiologies Men from Egypt and South African	3/128 (2.0%)	0/126	Flexible 25– 100 mg	<ul style="list-style-type: none"> Myocardial infarction (IG) Accidental vertebral fracture (IG) Diverticulitis (IG)
DeBusk (2004)	Stable coronary artery disease UK–NR	1/75 (1.4%)	2/76 (2.6%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> Atypical chest pain (IG) Acute UTI (CG) Severe angina pectoris (CG)
Tan (2000)	All etiologies Men from Malaysia, Singapore and Philippines	1/127 (<1%)	1/127 (<1%)	Flexible 25– 100 mg; IG pts on 100 mg	<ul style="list-style-type: none"> Severe angina pectoris 4 hr post 100 mg sildenafil (pts with CAD) Accidental hand injury (CG)
Meuluman (2001)	All causes Europe and US– NR	2/159 (1.3%)	0/156	Flexible 25– 100 mg	<ul style="list-style-type: none"> Death due to accident (IG) Death due to cardiac arrest (IG)
Young (2002)	All causes North America, Hispanic	1/98	0/99	Flexible 25– 100 mg	<ul style="list-style-type: none"> NR (IG)
Eardley (2001)	All causes UK–NR	0/44	1/44 (2.3%)	Flexible dose 25–75 mg	<ul style="list-style-type: none"> Myocardial infarction in a pt during 2nd 28 d phase (CG)
Price (1998)	Diabetes type I and II UK–NR	1/21 (4.7%)	0/21	25 mg	<ul style="list-style-type: none"> Pneumococcal pneumonia (IG)
Christiansen (2000)	All etiologies Europe-NR	24/205 (11.7%), Group designation not reported		10 or 25 mg	<ul style="list-style-type: none"> Death (open label phase, 10 mg) Other events not described
Olsson (2000)	All etiologies Europe-NR	3/351 (<1%); Group designation not reported		Fixed 25, 50, 100 mg	<ul style="list-style-type: none"> Myocardial infarction (NR) Renal cell carcinoma (NR) Epileptic crisis (NR)
Chen (2001)	All etiologies Taiwan-Asian	4/119 (3.0%)	4/117 (3.0%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> No data provided
Fowler (2004)	Multiple sclerosis UK–NR	3/104 (2.7%)	3/113 (2.9%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> NR (NR) 12 (6%) of pts experienced SAE (relapse) during open label
Katz (2005)	Stable coronary heart failure Multi-Nation	2/63 (3.0%)	4/74 (5.0%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> NR
Seibel (2002)	Renal failures Brazil-NR	0/24	2/24 (8.0%)	Fixed 50 mg	<ul style="list-style-type: none"> Deaths (CG)
Becher (2002)	All etiologies South America, Chile-Hispanic	2/72 (2.8%)	1/71 (1.4%)	Flexible 25– 100 mg	<ul style="list-style-type: none"> Death due to myocardial infarction (CG) Remaining SAEs not

Author year	ED Population Country/Ethnicity	Serious Adverse Events n/N (%)		Active dose	Description of Adverse Events (study arm)
		Sildenafil	Placebo		
					described
Cappelleri (2000)	All etiologies US-NR	3/124 (2.0%)	3/123 (2.0%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> NR
Albuquerque (2005)	Hypertensive men Brazil	3/61 (5.0%)	1/59 (1.7%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> Cerebrovascular accident (IG) Pulmonary edema/heart failure (IG) Atrial fibrillation/arrhythmia (IG) polytrauma (CG)
Pickering (2004)	Men with history of atrial hypertension Italy-NR	2/281 (<1%)	2/287 (<1%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> NR
Glina (2001)	All etiologies Mexico- Brazilian/Mexican	1/124 (<1%)	5/121 (4%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> NR
McVary (2007)	Men with lower urinary tract syndromes associated with prostatic hyperplasia US: 82% White	2/189 (1.0%)	3/181 (2.0%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> Worsening of knee arthralgia (100 mg/ IG) Severe acute cerebrovascular stroke (100 mg/ IG) Remaining 3 cases were not described
Althof (2006)	All causes Multi-nation: White 55.5%; Black 15%; Asian 5.5%; Other 23.5%	1/274 (<1%)	1/279 (<1%)	NR	<ul style="list-style-type: none"> Severe coronary artery disease (IG) Urinary tract infection (CG)
O'Leary (2006)	All causes (also with low self- esteem) US: 62% White; 25% Black	0/129	1/127 (<1%)	Flexible 25- 100 mg	<ul style="list-style-type: none"> Death (CG)

NR=not reported; CG=control group; IG=intervention group; pt(s)=patient(s)

Table 11: Efficacy Results of Tadalafil by ED Severity Groups

Study ID	Dose	Mild ED	Moderate ED	Severe ED
Mean change in IIEF-EF scores from baseline				
McMahon (2005)	20 mg	3.0	10.7	11.6
Eardley (2004)	20 mg	6.1	13.2	14.3
Seftel (2004)	20 mg	5.6	10.7	11.0
Carrier (2005)	10 mg	4.5	8.4	8.3
Carrier (2005)	20 mg	5.2	9.0	11.5
Costa, (2006)	On demand	6.2	11.5	14.2
Costa (2006)	3 x week	6.4	11.8	14.6
Saylan (2006)	20 mg	6.3	8.2	14.8
Yip (2006)	20 mg	5.3	9.1	12.5
EF mean end point scores				
McMahon (2005)	20 mg	24.4	23.9	19.0
Rajfer (2007)	2.5 mg	24.3	21.0	13.8
Rajfer (2007)	5 mg	26.2	21.9	15.5
Guo(2006)	10 mg	24.0	22.3	18.1
Guo(2006)	20 mg	23.5	23.0	21.6
Nagao (2006)	5 mg	25.6	22.7	15.8
Nagao (2006)	10 mg	26.0	24.0	20.2
Nagao (2006)	20 mg	25.3	23.0	21.9
Patients with normal EF at end point (%)				
Eardley (2004)	20 mg	80	73	55
Seftel (2004)	20 mg	72.1	52.4	34.3
Saylan (2006)	20 mg	84.4	43.2	40.7
Change from baseline in SEP-3 (% of patients with successful penetration)				
Young (2005)	10 mg*	13.1	46.0	29.2
Young (2005)	20 mg*	38.5	68.9	41.3
Costa, (2006)	On demand	41.7	59.7	55.8
Costa, (2006)	3 x week	44.4	61.3	57.1
Rajfer (2007)	2.5 mg	72.5	56.3	27.4
Rajfer (2007)	5 mg	82.2	61.3	32.6
Nagao (2006)	5 mg	74.2	50.3	31.1
Nagao (2006)	10 mg	80.4	64.5	49.4
Nagao (2006)	20 mg	76.8	67.8	62.1
Change from baseline in SEP-2 (% of patients with successful penetration)				
Rajfer (2007)	2.5 mg	90.0	74.8	38.9
Rajfer (2007)	5 mg	91.9	82.2	44.9
Nagao (2006)	5 mg	89.2	79.2	48.7
Nagao (2006)	10 mg	98.8	84.2	63.4
Nagao (2006)	20 mg	94.2	80.8	73.1

Table 12: Intracavernosal Injection: Sexual Intercourse Success

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Prostaglandins vs. Papaverine				
Earle 1990	Physiologic: 62% Idiopathic: 27% Unclear: 10%	31% (40/129) Over 4 weeks	33% (43/129) Over 4 weeks	0.93 [0.65–1.33]

Table 13: Intracavernosal Injection: Improvement in Erections*

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Prostaglandins (PgE₁) vs. Placebo				
Bechara 1997	NR	50 (30/60)	0 (0/60)	
Colli 1996	Psychogenic: 53% Physiologic: 31% Mixed: 11%	28.9 (39/135) All doses	0 (0/45)	–
Garceau 1996	Psychogenic: 27% Physiologic: 43.8% Mixed: 20.3% Other 8.2%	48.1 (26/54) All doses	NR	–
Linet 1996	Psychogenic: 13% Physiologic: 57% Mixed: 29%	A. Rigiscan 31.6 (75/237) By dose** 2.5 µg: 21% 5 µg: 31% 10 µg: 27% 20 µg: 45%	A. Rigiscan 0 (0/59)	–
		B. Clinical (Full rigidity) 35 (83/237) By dose** 2.5 µg: 17% 5 µg: 27% 10 µg: 45% 20 µg: 50%	B. Clinical (Full rigidity) 0 (0/59)	–
Range of treatment improvement (%)		28.9–66.0	0	NA
PgE₁ vs. Papaverine				

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Earle 1990	Physiologic: 62% Idiopathic: 27% Unclear: 10%	26.4 (34/129)	13.2 (17/129)	2.00 [1.18–3.39]
Kattan 1991	Physiologic: 100%	46 (23/50)	14 (7/50)	3.29 [1.55–6.95]
Kunelius 1998	NR	40 (12/30)	10 (3/30)	4.00 [1.25–12.75]
Mahmoud 1992	Psychogenic: 19% Physiologic: 66% Mixed: 15%	80.8 (42/52)	63.5 (33/52)	1.27 [1.00–1.63]
Range of treatment improvement (%)		26.4–80.8	10.0–63.5	NA
PgE₁ vs. PgE₁ + Papaverine				
Floth 1991	Psychogenic: 10.5% Physiologic: 92%	60.5 (23/38)	73.7 (28/38)	0.82 [0.60–1.13]
PgE₁ vs. Papaverine + Phentolamine				
Bechara 1997	NR	50 (30/60)	56.7 (34/60)	0.88 [0.63–1.23]
PgE₁ vs. Phentolamine+ PgE₁				
Aversa 1996a	Psychogenic: 100%	20.8 (5/24)	54.2 (13/24)	0.38 [0.16–0.91]
Aversa 1996b	Psychogenic:100%	30 (3/10)	60 (6/10)	0.50 [0.17–1.46]
Range of treatment improvement (%)		20.8–30.0	54.2–60.0	NA
PgE₁ vs. Trimix				
Bechara 1996	NR	21.9 (7/32)	50.0 (16/32)	0.44 [0.21–0.92]
Seyam 2005	Psychogenic: 8.9% Physiologic: 53.7% Mixed: 37.4%	67.8 (122/180)	66.7 (120/180)	0.98 [0.85–1.14]
Range of treatment improvement (%)		21.9– 67.8	50.0–66.7	NA
PgE₁ vs. Moxisylyate				
Kunelius 1998	NR	40.0 (12/30)	6.7 (2/30)	6.00 [1.47–24.55]
Buvat 1998	Psychogenic: 46% Physiologic: 26%	85.3 (58/68) <i>At home</i>	60.7 (37/61) <i>At home</i>	1.41 [1.12–1.76]

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
	Mixed: 28%	81.3 (61/75) <i>Investigator assessment</i>	45.7 (37/81) <i>Investigator assessment</i>	1.78 [1.37–2.31]
PgE₁ vs. Nitroprusside (300 µg or 400 µg)				
Martinez-Piñeiro 1995	NR	20.0 (12/60)	15.0 (9/60) 300 µg	1.33 [0.61–2.93]
		20.0 (7/35)	14.3 (5/35) 400 µg	1.40 [0.49–3.99]
PgE₁ vs. Linsidomine				
Porst 1993	Psychogenic: 60% Physiologic: 40%	65.0 (26/40)	12.5 (5/40)	5.20 [2.22–12.18]
Wegner 1995	NR	40.0 (16/40)	7.5 (3/40)	5.33 [1.68–16.89]
Wegner 1994	NR	30.0 (6/20)	10.0 (4/40)	3.00 [0.95–9.43]
Range of treatment improvement (%)		30.0–65.0	7.5–12.5	NA
PgE₁ vs. Linsidomine + Urapidil				
Wegner 1995	NR	40.0 (16/40)	25.0 (10/40)	1.60 [0.83–3.09]
PgE₁ vs. PgE₁ + Lidocaine				
Kattan 1995	NR DM: 68% Low testosterone: 12%	27.3 (6/22)	63.6 (14/22)	0.43 [0.20–0.91]
PgE₁ vs. PgE₁ + Procaine				
Shramek 1994	Psychogenic: 12.5% Physiologic: 87.5%	66.7 (16/24)	66.7 (16/24)	1.00 [0.67–1.49]
Trimix vs. Trimix + Sodium Bicarbonate				
Moriel 1993	NR	68.4 (13/19)	78.9 (15/19)	0.87 [0.59–1.27]
Trimix vs. Trimix + Atropine				
Sogari 1997	NR Risk factors: DM, hypertension, alcoholism, smoking, Peyronie's disease)	45.6 (52/114)	45.6 (52/114)	–
Papaverine + Phentolamine vs. Placebo				

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Bechara 1997	NR	56.7 (34/60)	0 (0/60)	–
Papaverine + Phentolamine + Sexual counseling vs. Papaverine + Phentolamine				
Van der Windt 2002	Psychogenic: 35.7% Physiologic: 11.4% Mixed: 34.3%	84 (subjective erection score, range 0–100)	79 (subjective erection score, range 0–100)	–
PgE₁ + Papaverine vs. Papaverine + Phentolamine				
Floth 1991	Psychogenic: 12.3% Physiologic: 100% (Patients could have both)	77.6 (38/49)	57.1 (28/49)	1.36 [1.02–1.81]
Papaverine vs. Moxisylate				
Kunelius 1998	NR	10.0 (3/30)	7.0 (2/30)	1.50 [0.27–8.34]
Moxisylate vs. Placebo				
Costa 1993	Psychogenic: 32%	86.9 (53/61)	27.9 (17/61)	3.12 [2.06–4.72]
Vasoactive Intestinal Polypeptide + Phentolamine vs. Placebo				
Sandhu 1999	Physiologic: 47% Mixed: 53% (Dose assessment phase) Results: Phase 1-2 combined. Phase 1 criteria met by 133 patients and phase 2 criteria met by 126 patients (94.7%) ITT population: 172 of 195 of those who received at least one injection of active treatment and placebo	<i>Erections suitable for intercourse</i> 25 µg dose: 75.1% (1417/1886 injections) 2 mg dose: 66.5% (257/386 injections) <u>ITT analysis</u> 25 µg dose: 73.7% (1576/2137 injections) 2 mg dose: 69.1% (397/574 injections)	<i>Erections suitable for intercourse</i> 25 µg dose: 12.1% (45/373 injections) 2 mg dose: 10.3% (8/78 injections) <u>ITT analysis</u> 25 µg dose: 12.9% (55/426 injections) 2 mg dose: 13.7% (16/116 injections)	p <0.001 p <0.001 p <0.001 p <0.001
Timing of PgE₁ and/or use in post-prostatectomy populations PgE₁ (early intervention) vs. PgE₁ (late intervention): post non-nerve-sparing radical prostatectomy				
Gontero 2003	All men had prostate cancer†	72.2 (26/36)	43.2 (16/37)	1.67 [1.10–2.54]

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
PgE₁ vs. No Treatment: post-nerve-sparing radical retropubic prostatectomy				
Montorsi 1997	All men had prostate cancer†	66.7 (8/12)	20 (3/15)	3.33 [1.12–9.90]
PgE₁ + Sexual Counseling vs. PgE₁: post-nerve-sparing radical retropubic prostatectomy or cystectomy				
Titta 2006	Men had either prostate and/or bladder cancer†	<i>Mean IIEF score</i> 26.6 (before surgery) 8.4 (before ICI) 23.4 (3 months after surgery) 26.5 (18 months after surgery) 75.8 (22/29) No ED at end of study	<i>Mean IIEF score</i> 26.1 (before surgery) 8.4 (before ICI) 21.7 (3 months after surgery) 24.3 (18 months after surgery) 50.0 (14/28) No ED at end of study	– – p <0.05 1.52 [0.99–2.32]

* Defined as full erection or “positive response,” Grade 4/5 erections, or erections sufficient for intercourse or Rigiscan assessment $\geq 70\%$ rigidity base or tip lasting ≥ 10 minutes

** Numbers extracted from graph

† All men were potent or had normal International Index of Erectile Dysfunction (IIEF) scores at baseline

†† Percentage of sexual situations producing an erection

Table 14: Intracavernosal Injection: Patients with Adverse Events

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Prostaglandins (PgE₁) vs. Placebo				
Bechara 1997	Pain	35.0 (21/60)	0	–
Linnet 1996	Penile pain	22.7 (54/237)	NR	–
	Priapism	2.5 (6/237)	NR	–
Vanderschueren 1995	Penile pain	11.7 (74/630)	10.9 (23/210)	1.0 [-4.0, 6.0]
von Heyden 1993	Penile pain/burning sensation	13.3 (18/135)	NR	–
Range of reported pain/discomfort (%)		11.7–35.0	0–10.9	NA
Bechara 1997	Prolonged erection	15.0 (9/60)	0 (0/60)	–
von Heyden 1993	Hematoma	1.5 (2/135)	NR	–
Colli 1996	Treatment-related	2.2 (3/135)	2.2 (1/45)	–
von Heyden 1993	Treatment-related	16.3 (22/135)	NR	–
PgE₁ vs. Papaverine				
Earle 1990	Pain during injection	8.5 (11/129)	4.7 (6/129)	4.0 [-2.0, 10.0]
Kattan 1991	Pain during injection	46.0 (23/50)	44.0 (22/50)	2.0 [-17.0, 21.0]
Mahmoud 1992	Penile pain	11.5 (6/52)	32.7 (17/52)	-21.0 [-37.0, -6.0]
Range of reported pain/discomfort (%)		8.5–46.0	4.7–44.0	NA
Earle 1990	Prolonged erection	0	<1 (1/129)	–
Kattan 1991	Priapism	0	0	–
Kunelius 1998	Prolonged erection	10.0 (3/30)	6.7 (2/30)	3.0 [-11.0, 17.0]
Mahmoud 1992	Priapism	0	0	–
Range of prolonged erection/priapism (%)		0–10.0	0–6.7	NA
Kattan 1991	Dizziness/headache	2.0 (1/50)	4.0 (2/50)	-2.0 [-9.0, 5.0]
PgE₁ vs. Papaverine + PgE₁				
Floth 1991	Pain	34.2 (13/38)	18.4 (7/38)	16.0 [-4.0, 35.0]

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
	Prolonged erection	0	10.5 (4/38)	–
PgE₁ vs. Papaverine + Phentolamine				
Bechara 1997	Pain	35.0 (21/60)	15.0 (9/60)	20.0 [5.0–35.0]
	Prolonged erection	15.0 (9/60)	18.3 (11/60)	-3.0 [-17.0, 10.0]
PgE₁ vs. Phentolamine+ PgE₁				
Aversa 1996a	Prolonged erection	4.2 (1/24)	4.2 (1/24)	–
PgE₁ vs. Trimix				
Bechara 1996	Pain	40.6 (13/32)	12.5 (4/32)	28.0 [8.0–49.0]
Seyam 2005	Pain	17.3 (31/179)	14.4 (26/179)	-3.0 [-11.0, 4.0]
Range of reported pain/discomfort (%)		14.4–40.6	12.5–17.8	NA
Seyam 2005	Priapism	<1.0 (1/179)	5.0 (9/170)	-5.0 [-8.0, -1.0]
PgE₁ vs. Moxisylyate				
Buvat 1998	Pain during injection: clinic	13.3 (10/75)	14.8 (12/81)	-1.0 [-12.0, 9.0]
	Pain during injection: home	25.0 (17/68)	14.8 (9/61)	10.0 [-3.0, 24.0]
	Pain during erection: clinic	17.3 (13/75)	2.5 (2/81)	15.0 [6.0–24.0]
	Pain during erection: home	23.5 (16/68)	4.9 (3/61)	19.0 [7.0–30.0]
	Pain after erection: clinic	6.7 (5/75)	0 (0/81)	–
	Pain after erection: home	19.1 (13/68)	4.9 (3/61)	14.0 [3.0–25.0]
	Prolonged erection: clinic	5.3 (4/75)	0 (0/81)	–
	Prolonged erection: home	4.4 (3/68)	1.6 (1/61)	3.0 [-3.0, 9.0]
	Bleeding: clinic	2.7 (2/75)	2.5 (2/81)	0.0 [-5.0, 5.0]
	Bleeding: home	14.7 (10/68)	4.9 (3/61)	10.0 [0.0–20.0]
	Dizziness/hypotension: home	1.5 (1/68)	8.2 (5/61)	-7.0 [-14.0, 1.0]
	Kunelius 1998	Prolonged erection	10.0 (3/30)	3.3 (1/30)
PgE₁ vs. Nitroprusside (100 µg, 300 µg or 400 µg)				

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Martinez-Piñeiro 1995	Pain during injection	6.7 (7/105)	0	7.0 [2.0–12 .0]
	Dizziness	3.8 (4/105)	6.7 (7/105)	-3.0 [-9.0, 3.0]
	Hematoma	1 subject	1 subject	–
PgE₁ vs. Linsidomine				
Porst 1993	Penile pain	17.5 (7/40)	NR	–
Wegner 1995	Pain during injection	7.5 (3/40)	2.5 (1/40)	5.0 [-4.0, 14.0]
Range of reported pain/discomfort (%)		7.5–17.5	NA	NA
Porst 1993	Moderate/severe headache	NR	7.5 (3/40)	–
PgE₁ vs. Linsidomine + Urapidil				
Wegner 1995	Pain during injection	7.5 (3/40)	7.5 (3/40)	–
	Severe hypotension	0	12.5 (5/40)	–
PgE₁ (fast injection) vs. PgE₁ (slow injection)				
Gherchiu 1996	Pain during injection	54.5 (6/11)	18.2 (2/11)	36.0 [-1.0, 74.0]
PgE₁ vs. PgE₁ + Local Anesthetic				
Kattan 1995	Pain	86.4 (19/22)	45.4 (10/22) Lidocaine	41.0 [16.0–66.0]
Shramek 1994	Pain, moderate to severe	83.3 (20/24) (11 patients with severe ED)	62.5 (15/24) + Procaine (4 patients with severe ED)	21.0 [-4.0, 45.0]
Range of reported pain/discomfort (%)		–	–	NA
PgE₁ vs. PgE₁ + Sodium Bicarbonate				
Godschalk 1996	Pain	80.0 (8/10)	70.0 (7/10)	10.0 [-28.0, 48.0]
PgE₁ + Papaverine vs. Papaverine + Phentolamine				
Floth 1991	Pain	16.3 (8/49)	0	–
	Prolonged erection	8.2 (4/49)	8.2 (4/49)	–

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Trimix vs. Trimix + Sodium Bicarbonate				
Moriel 1993	Pain/discomfort	57.9 (11/19)	5.3 (1/19)	53.0 [28.0–77.0]
Trimix vs. Trimix + Atropine				
Sogari 1997	Pain	50.0 (57/114)	55.3 (63/114)	-5.0 [-18.0, 8.0]
Papaverine +Phentolamine vs. Placebo				
Bechara 1997	Pain	15.0 (9/60)	0	–
	Prolonged erection	18.3 (11/60)	0	–
Papaverine + Phentolamine + Sexual Counseling vs. Papaverine + Phentolamine				
Van der Windt 2002	12% discontinued because of prolonged erection Priapism: 3 patients Hematoma: 4 patients Curvature of the penis: 1 patient AE similar between groups			–
Papaverine vs. Moxisylate				
Kunelius 1998	Prolonged erection	6.7 (2/30)	3.3 (1/30)	3.0 [-8.0, 14.0]
Moxisylate vs. Placebo				
Costa 1993	Prolonged erection	1.6 (1/61)	0	–
	Mild pain	3.3 (2/61)	0	–
	Faintness (normal BP)	3.3 (2/61)	0	–
	Hypotension, nausea, or bradycardia	1.6 (1/61)	0	–
	Hot flushes	1.6 (1/61)	0	–
	Vagal shock after sharp pain during injection	0	1.6 (1/61)	–
Vasoactive Intestinal Polypeptide + Phentolamine vs. Placebo				
Sandhu 1999	Bruising	43.1 (84/195)	12.3 (24/195)	31.0 [22.0–39.0]
	Bleeding at injection site	20.5 (40/195)	5.1 (10/195)	15.0 [9.0–22.0]

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
	Pain on injection	4.6 (9/195)	8.2 (16/195)	-4.0 [-8.0, 1.0]
	Urethral bleeding	12.3 (24/195)	2.6 (5/195)	10.0 [5.0–15.0]
	Priapism	<1.0 (1/195)	0	–
	Flushing	74.4 (145/195)	13.3 (26/195)	61.0 [53.0–69.0]
	Headache	3.6 (7/195)	1.5 (3/195)	2.0 [-1.0, 5.0]
	Palpitation	7.7 (15/195)	0	–
	Tachycardia	5.1 (10/195)	<1.0 (1/195)	5.0 [1.0–8.0]
Timing of PgE1 PgE₁ (early intervention) vs. PgE₁ (late intervention): post non-nerve-sparing radical prostatectomy				
Gontero 2003	Prolonged erection	8.3 (3/36)	0 (0/37)	–
PgE₁ vs. No Treatment: post-nerve-sparing radical retropubic prostatectomy				
Montorsi 1997)	Prolonged erection	6.7 (1/15)	0 (0/15)	–
	Hematoma	13.3 (2/15)	0 (0/15)	–
PgE₁ + Sexual Counseling vs. PgE₁: post-nerve-sparing radical retropubic prostatectomy or cystectomy				
Titta 2006	Moderate pain	34.5 (10/29)	42.9 (12/28)	-8.0 [-34.0, 17.0]
	Severe pain	13.8 (4/29)	10.7 (3/28)	3.0 [-14.0, 20.0]
	Prolonged erection	17.2 (5/29)	17.8 (5/28)	-1.0 [-20.0, 19.0]
	Hematoma	6.9 (2/29)	10.7 (3/28)	-4.0 [-19.0, 11.0]
	Priapsim	0	0	–
	Nodule	0	0	–
Vasoactive Intestinal Polypeptide + Phentolamine (2 arms) vs. Placebo				
Dinsmore 1999	Bruising	5.5–7.2 (range)	5.1	–
	Bleeding at injection site	4.0–4.6 (range)	3.0	–

Study	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
	Pain on injection	0	7.7	–
	Urethral bleeding	2.2–2.5 (range)	0.4	–
	Priapism	0.1	0	–
	Flushing	47.0–50.0 (range)	9	–
Papaverine followed by Sildenafil vs. Sildenafil followed by Papaverine				
Viswaroop 2005	Priapism	Both arms combined		
	Headache	10.0 (5/50)		–
	Blurred vision	4.0 (2/50)		–
	Dyspepsia	2.0 (1/50)		–
		2.0 (1/50)		–

Table 15: Subcutaneous Injection: Improvement in Erections

Study / Type of Patients	Outcome Definition	Treatment Group % (n/N)	Control Group % (n/N)	Relative risk (RR) [95% CI] or p value
Melanotan II vs. Placebo				
Wessells 2000	Subject reported "subjectively apparent erections" on at least one of two injections	85.0 (17/20)	NR	–
Psychogenic: 10 patients				
Physiologic: 10 patients	Subjective erectile activity	69.2 (27/39) Based on number of injections	2.4 (1/41) Based on number of injections	–
Analysis: 10 patients with physiologic ED	Subject reported "subjectively apparent erections" on at least one of two injections	90.0 (9/10)	10.0 (1/10)	9.00 [1.39–58.44]

Study / Type of Patients	Outcome Definition	Treatment Group% (n/N)	Control Group % (n/N)	Relative risk (RR) [95% CI] or p value
	Subjective erectile activity	63.2 (12/19) Based on number of injections	4.8 (1/21) Based on number of injections	–
PT–141 (cyclic heptapeptide melanocortin analog) vs. Placebo				
Rosen 2004 25 patients with moderate-severe ED with inadequate response to sildenafil.		NR		
		NR		
		NR		

Table 16: Subcutaneous Injection: Patients with Adverse Events

Study	Adverse event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute risk difference (%) [95% CI]
Melanotan II vs. Placebo				
Wessells 2000		<i>Number of injections</i>	<i>Number of injections</i>	
Psychogenic and physiologic ED subgroups combined	Nausea (any)	38.5 (15/39)	9.8 (4/41)	NA
	Nausea (severe)	15.4 (6/39)	2.4 (1/41)	
	Yawning/stretching (any)	56.4 (22/39)	12.2 (5/41)	
	Yawning/stretching (severe)	7.7 (3/39)	0 (0/41)	
Analysis of the 10 patients with physiologic ED	Nausea (any)	42.1 (8/19)	9.5 (2/21)	
	Nausea (severe)	21.1 (4/19)	0 (0/21)	
	Yawning/stretching (any)	42.1 (8/19)	0 (0/21)	
	Yawning/stretching (severe)	15.8 (3/19)	0 (0/21)	
PT–141 (cyclic heptapeptide melanocortin analog) vs. Placebo				

Study	Adverse event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute risk difference (%) [95% CI]
Rosen 2004 AE > 5% in both treatment arms	Nausea	24.0 (6/25) 4 mg 36.4 (8/22) 6 mg	0 (0/24)	–
	Headache	36.0 (9/25) 4 mg 27.3 (6/22) 6 mg	0 (0/24)	–
	Vomiting	8.0 (2/25) 4 mg 9.1 (2/22) 6 mg	0 (0/24)	–
	Diaphoresis	8 (2/25) 4 mg 9.1 (2/22) 6 mg	0 (0/24)	–
	Exacerbation of hypertension	9.1 (2/22) 4 mg	0 (0/24)	–
Apomorphine vs. Placebo				
Segraves 1991	Eight of 12 patients reported adverse events: yawning, drowsiness and nausea. Two patients had severe nausea and hypotension			

Table 17: Intra-urethral Treatment: Sexual Intercourse

Study	ED Etiology	Outcome	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Alprostadil vs. Placebo. Patients randomized included only men who had a maximal penile response (Grade of 4 or 5 on the Erection Assessment Scale) with at least one dose of alprostadil					
Padma-Nathan* 1997	Physiologic: 100%	Total successful attempts (diary self-report) after 3 months	50.4 (2485/4933)	10.4 (454/4346)	4.82 [4.40–28.00]
		Total successful			

Study	ED Etiology	Outcome	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Williams* 1998	Physiologic: 100%	attempts (diary self-report) after 3 months	51.1 (390/763)	7.5 (46/611)	6.79 [5.10–9.04]
I					
Padma-Nathan* 1997	Physiologic: 100%	Total successful attempts for men who had successful intercourse at least once (diary self-report) after 3 months	69.2 (2485/3593)	10.4 (454/4346)	6.62 [6.05–7.24]
Williams* 1998	Physiologic: 100%	Total successful attempts for men who had successful intercourse at least once (diary self-report) after 3 months	61.4 (390/635)	7.5 (46/611)	8.16 [6.14–10.84]
II					
Padma-Nathan* 1997	Physiologic: 100%	Total successful intercourse attempts or orgasm (diary self-report) after 3 months	56.3 (2770/4921)	15.4 (668/4331)	3.65 [3.39–3.93]
Padma-Nathan* 1997	Physiologic: 100%	Patients reporting successful intercourse at least once (diary self-report) after 3 months	61.6 (299/485) <i>All men randomized</i>	18.2 (93/511) <i>All men randomized</i>	3.39 [2.78–4.12]
Williams* 1998	Physiologic: 100%	Patients reporting successful intercourse at least once (diary self-report) after 3 months	59.0 (46/78) <i>All men randomized</i>	9.9 (8/81) <i>All men randomized</i>	5.97 [3.01–11.83]
III					
Padma-Nathan* 1997	Physiologic: 100%	Patients reporting successful intercourse at least once (diary self-report) after 3 months	64.9 (299/461) <i>Men with ≥ 1 administration</i>	18.6 (93/500) <i>Men with ≥ 1 administration</i>	3.49 [2.87–4.24]
Williams* 1998	Physiologic: 100%	Patients reporting successful intercourse at least once (diary self-report) after 3 months	68.7 (46/67) <i>Men with ≥ 1 administration</i>	7.5 (8/73) <i>Men with ≥ 1 administration</i>	6.26 [3.19–12.29]
Alprostadil (IU) vs. Alprostadil (ICI)					
Shokeir 1999	Physiologic: 100%	Total successful attempts (diary self-report) after 3 months	55.0 (198/360)	85.1 (206/242)	0.65 [0.58–0.72]
Shokeir 1999	Physiologic: 100%	Patients reporting successful intercourse at least once	53.3 (16/30)	86.7 (26/30)	0.62 [0.43–0.88]

Study	ED Etiology	Outcome	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Alprostadil (titrated; starting dose 250 µg,) vs. Alprostadil (titrated; starting dose 500 µg)					
Ekman 2000	NR Vascular: 43%–47% Diabetes: 21% Psychogenic: 7%–12%	Patients reporting successful intercourse at least once	68.1 (113/166)		–

Table 18: Intra-urethral Treatment: Improvement in Erections*

Study	ED etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Alprostadil vs. Placebo				
Padma-Nathan 1997	Physiologic: 100%	65.9 (996/1511)** <i>Dosing phase</i>	NA	–
Williams 1998	Physiologic: 100%	63.9 (159/249)** <i>Dosing phase</i>	NA	–
Alprostadil vs. Prazosin (IU)				
Peterson 1998	Physiologic: 100%	<i>Range for % response (dose)</i> 14.1 (125 mcg) – 31.0 (500 mcg)	<i>% Response (dose)</i> 3.0 (2000 mcg)	–
Alprostadil + Prazosin (IU) vs. Placebo				
Peterson 1998	Physiologic: 100%	<i>Range for % response (Alprostadil dose/Prazosin dose)</i> 30.4 (125 mcg/500 mcg) – 35.7 (500 mcg/2000 mcg)	0.4	–
Alprostadil (IU) vs. Alprostadil (ICI)				
Shabsigh 2000	NR	21.1 (20/95) <i>In-office titration phase, Positive buckling test</i> 61.8 (42/68) <i>At-home phase, ≥ 1 erection sufficient for intercourse</i>	61.1 (58/95) <i>In-office titration phase, Positive buckling test</i> 92.6 (63/68) <i>At-home phase, ≥ 1 erection sufficient for intercourse</i>	0.34 [0.23–0.53] 0.67 [0.55–0.81]

Shokeir 1999	Physiologic: 100%	60.0 (18/30)	90.0 (27/30)	0.67 [0.49–0.91]
Alprostadil (starting dose 250 µg) vs. Alprostadil (starting dose 500 µg)				
Ekman 2000	NR Vascular: 43%– 47% Diabetes: 21% Psychogenic: 7%–12%	73.5 (122/166)		–
Prazosin (IU) vs. Placebo				
Peterson 1998	Physiologic: 100%	% Response (dose) 3.0 (2000 mcg)	% Response 0.4	–

* Defined as full erection or “positive response,” Grade 4/5 erections, erections sufficient for intercourse, or Rigiscan assessment ≥ 70% rigidity base or tip lasting ≥ 10 minutes

** Patients achieving an adequate erectile response were then randomized in the double blind placebo controlled home phase

Table 19: Intra-urethral Treatment: Patients with Adverse Events

Study	Adverse Event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Alprostadil vs. Placebo				
Padma-Nathan 1997	Penile pain	32.8 (159/485)	3.3 (17/511)	29.0 [25.0–34.0]
Williams 1998	Penile pain	5.0 (4/78)	1.2 (1/81)	4.0 [-2.0, 9.0]
Padma-Nathan 1997	Minor urethral trauma	5.2 (25/485)	<1.0 (5/511)	4.0 [2.0–6.0]
Williams 1998	Minor urethral trauma	1.3 (1/78)	1.2 (1/81)	0.0 [-2.0, 7.0]
Padma-Nathan 1997	Dizziness	1.9 (9/485)	<1.0 (1/511)	2.0 [0.0–3.0]
Williams 1998	Dizziness	2.6 (2/78)	0 (0/81)	–
Padma-Nathan 1997	Prolonged erection	0	0	–
Williams 1998	Prolonged erection	1.3 (1/78)	0	–
Williams 1998	Urogenital pain/burning	6.4 (5/78)	0	–
Padma-Nathan 1997	Other events: Priapism or fibrosis	0	0	–
	Urinary tract infection	<1 (1/485)	<1 (3/511)	–
Williams 1998	Testicular pain	2.6 (2/78)	0	–
	Priapism or fibrosis	0	0	–
	Urinary tract infection	0	0	–
Alprostadil vs. Prazosin (IU)				

Study	Adverse Event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Peterson 1998		<i>Dose range</i> 125–1000 mcg	<i>Dose range</i> 250-2000 mcg	
		% Range 17.0–23.6	% Range 0.7 –5.5	
	Penile pain	1.0–9.1	0–2.1	–
	Urethral pain	2.0–4.4	0–1.4	–
	Testicular pain	0–5.5	0–0.7	–
	Dizziness	1.0–3.6	0–1.8	–
	Hypotension	0	0	–
	Priapism or fibrosis	0	0	–
	There were 12 cases of minor urethral bleeding and 2 cases of prolonged erections (no treatment arms reported).			
Alprostadil + Prazosin (IU) vs. Placebo				
Peterson 1998	Penile pain Urethral pain Testicular pain Dizziness Hypotension Priapism or fibrosis	<i>Alprostadil (dose range: 125–1000 mcg) + Prazosin (dose range: 250-2000 mcg)</i>		
		% Range 17.0–31.6	1.7 1.7	– –
		1.9–13.5	0.4	–
		1.8–6.8	0	–
		0–11.5	0	–
		0–14.0	0	–
		0		
Alprostadil (IU) vs. Alprostadil (ICI)				
Shabsigh 2000	Patients with ≥ 1 AE	55.8 (53/95) <i>Office</i>	30.5 (29/95) <i>Office</i>	25.0 [12.0–39.0]
		57.4 (39/68) <i>Home</i>	52.9 (36/68) <i>Home</i>	4.0 [-12.0, 21.0]
	Penile pain	30.5 (29/95) <i>Office</i>	20 (19/95) <i>Office</i>	11.0 [-2.0, 23.0]
		25.0 (17/68) <i>Home</i>	33.8 (23/68) <i>Home</i>	-9.0 [-24.0, 6.0]
	Prolonged erections	0 <i>Office</i>	2.1 (2/95) <i>Office</i>	–

Study	Adverse Event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
	Local bleeding	0 <i>Home</i>	2.9 (2/68) <i>Home</i>	–
		4.2 (4/95) <i>Office</i>	1.1 (1/95) <i>Office</i>	3.0 [-1.0, 8.0]
		2.9 (2/68) <i>Home</i>	1.5 (1/68) <i>Home</i>	1.0 [-3.0, 6.0]
Alprostadil (starting dose 250 µg) vs. Alprostadil (starting dose 500 µg)				
Shokeir 1999	Urogenital pain	6.7 (2/30)	46.7 (14/30)	-40.0 [-20.0, -60.0]
	Urethral bleeding	3.3 (1/30)	0	–
	Dizziness	6.7 (2/30)	0	–
Alprostadil (starting dose 250 µg) vs. Alprostadil (starting dose 500 µg)				
Ekman 2000	Pain	30.1 (50/166) 2% rated severe		–
Prazosin vs. Placebo				
Peterson 1998		<i>% Range</i>		
	Penile pain	0.7–5.5	1.7	–
	Urethral pain	0–2.1		
	Testicular pain	0–1.0		
	Dizziness	0–1.0		
	Hypotension	0–2.0		
	Priapism or fibrosis	0		

Table 20: Alprostadil (Topical Cream) vs. Placebo: Sexual Encounter Profile (SEP)

Study / Duration		Placebo (%)	Alprostadil Topical Cream			
			50 µg (%)	100 µg (%)	200 µg (%)	300 µg (%)
1. Rate of successful vaginal penetration/total attempts (SEP Question): Were you able to insert your penis into your partners' vagina? (yes/no)						
Padma-Nathan 2003 6 weeks Patients with mild-to-moderate ED (Study a)	Number of patients	31	31	29	26	NA
	Baseline	NR	NR	NR	NR	
	End point success rate ± standard deviation	55.3 ± 40.0	69.4 ± 34.2	69.1 ± 39.3	82.9 ± 24.6	
	Mean change	NR	NR	NR	NR	
	p value vs. placebo	NA	NS	NS	0.01	
Padma-Nathan 2003 6 weeks Patients with severe ED (study b)	Number of patients	35	NA	34	29	29
	Baseline success rate	NR		NR	NR	NR
	End point success rate ± standard deviation	15.6 ± 17.2		32.3 ± 18.0	36.2 ± 29.3	38.6 ± 22.8
	Mean change	NR		NR	NR	NR
	p value vs. placebo	NA		NS	NS	NS

Table 21: Topical Treatment: Improvement in Erections*

Study	ED Etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
Alprostadil vs. Placebo				
Goldstein 2001	Vascular: 97%	38.7 (12/31)	6.9 (2/29)	5.61 [1.37–22.96]
Padma-Nathan 2003 6 weeks Patients with	NR	80.2 (69/86) All doses	54.8 (17/31)	1.46 [1.05–2.05]
		81.0 (25/31) 50 µg	54.8 (17/31)	1.47 [1.02–2.11]
		69.0 (20/29) 100 µg	54.8 (17/31)	1.26 [0.84–1.88]

Study	ED Etiology	Treatment Group % (n/N)	Control Group % (n/N)	Relative Risk [95% CI]
mild-to-moderate ED (Study a)		92.0 (24/26) 200 µg	54.8 (17/31)	1.68 [1.20–2.36]
Padma-Nathan 2003 6 weeks Patients with severe ED (study b)	NR	71.7 (66/92) All doses	25.7 (9/35)	2.79 [1.57–4.97]
		58.8 (20/34) 100 µg	25.7 (9/35)	2.29 [1.22–4.29]
		75.9 (22/29) 200 µg	25.7 (9/35)	2.95 [1.62–5.37]
		82.7 (24/29) 300 µg	25.7 (9/35)	3.22 [1.79–5.79]
Aminophylline + Isosorbide dinitrate + Co-dergocrine vs. Placebo,				
Gomaa 1996	Physiologic: 52.3% Psychogenic: 25% Mixed: 22.2%	58.3 (21/36)	8.3 (3/36)	7.00 [2.29–21.41]
Le Roux 1999	Physiologic: 28.6% Psychogenic: 71.4%	3.9 (3/77 applications, 8 patients)	5.3 (4/76 applications, 8 patients)	0.74 [0.17–3.20]
Minoxidil vs. Nitroglycerin				
Cavallini 1994	Physiologic: 100%	44.0 (51/116)	20.7 (24/116)	2.13 [1.41–3.21]
Minoxidil vs. Placebo				
Cavallini 1994	Physiologic: 100%	44.0 (51/116)	1.7 (2/116)	25.5 [6.36–102.29]
Nitroglycerine plasters vs. Placebo plasters				
Gramkow 1999	Physiologic: 27.8% Psychogenic: 66.7% Mixed: 5.6%	16.7 (3/18)	11.1 (2/18)	1.50 [0.28–7.93]
Topical sildenafil + Oral placebo vs. Oral sildenafil + Topical placebo,				
Yonessi 2005	Physiologic: 41.3% Psychogenic: 58.8%	12.5 (5/40)	70.0 (28/40)	0.18 [0.08–0.42]

* Defined as full erection, erections sufficient for intercourse, improved erections based on Global Assessment Questionnaire, or RigiScan assessment \geq 60% rigidity (“good to excellent effect”)

** Intention-to-treat population, defined as patients receiving \geq one dose of study medication and \geq one post-baseline efficacy evaluation. Of a total of 1732 patients, 83 patients (4.8%) were not evaluated

† Includes only patients from the cohort for the primary efficacy endpoint analysis, defined as (a) used \geq three doses of study medication in conjunction with attempts at sexual intercourse between visits 2 and 4, (b) reported both baseline and end of treatment efficacy data (International Index of Erectile Function (IIEF)), (c) reported a baseline score for the IIEF EF domain of \leq 21, and (d) tolerated the test dose at visit 2 †† Based on a difficulties in maintaining an erection during intercourse scale, scored from 1 (always) to 6 (never). A score of 3 indicates difficulties 50% of the time.

Table 22: Topical Treatment: Patients with Adverse Events

Study	Adverse Event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Alprostadil vs. Placebo				
Goldstein 2001	Patients withdrawn from therapy due to adverse events	0/31	0/29	–
	Penile erythema	NR		–
	Mild/minor warmth or burning, tingling, and coolness	Reported by most patients after both alprostadil and placebo application		–
Padma-Nathan 2003 6 weeks Patients with mild-to-moderate ED (Study a)	Urogenital pain	13.2% (16/121) 12%: 50µg 15%: 100µg 13%: 200µg	0 (0/40) NR	–
	Hypotension	5.0% (6/121) 2.0%: 50µg 3.0%: 100µg 1.0%: 200µg	0 (0/40) NR	–
Padma-Nathan 2003 6 weeks Patients with severe ED (Study b)	Urogenital pain	5.5% (6/109) 0%: 100µg 9.0%: 200µg 8.0%: 300µg	0 (0/35) NR	–
	Hypotension	6.4% (7/109) 0%: 100µg 11.0%: 200µg 8.0%: 300µg	0 (0/35) NR	–
Topical PgE1 with or without Calcium Thioglycolate or Methyl Salicylate vs. Placebo				
Foldavi 1998	Patients with ≥ 1 AE	No local AEs were observed during the study		–
Aminophylline + Isosorbide dinitrate + Co-Dergocrine vs. Placebo,				
Gomaa 1996	Patients with ≥ 1 AE	No Patient reported prolonged erection/priapism, clinically significant cardiovascular events or complaints from patients' partners		–
Le Roux 1999	No AE reported	–	–	–
Nitroglycerin vs. Placebo				
Cavallini 1994	Patients with ≥ 1 AE	44.8 (52/116)	0 (0/116)	45.0 [36.0–54.0]
	Burning at application site	12.6 (14/116)	0 (0/116)	12.0 [6.0–18.0]
	Hypotension	10.3 (12/116)	0 (0/116)	10.0 [5.0–16.0]

Study	Adverse Event	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Cavallini 1991	Patients with ≥ 1 AE (burning at application site, headache, hypotension)	45.5 (15/33)	0 (0/33)	–
Nitroglycerin vs. Minoxidil				
Cavallini 1994	Patients with ≥ 1 adverse event	44.8 (52/116)	6.0 (7/116)	39.0 [29.0–49.0]
	Burning at application site	12.6 (14/116)	6.0 (7/116)	6.0 [-1.0, 13.0]
	Hypotension	10.3 (12/116)	0 (0/116)	–
Minoxidil vs. Placebo				
Cavallini 1994	Patients with ≥ 1 AE	6.0 (7/116)	0 (0/116)	–
	Burning at application site	6.0 (7/116)	0 (0/116)	–
	Hypotension	0 (0/116)	0 (0/116)	–
Cavallini 1991	Patients with ≥ 1 adverse event (burning at application site)	6.1 (2/33)	0 (0/33)	–
Nitroglycerine vs. Placebo				
Gramkow 1999	Patients withdrawn from therapy due to adverse events	1/18 due to severe pain from plaster	0/18	–
	Headache (mild)	35.4 (35/99) plasters used	1.1 (1/92) plasters used	34.0 [25.0–44.0]
	Smarting pain	23.2 (23/99) plasters used	1.1 (1/92) plasters used	22.0 [14.0–31.0]
Claes 1992	Patients withdrawn from therapy due to AEs	4 patients due to headache (unclear if due to active treatment)		–
Topical sildenafil + Oral Placebo vs. Oral Sildenafil + Topical Placebo				
Yonessi 2005	Headache	10.0 (4/40)	5.0 (2/40) 1 case each of dyspepsia and visual disturbance	5.0 [-6.0, 16.0]
Intranasal Cyclic Heptapeptide Melanocortin Analog (PT-141) vs. Placebo				
Diamond 2004	Flushing	16.7 (8/48)	4.2 (1/24)	13.0 [-1.0, 26.0]
	Nausea	10.4 (5/48)	0 (0/24)	–
	Feeling hot	4.2 (2/48)	4.2 (1/24)	–

Table 23: Testosterone: Improvement in Sexual Intercourse Outcomes

Study/patient Characteristics		Intervention Group 1	Intervention Group 2	Intervention Group 3	Intervention Group 4
Cavallini 2004 Men >60 with symptoms of androgen decline and depressed mood	Treatment type	T 160 mg/d oral	Placebo	NA	NA
	Number of patients at baseline	40	45	-	-
	IIEF "Intercourse Satisfaction" (range 0–15): Median score at baseline (range)	4 (3–6)	4 (2–5)	-	-
	IIEF "Intercourse Satisfaction": Median score at end of therapy (6 months)	5 (3–10) p <0.01 vs. baseline	4 (3–5)	-	-
Seftel 2004 Hypogonadal men (secondary to aging and normogonadotrophic)	Treatment type	T gel 50 mg/d	T gel 100 mg/d	T patch ~25mg/d	Placebo
	Number of patients at baseline	99	106	102	99
	Percentage of patients reporting no intercourse during baseline period	45	47	49	43
	% Improvement in frequency of intercourse from baseline at day 30	+31 <i>Extracted from graph</i> p value vs. placebo <0.05 p value vs. T patch NS	+39 p value vs. placebo 0.0096 p value vs. T patch 0.0356	+21 p value vs. placebo NS	+24 p value vs. T gel (50mg/d or 100mg/d) < 0.05 p value vs. T patch NS
Schiavi 1997 Men with ED and hypoactive sexual desire	Treatment type	T (IM) 200 mg	Placebo	NA	NA
	Number of patients at baseline	18 Crossover study (Washout period: 4 weeks)	18 Crossover study (Washout period: 4 weeks)	-	-

Study/patient Characteristics		Intervention Group 1	Intervention Group 2	Intervention Group 3	Intervention Group 4
	Frequency of intercourse at baseline	NR	NR	-	-
	Median frequency of "sex with partner" per week at week 6	1.25 (0–2) vs. Placebo: p value (NS)	0.54 (0–2.7) vs. T (IM): p value (NS)	-	-
	p value vs. placebo	NS	–	-	-
Gooma 2006 89 men with low testosterone levels and psychogenic and organic ED	Treatment type	T 0.8% + Isosorbide Dinitrate + Co-dergocrine Cream	Placebo	NA	NA
	Number of patients at baseline	45	44	-	-
	Number of patients having full erections with successful intercourse at study end	40% (18/45)	0/44	-	-
Gomaa 2001 Aged men with ED and hypoactive sexual desire	Treatment type	T 0.8% + Isosorbide Dinitrate + Co-Dergocrine Cream	T 0.8% cream	NA	NA
	Number of patients at baseline	42 Crossover study (washout period: 1 week)	42 Crossover study (washout period: 1 week)	-	-
	Frequency of intercourse at baseline	NR	NR	-	-
	Mean number of full erections with satisfactory intercourse at 1 month (standard deviation)	6.46 (2.7)	4.05 (1.8)	-	-

Study/patient Characteristics		Intervention Group 1	Intervention Group 2	Intervention Group 3	Intervention Group 4
	Number of patients with full erections and satisfactory intercourse at 1 month	66.7% (28/42) All patients 84.2% (16/19) Psychogenic 55.6% (10/18) Vascular 40% (2/5) Neurogenic	31% (13/42) All patients 57.9% (11/19) Psychogenic 11.1% (2/18) Vascular 0% (0/5) Neurogenic	-	-
Cavallini 2004 Men >60 with symptoms of androgen decline	Treatment type	T (oral) 160 mg/d	Propionyl-L Carnitine + Acetyl-L Carnitine 2 g/d	NA	NA
	Number of patients at baseline	40	45	-	-
	IIEF Intercourse satisfaction): Median score at baseline	4 (3–6)	4 (3–7)	-	-
	IIEF Intercourse satisfaction): Median score at end of therapy (6 months)	5 (3–10) p <0.01 vs. baseline	6 (3–10) p <0.01 vs. baseline	-	-

Table 24: Testosterone (T) Combined with PDE–5 inhibitors: Improvement in Sexual Intercourse Outcomes

Study/patient Characteristics		Testosterone Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI]
Shabsigh 2004 Hypogonadal men, non-responders to sildenafil therapy	Treatment type	T 1% gel + Sildenafil 100mg	Placebo gel + Sildenafil 100mg	
	Number of patients at baseline	39	36	
	Mean number of successful sexual attempts per week	1.7–2.1	1.5–2.4	–

	Proportion (%) of successful sexual attempts per week	49–59	43–50	–
Aversa 2003 Men with arteriogenic ED	Treatment type	T 5 mg/d patch + Sildenafil 100mg	Placebo patch + Sildenafil 100mg	
	Number of patients at baseline	10	10	
	Mean frequency of intercourse at baseline (SD)	1.4 (0.6)	NR	NA
	Mean frequency of intercourse at 1 month	2.8 (0.9)	1.5 (0.5)	WMD = 1.30 [0.66–1.94]
	IIEF** Intercourse satisfaction (range 0–15): mean score at baseline	7.1 (1.4)	7.8 (1.8)	WMD = -0.70 [-2.11, 0.71]
	IIEF Intercourse satisfaction: mean score at 1 month	12.1 (1.6)	7.7 (1.2)	WMD = 4.40 [3.16–5.64]
Yassin 2006 Hypogonadal men, non-responders to tadalafil therapy	Treatment type	T 50 mg/d gel + Tadalafil 20 mg	T 50 mg/d gel	
	Number of patients at baseline	34	35	NA
	IIEF Intercourse satisfaction (range 0–15): mean score at baseline	8.9 (2.8)		NA
	IIEF Intercourse satisfaction: mean score at 10 weeks	13.1 (0.8)	12.8 (0.9)	WMD = 0.30 [-0.10, 0.70]

* International Index of Erectile Dysfunction

Table 25: Testosterone Treatment: Improvement in Erections

Study/patient Characteristics	Outcome	Treatment Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI] or p value
Testosterone (IM) vs. Placebo				
Seidman 2006 32 hyogonadal men with major depressive disorder	Full erection during phases of a normal sexual response cycle (foreplay through intercourse and orgasm) at baseline (standard deviation). Based on DSPTS (range 0–8)*	1.54 (1.94)	1.18 (1.78)	NR
	Full erection during phases of a normal sexual response cycle (foreplay through intercourse and orgasm) at study end.	1.77 (2.17) Mean change = 0.23	1.53 (1.62) Mean change = 0.35	p value (NS)
	A satisfying orgasm at baseline. Based on DSPTS (range 0–8)*	1.92 (1.44)	1.82 (1.81)	NR
	A satisfying orgasm at end of study period	2.31 (2.06) Mean change = 0.23	2.06 (1.44) Mean change = 0.35	p value (NS)
Rabkin 2000 74 HIV positive men with hypogonadal symptoms	Completers who experienced ED rated as much to very much improved based on the Clinical Global Impression Scale	62.5% (20/32)	20.0% (4/20)	RR = 3.12 [1.25–7.82]
Clopper 1993 9 gonadotropin-deficient hypopituitary men	Self-reported weekly frequency of erection	7.9 (6.1)	4.9 (3.3)	p value (NS)
Testosterone (IM) vs. Human Chorionic Gonadotropin (IM)				

Study/patient Characteristics	Outcome	Treatment Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI] or p value
Clopper 1993 9 gonadotropin-deficient hypopituitary men	Self-reported weekly frequency of erection	7.9 (6.1)	8.2 (7.1)	p value (NS)
Testosterone (oral) vs. Placebo				
Haran 2005	"Are your erections less strong?" % reporting yes after 12 months	86%	93%	p = 0.059
Cavallini 2004 95 men > 60 with symptoms of androgen decline	IIEF Erectile function (range 1–30): Median score at baseline (range)	8 (5–19)	8 (5–21)	NR
	IIEF Erectile function: Median score at end of therapy (6 months)	16 (6–29)	8 (5-21)	Testosterone p <0.01 vs. baseline
Testosterone (oral) vs. No Treatment				
Boyanov 2003 48 middle-aged men, with type 2 diabetes, obesity, and symptoms of androgen deficiency	IIEF–5 to assess erectile function, score at baseline (absent-1 to severe-5)	2.25 (0.68)	2.50 (0.75)	NR
	IIEF–5 score after treatment (3 months)	1.062 (0.90)	2.25 (0.88)	p <0.05
Dihydrotestosterone Gel vs. Placebo Gel				
Kunelius 2002 120 men with andropause symptoms	Based on difficulties in maintaining an erection during intercourse scale, scored from 1 (always) to 6 (never). A score of 3 indicates difficulties 50% of the time.	3.24 (1.35)	2.81 (1.56)	NA
Testosterone 50 mg Gel (T 50) vs. Testosterone 100 mg Gel (T 100) vs. Andropatch				

Study/patient Characteristics	Outcome	Treatment Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI] or p value
McNicholas 2002 208 aging, hypogonadal men	Mean number of spontaneous erections/week at baseline	T 50: 0.8 T 100: 0.8	Andropatch 0.9	
	Mean change in spontaneous erections/week after therapy (90 days)	T 50: +0.6 T 100: +0.5	Andropatch +0.3	T 50: p <0.05 vs. baseline T 100: p <0.05 vs. baseline
Wang 2000 227 hypogonadal men	% of full erections at baseline (estimated from graph)	T 50: 53 T 100: 60	Andropatch 57%	NR
	% of full erections at day 90 (estimated from graph)	T 50: 67 T 100: 68	Andropatch 65%	p = 0.0001 for all groups vs. baseline
Testosterone 0.8% + Isosorbide Dinitrate + Co-Dergocrine Cream vs. Placebo				
Gooma 2006 89 men with low testosterone levels	Full erection after treatment (2 months)	40.0% (18/45) <i>All patients</i> 68.8% (11/16) <i>Psychogenic</i> 11.1% (1/9) <i>Vascular</i> 37.5% (3/8) <i>Neurogenic</i> 25% (3/12) <i>Mixed</i>	0/44	–
Testosterone 0.8% + Isosorbide Dinitrate + Co-Dergocrine Cream vs. Testosterone 0.8% cream				
Gomaa 2001 42 aged men with ED and hypoactive sexual desire	Mean number of full erections with satisfactory intercourse at 1 month.	6.46 (2.7)	4.05 (1.8)	WMD = 2.41 [1.43–3.39]

Study/patient Characteristics	Outcome	Treatment Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI] or p value
	Number of patients with full erections and satisfactory intercourse at 1 month	66.7% (28/42) <i>All patients</i>	31.0% (13/42) <i>All patients</i>	RR = 2.15 [1.31–3.55]
		84.2% (16/19) <i>Psychogenic</i>	57.9% (11/19) <i>Psychogenic</i>	RR = 1.45 [0.95–2.24]
		55.6% (10/18) <i>Vascular</i>	11.1% (2/18) <i>Vascular</i>	RR = 5.00 [1.27–19.68]
		40.0% (2/5) <i>Neurogenic</i>	0% (0/5) <i>Neurogenic</i>	–
Testosterone (oral) vs. Propionyl-L carnitine + Acetyl-L carnitine				
Cavallini 2004	IIEF Erectile function (range 1–30): Median score at baseline	8 (5–19)	8 (5–22)	NR
95 men > 60 with symptoms of androgen decline and depressed mood	IIEF Intercourse satisfaction: Median score at end of therapy (6 months)	16 (6–29)	24 (8–29)	Testosterone p <0.01 vs. baseline Carnitines p <0.01 vs. baseline
Testosterone 5 mg/d Patch + Sildenafil 100mg vs. Placebo Patch + Sildenafil 100mg				
Aversa 2003	Global Assessment Questionnaire: “has treatment improved erections”	80% (8/10)	10% (1/10)	RR = 8.00 [1.21–52.69]
20 men with arteriogenic ED	IIEF** Intercourse satisfaction (range 1–30): mean score at baseline	14.4 (1.4)	13.2 (1.1)	WMD = 1.20 [0.10–2.30]
	IIEF Intercourse satisfaction: mean score at 1 month	21.8 (2.1)	14.2 (0.7)	WMD = 7.60 [6.23–8.97]
Testosterone 1% Gel + Sildenafil 100mg vs. Placebo Gel + Sildenafil 100mg				

Study/patient Characteristics	Outcome	Treatment Group	Control Group	Relative risk (RR) or weighted mean difference (WMD) [95% CI] or p value
Shabsigh 2004 75 hypo-gonadal men, non-responders to sildenafil therapy	Patients with IIEF-Q3/Q4: 4-5 ** at study end	51.4% (19/37)	39.4% (13/33)	RR = 1.30 [0.77–2.21]
	Patients who increased functioning by at least 1 category over baseline for either IIEF Q3 or Q4 at week 12	78.8% (26/33)	71.0% (13/31)	RR = 1.11 [0.83–1.48]
Testosterone (oral) + Sildenafil (50 or 100mg) vs. Testosterone (oral): sildenafil non-responder men				
Shamloul 2005 Study a 20 men with ED associated with PADAM (partial androgen deficiency in aging men)	IIEF–5 to assess erectile function, score at baseline	10.1 (1.3) <i>Baseline</i>	9.9 (1.4) <i>Baseline</i>	
	IIEF–5 score after treatment	15.0 (1.4) p <0.01 vs. baseline	11.1 (1.5) p = 0.27 vs. baseline	WMD = 3.90 [2.63–5.17]
Testosterone (oral) + Sildenafil (50 or 100mg) vs. Sildenafil (50 or 100mg): men partially responding to sildenafil				
Shamloul 2005 Study b 20 men with ED associated with PADAM (partial androgen deficiency in aging men)	IIEF–5 to assess erectile function, score at baseline	15.3 (1.6) <i>Baseline</i>	15.4 (1.2) <i>Baseline</i>	–
	IIEF–5 score after treatment	17.5 (1.8) p <0.01 vs. baseline	15.9 (1.3) p = 0.24 vs. baseline	WMD = 1.60 [0.22–2.98]

* Derogatis Sexual performance Scale. Range 0 (not at all) to 8 (4 or more times/day)

** Question 3: “Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate your partner?” and Question 4: Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your erection after you penetrated your partner?”

Table 26: Testosterone Treatment: Patients with Adverse Events

Study/patient Characteristics	Adverse Events	Treatment Group % (n/N)	Control Group % (n/N)	Absolute Risk Difference [95% CI]
Testosterone (IM) vs. Placebo				
Seidman 2006	No adverse events occurred except one placebo subject had a myocardial infarction.			
Rabkin 2000	Patients with ≥ 1	41 (16/39)	20 (7/35)	21.0 [1.0–41.0]
	Irritability	17.9 (7/39)	17.1 (6/35)	1.0 [-17.0, 18.0]
	Acne	20.5 (8/39)	0/35	21.0 [7.0–34.0]
	Testicular atrophy	5.1 (2/39)	0/35	–
	Decreased ejaculate	2.6 (1/39)	2.9 (1/35)	-0.3 [-8.0, 7.0]
		Hair loss (n=1)	0	–
		Bossiness (n=1)	0	–
Testosterone (oral) vs. Placebo				
Cavallini 2004	Mild epigastralgia	2.5 (1/40)	2.2 (1/45)	0.3 [-6.0, 7.0]
Testosterone (oral) vs. No Treatment				
Boyanov 2003	No AE were reported during the study			
Testosterone (Cream) vs. Placebo				
Gooma 2006	Headaches (transient)	11.1 (5/45)	0 (0/44)	–
	Skin irritation	2.2 (1/45)	0 (0/44)	–
	Prolonged erections/priarism	0	0	–
Testosterone (Gel) vs. Placebo				
Seftel 2004	Treatment-related (application site reactions, BPH, increases in blood pressure and hematocrit/hemoglobin, gynecomastia, headache, hot flashes, insomnia, mood swings, spontaneous erections)	29.3 (29/99) T 50	40.4 (40/99)	-11.0 [-24.0, 2.0]
		36.8 (39/106) T 100		-4.0 [-17 to 10]
	Skin reaction leading to	0	0	

	study withdrawal			
Dihydrotestosterone Gel vs. Placebo Gel				
Kunelius 2002	Mild headache	5.0 (3/60)	3.3 (2/60)	2.0 [-5.0, 9.0]
	Mild depression	3.3 (2/60)	3.3 (2/60)	–
	Hair growth	1 patient		
Testosterone 0.8% + Isosorbide Dinitrate + Co-Dergocrine Cream vs. Testosterone 0.8% Cream				
Gomaa 2001	Mild transient headache PSA values: no significant increase of reported	N = 5 (phase 1 and 2)	0	–
Testosterone (patch) vs. Placebo				
Merza 2005	Increase in hematocrit	15 (3/20) n = 2 withdrawals in phase 2	5.3 (1/19)	10 [-9 to 28]
	Significant difference in the percentage change of hemoglobin between the two groups of 4% during phase 1 (p = 0.036). PSA: 25% increase testosterone vs. 6% for placebo (difference between the two means: NS)		n = 1 (angina)	
Seftel 2004	Treatment-related	62.7 (64/102)	40.4 (40/99)	22.0 [9.0–36.0]
	Skin reaction leading to study withdrawal	n = 15	0	–
Testosterone 5 mg/d Patch + Sildenafil 100mg vs. Placebo Patch + Sildenafil 100mg				
Aversa 2003	No clinically significant adverse events were observed with both treatments			
Testosterone 50 mg Gel (T 50) vs. Testosterone 100 mg Gel (T 100) vs. Andropatch				

McNicholas 2002	Patients reporting ≥ 1 treatment-emergent (erythema, irritation and reactions at application site)	35.3 (24/68) T 50 29.2 (21/72) T 100	63.2 (43/68) Patch	-28.0 [-44.0, -12.0] -34.0 [-50.0, -19.0]	
	Skin irritation	"Very low Incidence" – both groups	47% at day 30 and 53% after 90 days	–	
Wang 2000	Skin irritation	5.7 (3/53) T 50	65.8 (50/76) Patch	-60.0 [-72.0, -48.0]	
		5.3 (3/57) T 100		-61.0 [-73.0, -48.0]	
	Urogenital events	9.6 (7/73) T 50	0 (0/76) Patch	–	
		5.1 (4/78) T 100		–	
	Serum PSA levels elevated to above the normal range	1.4 (1/73) T 50	0 (0/76) Patch	–	
		5.1 (4/78) T 100		–	
	Gynecomastia (2 of the patients had preexisting gynecomastia)	1.4 (1/73) T 50	0 (0/76) Patch	–	
		3.8 (3/78) T 100		–	
	One patient in T 50 group had depression (discontinued); one patient in T 100 group had high blood pressure (discontinued), and one patient had memory loss/sadness (discontinued); One patient in Patch group discontinued due to elevated hematocrit and hemoglobin				
	Testosterone (oral) vs. Propionyl-L Carnitine + Acetyl-L Carnitine				
Cavallini 2004	Mild headache	0 (0/40)	2.2 (1/45)	–	

Testosterone 1% Gel + Sildenafil 100mg vs. Placebo Gel + Sildenafil 100mg				
Shabsigh 2004	One patient on testosterone withdrew from the study because of an AE. No further details were provided.			
Testosterone (oral) + Sildenafil (50 or 100mg) vs. Testosterone alone or Sildenafil (50 or 100mg) alone				
Shamloul 2005	No significant adverse events observed (mild headache in three patients on sildenafil 100mg) Slight increase in serum PSA (NS)			
Testosterone 50 mg/d Gel + Tadalafil 20 mg vs. Testosterone 50 mg Gel				
Yassin 2006	No adverse events observed			

* Derogatis Sexual Performance Scale. Range 0 (not at all) to 8 (4 or more times/day)

Table 27: Miscellaneous Treatments: Efficacy and Adverse Events

Author (year) Country	Study Population	Interventions (Dose and duration)	Outcomes		<ul style="list-style-type: none"> Any Event Serious Event Withdrawals Due to Adverse Event n (%)
			Self rated Erection End Points	RigiScan Measures	
Mann (2001) Germany	13 (6/7) men diagnosed with psychogenic ED	<ul style="list-style-type: none"> Oral moclobemide, 450–600 mg/wk; 8 wks Placebo 	<ul style="list-style-type: none"> Clinical Global Impression (GCI), NS between groups 	Nocturnal penile response: improvement NS between groups	<ul style="list-style-type: none"> 3 (50) vs. 3 (43) 0 NR
Piha (2003) Finland	11 hypertensive men 41–58 years old	<ul style="list-style-type: none"> Oral moxonidine, 0.4–0.6 mg/d; 8 wks Oral metoprolol, 100–200 mg/d; 8 wks 	<ul style="list-style-type: none"> IIEF–5: positive changes in 9/11 (82%) vs. 0, p<0.0002 	NR	NR
Reiter (1998) Austria	40 (20/20) men with low serum DHEAS (<1.5 µmol/L), and ED unrelated to any other known organic cause	<ul style="list-style-type: none"> Oral dehydro-epiandrosterone (DHEA) Placebo 	<ul style="list-style-type: none"> IIEF, mean scores in all 5 domains improved in DHAE vs. placebo 	NR	<ul style="list-style-type: none"> 0 0 0
Safarinejad (2001) Iran	44 men 28–55 years old with vasculogenic ED	<ul style="list-style-type: none"> Oral isoxsuprine hydrochloride, 60 mg/d; 30 d Placebo 	<ul style="list-style-type: none"> Complete erectile response 8.3% vs. 8.3% (NS) 	NR	<ul style="list-style-type: none"> 70% vs. 15% 1 (2.3) vs. 0 NR
Sommer (2006) Germany	18 (NR) men with ED (no etiology reported)	<ul style="list-style-type: none"> Oral (BH4) + VSS, 200 or 500 mg; once Placebo; once 	<ul style="list-style-type: none"> NR 	Improved duration of >60%: at base 33.1 and 36.1 min; at tip by 29.4 and 33.7 min (200 and 500 mg respectively)	<ul style="list-style-type: none"> 3 (17) vs. 1 (5.6) NR NR
Sommer (2006) Italy	176 (NR) men with DM type II and ED of longer than	<ul style="list-style-type: none"> Oral myoinositol + folic acid Combination, 4g + 400µg; 12 wks Placebo; 12 wks 	<ul style="list-style-type: none"> Mean IIEF–5 change: 8 vs. -1 	NR	<ul style="list-style-type: none"> NR

Author (year) Country	Study Population	Interventions (Dose and duration)	Outcomes		<ul style="list-style-type: none"> Any Event Serious Event Withdrawals Due to Adverse Event n (%)
			Self rated Erection End Points	RigiScan Measures	
	6 mo of organic cause				
Sommer (2006) Canada	68 men > 18 years old diagnosed with depressive disorder and ED for longer than 6 mo	<ul style="list-style-type: none"> Oral tianeptine, NR; 8 wks Placebo; 8 wks 	<ul style="list-style-type: none"> Patients with full response to treatment: 72.7% vs. 27.9% Patients with successful sexual intercourse: 89.4% vs. 50.0% 	NR	<ul style="list-style-type: none"> 5 (7.4) vs. 1 (1.5) <ul style="list-style-type: none"> NR NR
Speel (2005) the Netherlands	59 men with mean age of 60 years old, and atherosclerosis ED	<ul style="list-style-type: none"> Oral angiotensin-converting enzyme (ACE), 20 mg/d; 26–46 wks Placebo 	<ul style="list-style-type: none"> IIEF–EF: severity of ED improved in both groups (NS between groups) 	NR	<ul style="list-style-type: none"> 11 (37) vs. 4 (14) <ul style="list-style-type: none"> NR NR
Van Ahlen (1995) Germany	20 men with mean age of 46 y, and idiopathic ED	<ul style="list-style-type: none"> Oral Naltrexone (NTX), 25 or 50 mg/d; 3 mo Placebo; 3 mo 	<ul style="list-style-type: none"> Early morning erections change from baseline 1.39 vs. 0.22 (p<0.05) 	NR	<ul style="list-style-type: none"> NR

Table 28: Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

Study	Study Design	Subject(s) (number, age, co-morbidities, medical history)	Treatment (type, dose)	Visual Complaint (or diagnosis)	Relative Risk (RR) 95% CI
Akash (2002)	Case report	n = 1 54 years Caucasian None	100 mg 2–3/week; one time overdose: 200 mg	Blindness in left eye hours post overdose Left combined NAION w+ cilioretinal artery occlusion	NA
Cunningham (2001)	Case report	n = 1 42 years Depression	50 mg/d; 3 doses	Blurred vision post 2 nd and 3 rd dosing NAION	NA
Dheer (2002)	Case report	n = 1 48 years None	100 mg/d; two doses	Blue flashes and blurring vision in both eyes NAION	NA
Egan (2000)	Case report	n = 1 52 years Transurethral resection for prostate cancer	50 mg; single dose	Bilateral blue lightning bolts and blurry vision within 1 hr post dosing NAION	NA
Gedik (2006)	Case report	n = 1 36 years NR	100 mg; two separate dosing 4 months apart	Blurred vision deteriorated to light perception in both dosing cases NAION	NA
Grugn (2004)	Case report	n = 1 69 years (only case reported to date in Scandinavia)	50 mg (single dose)	Abnormal vision in right eye NAION	NA
Margo (2007)	Retrospective cohort	n = 479,489 Veterans ≥50 years; documented PDE–5 inhibitor use	100 mg in 99.4% of pts	NR Diagnosed NAION: n = 442 (<1%) Possible NAION: n = 228 (<1%)	RR for diagnosed NAION = 1.02 (95% CI 0.92–1.12)* RR for possible NAION = 1.34 (95% CI: 1.17–1.55)

Pomeranz (2002)	Case series	n = 5 42–69 years, elevated lipids, smoking, diabetes, coronary artery disease, diagnosis of NAION (n = 1)	50–100 mg	Loss of vision in the affected eye within min to hrs post dosing NAION	NA
Pomeranz (2005)	Case series	n = 7 50–69 years, hypertension, diabetes, elevated cholesterol, or hyperlipidemia	25–50 mg (dosing regiment ranged from single dose to sporadic use over several years)	Vision loss [unilateral (n=6), bilateral (n=1)] NAION	NA
Sinha (2004)	Case report	n = 1 61 years, smoking	200 mg at once (usual dose of 100 mg)	Loss of vision in right eye Possible NAION	NA

* Relative risk was calculated as ratio of risks in men exposed to PDE-5 inhibitors those unexposed.

Table 29: Penile Fibrosis in Studies of Intracavernosal Injection (Non-randomized)

Study	Study Design	Patients	Treatment(s)	Treatment Duration	Fibrosis % (n/N) by Treatment Group
Perimenis 2006	Clinical trial	38 Greek men Mean age 56.4 (range 42–62) years With diabetes mellitus (DM) (type I and II)	1. Prostaglandin (PGE ₁) 5–20 µg 2. Papaverine (PAP) ≥8 mg 3. PGE ₁ + PAP 20 µg/ 8 mg	10 years	13.2% (5/38)
Althof 1991	Clinical trial	42 American men, mean age 54.4 years	PAP + phentolamine, NR	12 months	26%
Canale 1996	Clinical trial	68 Italian men, mean age 50.5 (22-70) years	PGE ₁ , 20 µg/ml /wk (20-60 µg/2-3 d in one case)	> 12 months	4.4% (3/68)
Porst 1998	Clinical trial	162 European men, mean age 54 (22-70) years	PGE ₁ , NR	1- 4 y	11.7% (19/162) 1 st y: 6.8% 2 nd y: 2.5% 3 rd y: 7.3% 4 th y: 1.7%
Claro 2001	Retrospective cohort	168 Brazilian men, median age 61 (43–78) years, had undergone prostatectomy for localized prostate cancer	1. PAP + Phentolamine (PHEN) + PGE ₁ 22.6 mg / 1.34 mg/ 13.4 mg	NR	0%
Lepore 2001	Clinical trial	52 Italian men, mean age 56.7 (range 35–74) years With diabetes	1. PGE ₁ NR 2. Sildenafil	3 months	0%
Perimenis 2001	Clinical trial	40 Greek men 18 diabetic and 22 non-diabetic controls Mean age 55.6 (48–64)	1. PGE ₁ 5–20 µg 2. PAP 8–16 mg 3. PGE ₁ + PAP 20 µg/ 8–16 mg	7 years	17.5% (7/40) One non-diabetic control developed early Peyronie's plaque leading to study withdrawal
Wespes 2000	Clinical trial	10 Belgian men, mean age 56.5 (46–69) years	1. PGE ₁ 6–20 ug	NR	0%
Shmueli 1999	Clinical trial	452 Israeli men, mean age 59.5 (26–85) years	Protocol I: PAP + PHEN 6–25 mg/ 0.05–1.5 mg.	6 months	0% Small nodules

Study	Study Design	Patients	Treatment(s)	Treatment Duration	Fibrosis % (n/N) by Treatment Group
			Patients who failed received Protocol II: PGE ₁ 10–25 µg. Patients who failed received Protocol III: PAP + Phentolamine + PGE ₁ Patients who failed received Protocol VI: PAP + Phentolamine + PGE ₁ + atropine 0.02–0.06 mg		Protocol I: 0.6% (3/452) Protocol II: 2% (3/147) Protocol III: 3.5% (3/86) Protocol IV: 9.7% (3/31)
Chew 1997	Retrospective cohort	245 Australian men, mean age 62 (21–79) years, hypertension (22.8%), DM (8.5%)	1. PGE ₁ 2–60 µg (mean 13 µg)	2.1 years (up to 86 months)	23.3% (57/245)
Sundaram 1997	Retrospective cohort	160 American men Age not reported	1. PAP 30 mg 2. PAP + PHEN 25 mg + 0.83 mg 3. PGE ₁ NR (alternative therapy)	1–5 years	<1% (1 patient)
Gupta 1997	Retrospective cohort	1089 American men, mean age 62 (21–94) years	1. PGE ₁ 5–10 µg 2. TRIMIX 4.41 mg/ 0.5 mg/ 1.47 µg 3. PGE ₁ + PAP 5–10 µg/ 30 mg 4. PAP + PHEN 30 mg/ 0.5 mg	Up to 80 months	Penile scarring /nodules in patients discontinuing therapy 1. PGE ₁ 10.7% (8/75) 2. TRIMIX 23.1% (6/26) 3. PAP + PHEN 11.1% (4/36)
Flynn 1996	Retrospective cohort	126 British men, mean age 57 (27–77) years, 40% had co-morbidities	1. PAP NR 2. PAP + PHEN NR	3.9 years	<1% (1 subject)
Chen 1996	Retrospective cohort	92 American men, mean age 58.6 (32–78) years, 67% had co-morbidities	1. PGE ₁ initial dose <10 µg/ml in most cases	1–56 months	16.3% (15/92)
Bolayir 1994	Clinical trial	40 Cypriot men,	1. PAP +	1 year	2.5% (1/40)

Study	Study Design	Patients	Treatment(s)	Treatment Duration	Fibrosis % (n/N) by Treatment Group
		age range 40–75 years	Verapamil 20–35 mg/5 mg		
Hattat 1994	Clinical trial	69 Turkish men, mean age 52.6 (31–71) years	1. PGE ₁ NR 2. PAP NR	13.6 months	3.6% (2/56) PAP 0 (0/13) PGE ₁
Betts 1994	Clinical trial	46 British men, mean age 39 (26–58) with multiple sclerosis	1. PAP 10–80 mg	NR	2.2% (1/46)
Chiang 1992	Clinical trial	51 Taiwanese men, mean age 58.3 (29–79) years	1. PGE ₁ 5–40 µg 2. PAP 15–60 mg	1 year	3.9% (2/51)
Kerfoot 1991	Retrospective cohort	119 American men Group 1 (n = 65): Geriatric (>65), mean age 70 years Group 2 (n = 54): younger, mean age 47	1. PAP + PHEN 30 mg / 1.0 mg (titrated up to 1.5 if no response)	> 6 months	2.5% (3/119)
Schramek 1990	Clinical trial	149 Austrian men, Mean age 56.5 (25–76) years	1. PGE ₁ 10–40 µg	NR	0%

Figures

Note: Figure 1 (Analytic Framework) and Figure 2 (Quorum Flow Chart) are found in Chapter 2.

Figure 3. The mean IIEF “EF domain” score

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 01 Mean IIEF 'EF domain' Score

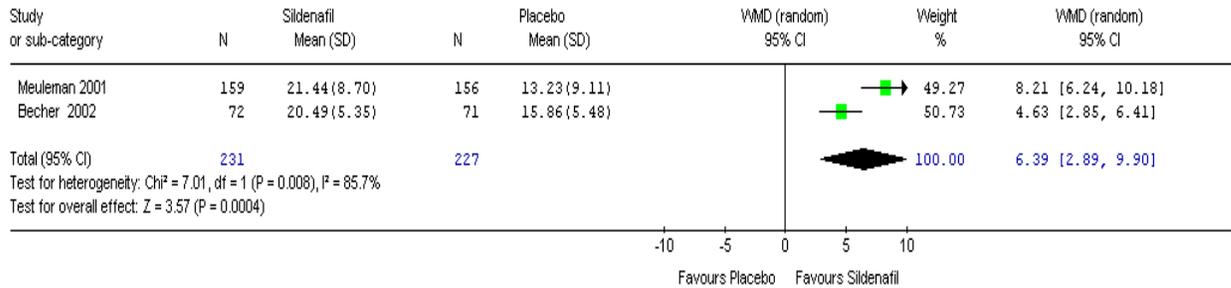


Figure 4. The mean IIEF–Q3 score

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 02 Mean IIEF-Q3 score

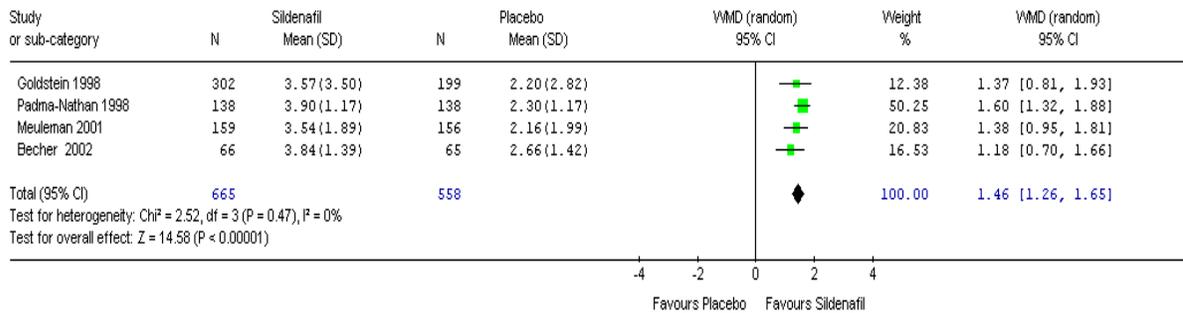


Figure 5. The mean IIEF–Q4 score

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 03 Mean IIEF-Q4 score

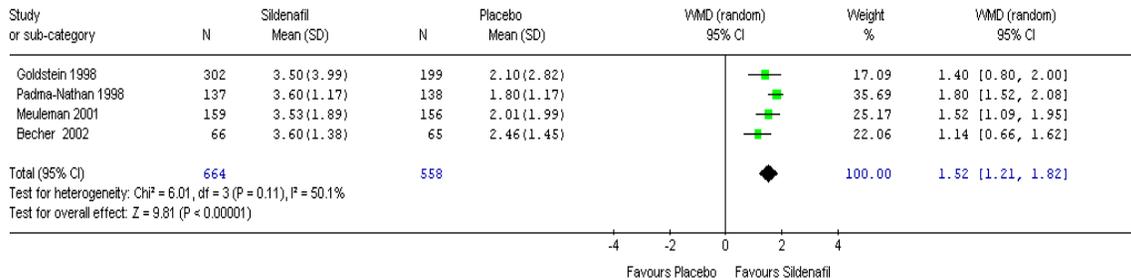


Figure 6. Improved erection (GEQ-Q1)

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 05 Patients with Improved Erections (GEQ-Q1)

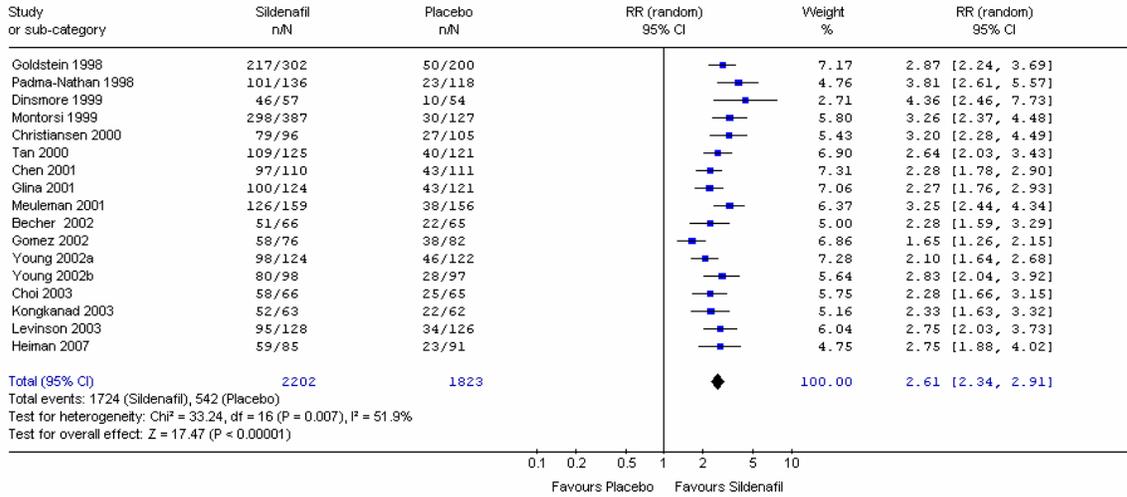


Figure 7. Any adverse events (all cause)

Review: Sildenafil
 Comparison: 01 Sildenafil (Any dose/dosing) vs. Placebo
 Outcome: 08 Proportion of patients with at least one adverse event (all cause)

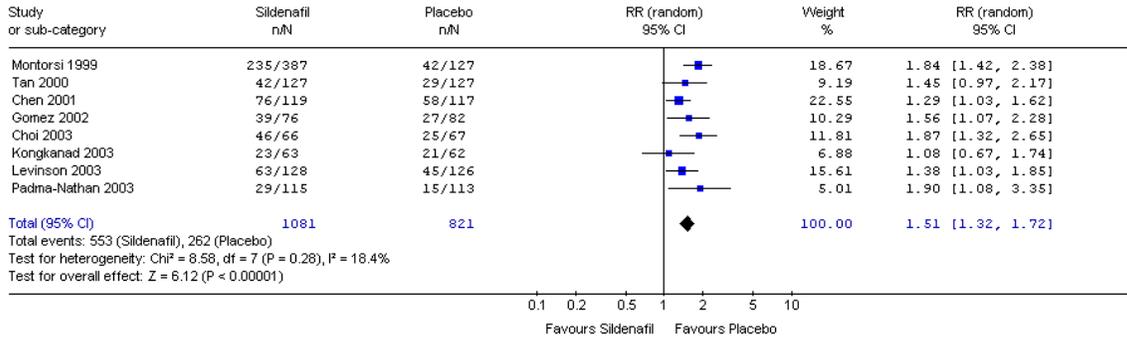


Figure 8. Any adverse events (treatment-related)

Review: Sildenafil
 Comparison: 01 Sildenafil (Any dose/dosing) vs. Placebo
 Outcome: 09 Proportion of patients with at least one adverse event (treatment-related)

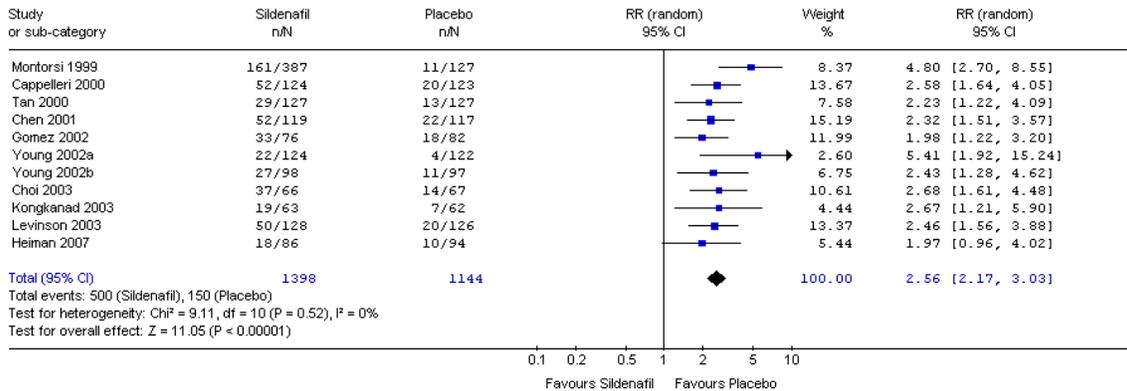


Figure 9. Headache (all cause)

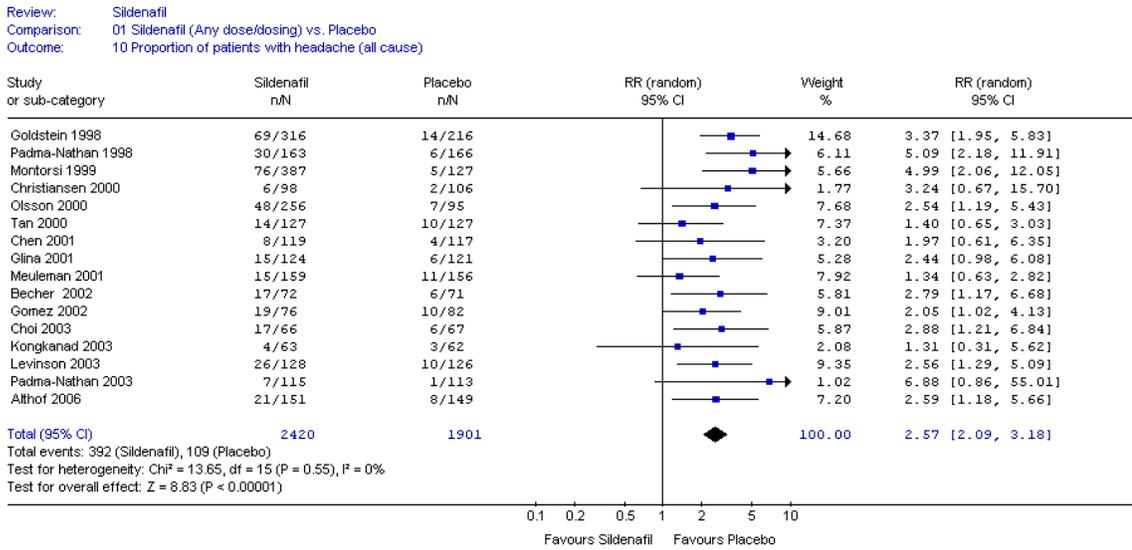


Figure 10. Flushing (all cause)

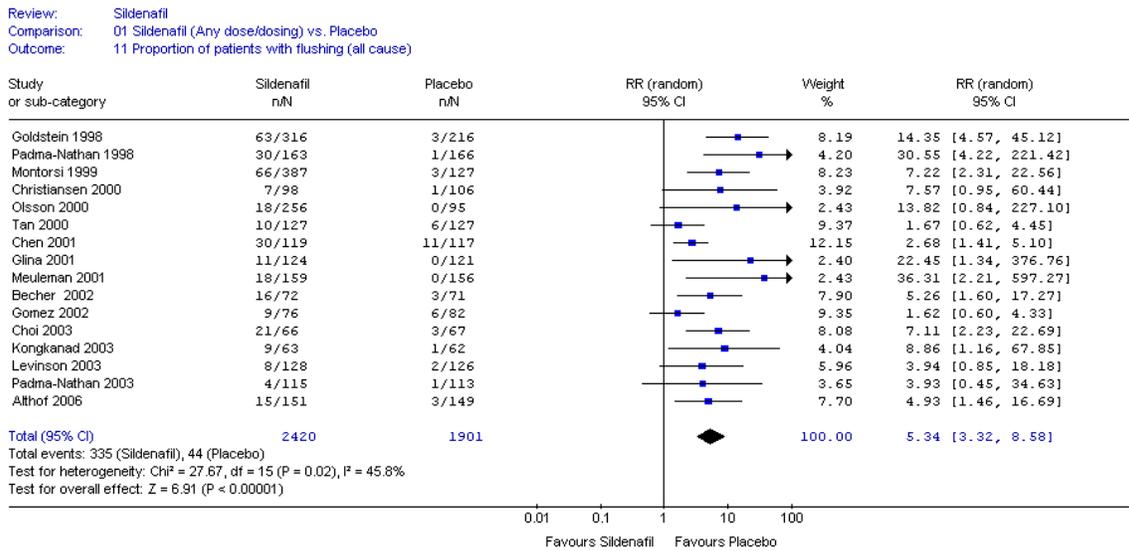


Figure 11. Visual disturbances (all cause)

Review: Sildenafil
 Comparison: 01 Sildenafil (Any dose/dosing) vs. Placebo
 Outcome: 12 Proportion of patients with visual disturbances (all cause)

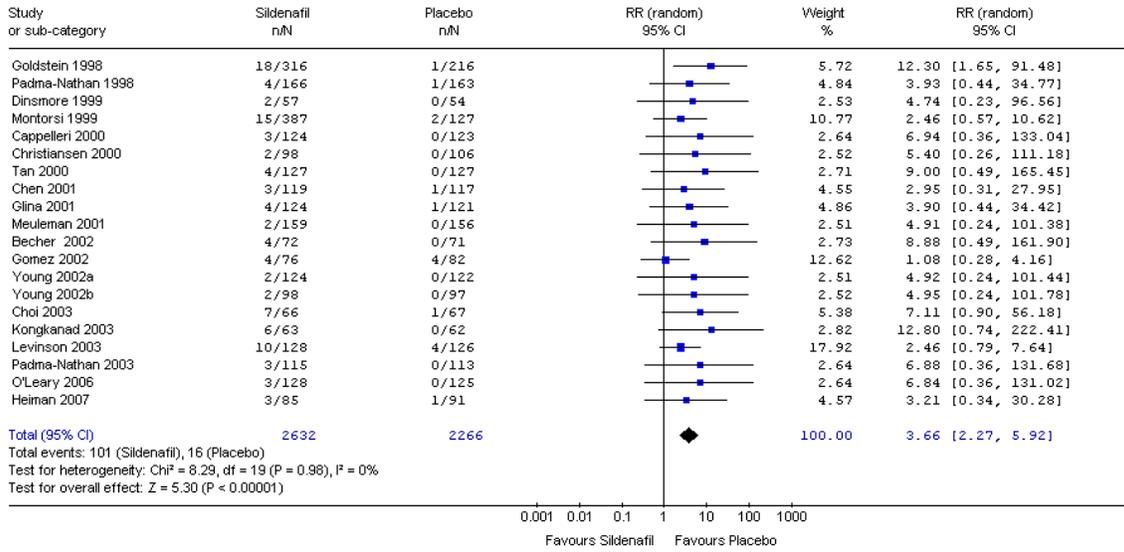


Figure 12. Improved erection (GEQ-Q1): Type I-II diabetes

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 05 Patients with Improved Erections (GEQ-Q1)

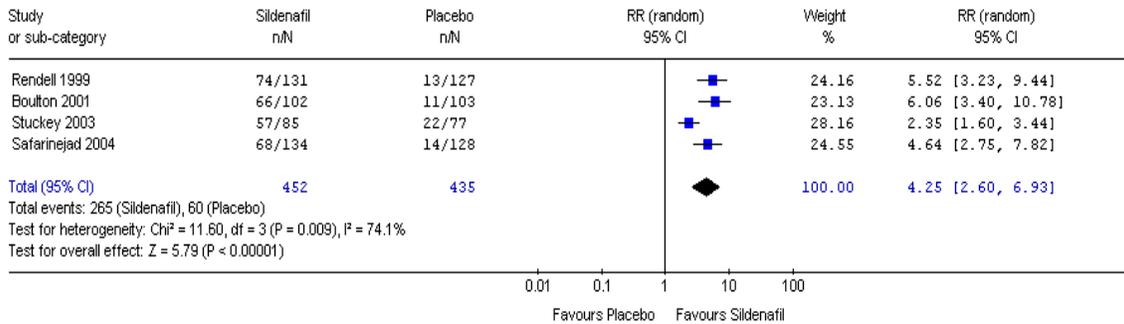


Figure 13. Improved erection (GEQ-Q1): Type II diabetes

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 05 Patients with Improved Erections (GEQ-Q1)

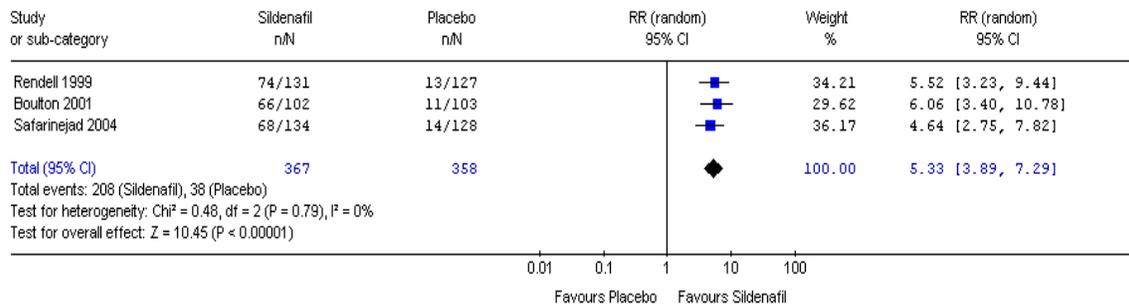


Figure 14. The mean IIEF-Q3 score: Type I-II diabetes

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 02 Mean IIEF-Q3 score

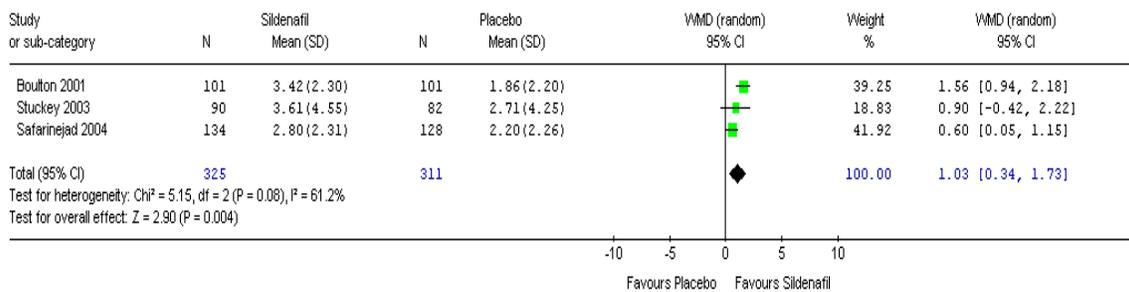


Figure 15. The mean IIEF-Q4 score: Type I-II diabetes

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 03 Mean IIEF-Q4 score

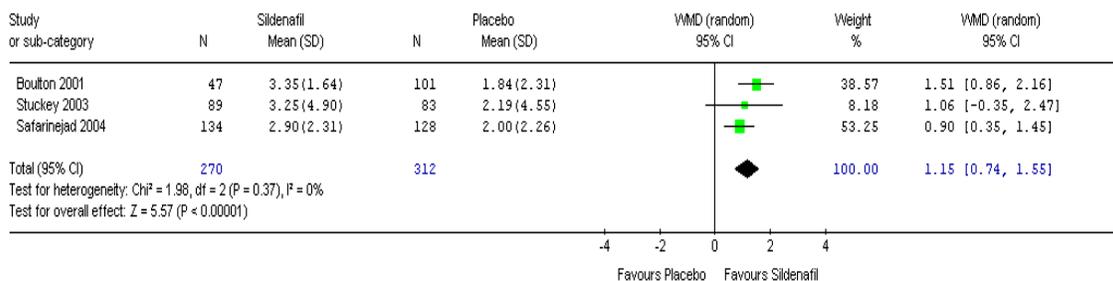


Figure 16. Any adverse events (treatment-related): Type I-II diabetes

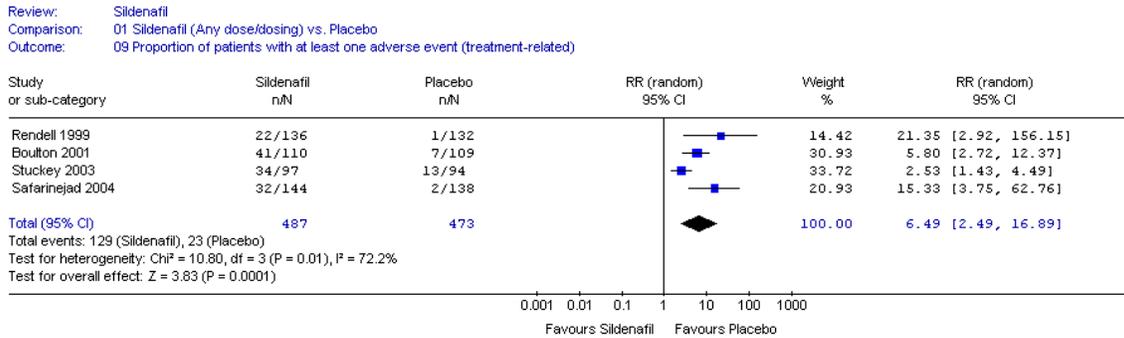


Figure 17. Any adverse events (treatment-related): Type II diabetes

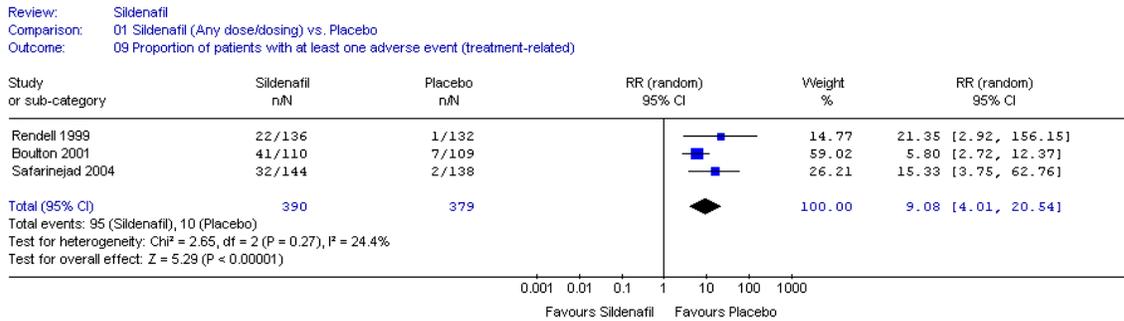


Figure 18. Successful intercourse attempts: major depressive disorder in remission

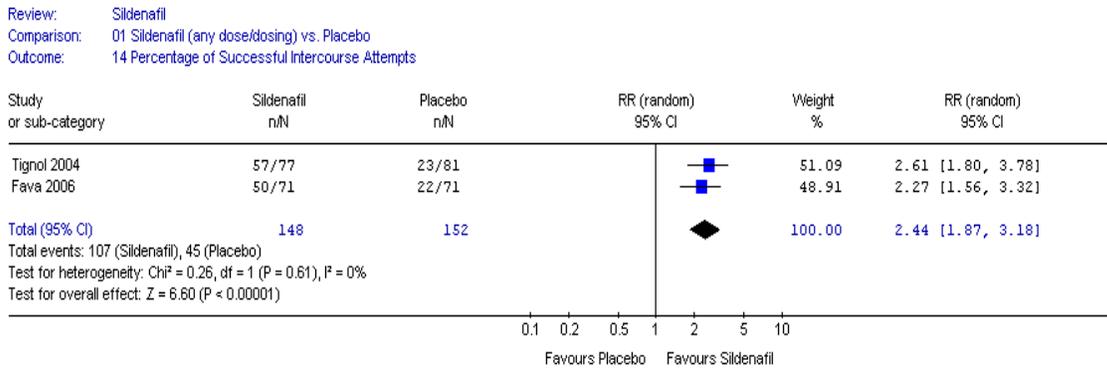


Figure 19. Improved erection (GEQ-Q1): major depressive disorder in remission

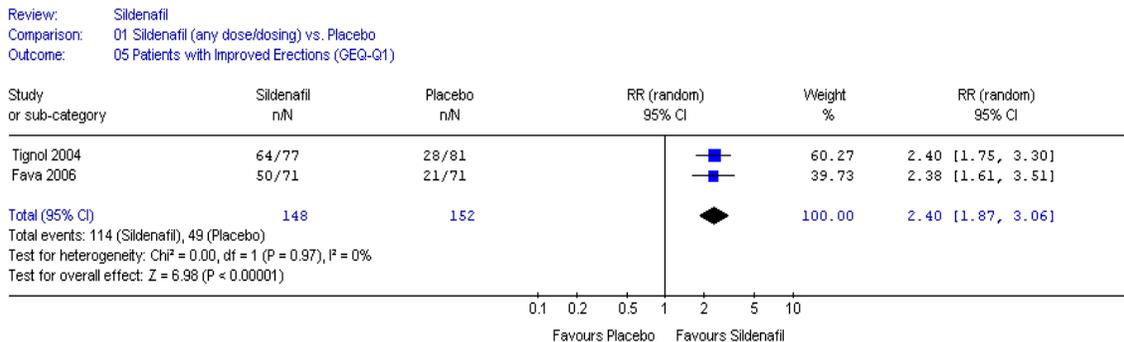


Figure 1. The mean IIEF–Q3 score: major depressive disorder in remission

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 02 Mean IIEF-Q3 score

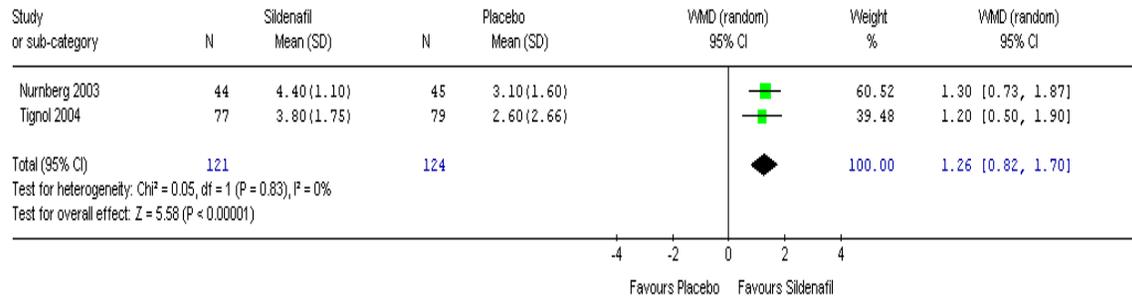


Figure 212. The mean IIEF–Q4 score: major depressive disorder in remission

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 03 Mean IIEF-Q4 score

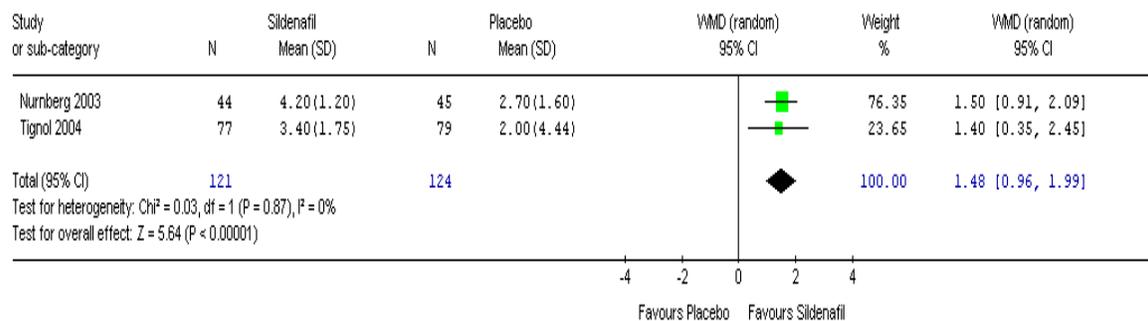


Figure 22. The mean IIEF–Q3 score: patients with hypertension taking anti-hypertensive drugs

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 02 Mean IIEF-Q3 score

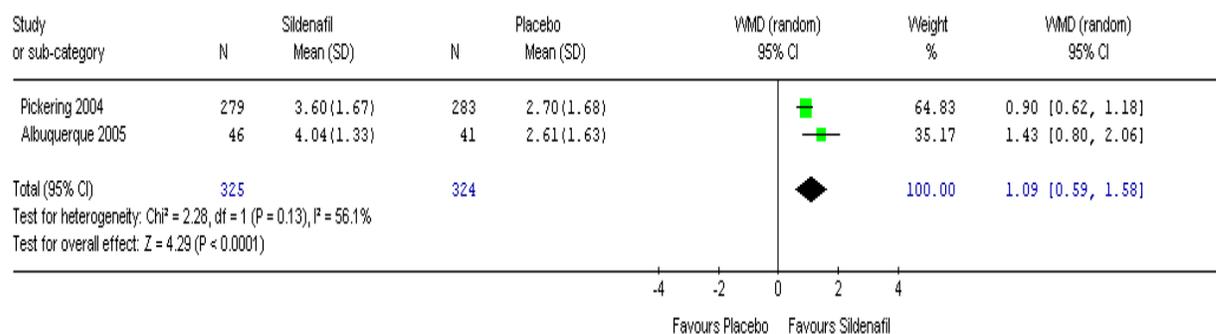


Figure 23. The mean IIEF–Q4 score: patients with hypertension taking anti-hypertensive drugs

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 03 Mean IIEF-Q4 score

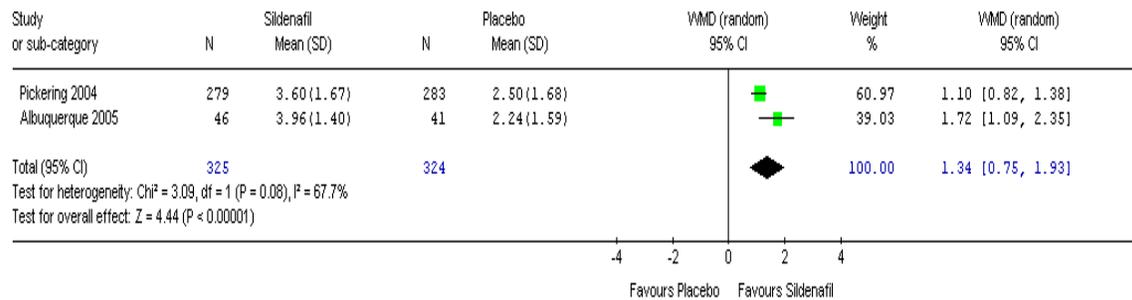


Figure 24. Improved erection (GEG–Q1): patients with hypertension taking anti-hypertensive drugs

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 05 Patients with Improved Erections (GEG-Q1)

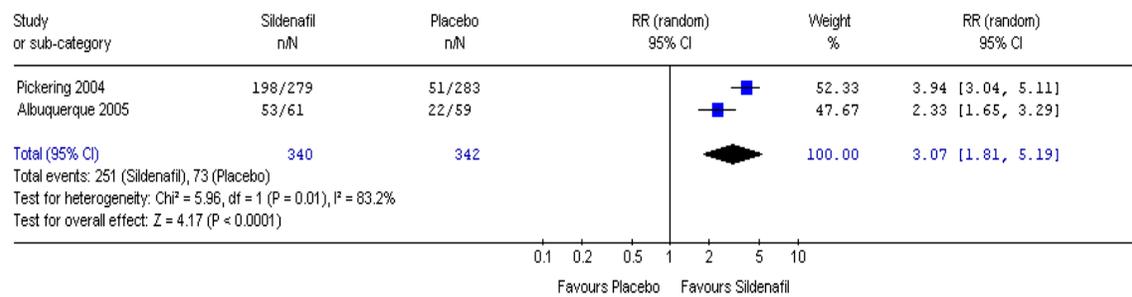


Figure 25. Successful intercourse attempts: patients with hypertension taking anti-hypertensive drugs

Review: Sildenafil
 Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
 Outcome: 04 Percentage of Successful Intercourse Attempts

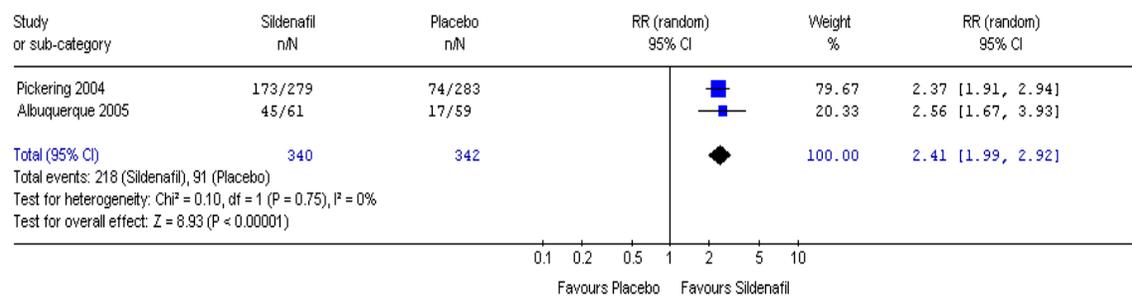


Figure 26. Any adverse event (all cause): patients with hypertension taking anti-hypertensive drugs

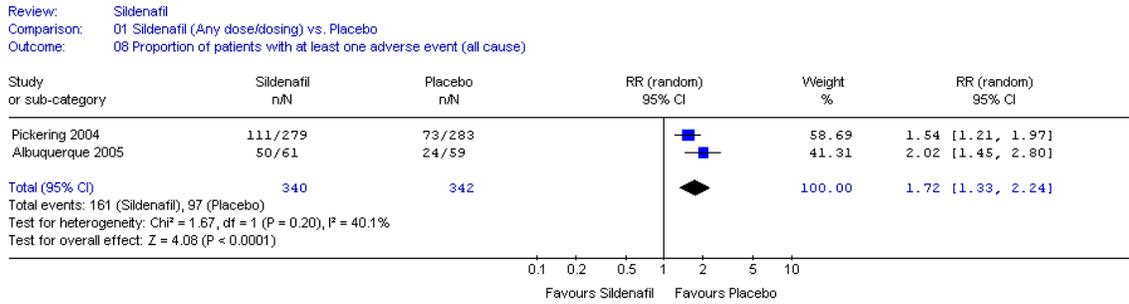


Figure 27. Headache (treatment-related): patients with hypertension taking anti-hypertensive drugs

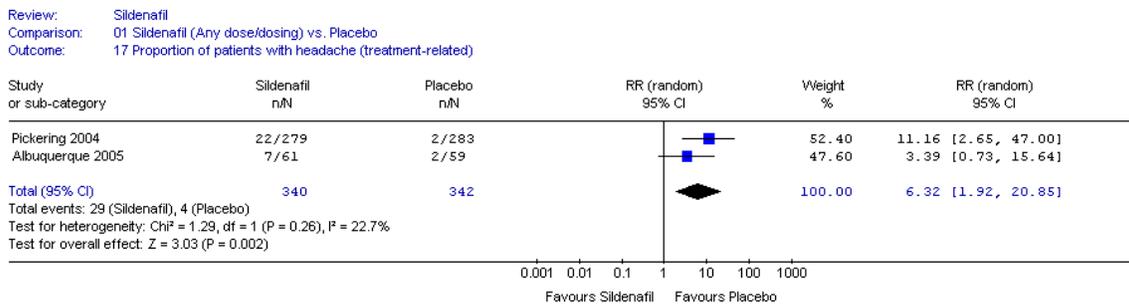


Figure 28. Dyspepsia (treatment-related): patients with hypertension taking anti-hypertensive drugs

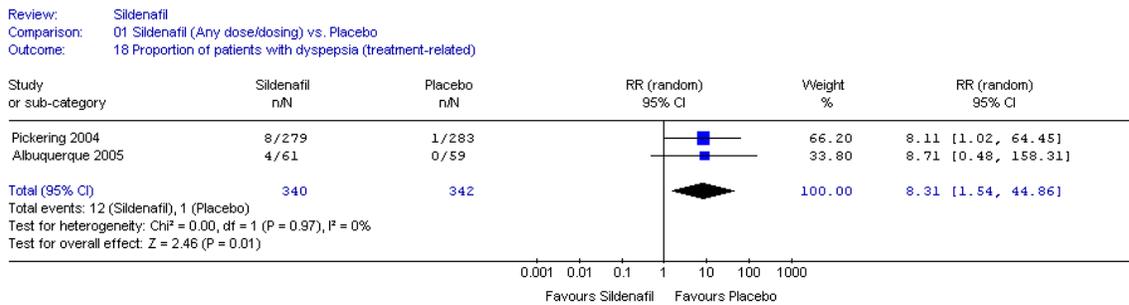


Figure 29. Flushing (treatment-related): patients with hypertension taking anti-hypertensive drugs

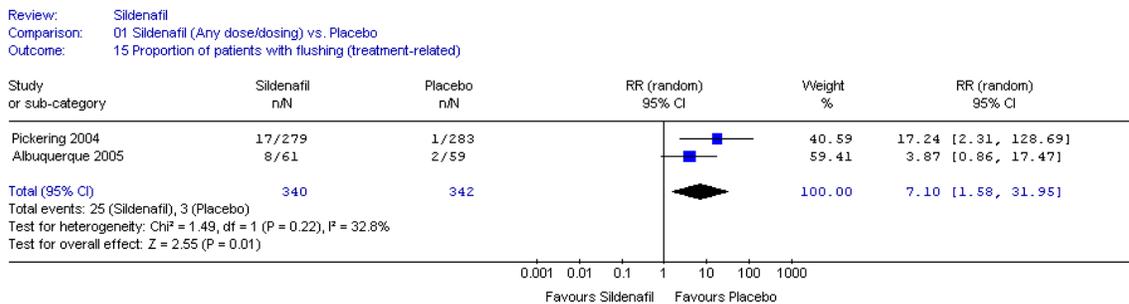


Figure 30. Improved erection (GEQ-Q1)

Review: Sildenafil
 Comparison: 02 Sildenafil (25 mg) vs. Sildenafil (50 mg)
 Outcome: 01 Proportion of patients with improved erection (GEQ-Q1)

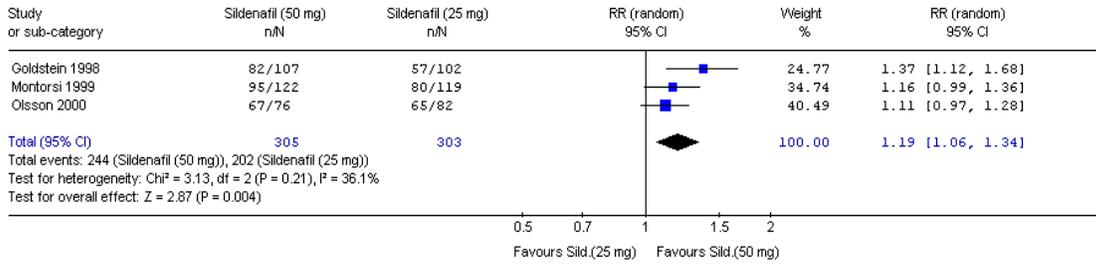


Figure 31. Headache (all cause)

Review: Sildenafil
 Comparison: 02 Sildenafil (25 mg) vs. Sildenafil (50 mg)
 Outcome: 02 Proportion of patients with headache (all cause)

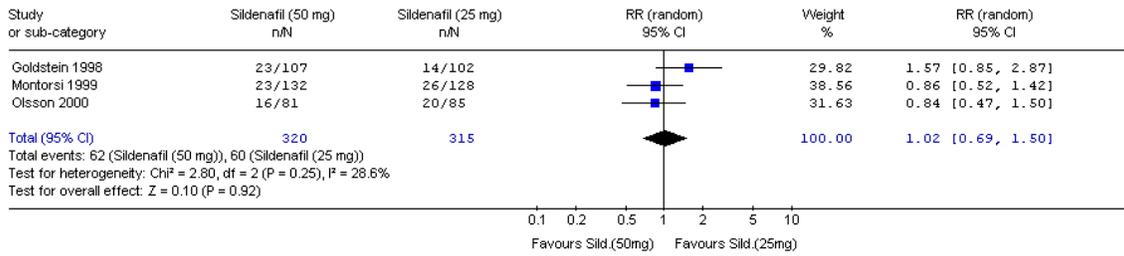


Figure 32. Flushing (all cause)

Review: Sildenafil
 Comparison: 02 Sildenafil (25 mg) vs. Sildenafil (50 mg)
 Outcome: 03 Proportion of patients with flushing (all cause)

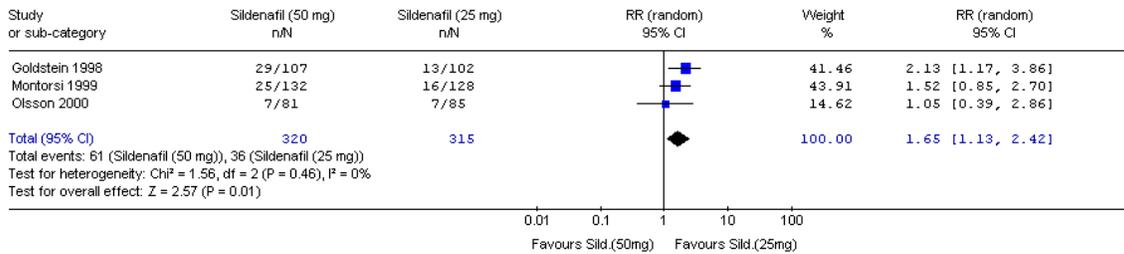


Figure 33. Visual disturbances (all cause)

Review: Sildenafil
 Comparison: 02 Sildenafil (25 mg) vs. Sildenafil (50 mg)
 Outcome: 04 Proportion of patients with visual disturbances (all cause)

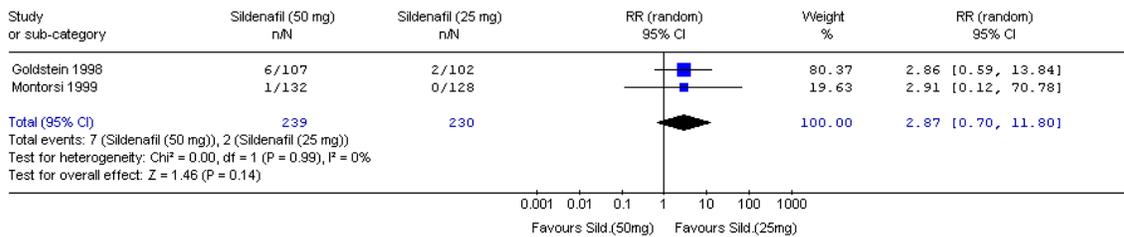


Figure 34. Improved erection (GEQ-Q1)

Review: Sildenafil
 Comparison: 04 Sildenafil (50 mg) vs. Sildenafil (100 mg)
 Outcome: 01 Proportion of patients with improved erection (GEQ-Q1)

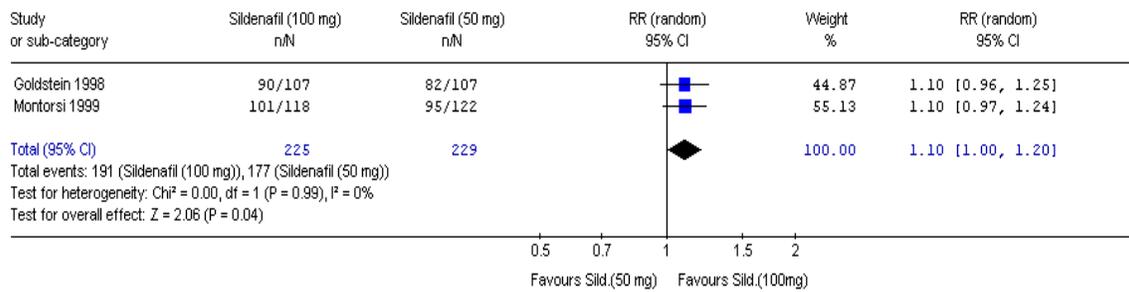


Figure 35. Headache (all cause)

Review: Sildenafil
 Comparison: 04 Sildenafil (50 mg) vs. Sildenafil (100 mg)
 Outcome: 02 Proportion of patients with headache (all cause)

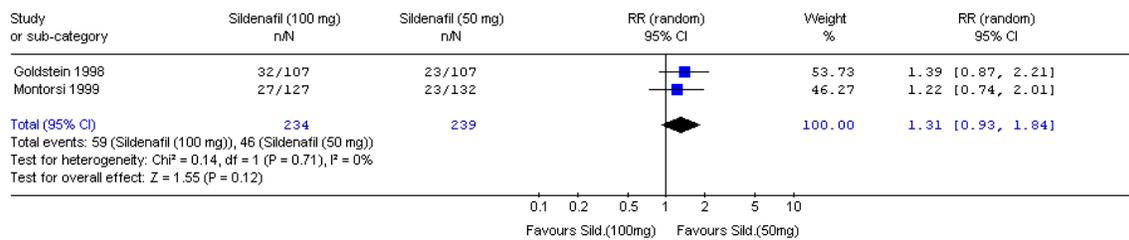


Figure 36. Flushing (all cause)

Review: Sildenafil
 Comparison: 04 Sildenafil (50 mg) vs. Sildenafil (100 mg)
 Outcome: 03 Proportion of patients with flushing (all cause)

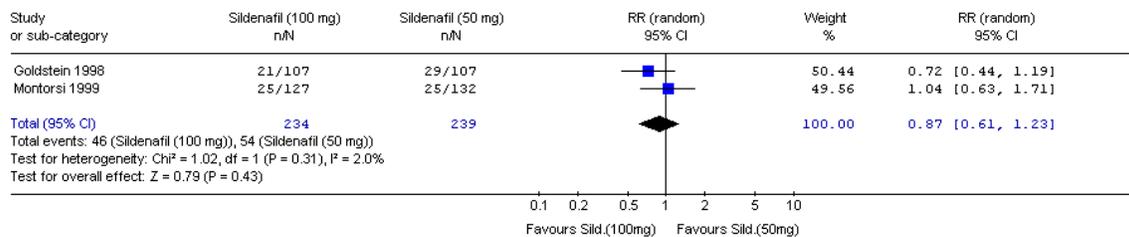


Figure 37. Visual disturbances (all cause)

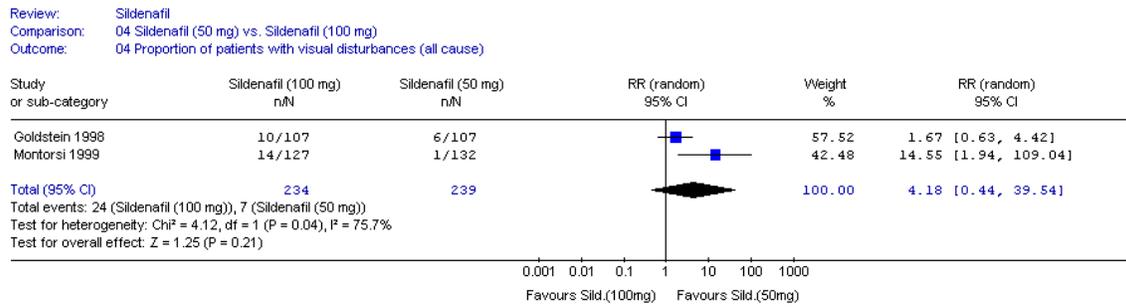


Figure 38. The mean IIEF “EF domain” score

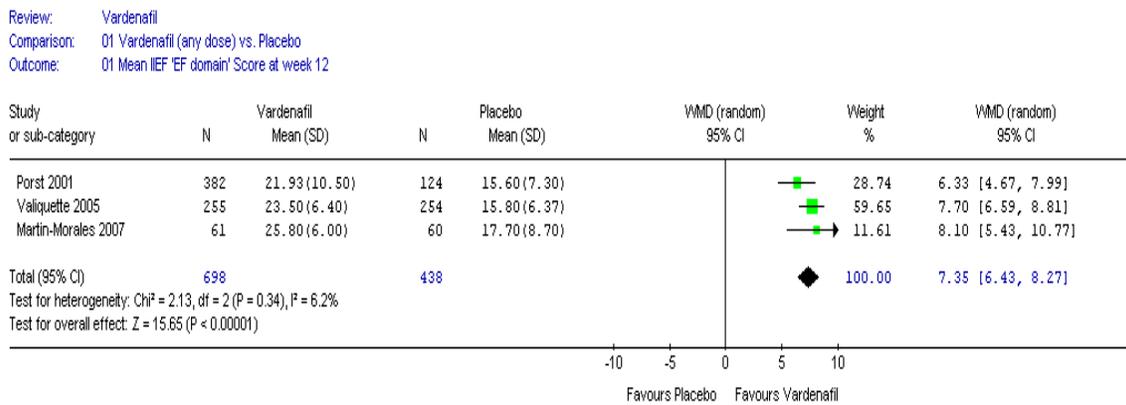


Figure 39. Successful intercourse attempts (SEP-Q2)

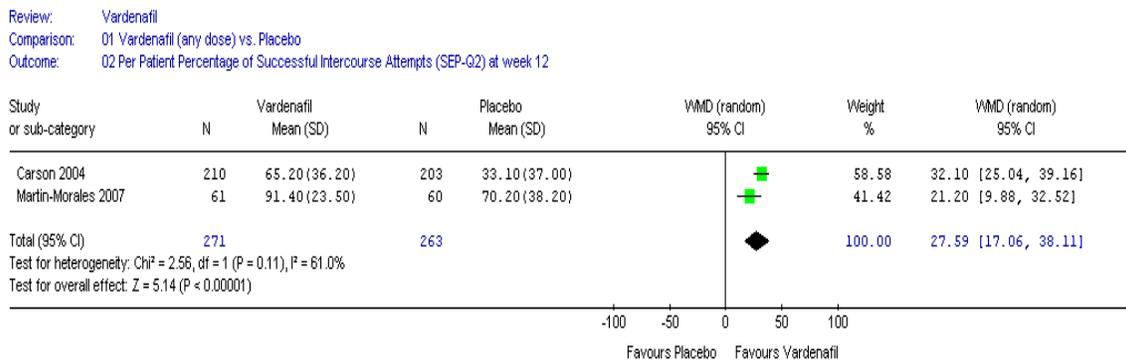


Figure 40. Successful intercourse attempts (SEP-Q3)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 03 Per Patient Percentage of Successful Intercourse Attempts (SEP-Q3) at week 12

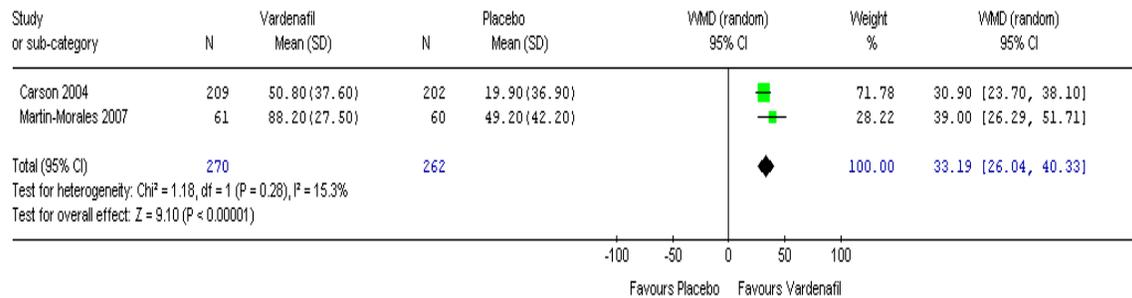


Figure 41. Improved erection (GAQ-Q1)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 04 Patients with improved erection (GAQ-Q1) at week 12

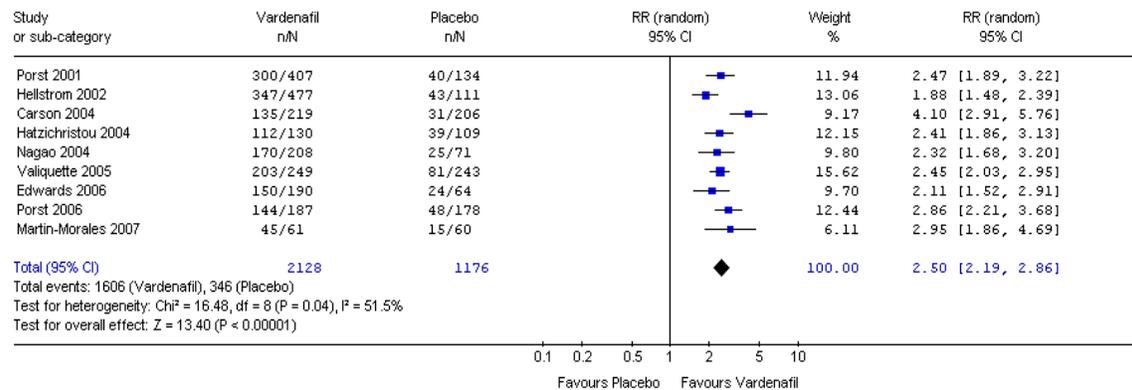


Figure 42. Improved erection without Carson 2004 (GAQ-Q1)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 04 Patients with improved erection (GAQ-Q1) at week 12

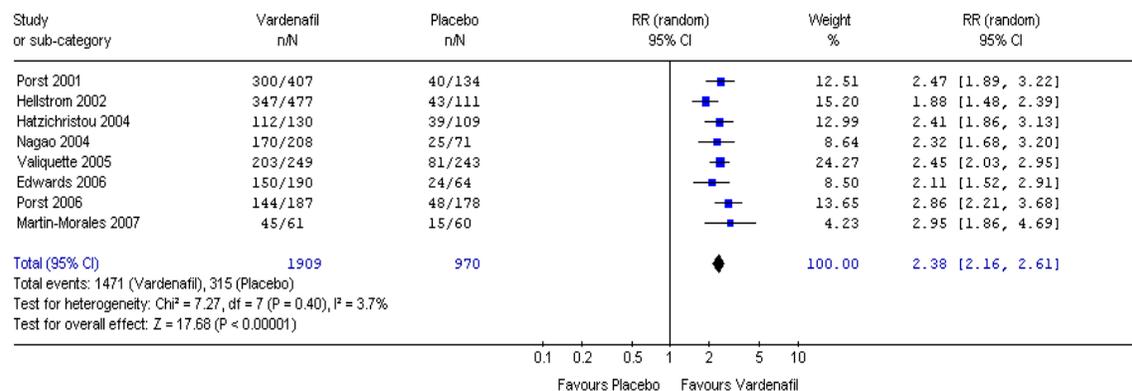


Figure 43. IIEF-EF \geq 26 at follow up (weeks 10–12)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 05 Patients with Mean IIEF 'EF domain' Score \Rightarrow 26 at weeks 10-12

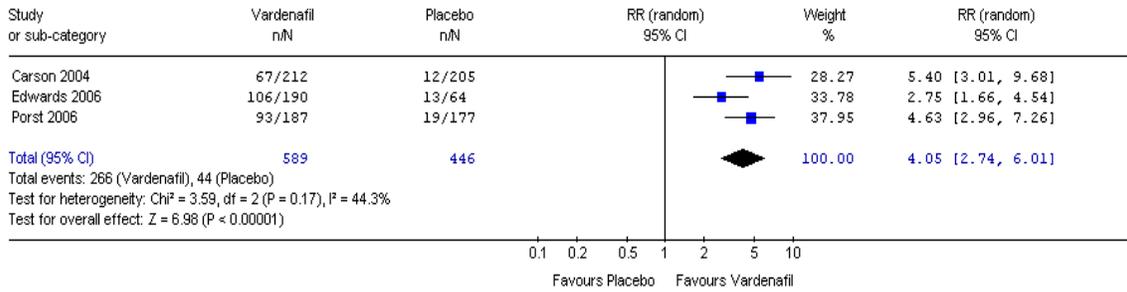


Figure 44. Any adverse events (all cause)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 07 Proportion of patients with at least one adverse event (all cause)

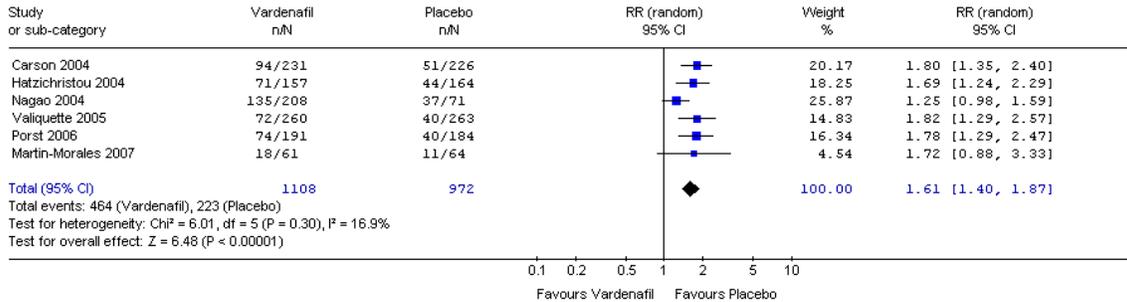


Figure 45. Withdrawals due to adverse events

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 08 Proportion of patients withdrawn due to adverse events

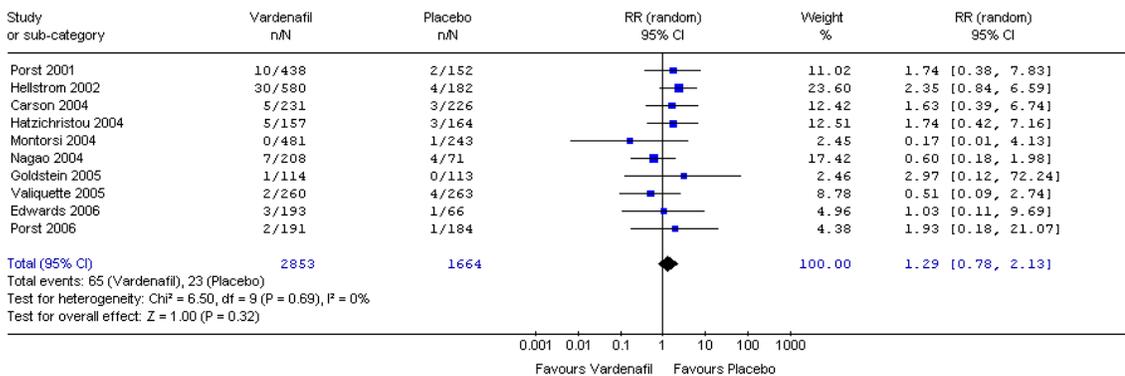


Figure 46. Serious adverse events

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 09 Proportion of patients with at least one serious adverse event (all cause)

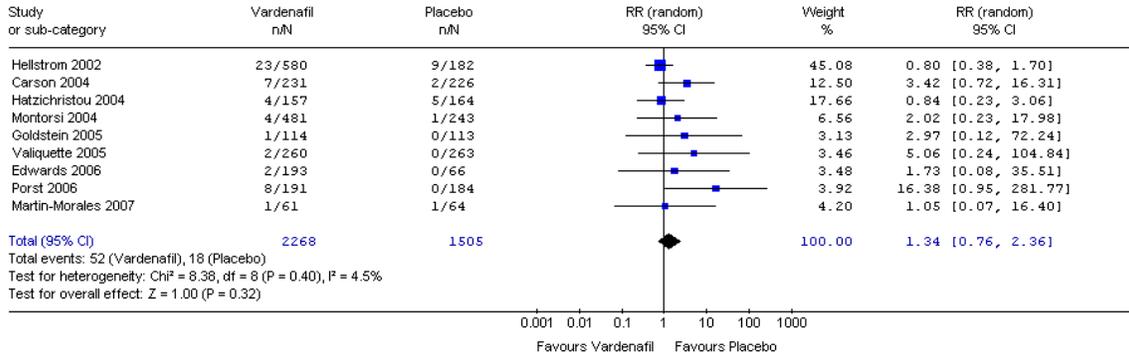


Figure 47. Headache (all cause)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 10 Proportion of patients with headache (all cause)

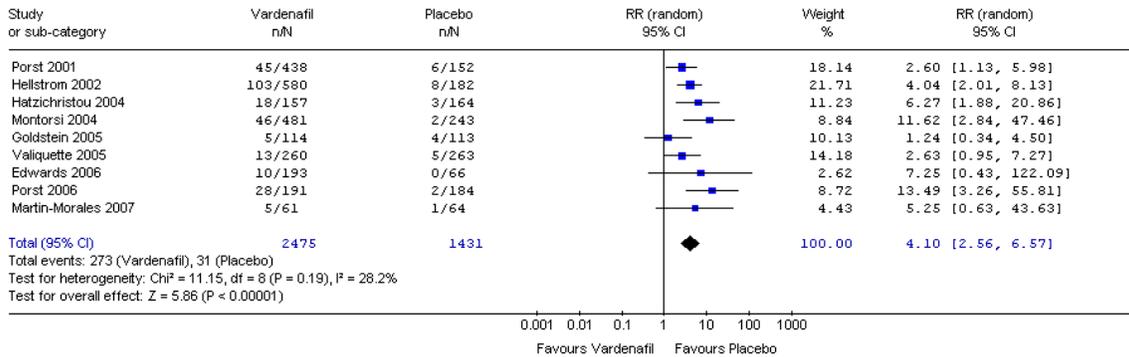


Figure 48. Flushing (all cause)

Review: Vardenafil
 Comparison: 01 Vardenafil (any dose) vs. Placebo
 Outcome: 11 Proportion of patients with flushing (all cause)

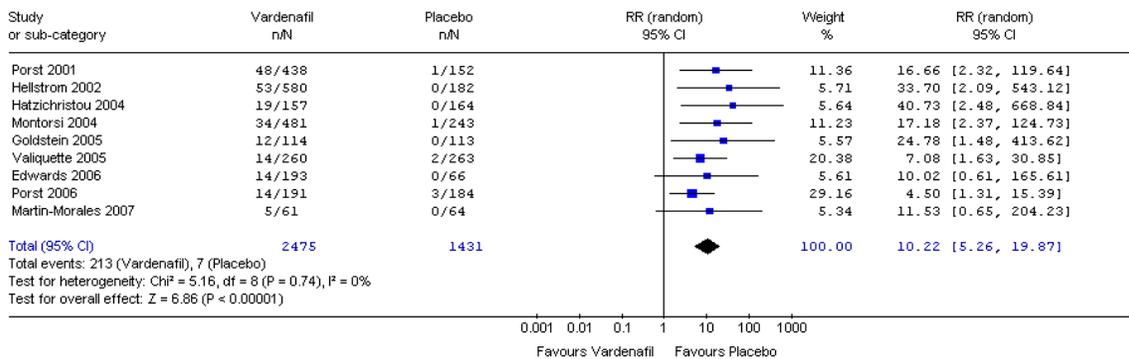


Figure 49. Dyspepsia (all cause)

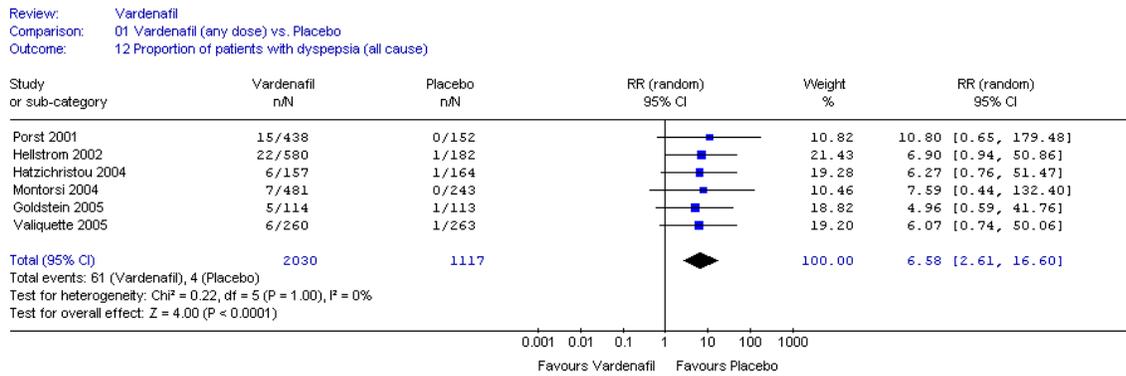


Figure 50. Serious adverse events: patients with diabetes

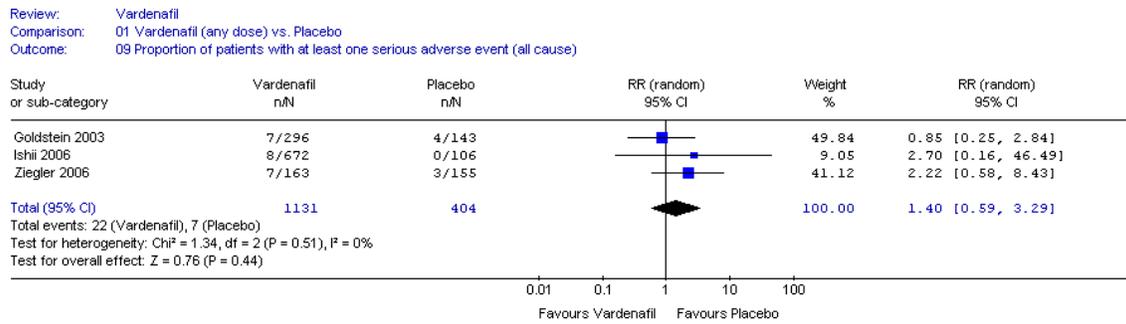


Figure 51. Withdrawals due to adverse events: patients with diabetes

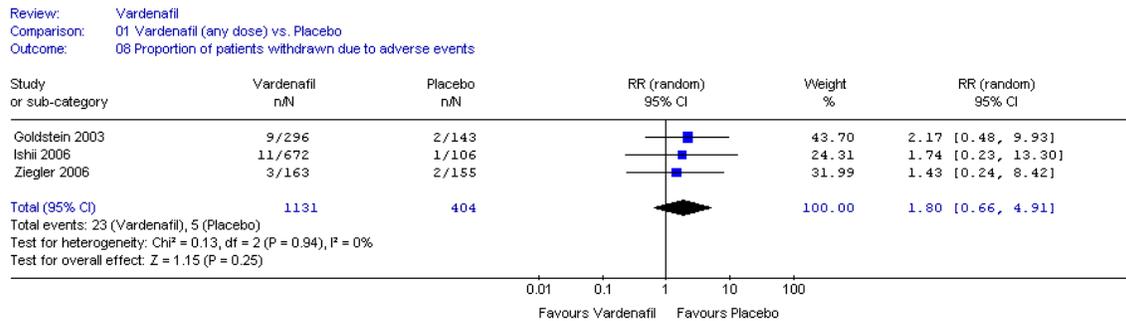


Figure 52. The mean IIEF “EF domain” score (at week 12–104)

Review: Vardenafil
 Comparison: 02 Vardenafil (20mg) vs. Vardenafil (10mg)
 Outcome: 01 Mean IIEF 'EF domain' Score

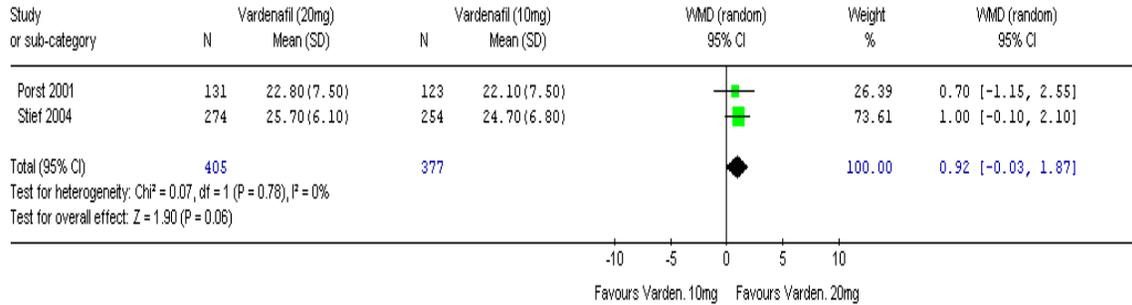


Figure 53. Improved erection (GAQ-Q1) (at week 12)

Review: Vardenafil
 Comparison: 02 Vardenafil (20mg) vs. Vardenafil (10mg)
 Outcome: 02 Patients with improved erection (GAQ-Q1)

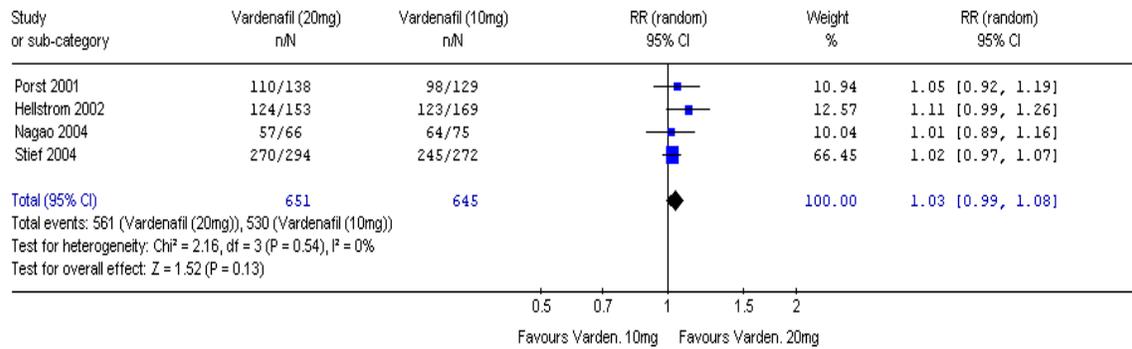


Figure 54. Any adverse events (all cause)

Review: Vardenafil
 Comparison: 02 Vardenafil (20mg) vs. Vardenafil (10mg)
 Outcome: 03 Proportion of patients with at least one adverse event (all cause)

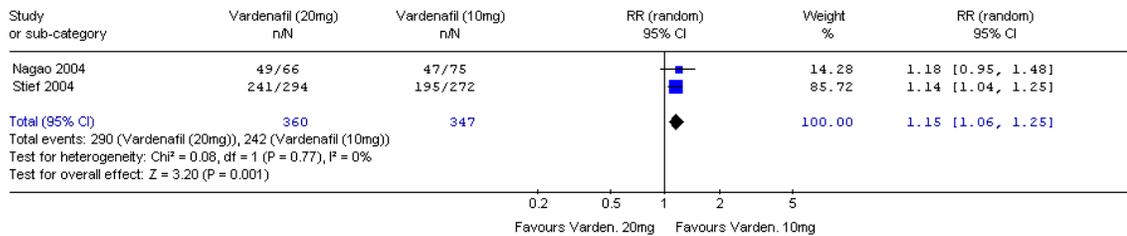


Figure 55. Serious adverse events (all cause)

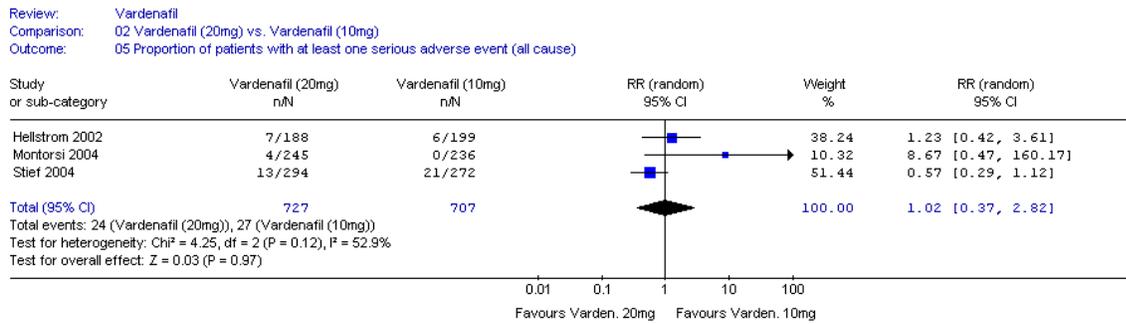


Figure 56. Withdrawals due to adverse events

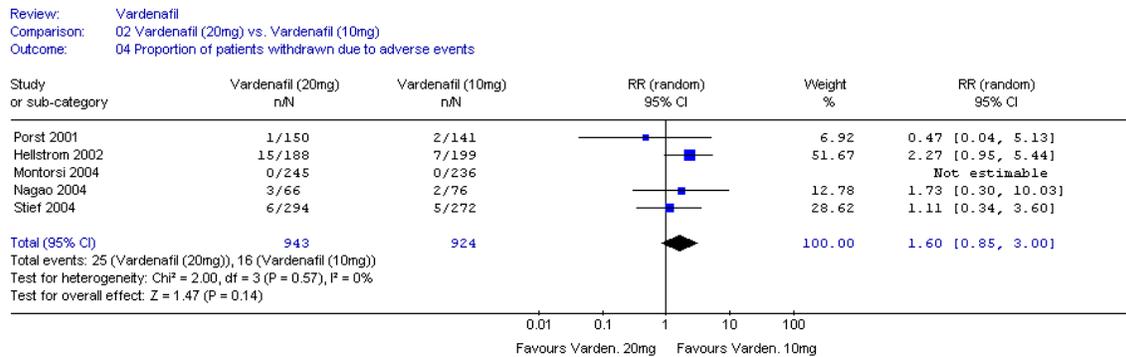


Figure 57. Headache (all cause)

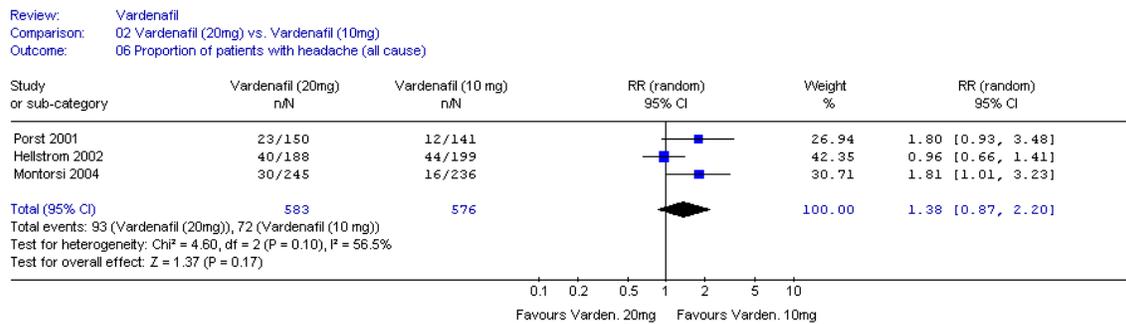


Figure 58. Flushing (all cause)

Review: Vardenafil
 Comparison: 02 Vardenafil (20mg) vs. Vardenafil (10mg)
 Outcome: 07 Proportion of patients with flushing (all cause)

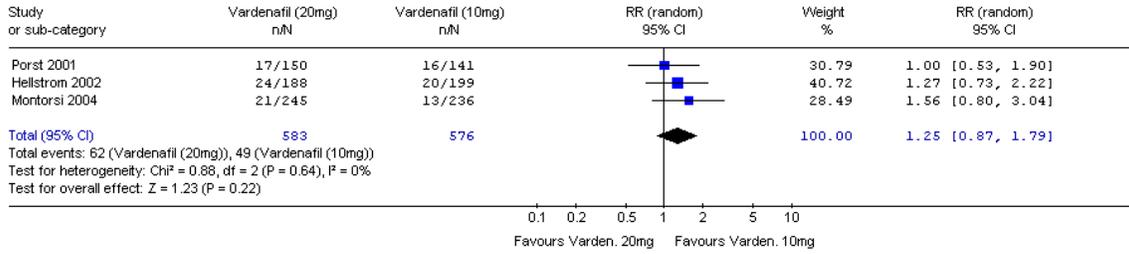


Figure 59. Dyspepsia (all cause)

Review: Vardenafil
 Comparison: 02 Vardenafil (20mg) vs. Vardenafil (10mg)
 Outcome: 08 Proportion of patients with dyspepsia (all cause)

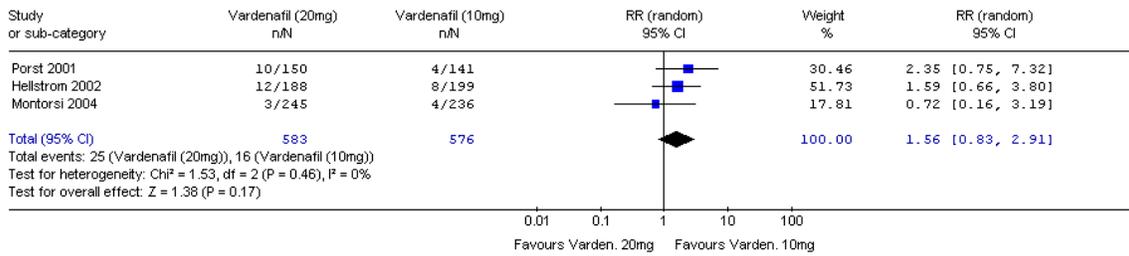


Figure 60. Absolute mean change in IIEF-EF score

Review: Tadalafil
 Comparison: 02 Tadalafil (10 mg or 20 mg) vs. Placebo
 Outcome: 01 IIEF-EF domain' mean score change

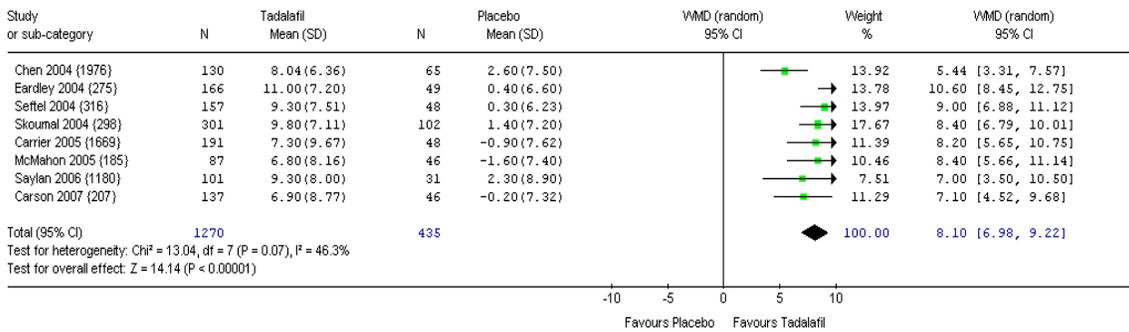


Figure 61. Mean per-patient percent absolute change from baseline in SEP-Q2

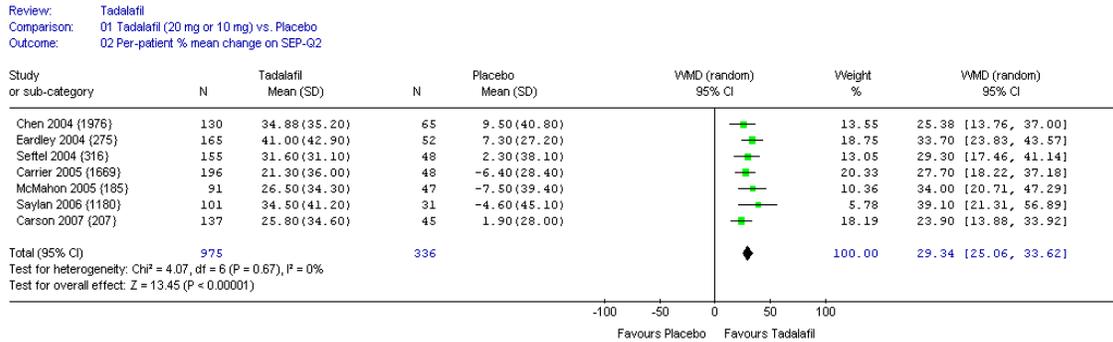


Figure 62. Improved erection (GAQ-Q1)

Review: Tadalafil
 Comparison: 01 Tadalafil (20 mg or 10 mg) vs. Placebo
 Outcome: 03 Proportion of patients with improved erection (GAQ-Q1)

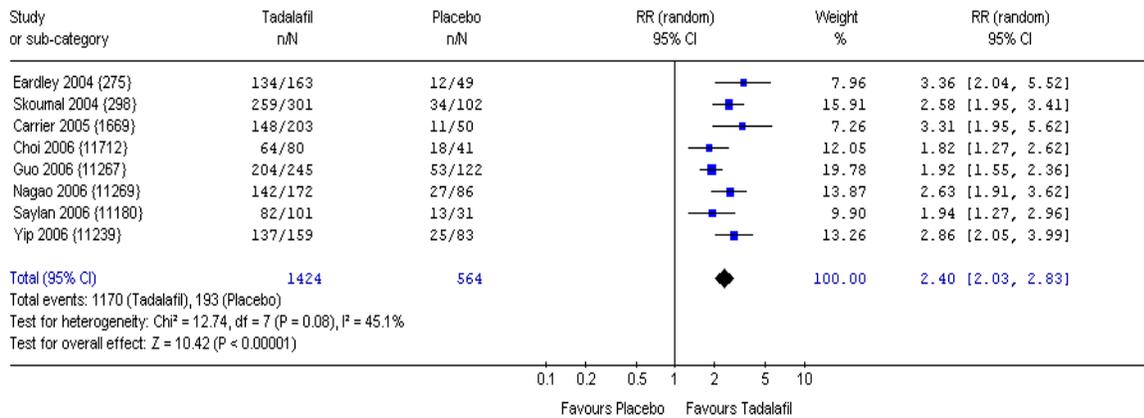


Figure 63. Absolute mean change from baseline in IIEF-EF score

Review: Tadalafil
 Comparison: 01 Tadalafil (20 mg) vs. Placebo
 Outcome: 01 IIEF-EF domain mean score change

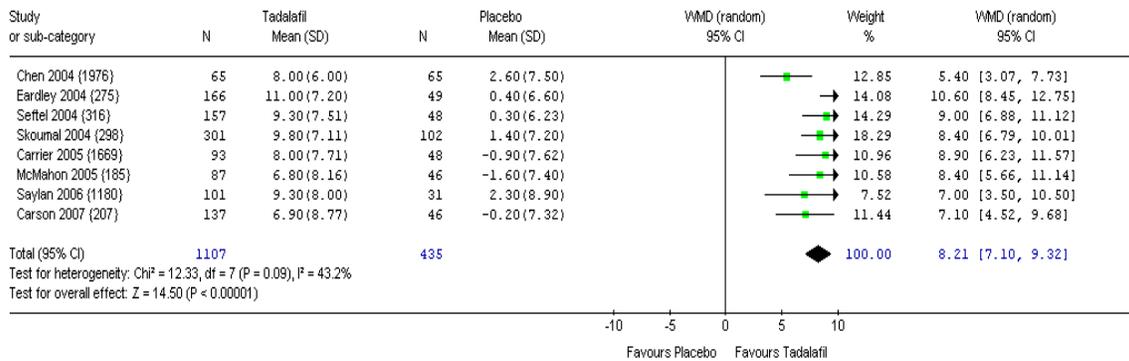


Figure 64. Mean per-patient percent absolute change from baseline in SEP-Q2

Review: Tadalafil
 Comparison: 01 Tadalafil (20 mg) vs. Placebo
 Outcome: 02 Per-patient % mean change on SEP-Q2

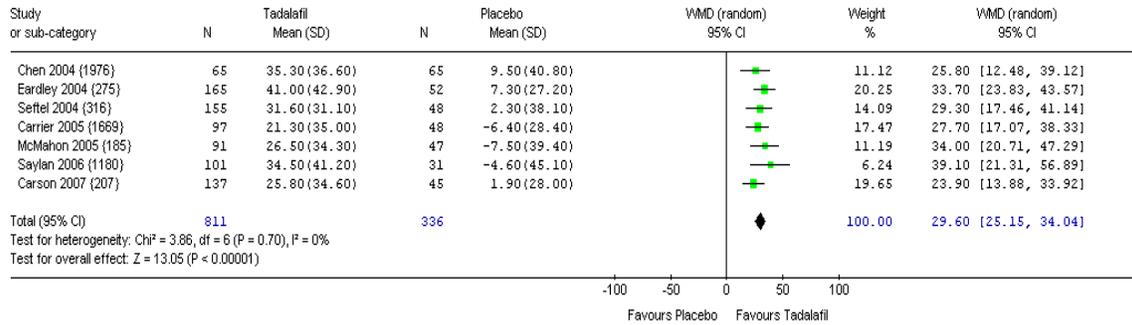


Figure 65. Improved erection (GAQ-Q)

Review: Tadalafil
 Comparison: 01 Tadalafil (20 mg) vs. Placebo
 Outcome: 03 Proportion of patients with improved erection (GAQ-Q1)

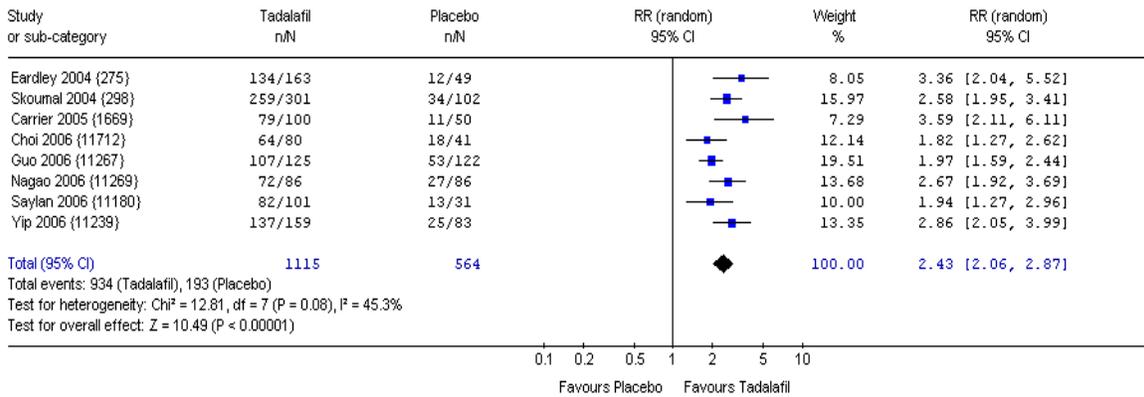


Figure 66. Any adverse events (all-cause)

Review: Tadalafil
 Comparison: 01 Tadalafil (20 mg) vs. Placebo
 Outcome: 04 Proportion of patients with at least one adverse event (all cause)

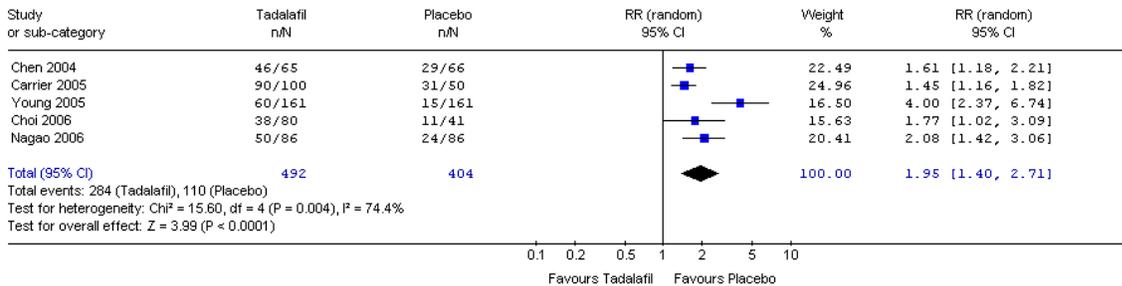


Figure 67. Any adverse events (all-cause)

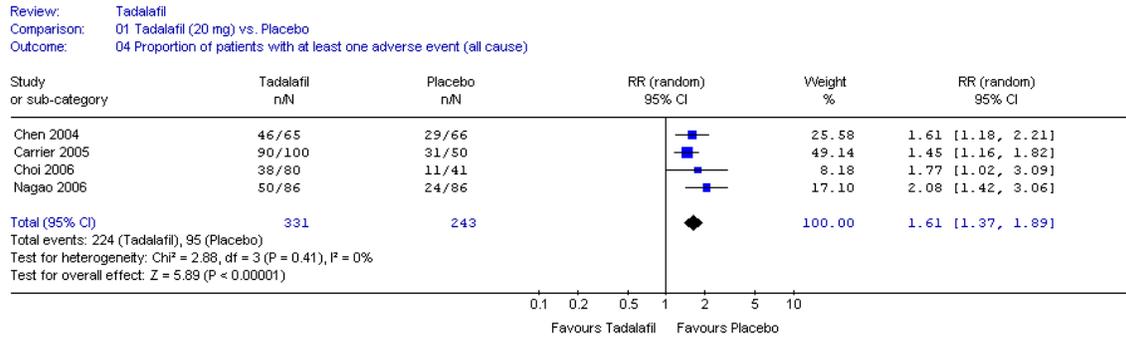


Figure 68. Mean change from baseline in IIEF-EF score

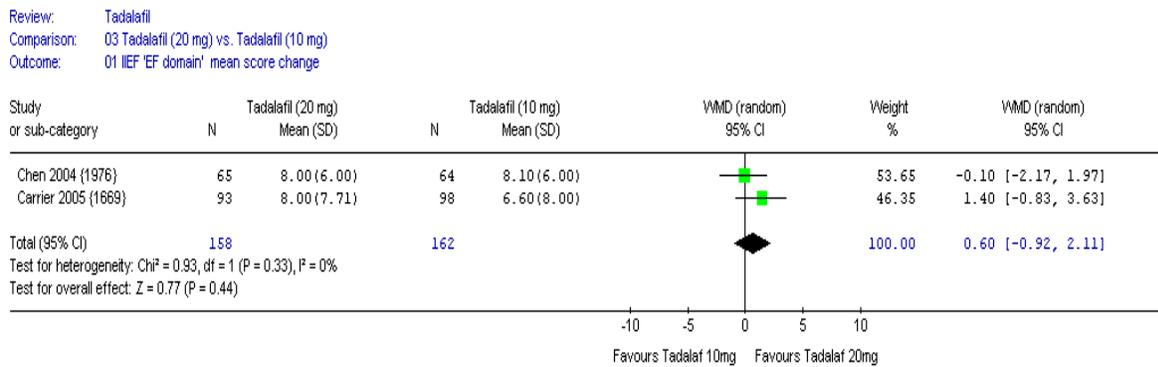


Figure 69. Mean per-patient percent absolute change from baseline in SEP-Q2

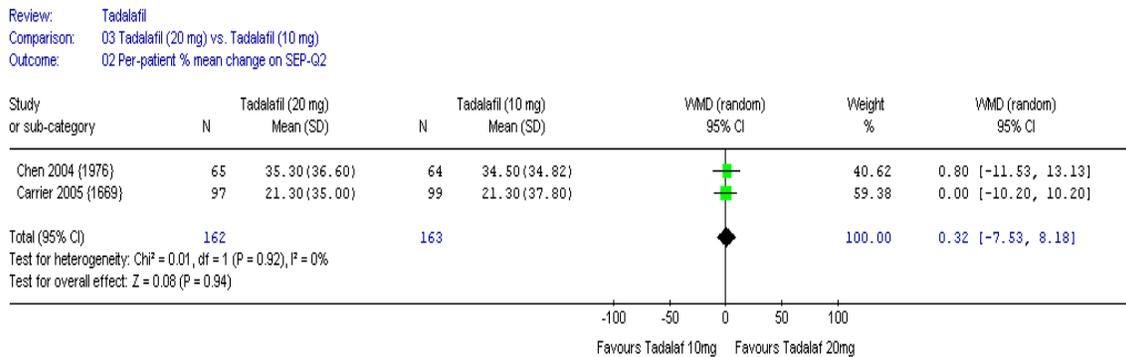


Figure 70. Improved erection (GAQ-Q1)

Review: Tadalafil
 Comparison: 03 Tadalafil (20 mg) vs. Tadalafil (10 mg)
 Outcome: 03 Proportion of patients with improved erection (GAQ-Q1)

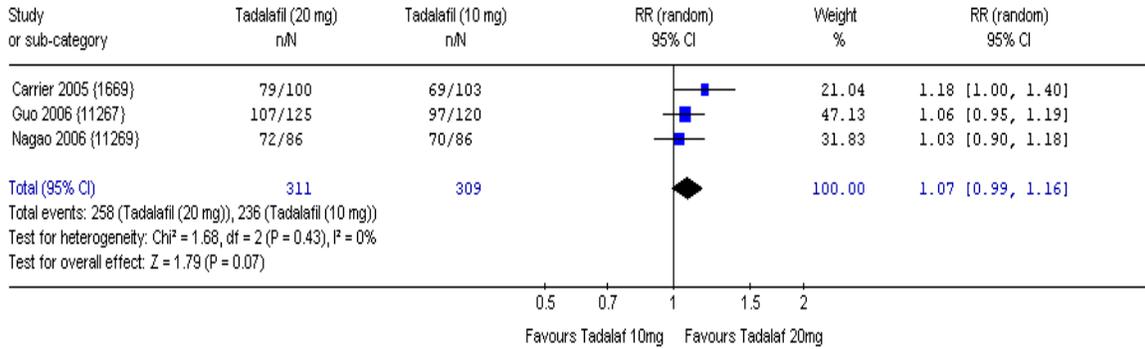


Figure 71. Any adverse events (all-cause)

Review: Tadalafil
 Comparison: 03 Tadalafil (20 mg) vs. Tadalafil (10 mg)
 Outcome: 04 Proportion of patients with at least one adverse event (all cause)

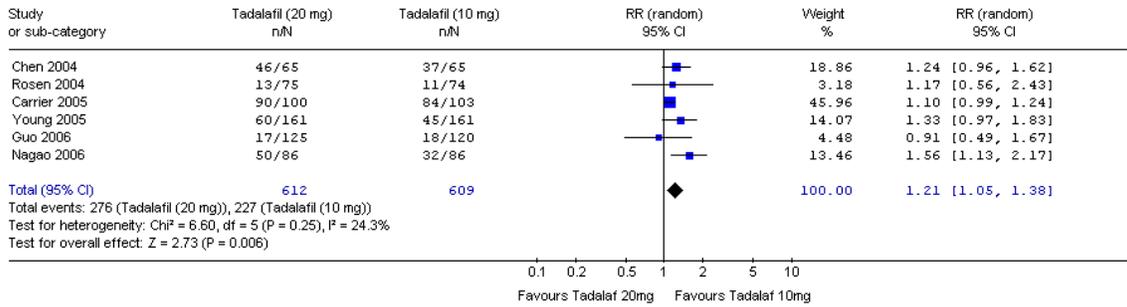


Figure 72. Any adverse events (all-cause)

Review: Tadalafil
 Comparison: 02 Tadalafil (10 mg) vs. Placebo
 Outcome: 01 Proportion of patients with at least one adverse event (all cause)

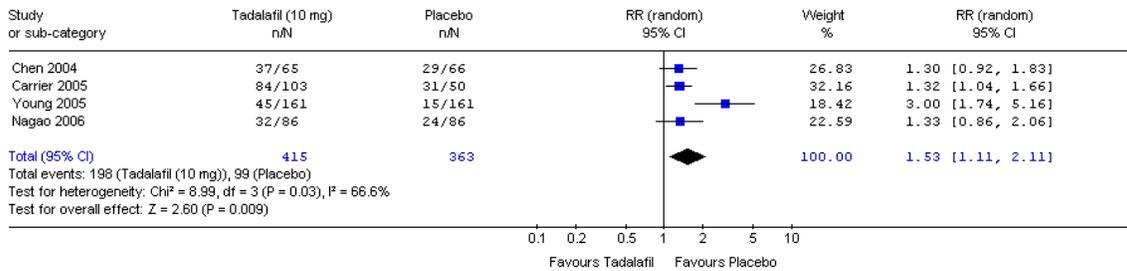
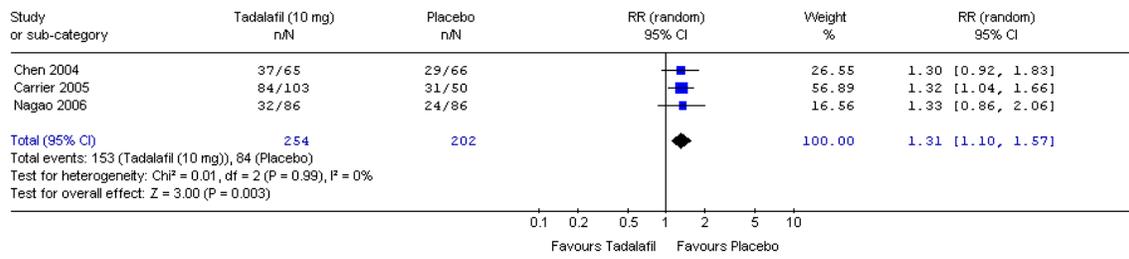


Figure 73. Any adverse events (all-cause)

Review: Tadalafil
 Comparison: 02 Tadalafil (10 mg) vs. Placebo
 Outcome: 01 Proportion of patients with at least one adverse event (all cause)



References and Included Studies

1. Anonymous. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *JAMA* 1993 Jul 7;270(1):83-90.
2. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994 Jan;151(1):54-61.
3. Bella A, Lue T. Male sexual dysfunction. In: Tanagho E, editors. *Smith's General Urology*, 17th ed. New York: Lange/McGraw Hill; 2008. p. 589-610.
4. Lin C, Lin G, Lue T. Cyclic nucleotide signaling in cavernous smooth muscle. *J Sex Med* 2005;2(4):478-91.
5. Shabsigh R, Kaufman JM, Steidle C, et al. Randomized study of testosterone gel as adjunctive therapy to sildenafil in hypogonadal men with erectile dysfunction who do not respond to sildenafil alone. *J Urol* 2004 Aug;172(2):658-63.
6. Musicki B, Burnett A. eNOS function and dysfunction in the penis. *Exp Biol Med* 2006;231(2):154-65.
7. Burnett AL. Role of nitric oxide in the physiology of erection. *Biol Reprod* 1995;52(3):485-9.
8. Lue TF. Erectile dysfunction. *N Engl J Med* 2000;342(24):1802-13.
9. Andersson KE, Wagner G. Physiology of penile erection. *Physiol Rev* 1995 Jan;75(1):191-236.
10. Jin L, Burnett AL. RhoA/Rho-kinase in erectile tissue: mechanisms of disease and therapeutic insights. *Clin Sci (Lond)* 2006 Feb;110(2):153-65.
11. Rehman J, Benet A, Minsky LS, et al. Results of surgical treatment for abnormal penile curvature: Peyronie's disease and congenital deviation by modified Nesbit plication (tunica shaving and plication). *J Urol* 1997 Apr;157(4):1288-91.
12. Brock G. Erectile dysfunction update education forum summary. *Can J Urol* 2000;8:1416-8.
13. Fazio L, Brock G. Erectile dysfunction: Management update. *CMAJ: Canadian Medical Association Journal* 2004;170(9):1429-37.
14. Montague DK, Jarow JP, Broderick GA, et al. Chapter 1: The management of erectile dysfunction: an AUA update. *J Urol* 2005 Jul;174(1):230-9.
15. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997 Jun;49(6):822-30.
16. Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11(6):319-26.
17. Althof SE, Corty EW, Levine SB, et al. EDITS: development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. *Urology* 1999 Apr;53(4):793-9.
18. Rosen RC, Cappelleri JC, Gendrano N, III. The International Index of Erectile Function (IIEF): a state-of-the-science review. [Review] [63 refs]. *Int J Impot Res* 2002 Aug;14(4):226-44.
19. Burnett AL, Johns DG, Kriegsfeld LJ, et al. Ejaculatory abnormalities in mice with targeted disruption of the gene for heme oxygenase-2. *Nat Med* 1998 Jan;4(1):84-7.
20. Johnson AR, III, Jarow JP. Is routine endocrine testing of impotent men necessary? *J Urol* 1992 Jun;147(6):1542-3.
21. Miller TA. Diagnostic evaluation of erectile dysfunction. *Am Fam Physician* 2000 Jan 1;61(1):95-10.
22. Ayta IA, McKinlay JB, Krane RJ. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. *BJU Int* 1999 Jul;84(1):50-6.
23. Johannes CB, Araujo AB, Feldman HA, et al. Incidence of erectile dysfunction in men 40 to 69 years old: longitudinal results from the Massachusetts male aging study.[see comment]. *J Urol* 2000 Feb;163(2):460-3.
24. Virag R. Indications and early results of sildenafil (Viagra) in erectile dysfunction. *Urology* 1999 Dec;54(6):1073-7.
25. Kendirci M, Trost L, Sikka SC, et al. The effect of vascular risk factors on penile vascular status

- in men with erectile dysfunction. *J Urol* 2007 Dec;178(6):2516-20.
26. Rosen RC, Leiblum SR, Spector IP. Psychologically based treatment for male erectile disorder: a cognitive-interpersonal model. *J Sex Marital Ther* 1994;20(2):67-85.
 27. Esposito K, Giugliano F, Di PC, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial.[see comment]. *JAMA* 2004 Jun 23;291(24):2978-84.
 28. Porst H. The rationale for prostaglandin E1 in erectile failure: a survey of worldwide experience. [Review] [219 refs]. *J Urol* 1996 Mar;155(3):802-15.
 29. Wessells H, Joyce GF, Wise M, et al. Erectile dysfunction. *J Urol* 2007 May;177(5):1675-81.
 30. Simmons M, Montague DK. Penile prosthesis implantation: past, present and future. *Int J Impot Res* 2008 Apr 3;
 31. Anonymous. Bayer Annual Report. 2005.
 32. Anonymous. Eli Lilly Annual Report. 2005.
 33. Wessells H. Pfizer Annual Report. 2007.
 34. Carson C. Long-term use of sildenafil. *Expert Opin Pharmacother* 2003;4(3):397-405.
 35. Hanson-Divers C, Jackson SE, Lue TF, et al. Health outcomes variables important to patients in the treatment of erectile dysfunction. *J Urol* 1998 May;159(5):1541-7.
 36. Carson C, Giuliano F, Goldstein I, et al. The 'effectiveness' scale--therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report. [Review] [7 refs]. *Int J Impot Res* 2004 Jun;16(3):207-13.
 37. Noldus J, Huland H. [Erectile dysfunction and hypogonadism. Is routine endocrine screening necessary?]. *Urologe A* 1994 Jan;33(1):73-5.
 38. Buvat J, Lemaire A. Endocrine screening in 1,022 men with erectile dysfunction: clinical significance and cost-effective strategy.[see comment]. [Review] [16 refs]. *J Urol* 1997 Nov;158(5):1764-7.
 39. Wespes E, Amar E, Hatzichristou D, et al. EAU Guidelines on Erectile Dysfunction: An Update. *Eur Urol* 2006;49(5):806-15.
 40. Miller TA. Diagnostic evaluation of erectile dysfunction. *Am Fam Physician* 2000 Jan 1;61(1):95-10.
 41. Bancroft J, Wu FC. Changes in erectile responsiveness during androgen replacement therapy. *Arch Sex Behav* 1983 Feb;12(1):59-66.
 42. Morelli A, Filippi S, Mancina R, et al. Androgens regulate phosphodiesterase type 5 expression and functional activity in corpora cavernosa. *Endocrinology* 2004 May;145(5):2253-63.
 43. Aversa A, Isidori AM, De Martino MU, et al. Androgens and penile erection: evidence for a direct relationship between free testosterone and cavernous vasodilation in men with erectile dysfunction. *Clin Endocrinol (Oxf)* 2000 Oct;53(4):517-22.
 44. Lue TF, Broderick G. Evaluation and nonsurgical management of erectile dysfunction and priapism. In: Walsh P, Retik A, Vaughan E, editors. *Campbell's Urology*, 7th ed Philadelphia, PA: Saunders; 1998. p. 1181-214.
 45. Kropman RF, Nijeholt AA, Zwartendijk J. Experiences with the Surgitek Art-1000 penile tumescence and rigidity monitor, and comparison with the RigiScan. *J Urol* 1991 Jul;146(1):43-5.
 46. Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003 Nov 10;3:25
 47. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996 Feb;17(1):1-12.
 48. Schulz KF, Grimes DA. Allocation concealment in randomised trials: defending against deciphering. *Lancet* 2002 Feb 16;359(9306):614-8.
 49. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986 Sep;7(3):177-88.
 50. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003 Sep 6;327(7414):557-60.
 51. Fleiss JL. The statistical basis of meta-analysis. *Stat Methods Med Res* 1993;2(2):121-45.

52. Deeks JJ, Higgins JP, Altman DG. Analysing and presenting results. In: *Cochrane Handbook for Systematic Reviews of Interventions*, 4.2.6 2006. 8 p. 97-165.
53. Egger M, Davey SG, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997 Sep 13;315(7109):629-34.
54. Lau J, Ioannidis JP, Terrin N, et al. The case of the misleading funnel plot. *BMJ* 2006 Sep 16;333(7568):597-600.
55. Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *J Clin Epidemiol* 2001 Oct;54(10):1046-55.
56. Netto Junior NR, Claro JA. The importance of hyperprolactinemia in impotence. *Rev Paul Med* 1993 Nov;111(6):454-5.
57. Citron J, Ettinger B, Rubinoff H, et al. Prevalence of hypothalamic-pituitary imaging abnormalities in impotent men with secondary hypogonadism. *J Urol* 1996;155(Feb.):529-33.
58. Hatzichristou D, Hatzimouratidis K, Bekas M, et al. Diagnostic steps in the evaluation of patients with erectile dysfunction. *J Urol* 2002;168(2):615-20.
59. Martinez-Jabaloyas JM, Queipo-Zaragoza A, Pastor-Hernandez F, et al. Testosterone levels in men with erectile dysfunction. *BJU Int* 2006 Jun;97(6):1278-83.
60. Acar D, Cayan S, Bozlu M, et al. Is routine hormonal measurement necessary in initial evaluation of men with erectile dysfunction? *Arch Androl* 2004 Jul;50(4):247-53.
61. Earle CM, Stuckey BG. Biochemical screening in the assessment of erectile dysfunction: what tests decide future therapy? *Urology* 2003 Oct;62(4):727-31.
62. Rhoden EL, Teloken C, Mafessoni R, et al. Is there any relation between serum levels of total testosterone and the severity of erectile dysfunction? *Int J Impot Res* 2002 Jun;14(3):167-71.
63. Bunch TJ, Abraham D, Wang S, et al. Pituitary radiographic abnormalities and clinical correlates of hypogonadism in elderly males presenting with erectile dysfunction. *Aging Male* 2002 Mar;5(1):38-46.
64. Fahmy AK, Mitra S, Blacklock AR, et al. Is the measurement of serum testosterone routinely indicated in men with erectile dysfunction? *BJU Int* 1999 Sep;84(4):482-4.
65. Akpunonu BE, Mutgi AB, Federman DJ, et al. Routine prolactin measurement is not necessary in the initial evaluation of male impotence. *J Gen Intern Med* 1994 Jun;9(6):336-8.
66. Drinka PJ, Voeks S, Bauwens S, et al. Sensitivity and positive predictive value of clinical signs of hypogonadism in elderly men. *South Med J* 1993 Nov;86(11):1264-5.
67. El-Sakka AI, Hassoba HM, Sayed HM, et al. Pattern of endocrinal changes in patients with sexual dysfunction. *J Sex Med* 2005;2(4):551-8.
68. Tsujimura A, Matsumiya K, Miyagawa Y, et al. Comparative study on evaluation methods for serum testosterone level for PADAM diagnosis. *Int J Impot Res* 2005;17(3):259-63.
69. Guay AT, Bansal S, Hodge MB. Possible hypothalamic impotence: Male counterpart to hypothalamic amenorrhea? *Urology* 1991;38(4):317-22.
70. Forsberg L, Gustavii B, Hojerback T, et al. One hundred impotent men. *Scand J Urol Nephrol* 1990;24(2):83-7.
71. Reyes-Vallejo L, Lazarou S, Morgentaler A. Subjective sexual response to testosterone replacement therapy based on initial serum levels of total testosterone. *J Sex Med* 2006 Nov 6;4(6):1757-62.
72. El-Sakka AI, Hassoba HM. Age related testosterone depletion in patients with erectile dysfunction. *J Urol* 2006 Dec;176(6 Pt 1):2589-93.
73. Low W-Y, Khoo E-M, Tan H-M, et al. Depression, hormonal status and erectile dysfunction in the aging male: results from a community study in Malaysia. *J Mens Health Gend* 2006;3(3):263-70.
74. Guay A, Jacobson J. The relationship between testosterone levels, the metabolic syndrome (by two criteria), and insulin resistance in a population of men with organic erectile dysfunction. *J Sex Med* 2007 Jul;4(4 Pt 1):1046-55.
75. Zohdy W, Kamal EE, Ibrahim Y. Androgen deficiency and abnormal penile duplex

- parameters in obese men with erectile dysfunction. *J Sex Med* 2007 May;4(3):797-808.
76. Rhoden EL, Teloken C, Sogari PR, et al. The relationship of serum testosterone to erectile function in normal aging men. *J Urol* 2002 Apr;167(4):1745-8.
 77. Aversa A, Isidori AM, Spera G, et al. Androgens improve cavernous vasodilation and response to sildenafil in patients with erectile dysfunction. *Clin Endocrinol (Oxf)* 2003 May;58(5):632-8.
 78. Palmer JS, Kaplan WE, Firlit CF. Erectile dysfunction in patients with spina bifida is a treatable condition. *J Urol* 2000 Sep;164(3 Pt 2):958-61.
 79. Seidman SN, Roose SP, Menza MA, et al. Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. *Am J Psychiatry* 2001 Oct;158(10):1623-30.
 80. Kongkanand A, Ratana-Olarn K, Ruangdilokrat S, et al. The efficacy and safety of oral sildenafil in Thai men with erectile dysfunction: a randomized, double-blind, placebo controlled, flexible-dose study. *J Med Assoc Thai* 2003 Mar;86(3):195-205.
 81. Stuckey BG, Jadzinsky MN, Murphy LJ, et al. Sildenafil citrate for treatment of erectile dysfunction in men with type 1 diabetes: results of a randomized controlled trial. *Diabetes Care* 2003 Feb;26(2):279-84.
 82. Choi HK, Ahn TY, Kim JJ, et al. A double-blind, randomised- placebo, controlled, parallel group, multicentre, flexible-dose escalation study to assess the efficacy and safety of sildenafil administered as required to male outpatients with erectile dysfunction in Korea. *Int J Impot Res* 2003 Apr;15(2):80-6.
 83. Levinson IP, Khalaf IM, Shaer KZ, et al. Efficacy and safety of sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men in Egypt and South Africa. *Int J Impot Res* 2003 Apr;15(Suppl 1):25-9.
 84. DeBusk RF, Pepine CJ, Glasser DB, et al. Efficacy and safety of sildenafil citrate in men with erectile dysfunction and stable coronary artery disease. *Am J Cardiol* 2004 Jan 15;93(2):147-53.
 85. Boolell M, Gepi-Attee S, Gingell JC, et al. Sildenafil, a novel effective oral therapy for male erectile dysfunction. *Br J Urol* 1996 Aug;78(2):257-61.
 86. Goldstein I, Lue TF, Padma-Nathan H, et al. Oral sildenafil in the treatment of erectile dysfunction. Sildenafil Study Group. *N Engl J Med* 1998 May 14;338(20):1397-404.
 87. Tan HM, Moh CL, Mendoza JB, et al. Asian sildenafil efficacy and safety study (ASSESS-1): a double-blind, placebo-controlled, flexible-dose study of oral sildenafil in Malaysian, Singaporean, and Filipino men with erectile dysfunction. The Assess-1 Study Group. *Urology* 2000 Oct 1;56(4):635-40.
 88. Meuleman E, Cuzin B, Opsomer RJ, et al. A dose-escalation study to assess the efficacy and safety of sildenafil citrate in men with erectile dysfunction. *BJU Int* 2001 Jan;87(1):75-81.
 89. Eardley I, Morgan R, Dinsmore W, et al. Efficacy and safety of sildenafil citrate in the treatment of men with mild to moderate erectile dysfunction. *Br J Psychiatry* 2001 Apr;178(Apr.):325-30.
 90. Young JM, Bennett C, Gilhooly P, et al. Efficacy and safety of sildenafil citrate (Viagra) in black and Hispanic American men. *Urology* 2002 Sep;60(2 Suppl 2):39-48.
 91. Nurnberg HG, Hensley PL, Gelenberg AJ, et al. Treatment of antidepressant-associated sexual dysfunction with sildenafil: a randomized controlled trial. *JAMA* 2003 Jan 1;289(1):56-64.
 92. Incrocci L, Hop WC, Slob AK. Efficacy of sildenafil in an open-label study as a continuation of a double-blind study in the treatment of erectile dysfunction after radiotherapy for prostate cancer. *Urology* 2003 Jul;62(1):116-20.
 93. Price DE, Gingell JC, Gepi-Attee S, et al. Sildenafil: study of a novel oral treatment for erectile dysfunction in diabetic men. *Diabet Med* 1998 Oct;15(10):821-5.
 94. Rendell MS, Rajfer J, Wicker PA, et al. Sildenafil for treatment of erectile dysfunction in men with diabetes: a randomized controlled trial. Sildenafil Diabetes Study Group. *JAMA* 1999 Feb 3;281(5):421-6.
 95. Christiansen E, Guirguis WR, Cox D, et al. Long-term efficacy and safety of oral Viagra (sildenafil citrate) in men with erectile dysfunction and the effect of randomised

- treatment withdrawal. *Int J Impot Res* 2000 Jun;12(3):177-82.
96. Olsson AM, Speakman MJ, Dinsmore WW, et al. Sildenafil citrate (Viagra) is effective and well tolerated for treating erectile dysfunction of psychogenic or mixed aetiology. *Int J Clin Pract* 2000 Nov;54(9):561-6.
 97. Chen KK, Hsieh JT, Huang ST, et al. ASSESS-3: a randomised, double-blind, flexible-dose clinical trial of the efficacy and safety of oral sildenafil in the treatment of men with erectile dysfunction in Taiwan. *Int J Impot Res* 2001 Aug;13(4):221-9.
 98. Boulton AJ, Selam JL, Sweeney M, et al. Sildenafil citrate for the treatment of erectile dysfunction in men with Type II diabetes mellitus. *Diabetologia* 2001 Oct;44(10):1296-301.
 99. Hussain IF, Brady CM, Swinn MJ, et al. Treatment of erectile dysfunction with sildenafil citrate (Viagra) in parkinsonism due to Parkinson's disease or multiple system atrophy with observations on orthostatic hypotension. *J Neurol Neurosurg Psychiatry* 2001 Sep;71(3):371-4.
 100. Lewis R, Bennett CJ, Borkon WD, et al. Patient and partner satisfaction with Viagra (sildenafil citrate) treatment as determined by the Erectile Dysfunction Inventory of Treatment Satisfaction Questionnaire. *Urology* 2001 May;57(5):960-5.
 101. Safarinejad MR. Oral sildenafil in the treatment of erectile dysfunction in diabetic men: a randomized double-blind and placebo-controlled study. *J Diabetes Complications* 2004 Jul;18(4):205-10.
 102. Webster LJ, Michelakis ED, Davis T, et al. Use of sildenafil for safe improvement of erectile function and quality of life in men with New York Heart Association classes II and III congestive heart failure: a prospective, placebo-controlled, double-blind crossover trial. *Arch Intern Med* 2004 Mar 8;164(5):514-20.
 103. Eardley I, Mirone V, Montorsi F, et al. An open-label, multicentre, randomized, crossover study comparing sildenafil citrate and tadalafil for treating erectile dysfunction in men naive to phosphodiesterase 5 inhibitor therapy. *BJU Int* 2005 Dec;96(9):1323-32.
 104. Cavallini G, Modenini F, Vitali G, et al. Acetyl-L-carnitine plus propionyl-L-carnitine improve efficacy of sildenafil in treatment of erectile dysfunction after bilateral nerve-sparing radical retropubic prostatectomy. *Urology* 2005 Nov;66(5):1080-5.
 105. Diamond LE, Earle DC, Garcia WD, et al. Co-administration of low doses of intranasal PT-141, a melanocortin receptor agonist, and sildenafil to men with erectile dysfunction results in an enhanced erectile response. *Urology* 2005 Apr;65(4):755-9.
 106. Melnik T, Abdo CH. Psychogenic erectile dysfunction: comparative study of three therapeutic approaches. *J Sex Med* 2005 May;31(3):243-55.
 107. Fowler CJ, Miller JR, Sharief MK, et al. A double blind, randomised study of sildenafil citrate for erectile dysfunction in men with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2005 May;76(5):700-5.
 108. Mahon A, Sidhu PS, Muir G, et al. The efficacy of sildenafil for the treatment of erectile dysfunction in male peritoneal dialysis patients. *Am J Kidney Dis* 2005 Feb;45(2):381-7.
 109. Katz SD, Parker JD, Glasser DB, et al. Efficacy and safety of sildenafil citrate in men with erectile dysfunction and chronic heart failure. *Am J Cardiol* 2005 Jan 1;95(1):36-42.
 110. Abdel-Naser MB, Imam A, Wollina U. Sildenafil citrate significantly improves nocturnal penile erections in sildenafil non-responding patients with psychogenic erectile dysfunction. *Int J Impot Res* 2004 Dec;16(6):552-6.
 111. Deveci S, Peskircioglu L, Aygun C, et al. Sublingual sildenafil in the treatment of erectile dysfunction: faster onset of action with less dose. *Int J Urol* 2004 Nov;11(11):989-92.
 112. Gentile V, Vicini P, Prigiotti G, et al. Preliminary observations on the use of propionyl-L-carnitine in combination with sildenafil in patients with erectile dysfunction and diabetes. *Curr Med Res Opin* 2004 Sep;20(9):1377-84.
 113. Rosen RC, Seidman SN, Menza MA, et al. Quality of life, mood, and sexual function: a path analytic model of treatment effects in men with erectile dysfunction and depressive symptoms. *Int J Impot Res* 2004 Aug;16(4):334-40.
 114. Perimenis P, Markou S, Gyftopoulos K, et al. Efficacy of apomorphine and sildenafil in men with nonarteriogenic erectile dysfunction. *A*

- comparative crossover study. *Andrologia* 2004 Jun;36(3):106-10.
115. Tignol J, Furlan PM, Gomez-Beneyto M, et al. Efficacy of sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men in remission from depression. *Int Clin Psychopharmacol* 2004 Jul;19(4):191-9.
 116. Perimenis P, Karkoulias K, Markou S, et al. Erectile dysfunction in men with obstructive sleep apnea syndrome: a randomized study of the efficacy of sildenafil and continuous positive airway pressure. *Int J Impot Res* 2004 Jun;16(3):256-60.
 117. Eardley I, Wright P, MacDonagh R, et al. An open-label, randomized, flexible-dose, crossover study to assess the comparative efficacy and safety of sildenafil citrate and apomorphine hydrochloride in men with erectile dysfunction. *BJU Int* 2004 Jun;93(9):1271-5.
 118. von Keitz A, Rajfer J, Segal S, et al. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil. *Eur Urol* 2004;45(4):499-507.
 119. Mancini M, Raina R, Agarwal A, et al. Sildenafil citrate vs intracavernous alprostadil for patients with arteriogenic erectile dysfunction: a randomised placebo controlled study. *Int J Impot Res* 2004 Feb;16(1):8-12.
 120. Perimenis P, Gyftopoulos K, Giannitsas K, et al. A comparative, crossover study of the efficacy and safety of sildenafil and apomorphine in men with evidence of arteriogenic erectile dysfunction. *Int J Impot Res* 2004 Feb;16(1):2-7.
 121. Govier F, Potempa AJ, Kaufman J, et al. A multicenter, randomized, double-blind, crossover study of patient preference for tadalafil 20 mg or sildenafil citrate 50 mg during initiation of treatment for erectile dysfunction. *Eur Urol* 2003 Nov;25(11):2709-23.
 122. Padma-Nathan H, Stecher VJ, Sweeney M, et al. Minimal time to successful intercourse after sildenafil citrate: results of a randomized, double-blind, placebo-controlled trial. *Urology* 2003 Sep;62(3):400-3.
 123. Seibel I, Poli de Figueiredo CE, Teloken C, et al. Efficacy of oral sildenafil in hemodialysis patients with erectile dysfunction. *J Am Soc Nephrol* 2002 Nov;13(11):2770-5.
 124. Ugarte F, Hurtado-Coll A. Comparison of the efficacy and safety of sildenafil citrate (Viagra) and oral phentolamine for the treatment of erectile dysfunction. *Int J Impot Res* 2002 Aug;14(Suppl 2):48-53.
 125. Gomez F, Davila H, Costa A, et al. Efficacy and safety of oral sildenafil citrate (Viagra) in the treatment of male erectile dysfunction in Colombia, Ecuador, and Venezuela: a double-blind, multicenter, placebo-controlled study. *Int J Impot Res* 2002 Aug;14(Suppl 2):42-7.
 126. Becher E, Tejada NA, Gomez R, et al. Sildenafil citrate (Viagra) in the treatment of men with erectile dysfunction in southern Latin America: a double-blind, randomized, placebo-controlled, parallel-group, multicenter, flexible-dose escalation study. *Int J Impot Res* 2002 Aug;14(Suppl 2):33-41.
 127. Glina S, Bertero E, Claro J, et al. Efficacy and safety of flexible-dose oral sildenafil citrate (Viagra) in the treatment of erectile dysfunction in Brazilian and Mexican men. *Int J Impot Res* 2002 Aug;14(Suppl 2):27-32.
 128. Lindsey I, George B, Kettlewell M, et al. Randomized, double-blind, placebo-controlled trial of sildenafil (Viagra) for erectile dysfunction after rectal excision for cancer and inflammatory bowel disease. *Dis Colon Rectum* 2002 Jun;45(6):727-32.
 129. Lim PH, Ng FC, Cheng CW, et al. Clinical safety profile of sildenafil in Singaporean men with erectile dysfunction: pre-marketing experience (ASSESS-I evaluation). *J Int Med Res* 2002 Mar;30(2):137-43.
 130. Eardley I, Ellis P, Boolell M, et al. Onset and duration of action of sildenafil for the treatment of erectile dysfunction. *Br J Clin Pharmacol* 2002;53(Suppl 1):61-5.
 131. Incrocci L, Koper PC, Hop WC, et al. Sildenafil citrate (Viagra) and erectile dysfunction following external beam radiotherapy for prostate cancer: a randomized, double-blind, placebo-controlled, cross-over study. *Int J Radiat Oncol Biol Phys* 2001 Dec 1;51(5):1190-5.
 132. Choppin A, Blue DR, Hegde SS, et al. Evaluation of oral ro70-0004/003, an alpha1A-adrenoceptor antagonist, in the treatment of male erectile dysfunction. *Int J Impot Res* 2001 Jun;13(3):157-61.

133. Olsson AM, Persson CA, Swedish Sildenafil Investigators Group. Efficacy and safety of sildenafil citrate for the treatment of erectile dysfunction in men with cardiovascular disease. *Int J Clin Pract* 2001 Apr;55(3):171-6.
134. Montorsi F, Maga T, Strambi LF, et al. Sildenafil taken at bedtime significantly increases nocturnal erections: results of a placebo-controlled study. *Urology* 2000 Dec 20;56(6):906-11.
135. Cappelleri JC, Siegel RL, Osterloh IH, et al. Relationship between patient self-assessment of erectile function and the erectile function domain of the international index of erectile function. *Urology* 2000 Sep 1;56(3):477-81.
136. Palmer JS, Kaplan WE, Firlit CF. Erectile dysfunction in spina bifida is treatable. *Lancet* 1999 Jul 10;354(9173):125-6.
137. Montorsi F, McDermott TE, Morgan R, et al. Efficacy and safety of fixed-dose oral sildenafil in the treatment of erectile dysfunction of various etiologies. *Urology* 1999 May;53(5):1011-8.
138. Dinsmore WW, Hodges M, Hargreaves C, et al. Sildenafil citrate (Viagra) in erectile dysfunction: near normalization in men with broad-spectrum erectile dysfunction compared with age-matched healthy control subjects.[erratum appears in *Urology* 1999 May;53(5):1072]. *Urology* 1999 Apr;53(4):800-5.
139. Eardley I, Brooks J, Yates PK, et al. Sildenafil citrate (VIAGRA): an oral treatment for erectile function with activity for up to four hours' duration. *Int J Clin Pract* 1999 Jun;102(Suppl Jun.):102-4.
140. Hartmann U, Meuleman EJ, Cuzin B, et al. Sildenafil citrate (VIAGRA): analysis of preferred doses in a European, six-month, double-blind, placebo-controlled, flexible dose-escalation study in patients with erectile dysfunction. Multicentre Study Group. *Int J Clin Pract* 1999 Jun;102(Suppl Jun.):102-9.
141. Young J. Sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: a 12-week, flexible-dose study to assess efficacy and safety. *Int J Clin Pract* 1999 Jun;102(Suppl Jun.):6-7.
142. Padma-Nathan H, Steers WD, Wicker PA. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction: a double-blind, placebo-controlled study of 329 patients. Sildenafil Study Group. *Int J Clin Pract* 1998 Sep;52(6):375-9.
143. Albuquerque DC, Miziara LJ, Saraiva JFK, et al. Efficacy, safety and tolerability of sildenafil in Brazilian hypertensive patients on multiple antihypertensive drugs. *Int Braz J Urol* 2005;31(4):342-55.
144. Yonessi M, Saeedi M. A double-blind placebo-controlled evaluation of the effect of topical sildenafil on erectile dysfunction. *J App Res* 2005;5(2):289-94.
145. Shamloul R, Ghanem H, Fahmy I, et al. Testosterone therapy can enhance erectile function response to sildenafil in patients with PADAM: A pilot study. *J Sex Med* 2005;2(4):559-64.
146. Gingell C, Sultana SR, Wulff MB, et al. Duration of action of sildenafil citrate in men with erectile dysfunction. *J Sex Med* 2004;1(2):179-84.
147. Pickering TG, Shepherd AMM, Puddey I, et al. Sildenafil citrate for erectile dysfunction in men receiving multiple antihypertensive agents: A randomized controlled trial. *Am J Hypertens* 2004;17(12):1135-42.
148. Pavone C, Curto F, Anello G, et al. Prospective, randomized, crossover comparison of sublingual apomorphine (3 mg) with oral sildenafil (50 mg) for male erectile dysfunction. *J Urol* 2004;172(6 Pt 1):2347-9.
149. Bawa AS, Sharma DR, Singh R, et al. Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo-controlled, crossover study. *Indian J Pharmacol* 2004;36(5):317
150. Dünzendorfer U, Behm A, Dünzendorfer E, et al. Drug combinations in the therapy of low response to phosphodiesterase 5 inhibitors in patients with erectile dysfunction. *In Vivo* 2002;16(5):345-8.
151. Glina S, Bertero E, Claro J, et al. Efficacy and safety of sildenafil citrate for the treatment of erectile dysfunction in Latin America. *Braz J Urol* 2001;27(2):148-54.
152. Barry MJ. Sildenafil improved sexual function in erectile dysfunction. *Int J Impot Res* 1998;3(6):184

153. Shabsigh R. Efficacy of sildenafil citrate (VIAGRA) is not affected by aetiology of erectile dysfunction. *Int J Clin Pract* 1999 Jan;102(Jun.):19-20.
154. Padma-Nathan H. Oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: assessment of erections hard enough for sexual intercourse. *Int J Clin Pract* 1999 Jan;102(Jun.):13-5.
155. Perimenis P, Karkoulias K, Konstantinopoulos A, et al. Sildenafil versus continuous positive airway pressure for erectile dysfunction in men with obstructive sleep apnea: a comparative study of their efficacy and safety and the patient's satisfaction with treatment. *Asian J Androl* 2007 Mar;9(2):259-64.
156. Heiman JR, Talley DR, Bailen JL, et al. Sexual function and satisfaction in heterosexual couples when men are administered sildenafil citrate (Viagra) for erectile dysfunction: a multicentre, randomised, double-blind, placebo-controlled trial. *BJOG* 2007 Apr;114(4):437-47.
157. Sommer F, Klotz T, Engelmann U. Improved spontaneous erectile function in men with mild-to-moderate arteriogenic erectile dysfunction treated with a nightly dose of sildenafil for one year: a randomized trial. *Asian J Androl* 2007 Jan;9(1):134-41.
158. Bank AJ, Kelly AS, Kaiser DR, et al. The effects of quinapril and atorvastatin on the responsiveness to sildenafil in men with erectile dysfunction. *Vasc Med* 2006 Nov;11(4):251-7.
159. Porst H, Behre HM, Jungwirth A, et al. Comparative trial of treatment satisfaction, efficacy and tolerability of sildenafil versus apomorphine in erectile dysfunction--an open, randomized cross-over study with flexible dosing. *Eur J Med Res* 2007 Feb 26;12(2):61-7.
160. McVary KT, Monnig W, Camps JL, Jr., et al. Sildenafil citrate improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: a randomized, double-blind trial. *J Urol* 2007 Mar;177(3):1071-7.
161. Zinner N. Do food and dose timing affect the efficacy of sildenafil? A randomized placebo-controlled study. *J Sex Med* 2007 Jan;4(1):137-44.
162. Safarinejad MR. Salvage of sildenafil failures with cabergoline: a randomized, double-blind, placebo-controlled study. *Int J Impot Res* 2006 Nov;18(6):550-8.
163. Tolra JR, Campana JM, Ciutat LF, et al. Prospective, randomized, open-label, fixed-dose, crossover study to establish preference of patients with erectile dysfunction after taking the three PDE-5 inhibitors. *J Sex Med* 2006 Sep;3(5):901-9.
164. Orr G, Weiser M, Polliack M, et al. Effectiveness of sildenafil in treating erectile dysfunction in PTSD patients: a double-blind, placebo-controlled crossover study. *J Clin Psychopharmacol* 2006 Aug;26(4):426-30.
165. Sharma RK, Prasad N, Gupta A, et al. Treatment of erectile dysfunction with sildenafil citrate in renal allograft recipients: a randomized, double-blind, placebo-controlled, crossover trial. *Am J Kidney Dis* 2006 Jul;48(1):128-33.
166. Althof SE, O'Leary MP, Cappelleri JC, et al. Sildenafil citrate improves self-esteem, confidence, and relationships in men with erectile dysfunction: Results from an international, multicenter, double-blind, placebo-controlled trial. *J Sex Med* 2006 May;3(3):521-9.
167. Fava M, Nurnberg HG, Seidman SN, et al. Efficacy and safety of sildenafil in men with serotonergic antidepressant-associated erectile dysfunction: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2006 Feb;67(2):240-6.
168. Gopalakrishnan R, Jacob KS, Kuruvilla A, et al. Sildenafil in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover trial. *Am J Psychiatry* 2006 Mar;163(3):494-9.
169. Herrmann HC, Levine LA, Macaluso J, Jr., et al. Can atorvastatin improve the response to sildenafil in men with erectile dysfunction not initially responsive to sildenafil? Hypothesis and pilot trial results. *J Sex Med* 2006 Mar;3(2):303-8.
170. Rochira V, Balestrieri A, Madeo B, et al. Sildenafil improves sleep-related erections in hypogonadal men: evidence from a randomized, placebo-controlled, crossover study of a synergic role for both testosterone and sildenafil on penile erections.[erratum appears in *J Androl*. 2006

- May-Jun;27(3):480]. *J Androl* 2006 Mar;27(2):165-75.
171. O'Leary MP, Althof SE, Cappelleri JC, et al. Self-esteem, confidence and relationship satisfaction of men with erectile dysfunction treated with sildenafil citrate: a multicenter, randomized, parallel group, double-blind, placebo controlled study in the United States. *J Urol* 2006 Mar;175(3 Pt 1):1058-62.
172. Viswaroop B, B A, Gopalakrishnan G. Evaluating erectile dysfunction: oral sildenafil versus intracavernosal injection of papaverine. *Natl Med J India* 2005 Nov;18(6):299-301.
173. Kaplan SA, Gonzalez RR, Te AE. Combination of alfuzosin and sildenafil is superior to monotherapy in treating lower urinary tract symptoms and erectile dysfunction. *Eur Urol* 2007;51(6):1717-23.
174. Salonia A. Sildenafil citrate: A safe and effective treatment for erectile dysfunction after renal transplantation? Commentary. *Nature Clinical Practice Nephrology* 2007;3(2):80-1.
175. Koulikov D, Fridmans A, Chertin B, et al. Is sildenafil citrate associated with an amelioration of the symptomatology of androgen decline in the aging male? *J Urol* 2007 Jun;177(6):2267-71.
176. Gray PB, Singh AB, Woodhouse LJ, et al. Dose-dependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. *J Clin Endocrinol Metab* 2005 Jul;90(7):3838-46.
177. Karkos CD, Wood A, Bruce IA, et al. Erectile dysfunction after open versus angioplasty aortoiliac procedures: a questionnaire survey. *Vascular & Endovascular Surgery* 2004 Mar;38(2):157-65.
178. Giuliano F, Donatucci C, Montorsi F, et al. Vardenafil is effective and well-tolerated for treating erectile dysfunction in a broad population of men, irrespective of age. *BJU Int* 2005 Jan;95(1):110-6.
179. Hatzichristou D, Vardi Y, Papp G, et al. Effect of tadalafil on sexual timing behavior patterns in men with erectile dysfunction: integrated analysis of randomized, placebo controlled trials. *J Urol* 2005 Oct;174(4 Pt 1):1356-9.
180. Mazo E, Gamidov S, Iremashvili V. The effect of vardenafil on endothelial function of brachial and cavernous arteries. *Int J Impot Res* 2006 Sep;18(5):464-9.
181. Goldstein I, Young JM, Fischer J, et al. Vardenafil, a new phosphodiesterase type 5 inhibitor, in the treatment of erectile dysfunction in men with diabetes: a multicenter double-blind placebo-controlled fixed-dose study. *Diabetes Care* 2003 Mar;26(3):777-83.
182. Valiquette L, Young JM, Moncada I, et al. Sustained efficacy and safety of vardenafil for treatment of erectile dysfunction: a randomized, double-blind, placebo-controlled study. *Mayo Clin Proc* 2005 Oct;80(10):1291-7.
183. Nehra A, Grantmyre J, Nadel A, et al. Vardenafil improved patient satisfaction with erectile hardness, orgasmic function and sexual experience in men with erectile dysfunction following nerve sparing radical prostatectomy. *J Urol* 2005 Jun;173(6):2067-71.
184. Carson CC, Hatzichristou DG, Carrier S, et al. Erectile response with vardenafil in sildenafil nonresponders: a multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial.[erratum appears in *BJU Int*. 2005 Aug;96(3):466]. *BJU Int* 2004 Dec;94(9):1301-9.
185. Porst H, Young JM, Schmidt AC, et al. Efficacy and tolerability of vardenafil for treatment of erectile dysfunction in patient subgroups. *Urology* 2003 Sep;62(3):519-23.
186. Fisher WA, Rosen RC, Mollen M, et al. Improving the sexual quality of life of couples affected by erectile dysfunction: A double-blind, randomized, placebo-controlled trial of vardenafil. *J Sex Med* 2005;2(5):699-708.
187. Brock G, Nehra A, Lipshultz LI, et al. Safety and efficacy of vardenafil for the treatment of men with erectile dysfunction after radical retropubic prostatectomy. *J Urol* 2003 Oct;170(4 Pt 1):1278-83.
188. Hatzichristou DG, Aliotta P, Auerbach S, et al. Erectile response to vardenafil in men with a history of nonresponse to sildenafil: A time-from-dosing descriptive analysis. *Eur Urol* 2005;27(9):1452-61.
189. Nagao K, Ishii N, Kamidono S, et al. Safety and efficacy of vardenafil in patients with erectile dysfunction: result of a bridging study in Japan. *Int J Urol* 2004 Jul;11(7):515-24.

190. Stief C, Porst H, Saenz dT, I, et al. Sustained efficacy and tolerability with vardenafil over 2 years of treatment in men with erectile dysfunction. *Int J Clin Pract* 2004 Mar;58(3):230-9.
191. Hatzichristou D, Montorsi F, Buvat J, et al. The efficacy and safety of flexible-dose vardenafil (levitra) in a broad population of European men. *Eur Urol* 2004;45(5):634-41.
192. Hellstrom WJ, Gittelman M, Karlin G, et al. Vardenafil for treatment of men with erectile dysfunction: efficacy and safety in a randomized, double-blind, placebo-controlled trial. *J Androl* 2002 Nov;23(6):763-71.
193. Stark S, Sachse R, Liedl T, et al. Vardenafil increases penile rigidity and tumescence in men with erectile dysfunction after a single oral dose. *Eur Urol* 2001;40(2):181-8.
194. Porst H, Rosen R, Padma-Nathan H, et al. The efficacy and tolerability of vardenafil, a new, oral, selective phosphodiesterase type 5 inhibitor, in patients with erectile dysfunction: the first at-home clinical trial. *Int J Impot Res* 2001 Aug;13(4):192-9.
195. Klotz T, Sachse R, Heidrich A, et al. Vardenafil increases penile rigidity and tumescence in erectile dysfunction patients: a RigiScan and pharmacokinetic study. *World J Urol* 2001 Feb;19(1):32-9.
196. van Ahlen H, Wahle K, Kupper W, et al. Safety and efficacy of vardenafil, a selective phosphodiesterase 5 inhibitor, in patients with erectile dysfunction and arterial hypertension treated with multiple antihypertensives. *J Sex Med* 2005;2(6):856-64.
197. Goldstein I, Fisher WA, Sand M, et al. Women's sexual function improves when partners are administered vardenafil for erectile dysfunction: A prospective, randomized, double-blind, placebo-controlled trial. *J Sex Med* 2005;2(6):819-32.
198. Montorsi F, Padma-Nathan H, Buvat J, et al. Earliest time to onset of action leading to successful intercourse with vardenafil determined in an at-home setting: A randomized, double-blind, placebo-controlled trial. *J Sex Med* 2004;1(2):168-78.
199. Rosen R, Shabsigh R, Berber M, et al. Efficacy and tolerability of vardenafil in men with mild depression and erectile dysfunction: The depression-related improvement with vardenafil for erectile response study. *Am J Psychiatry* 2006;163(1):79-87.
200. Martin-Morales A, Meijide F, Garcia N, et al. Efficacy of vardenafil and influence on self-esteem and self-confidence in patients with severe erectile dysfunction. *J Sex Med* 2007 Mar;4(2):440-7.
201. Edwards D, Hackett G, Collins O, et al. Vardenafil improves sexual function and treatment satisfaction in couples affected by erectile dysfunction (ED): a randomized, double-blind, placebo-controlled trial in PDE5 inhibitor-naive men with ED and their partners. *J Sex Med* 2006 Nov;3(6):1028-36.
202. Valiquette L, Montorsi F, Auerbach S, et al. First-dose success with vardenafil in men with erectile dysfunction and associated comorbidities: RELY-I. *Int J Clin Pract* 2006 Nov;60(11):1378-85.
203. Porst H, Sharlip ID, Hatzichristou D, et al. Extended duration of efficacy of vardenafil when taken 8 hours before intercourse: a randomized, double-blind, placebo-controlled study. *Eur Urol* 2006 Nov;50(5):1086-94.
204. Ziegler D, Merfort F, Van AH, et al. Efficacy and safety of flexible-dose vardenafil in men with type 1 diabetes and erectile dysfunction. *J Sex Med* 2006 Sep;3(5):883-91.
205. Ishii N, Nagao K, Fujikawa K, et al. Vardenafil 20-mg demonstrated superior efficacy to 10-mg in Japanese men with diabetes mellitus suffering from erectile dysfunction. *Int J Urol* 2006 Aug;13(8):1066-72.
206. Demir E, Balal M, Paydas S, et al. Efficacy and safety of vardenafil in renal transplant recipients with erectile dysfunction. *Transplant Proc* 2006 Jun;38(5):1379-81.
207. Hatzichristou DG, Cuzin B, Martin-Morales A, et al. Vardenafil improves satisfaction rates, depressive symptomatology, and self-confidence in a broad population of men with erectile dysfunction. *J Sex Med* 2005;2(1):109-16.
208. Hellstrom WJ, Gittelman M, Karlin G, et al. Sustained efficacy and tolerability of vardenafil, a highly potent selective phosphodiesterase type 5 inhibitor, in men with erectile dysfunction: results of a randomized, double-blind, 26-week placebo-controlled pivotal trial. *Urology* 2003 Apr;61(4 Suppl 1):8-14.

209. Hellstrom WJ, Elhilali M, Homering M, et al. Vardenafil in patients with erectile dysfunction: achieving treatment optimization. *J Androl* 2005 Sep;26(5):604-9.
210. Donatucci C, Taylor T, Thibonnier M, et al. Verdenafil improves patient satisfaction with erection hardness, orgasmic function and overall sexual experience, while improving quality of life in men with erectile dysfunction. *J Sex Med* 2004;1(2):185-92.
211. Shafik A, Shafik I, El-Sibai O, et al. Overactive corpus cavernosum: a novel cause of erectile dysfunction. *Andrologia* 2004 Dec;36(6):378-83.
212. Dundar SO. Visual loss associated with erectile dysfunction drugs. *Can J Ophthalmol* 2007 Feb;42(1):10-2.
213. Gupta S, Salimpour P, Saenz dT, I, et al. A possible mechanism for alteration of human erectile function by digoxin: inhibition of corpus cavernosum sodium/potassium adenosine triphosphatase activity. *J Urol* 1998 May;159(5):1529-36.
214. Mirone V, Costa P, Damber JE, et al. An evaluation of an alternative dosing regimen with tadalafil, 3 times/week, for men with erectile dysfunction: SURE study in 14 European countries. *Eur Urol* 2005;47(6):846-54.
215. Young JM, Feldman RA, Auerbach SM, et al. Tadalafil improved erectile function at twenty-four and thirty-six hours after dosing in men with erectile dysfunction: US trial. *J Androl* 2005 May;26(3):310-8.
216. McMahon CG, Stuckey BG, Lording DW, et al. A 6-month study of the efficacy and safety of tadalafil in the treatment of erectile dysfunction: a randomised, double-blind, parallel-group, placebo-controlled study in Australian men. *Int J Clin Pract* 2005 Feb;59(2):143-9.
217. Carson C, Shabsigh R, Segal S, et al. Efficacy, safety, and treatment satisfaction of tadalafil versus placebo in patients with erectile dysfunction evaluated at tertiary-care academic centers. *Urology* 2005 Feb;65(2):353-9.
218. Rosano GM, Aversa A, Vitale C, et al. Chronic treatment with tadalafil improves endothelial function in men with increased cardiovascular risk. *Eur Urol* 2005;47(2):214-20.
219. De Rose AF, Gallo F, Carmignani G. Evaluation of sexual activity in patients treated with tadalafil: a randomized prospective placebo-controlled trial. *Int J Impot Res* 2005 Jan;17(1):76-9.
220. Eardley I, Gentile V, Austoni E, et al. Efficacy and safety of tadalafil in a Western European population of men with erectile dysfunction. *BJU Int* 2004 Oct;94(6):871-7.
221. Staab A, Tillmann C, Forgue ST, et al. Population dose-response model for tadalafil in the treatment of male erectile dysfunction. *Pharm Res* 2004 Aug;21(8):1463-70.
222. Montorsi F, Nathan HP, McCullough A, et al. Tadalafil in the treatment of erectile dysfunction following bilateral nerve sparing radical retropubic prostatectomy: a randomized, double-blind, placebo controlled trial.[erratum appears in *J Urol*. 2005 Feb;173(2):664]. *J Urol* 2004 Sep;172(3):1036-41.
223. Skoumal R, Chen J, Kula K, et al. Efficacy and treatment satisfaction with on-demand tadalafil (Cialis) in men with erectile dysfunction. *Eur Urol* 2004;46(3):362-9.
224. Seftel AD, Wilson SK, Knapp PM, et al. The efficacy and safety of tadalafil in United States and Puerto Rican men with erectile dysfunction.[erratum appears in *J Urol*. 2005 Feb;173(2):664]. *J Urol* 2004 Aug;172(2):652-7.
225. Porst H, Padma-Nathan H, Giuliano F, et al. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: a randomized controlled trial. *Urology* 2003;62(1):121-5.
226. Saenz dT, I, Anglin G, Knight JR, et al. Effects of tadalafil on erectile dysfunction in men with diabetes. *Diabetes Care* 2002 Dec;25(12):2159-64.
227. Carrier S, Brock GB, Pommerville PJ, et al. Efficacy and safety of oral tadalafil in the treatment of men in Canada with erectile dysfunction: A randomized, double-blind, parallel, placebo-controlled clinical trial. *J Sex Med* 2005;2(5):685-98.
228. McMahon C, Kloner RA, Hutter Jr AM, et al. Comparison of efficacy, safety, and tolerability of on-demand tadalafil and daily dosed tadalafil for the treatment of erectile dysfunction. *J Sex Med* 2005;2(3):415-27.
229. Chen KK, Jiann B-P, Lin JSN, et al. Efficacy and safety of on-demand oral tadalafil in the

- treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study. *J Sex Med* 2004;1(2):201-8.
230. Rosen RC, Padma-Nathan H, Shabsigh R, et al. Determining the earliest time within 30 minutes to erectogenic effect after tadalafil 10 and 20 mg: A multicenter, randomized, double-blind, placebo-controlled, at-home study. *J Sex Med* 2004;1(2):193-200.
 231. Yassin AA, Saad F, Diede HE. Testosterone and erectile function in hypogonadal men unresponsive to tadalafil: results from an open-label uncontrolled study. *Andrologia* 2006 Apr;38(2):61-8.
 232. Aversa A, Greco E, Bruzziches R, et al. Relationship between chronic tadalafil administration and improvement of endothelial function in men with erectile dysfunction: a pilot study. *Int J Impot Res* 2007 Mar;19(2):200-7.
 233. McVary KT, Roehrborn CG, Kaminetsky JC, et al. Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Urol* 2007 Apr;177(4):1401-7.
 234. Saylan M, Khalaf I, Kadioglu A, et al. Efficacy of tadalafil in Egyptian and Turkish men with erectile dysfunction. *Int J Clin Pract* 2006 Jul;60(7):812-9.
 235. Rajfer J, Aliotta PJ, Steidle CP, et al. Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double-blind, placebo-controlled study in the US. *Int J Impot Res* 2007 Jan;19(1):95-103.
 236. Yip WC, Chiang HS, Mendoza JB, et al. Efficacy and safety of on demand tadalafil in the treatment of East and Southeast Asian men with erectile dysfunction: a randomized double-blind, parallel, placebo-controlled clinical study. *Asian J Androl* 2006 Nov;8(6):685-92.
 237. Guo YL, Zhu JC, Pan TM, et al. Efficacy and safety of on-demand tadalafil for the treatment of erectile dysfunction in South-East Asian men. *Int J Urol* 2006 Jun;13(6):721-7.
 238. Nagao K, Kimoto Y, Marumo K, et al. Efficacy and safety of tadalafil 5, 10, and 20 mg in Japanese men with erectile dysfunction: results of a multicenter, randomized, double-blind, placebo-controlled study. *Urology* 2006 Oct;68(4):845-51.
 239. Incrocci L, Slagter C, Slob AK, et al. A randomized, double-blind, placebo-controlled, cross-over study to assess the efficacy of tadalafil (Cialis) in the treatment of erectile dysfunction following three-dimensional conformal external-beam radiotherapy for prostatic carcinoma. *Int J Radiat Oncol Biol Phys* 2006 Oct 1;66(2):439-44.
 240. Choi H-K, Kim JJ, Kim S-C, et al. A randomised, double-blind, parallel, placebo-controlled study of the efficacy and safety of Tadalafil administered on-demand to men with erectile dysfunction in Korea. *Taehan Pinyogikwa Hakhoe Chapchi* 2006;47(8):852-8.
 241. Dean J, Hackett GI, Gentile V, et al. Psychosocial outcomes and drug attributes affecting treatment choice in men receiving sildenafil citrate and tadalafil for the treatment of erectile dysfunction: results of a multicenter, randomized, open-label, crossover study. *J Sex Med* 2006 Jul;3(4):650-61.
 242. McMahon CG, Carson CC, Fischer CJ, et al. Tolerance to the therapeutic effect of tadalafil does not occur during 6 months of treatment: A randomized, double-blind, placebo-controlled study in men with erectile dysfunction. *J Sex Med* 2006 May;3(3):504-11.
 243. Carson CC. Efficacy and safety of tadalafil in men with severe erectile dysfunction in tertiary care academic centers. *Curr Urol Rep* 2005 Nov;6(6):437-8.
 244. Moncada I, Damber J-E, Mirone V, et al. Sexual intercourse attempt patterns with two dosing regimens of tadalafil in men with erectile dysfunction: Results from the SURE study in 14 European countries. *J Sex Med* 2005;2(5):668-74.
 245. Costa P, Buvat J, Holmes S, et al. Predictors of tadalafil efficacy in men with erectile dysfunction: the SURE study comparing two dosing regimens. *J Sex Med* 2006 Nov;3(6):1050-8.
 246. Wespes E, Moncada I, Schmitt H, et al. The influence of age on treatment outcomes in men with erectile dysfunction treated with two regimens of tadalafil: results of the SURE study. *BJU Int* 2007 Jan;99(1):121-6.
 247. Buvat J, Van AH, Schmitt H, et al. Efficacy and safety of two dosing regimens of tadalafil and patterns of sexual activity in men with diabetes mellitus and erectile dysfunction: Scheduled use versus on-demand regimen evaluation (SURE)

- study in 14 European countries. *J Sex Med* 2006 May;3(3):512-20.
248. von Keitz A, Stroberg P, Bukofzer S, et al. A European multicentre study to evaluate the tolerability of apomorphine sublingual administered in a forced dose-escalation regimen in patients with erectile dysfunction. *BJU Int* 2002 Mar;89(4):409-15.
 249. Gontero P, D'Antonio R, Pretti G, et al. Clinical efficacy of Apomorphine SL in erectile dysfunction of diabetic men. *Int J Impot Res* 2005 Jan;17(1):80-5.
 250. Hagemann JH, Berding G, Bergh S, et al. Effects of visual sexual stimuli and apomorphine SL on cerebral activity in men with erectile dysfunction. *Eur Urol* 2003 Apr;43(4):412-20.
 251. Lammers PI, Rubio-Aurioles E, Castell R, et al. Combination therapy for erectile dysfunction: a randomized, double blind, unblinded active-controlled, cross-over study of the pharmacodynamics and safety of combined oral formulations of apomorphine hydrochloride, phentolamine mesylate and papaverine hydrochloride in men with moderate to severe erectile dysfunction. *Int J Impot Res* 2002;14(1):54-9.
 252. Dula E, Bukofzer S, Perdok R, et al. Double-blind, crossover comparison of 3 mg apomorphine SL with placebo and with 4 mg apomorphine SL in male erectile dysfunction. *Eur Urol* 2001;39(5):558-3.
 253. Dula E, Keating W, Siami PF, et al. Efficacy and safety of fixed-dose and dose-optimization regimens of sublingual apomorphine versus placebo in men with erectile dysfunction. The Apomorphine Study Group. *Urology* 2000 Jul;56(1):130-5.
 254. rruda-Olson AM, Pellikka PA. Appropriate use of exercise testing prior to administration of drugs for treatment of erectile dysfunction. [Review] [47 refs]. *Herz* 2003 Jun;28(4):291-7.
 255. Seyam R, Mohamed K, Akhras AA, et al. A prospective randomized study to optimize the dosage of trimix ingredients and compare its efficacy and safety with prostaglandin E1. *Int J Impot Res* 2005 Jul;17(4):346-53.
 256. Gontero P, Fontana F, Bagnasacco A, et al. Is there an optimal time for intracavernous prostaglandin E1 rehabilitation following nonnerve sparing radical prostatectomy? Results from a hemodynamic prospective study. *J Urol* 2003 Jun;169(6):2166-9.
 257. Van der WF, Dohle GR, Van Der TJ, et al. Intracavernosal injection therapy with and without sexological counselling in men with erectile dysfunction. *BJU Int* 2002 Jun;89(9):901-4.
 258. Fu Q, Yao DH, Jiang YQ. A clinical comparative study on effects of intracavernous injection of sodium nitroprusside and papaverine/phentolamine in erectile dysfunction patients. *Asian J Androl* 2000 Dec;2(4):301-3.
 259. Baum N, Randrup E, Junot D, et al. Prostaglandin E1 versus sex therapy in the management of psychogenic erectile dysfunction. *Int J Impot Res* 2000 Jun;12(3):191-4.
 260. Sandhu D, Curless E, Dean J, et al. A double blind, placebo controlled study of intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector for the treatment of non-psychogenic erectile dysfunction. *Int J Impot Res* 1999 Apr;11(2):91-7.
 261. Dinsmore WW, Gingell C, Hackett G, et al. Treating men with predominantly nonpsychogenic erectile dysfunction with intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector system: a multicentre double-blind placebo-controlled study. *BJU Int* 1999 Feb;83(3):274-9.
 262. Buvat J, Costa P, Morlier D, et al. Double-blind multicenter study comparing alprostadil alpha-cyclodextrin with moxislyte chlorhydrate in patients with chronic erectile dysfunction. *J Urol* 1998 Jan;159(1):116-9.
 263. Montorsi F, Guazzoni G, Barbieri L, et al. Genital plus audiovisual sexual stimulation following intracavernous vasoactive injection versus re-dosing for erectile dysfunction--results of a prospective study. *J Urol* 1998 Jan;159(1):113-5.
 264. Sogari PR, Teloken C, Souto CA. Atropine role in the pharmacological erection test: study of 228 patients. *J Urol* 1997 Nov;158(5):1760-3.
 265. Montorsi F, Guazzoni G, Strambi LF, et al. Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: results of a prospective,

- randomized trial. *J Urol* 1997 Oct;158(4):1408-10.
266. Bechara A, Casabe A, Cheliz G, et al. Comparative study of papaverine plus phentolamine versus prostaglandin E1 in erectile dysfunction. *J Urol* 1997 Jun;157(6):2132-4.
267. Aversa A, Rocchietti-March M, Caprio M, et al. Anxiety-induced failure in erectile response to intracorporeal prostaglandin-E1 in non-organic male impotence: a new diagnostic approach. *Int J Androl* 1996 Oct;19(5):307-13.
268. Colli E, Calabro A, Gentile V, et al. Alprostadil sterile powder formulation for intracavernous treatment of erectile dysfunction. *Eur Urol* 1996;29(1):59-62.
269. Godschalk M, Gheorghiu D, Katz PG, et al. Alkalinization does not alleviate penile pain induced by intracavernous injection of prostaglandin E1. *J Urol* 1996 Sep;156(3):999-1000.
270. Gheorghiu D, Godschalk M, Gheorghiu S, et al. Slow injection of prostaglandin E1 decreases associated penile pain. *Urology* 1996 Jun;47(6):903-4.
271. Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. *N Engl J Med* 1996 Apr 4;334(14):873-7.
272. Bechara A, Casabe A, Cheliz G, et al. Prostaglandin E1 versus mixture of prostaglandin E1, papaverine and phentolamine in nonresponders to high papaverine plus phentolamine doses. *J Urol* 1996 Mar;155(3):913-4.
273. Wegner HE, Knispel HH, Klan R, et al. Efficacy of linsidomine chlorhydrate, a direct nitric oxide donor, in the treatment of human erectile dysfunction: results of a double-blind cross over trial. *Int J Impot Res* 1995 Dec;7(4):233-7.
274. Vanderschueren D, Heyrman RM, Keogh EJ, et al. A study in patients with erectile dysfunction comparing different formulations of prostaglandin E1. Alprostadil Study Group. *J Urol* 1995 Nov;154(5):1744-7.
275. el-Saleh JC, Keogh EJ, Chew KK, et al. Does compression of the base of the penis improve the efficacy of intracavernosal injection of prostaglandin E1 for impotence? A randomized controlled study. *Int J Impot Res* 1995 Mar;7(1):23-31.
276. Ogrinc FG, Linet OI. Evaluation of real-time RigiScan monitoring in pharmacological erection. *J Urol* 1995 Oct;154(4):1356-9.
277. Kattan S. Double-blind randomized crossover study comparing intracorporeal prostaglandin E1 with combination of prostaglandin E1 and lidocaine in the treatment of organic impotence. *Urology* 1995 Jun;45(6):1032-6.
278. Martinez-Pineiro L, Lopez-Tello J,onso Dorrego JM, et al. Preliminary results of a comparative study with intracavernous sodium nitroprusside and prostaglandin E1 in patients with erectile dysfunction. *J Urol* 1995 May;153(5):1487-90.
279. Wegner HE, Knispel HH, Klan R, et al. Prostaglandin E1 versus linsidomine chlorhydrate in erectile dysfunction. *Urol Int* 1994;53(4):214-6.
280. Schramek P, Plas EG, Hubner WA, et al. Intracavernous injection of prostaglandin E1 plus procaine in the treatment of erectile dysfunction. *J Urol* 1994 Oct;152(4):1108-10.
281. Godschalk MF, Chen J, Katz PG, et al. Treatment of erectile failure with prostaglandin E1: a double-blind, placebo-controlled, dose-response study. *J Urol* 1994 Jun;151(6):1530-2.
282. von Heyden B, Donatucci CF, Marshall GA, et al. A prostaglandin E1 dose-response study in man. *J Urol* 1993 Dec;150(6):1825-8.
283. Moriel EZ, Rajfer J. Sodium bicarbonate alleviates penile pain induced by intracavernous injections for erectile dysfunction. *J Urol* 1993 May;149(5 Pt 2):1299-300.
284. Porst H. Prostaglandin E1 and the nitric oxide donor linsidomine for erectile failure: a diagnostic comparative study of 40 patients. *J Urol* 1993 May;149(5 Pt 2):1280-3.
285. Costa P, Sarrazin B, Bressolle F, et al. Efficiency and side effects of intracavernous injections of moxisylyte in impotent patients: a dose-finding study versus placebo. *J Urol* 1993 Feb;149(2):301-5.
286. Allen RP, Engel RM, Smolev JK, et al. Objective double-blind evaluation of erectile function with intracorporeal papaverine in combination with phentolamine and/or

- prostaglandin E1. *J Urol* 1992 Oct;148(4):1181-3.
287. Mahmoud KZ, el Dakhli MR, Fahmi IM, et al. Comparative value of prostaglandin E1 and papaverine in treatment of erectile failure: double-blind crossover study among Egyptian patients. *J Urol* 1992 Mar;147(3):623-6.
 288. Kattan S, Collins JP, Mohr D. Double-blind, cross-over study comparing prostaglandin E1 and papaverine in patients with vasculogenic impotence. *Urology* 1991 Jun;37(6):516-8.
 289. Floth A, Schramek P. Intracavernous injection of prostaglandin E1 in combination with papaverine: enhanced effectiveness in comparison with papaverine plus phentolamine and prostaglandin E1 alone. *J Urol* 1991 Jan;145(1):56-9.
 290. Roy JB, Petrone RL, Said SI. A clinical trial of intracavernous vasoactive intestinal peptide to induce penile erection. *J Urol* 1990 Feb;143(2):302-4.
 291. Earle CM, Keogh EJ, Wisniewski ZS, et al. Prostaglandin E1 therapy for impotence, comparison with papaverine. *J Urol* 1990 Jan;143(1):57-9.
 292. Garceau RJ, Zhang IX, Jen L. Dose-response studies of intracavernous injection therapy with alprostadil in Asian and Australian men with erectile dysfunction. *Curr Ther Res Clin Exp* 1996;57(1):50-61.
 293. Kunelius P, Lukkarinen O. Intracavernous injection test in the evaluation of patients with erectile dysfunction: a blind, cross-over placebo-controlled study between three different vasoactive agents in 30 impotent inpatients. *Sexual Dysfunct* 1998;1(1):35-8.
 294. Titta M, Tavolini IM, Moro FD, et al. Sexual counseling improved erectile rehabilitation after non-nerve-sparing radical retropubic prostatectomy or cystectomy--results of a randomized prospective study. *J Sex Med* 2006 Mar;3(2):267-73.
 295. Wessells H, Levine N, Hadley ME, et al. Melanocortin receptor agonists, penile erection, and sexual motivation: human studies with Melanotan II. *Int J Impot Res* 2000 Oct;12(Suppl 4):74-9.
 296. Wessells H, Gralnek D, Dorr R, et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000 Oct 1;56(4):641-6.
 297. Segraves RT, Bari M, Segraves K, et al. Effect of apomorphine on penile tumescence in men with psychogenic impotence. *J Urol* 1991 Jun;145(6):1174-5.
 298. Rosen RC, Diamond LE, Earle DC, et al. Evaluation of the safety, pharmacokinetics and pharmacodynamic effects of subcutaneously administered PT-141, a melanocortin receptor agonist, in healthy male subjects and in patients with an inadequate response to Viagra. *Int J Impot Res* 2004 Apr;16(2):135-42.
 299. Ekman P, Sjogren L, Englund G, et al. Optimizing the therapeutic approach of transurethral alprostadil. *BJU Int* 2000 Jul;86(1):68-74.
 300. Shabsigh R, Padma-Nathan H, Gittleman M, et al. Intracavernous alprostadil alfadex is more efficacious, better tolerated, and preferred over intraurethral alprostadil plus optional actis: a comparative, randomized, crossover, multicenter study. *Urology* 2000 Jan;55(1):109-13.
 301. Shokeir AA, Alserafi MA, Mutabagani H. Intracavernosal versus intraurethral alprostadil: a prospective randomized study. *BJU Int* 1999 May;83(7):812-5.
 302. Williams G, Abbou CC, Amar ET, et al. Efficacy and safety of transurethral alprostadil therapy in men with erectile dysfunction. MUSE Study Group. *Br J Urol* 1998 Jun;81(6):889-94.
 303. Peterson CA, Bennett AH, Hellstrom WJ, et al. Erectile response to transurethral alprostadil, prazosin and alprostadil-prazosin combinations. *J Urol* 1998;159(5):1523-7.
 304. Padma-Nathan H, Hellstrom WJ, Kaiser FE, et al. Treatment of men with erectile dysfunction with transurethral alprostadil. Medicated Urethral System for Erection (MUSE) Study Group. *N Engl J Med* 1997 Jan 2;336(1):1-7.
 305. Lazzeri M, Barbanti G, Beneforti P, et al. Intraurethraly infused capsaicin induces penile erection in humans. *Scand J Urol Nephrol* 1994 Dec;28(4):409-12.
 306. Padma-Nathan H, Steidle C, Salem S, et al. The efficacy and safety of a topical alprostadil cream, Alprox-TD, for the treatment of erectile dysfunction: two phase 2 studies in mild-to-

- moderate and severe ED. *Int J Impot Res* 2003 Feb;15(1):10-7.
307. Cavallini G. Minoxidil versus nitroglycerin: a prospective double-blind controlled trial in transcutaneous erection facilitation for organic impotence. *J Urol* 1991 Jul;146(1):50-3.
308. Claes H, Smet G, Baert L. The influence of transcutaneous nitroglycerine on nocturnal erections. *J Drug Dev* 1992;4(4):229-33.
309. Diamond LE, Earle DC, Rosen RC, et al. Double-blind, placebo-controlled evaluation of the safety, pharmacokinetic properties and pharmacodynamic effects of intranasal PT-141, a melanocortin receptor agonist, in healthy males and patients with mild-to-moderate erectile dysfunction. *Int J Impot Res* 2004 Feb;16(1):51-9.
310. Foldvari M, Oguejiofor C, Afridi S, et al. Liposome encapsulated prostaglandin E1 in erectile dysfunction: correlation between in vitro delivery through foreskin and efficacy in patients. *Urology* 1998 Nov;52(5):838-43.
311. Goldstein I, Payton TR, Schechter PJ. A double-blind, placebo-controlled, efficacy and safety study of topical gel formulation of 1% alprostadil (Topiglan) for the in-office treatment of erectile dysfunction. *Urology* 2001 Feb;57(2):301-5.
312. Le Roux PJ, Naude JH. Topical vasoactive cream in the treatment of erectile failure: a prospective, randomized placebo-controlled trial. *BJU Int* 1999 May;83(7):810-1.
313. Cavallini G. Minoxidil versus nitroglycerine: a prospective, double-blind, controlled trial in transcutaneous therapy for organic impotence. *Int J Impot Res* 1994 Dec;6(4):205-12.
314. Gomaa A, Shalaby M, Osman M, et al. Topical treatment of erectile dysfunction: randomised double blind placebo controlled trial of cream containing aminophylline, isosorbide dinitrate, and co-dergocrine mesylate. *BMJ* 1996 Jun 15;312(7045):1512-5.
315. Gramkow J, Lendorf A, Zhu J, et al. Transcutaneous nitroglycerine in the treatment of erectile dysfunction: a placebo controlled clinical trial. *Int J Impot Res* 1999 Feb;11(1):35-9.
316. Haren M, Chapman I, Coates P, et al. Effect of 12 month oral testosterone on testosterone deficiency symptoms in symptomatic elderly males with low-normal gonadal status. *Ageing* 2005 Mar;34(2):125-30.
317. Seftel AD, Mack RJ, Secrest AR, et al. Restorative increases in serum testosterone levels are significantly correlated to improvements in sexual functioning. *J Androl* 2004 Nov;25(6):963-72.
318. Steidle C, Schwartz S, Jacoby K, et al. AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function. *J Clin Endocrinol Metab* 2003 Jun;88(6):2673-81.
319. Cavallini G, Caracciolo S, Vitali G, et al. Carnitine versus androgen administration in the treatment of sexual dysfunction, depressed mood, and fatigue associated with male aging. *Urology* 2004 Apr;63(4):641-6.
320. McNicholas TA, Dean JD, Mulder H, et al. A novel testosterone gel formulation normalizes androgen levels in hypogonadal men, with improvements in body composition and sexual function. *BJU Int* 2003 Jan;91(1):69-74.
321. Kunelius P, Lukkarinen O, Hannuksela ML, et al. The effects of transdermal dihydrotestosterone in the aging male: a prospective, randomized, double blind study. *J Clin Endocrinol Metab* 2002 Apr;87(4):1467-72.
322. Gomaa A, Eissa M, El-Gebaley A. The effect of topically applied vasoactive agents and testosterone versus testosterone in the treatment of erectile dysfunction in aged men with low sexual interest. *Int J Impot Res* 2001 Apr;13(2):93-9.
323. Clopper RR, Voorhess ML, MacGillivray MH, et al. Psychosexual behavior in hypopituitary men: A controlled comparison of gonadotropin and testosterone replacement. *Psychoneuroendocrinology* 1993;18(2):149-61.
324. Boyanov MA, Boneva Z, Christov VG. Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency. *Ageing Male* 2003 Mar;6(1):1-7.
325. Rabkin JG, Wagner GJ, Rabkin R. A double-blind, placebo-controlled trial of testosterone therapy for HIV-positive men with hypogonadal symptoms. *Arch Gen Psychiatry* 2000;57(2):141-7.
326. Schiavi RC, White D, Mandeli J, et al. Effect of testosterone administration on sexual behavior

- and mood in men with erectile dysfunction. *Arch Sex Behav* 1997 Jun;26(3):231-41.
327. Wang C, Swerdloff RS, Iranmanesh A, et al. Transdermal testosterone gel improves sexual function, mood, muscle strength, and body composition parameters in hypogonadal men. *J Clin Endocrinol Metab* 2000 Aug;85(8):2839-53.
 328. Seidman SN, Roose SP. The sexual effects of testosterone replacement in depressed men: randomized, placebo-controlled clinical trial. *J Sex Marital Ther* 2006 May;32(3):267-73.
 329. Gomaa AA, Hamed HA. Improvement of sexual function in partial testosterone-deficient ageing men treated with cream containing testosterone and vasoactive agents. *J Mens Health Gend* 2006;3(1):47-55.
 330. Merza Z, Blumsohn A, Mah PM, et al. Double-blind placebo-controlled study of testosterone patch therapy on bone turnover in men with borderline hypogonadism. *Int J Androl* 2006 Jun;29(3):381-91.
 331. Padma-Nathan H, Yeager JL. An integrated analysis of alprostadil topical cream for the treatment of erectile dysfunction in 1732 patients. *Urology* 2006 Aug;68(2):386-91.
 332. Knoll LD, Abrams JH. Nocturnal electrobioimpedance volumetric assessment of patients with erectile dysfunction. *Urology* 1999 Jun;53(6):1200-4.
 333. Hatzichristou DG, Apostolidis A, Tzortzis V, et al. Effects of oral phentolamine, taken before sleep, on nocturnal erectile activity: a double-blind, placebo-controlled, crossover study. *Int J Impot Res* 2001 Oct;13(5):303-8.
 334. Mann K, Pankok J, Leissner J, et al. Effects of moclobemide on sexual performance and nocturnal erections in psychogenic erectile dysfunction. *Psychopharmacology* 2001 Jun;156(1):86-91.
 335. Safarinejad MR. Therapeutic effects of high-dose isoxsuprine in the management of mixed-type impotence. *Urology* 2001 Jul;58(1):95-7.
 336. Enzlin P, Vanderschueren D, Bonte L, et al. Trazodone: a double-blind, placebo-controlled, randomized study of its effects in patients with erectile dysfunction without major organic findings. *Int J Impot Res* 2000 Aug;12(4):223-8.
 337. Costabile RA, Spevak M. Oral trazodone is not effective therapy for erectile dysfunction: a double-blind, placebo controlled trial. *J Urol* 1999 Jun;161(6):1819-22.
 338. Becker AJ, Stief CG, Machtens S, et al. Oral phentolamine as treatment for erectile dysfunction. *J Urol* 1998 Apr;159(4):1214-6.
 339. Meinhardt W, Schmitz PI, Kropman RF, et al. Trazodone, a double blind trial for treatment of erectile dysfunction. *Int J Impot Res* 1997 Sep;9(3):163-5.
 340. Peskircioglu L, Karabulut A, Deniz E, et al. The role of pentoxifylline in the treatment of erectile dysfunction due to borderline arterial insufficiency. *Br J Urol* 1996 Apr;77(4):563-5.
 341. Aydin S, Odabas O, Ercan M, et al. Efficacy of testosterone, trazodone and hypnotic suggestion in the treatment of non-organic male sexual dysfunction. *Br J Urol* 1996 Feb;77(2):256-60.
 342. van Ahlen H, Piechota HJ, Kias HJ, et al. Opiate antagonists in erectile dysfunction: a possible new treatment option? Results of a pilot study with naltrexone. *Eur Urol* 1995;28(3):246-50.
 343. Georgitis WJ, Merenich JA. Trial of pentoxifylline for diabetic impotence. *Diabetes Care* 1995 Mar;18(3):345-52.
 344. Kurt U, Ozkardes H, Altug U, et al. The efficacy of anti-serotonergic agents in the treatment of erectile dysfunction. *J Urol* 1994 Aug;152(2 Pt 1):t-9
 345. Korenman SG, Viosca SP. Treatment of vasculogenic sexual dysfunction with pentoxifylline. *J Am Geriatr Soc* 1993 Apr;41(4):363-6.
 346. Speel TGW, Kiemeny LA, Thien T, et al. Long-term effect of inhibition of the angiotensin-converting enzyme (ACE) on cavernosal perfusion in men with atherosclerotic erectile dysfunction: A pilot study. *J Sex Med* 2005;2(2):207-12.
 347. Piha J, Kaaja R. Effects of moxonidine and metoprolol in penile circulation in hypertensive men with erectile dysfunction: Results of a pilot study. *Int J Impot Res* 2003;15(4):287-9.
 348. Reiter WJ, Pycha A, Schatzl G, et al. Dehydroepiandrosterone in the treatment of erectile dysfunction: a prospective, double-blind,

- randomized, placebo-controlled study. *Urology* 1999 Mar;53(3):590-4.
349. Korenman SG, Viosca SP. Treatment of vasculogenic sexual dysfunction with pentoxifylline. *J Age Rel Dis* 1994;6(3):24-8.
 350. Nickel M, Moleda D, Loew T, et al. Cabergoline treatment in men with psychogenic erectile dysfunction: a randomized, double-blind, placebo-controlled study. *Int J Impot Res* 2007 Jan;19(1):104-7.
 351. Agostini R, Rossi F, Pajalich R. Myoinositol/folic acid combination for the treatment of erectile dysfunction in type 2 diabetes men: a double-blind, randomized, placebo-controlled study. *Eur Rev Med Pharmacol Sci* 2006 Sep;10(5):247-50.
 352. El-Shafey H, Atteya A, el-Maghd SA, et al. Tianeptine can be effective in men with depression and erectile dysfunction. *J Sex Med* 2006 Sep;3(5):910-7.
 353. Sommer F, Klotz T, Steinritz D, et al. Evaluation of tetrahydrobiopterin (BH4) as a potential therapeutic agent to treat erectile dysfunction. *Asian J Androl* 2006 Mar;8(2):159-67.
 354. Akash R, Hrishikesh D, Amith P, et al. Case report: association of combined nonarteritic anterior ischemic optic neuropathy (NAION) and obstruction of cilioretinal artery with overdose of Viagra. *J Ocul Pharmacol Ther* 2005 Aug;21(4):315-7.
 355. Cunningham AV, Smith KH. Anterior ischemic optic neuropathy associated with viagra. *J Neuroophthalmol* 2001 Mar;21(1):22-5.
 356. Dheer S, Rekhi GS, Merlyn S. Sildenafil associated anterior ischaemic optic neuropathy. *J Assoc Physicians India* 2002 Feb;50:265
 357. Egan R, Pomeranz H. Sildenafil (Viagra) associated anterior ischemic optic neuropathy. *Arch Ophthalmol* 2000 Feb;118(2):291-2.
 358. Gedik S, Yilmaz G, Akova YA. Sildenafil-associated consecutive nonarteritic anterior ischaemic optic neuropathy, cilioretinal artery occlusion, and central retinal vein occlusion in a haemodialysis patient [27]. *Eye* 2007;21(1):129-30.
 359. Gruhn N, Fledelius HC. Unilateral optic neuropathy associated with sildenafil intake. *Acta Ophthalmol Scand* 2005 Feb;83(1):131-2.
 360. Margo CE, French DD. Ischemic optic neuropathy in male veterans prescribed phosphodiesterase-5 inhibitors. *Am J Ophthalmol* 2007 Mar;143(3):538-9.
 361. Pomeranz HD, Smith KH, Hart WM, Jr., et al. Sildenafil-associated nonarteritic anterior ischemic optic neuropathy.[see comment]. *Ophthalmology* 2002 Mar;109(3):584-7.
 362. Pomeranz HD, Bhavsar AR. Nonarteritic ischemic optic neuropathy developing soon after use of sildenafil (viagra): a report of seven new cases.[see comment]. *J Neuroophthalmol* 2005 Mar;25(1):9-13.
 363. Sinha S, Pathak-Ray V, Ahluwalia H, et al. Viagra or what? *Eye* 2004 Apr;18(4):446-8.
 364. Porst H, Buvat J, Meuleman E, et al. Intracavernous Alprostadil Alfadex--an effective and well tolerated treatment for erectile dysfunction. Results of a long-term European study. *Int J Impot Res* 1998 Dec;10(4):225-31.
 365. Canale D, Giorgi PM, Lencioni R, et al. Long-term intracavernous self-injection with prostaglandin E1 for the treatment of erectile dysfunction. *Int J Androl* 1996;19(1):28-32.
 366. Perimenis P, Konstantinopoulos A, Perimeni PP, et al. Long-term treatment with intracavernosal injections in diabetic men with erectile dysfunction. *Asian J Androl* 2006 Mar;8(2):219-24.
 367. Claro JA, de Aboim JE, Maringolo M, et al. Intracavernous injection in the treatment of erectile dysfunction after radical prostatectomy: an observational study. *Sao Paulo Med J* 2001 Jul 5;119(4):135-7.
 368. Lepore G, Nosari I. Efficacy of oral sildenafil in the treatment of erectile dysfunction in diabetic men with positive response to intracavernosal injection of alprostadil. *Diabetes Care* 2001 Feb;24(2):409-11.
 369. Perimenis P, Gyftopoulos K, Athanasopoulos A, et al. Diabetic impotence treated by intracavernosal injections: high treatment compliance and increasing dosage of vaso-active drugs. *Eur Urol* 2001 Oct;40(4):398-402.
 370. Wespes E, Sattar AA, Noel JC, et al. Does prostaglandin E1 therapy modify the intracavernous musculature? *J Urol* 2000 Feb;163(2):464-6.

371. Shmueli J, Israilov S, Segenreich E, et al. Progressive treatment of erectile dysfunction with intracorporeal injections of different combinations of vasoactive agents. *Int J Impot Res* 1999 Feb;11(1):15-9.
372. Chew K-K, Stuckey BGA, Earle CM, et al. Penile fibrosis in intracavernosal prostaglandin E1 injection therapy for erectile dysfunction. *Int J Impot Res* 1997;9(4):225-30.
373. Sundaram CP, Thomas W, Pryor LE, et al. Long-term follow-up of patients receiving injection therapy for erectile dysfunction. *Urology* 1997 Jun;49(6):932-5.
374. Gupta R, Kirschen J, Barrow RC, et al. Predictors of success and risk factors for attrition in the use of intracavernous injection. *J Urol* 1997 May;157(5):1681-6.
375. Chen RN, Lakin MM, Montague DK, et al. Penile scarring with intracavernous injection therapy using prostaglandin E1: a risk factor analysis. *J Urol* 1996 Jan;155(1):138-40.
376. Hattat H, Ozkara H, Akkus E, et al. Our experience with pharmacological erection treatment of erectile dysfunction. *J Androl* 1994 Nov;15(Suppl):47S-9S.
377. Chiang H-S, Wen T-C, Wu C-C, et al. Intracavernous self-injection therapy for the treatment of erectile dysfunction. *J Formos Med Assoc* 1992;91(9):898-901.
378. Schramek P, Dorninger R, Waldhauser M, et al. Prostaglandin E1 in erectile dysfunction. Efficiency and incidence of priapism. *Br J Urol* 1990 Jan;65(1):68-71.
379. Flynn RJ, Williams G. Long-term follow-up of patients with erectile dysfunction commenced on self injection with intracavernosal papaverine with or without phentolamine. *Br J Urol* 1996 Oct;78(4):628-31.
380. Bolayir K, Goksin N. Intracavernous self-injection of papaverine and verapamil: a clinical experience. *Acta Chir Hung* 1994;34(3-4):253-6.
381. Betts CD, Jones SJ, Fowler CG, et al. Erectile dysfunction in multiple sclerosis. Associated neurological and neurophysiological deficits, and treatment of the condition. *Brain* 1994 Dec;117(Pt 6):1303-10.
382. Kerfoot WW, Carson CC. Pharmacologically induced erections among geriatric men. *J Urol* 1991 Oct;146(4):1022-4.
383. Althof SE, Turner LA, Levine SB, et al. Sexual, psychological, and marital impact of self-injection of papaverine and phentolamine: A long-term prospective study. *J Sex Marital Ther* 1991;17(2):101-12.
384. Fink HA, Mac DR, Rutks IR, et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002 Jun 24;162(12):1349-60.
385. Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *J Sex Med* 2005;2(5):658-67.
386. Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
387. Montague DK, Jarow J, Broderick GA, et al. AUA guideline on the pharmacologic management of premature ejaculation. *J Urol* 2004 Jul;172(1):290-4.
388. Wespes E, Amar E, Hatzichristou D, et al. Guidelines on erectile dysfunction. *Eur Urol* 2002;41(1):1-5.
389. Heaton JPW, Morales A. Hormonal evaluation and treatment in male sexual function: A guide to clinical management. In: Mulcahy J, editors. 2nd New Jersey: Humana; 2008. p. 123-33.
390. Porst H. IC351 (tadalafil, Cialis): update on clinical experience. *Int J Impot Res* 2002 Feb;14 Suppl 1:S57-S64
391. Anonymous. [Sildenafil Citrate (Viagra) - package insert]. 2002; U.S.A.: New York: Pfizer, Inc.
392. Bella AJ, Brock GB. Intracavernous pharmacotherapy for erectile dysfunction. *Endocrine* 2004;23(2-3):149-55.
393. El-Sakka AI. Intracavernosal prostaglandin E1 self vs office injection therapy in patients with erectile dysfunction. *Int J Impot Res* 2006 Mar;18(2):180-5.
394. Melman A, Serels S, Morales, et al. Priapism. *Int J Impot Res* 2000;12(SUPPL. 4):S133-S139

395. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *Ann Intern Med* 2001 Apr 17;134(8):657-62.

396. Swerdloff RS, Wang C. Androgens and the ageing male. *Best Practice & Research Clinical Endocrinology & Metabolism* 2004;18(3):349-62.

List of Acronyms/Abbreviations

CLINICAL

3DCRT	three-dimensional conformal external-beam radiotherapy
AMI	acute myocardial infarction
BMI	body mass index
BPH	benign prostatic hyperplasia
CAD	coronary artery disease
CHF	congestive heart failure
cGMP	cyclic guanosine monophosphate
CI	confidence interval
CRP	C-reactive protein
CT	computer tomography
CVD	cardiovascular disease
DBP	diastolic blood pressure
DM	diabetes mellitus
ECG	electrocardiogram
ED	erectile dysfunction
EDV	end-diastolic velocity
EID	endothelium-independent dilatation
FMD	flow mediated dilation
FSH	follicle-stimulating hormone (pituitary gland)
GnRH	gonadotropin-releasing hormone
HbA1C	hemoglobin,
HDL-c	high-density lipoprotein cholesterol
IC/I	intracavernosal/ injection
IIEF	International Index of Erectile Function
IM/I	intramuscular/ injection
IU	Intraurethral
LDL-c	low-density lipoprotein cholesterol
LH	luteinizing hormone (pituitary gland)
LUTS	lower urinary tract symptoms
MI	myocardial infarction
MuSE	Multiple Streaming Engine (intraurethral pellets of PGE1)
MRI	magnetic resonance imaging
NAION	nonarteritic ischemic optic neuropathy
NO	nitric oxide
nNOS	neuronal nitric oxide synthase
PADAM	partial androgen deficiency of the aging male
PC	prostate cancer
PDE-5/i	phosphodiesterase type 5/ inhibitor
PGE ₁	prostaglandin E ₁
PH	prostatic hyperplasia
PKG	protein kinase G
PRL	prolactin
PSA	prostate-specific antigen

PSV	peak systolic velocity
RCT	randomized controlled trial
RI	resistance index
RIA	Radioimmunoassay
SBP	systolic blood pressure
SC	Subcutaneous
SD	standard deviation
SE	standard error
T	Testosterone
TG	Triglycerides
TRT	testosterone replacement treatment
WMD	weighted mean difference

Specific Scales (subscales)

AMS	Aging Males Symptoms
CES-D	Center for Epidemiologic Studies Depression Scale
EDITS	Erectile Dysfunction Inventory of Treatment Satisfaction
GAQ	global assessment question
GEQ	global efficacy question
HARS	Hamilton Anxiety Rating Scale
HDRS	Hamilton Depression Rating Scale
IcS	intercourse satisfaction
IIEF	International Index of Erectile Function,
- EF	erectile function
- OF	orgasmic function
- OS	overall satisfaction
- SD	sexual desire
IIEF-5	modified 5-item IIEF
RAU	rigidity activity unit
SFP	sexual function profile
SHIM	Sexual Health Inventory for Men
TAU	tumescence activity unit
TICS	Trier Inventory for the Assessment of Chronic Stress

UNITS

µg	Micrograms
µg /L	micrograms per liter
µg /mL	micrograms per milliliter
µg/dL	micrograms per deciliter
µm	micromolar
µmol/L	micromoles per liter
cm	centimeters
cm/s	centimeters/second
Ibs	pounds
IU/L	international units per liter

IU/L	international units per liter
kg	kilograms
kg/m ²	kilograms per meter squared
m	meters
mg	milligrams
mg/d	milligrams per day
mL	milliliter
mmol/L	millimoles per liter
N	sample size
ng/dL	nanogram per deciliter
ng/L	nanogram per liter
ng/mL	nanograms per milliliter
nmol/L	nanomoles per liter
pg/mL	picograms per milliliter
pmol/L	picomoles per liter

STATISTICS

ANCOVA	analysis of covariance
ANOVA	analysis of variance
ARD	absolute risk difference
CCT	controlled clinical trial
CI	confidence interval
CV	coefficient of variation
HR	hazard ratio
IQR	interquartile range
ITT	intention to treat
LOCF	last observation carried forward
LS	Least square
NS	not significant
RCT	randomized controlled trial
S/sign.	significant
SD	standard deviation
SE/SEM	standard error
WMD	weighted mean difference

COMMONLY USED ABBREVIATIONS

#	Number
%	Percent
<	greater than
< or ≤/+	less than or equal to and
>	less than
> or ≥/=	greater than or equal to
▲/↑ or ▼/↓	increased, or decreased,
CG	control group
grp	group/s
ctrls	Controls

d	Day
Deg	Degrees
Dept.	department
F	Female
f/u	followup
FHx	family history
hr	Hour
Hx	History
IG	intervention group
M	Male
max	maximum
min	minimum
mo	Month
NA	not applicable
NIH	National Institute of Health
NR	not reported
prn	<i>pro re nata</i> (as required)
Q	Question
Tx	treatment
versus	Versus
wks	Weeks
y	Year

Appendix A. Search Strategies

Medline strategy: [variations of these strategies exist for a) Embase, b) CENTRAL CINAHL AMED, c) Biological abstracts]

Main Search

OVID MEDLINE Preliminary search

1. Impotence/
2. erectile dysfunction\$.mp.
3. 1 or 2
4. limit 3 to ebm reviews
5. limit 3 to systematic reviews
6. limit 3 to guideline
7. or/4-6

Diagnostic Questions – Ovid MEDLINE

1. Impotence/
2. erecti\$.tw.
3. 1 or 2
4. limit 3 to "diagnosis (sensitivity)"
5. routin\$.ti.
6. 3 and 5
7. or/4,6
8. follicle stimulating hormone/
9. (follicle stimulating hormone or fsh).tw.
10. Luteinizing Hormone/
11. (luteini?ing hormone or lh).tw.
12. Prolactin/
13. prolactin.tw.
14. Testosterone/
15. testosterone.tw.
16. or/8-15
17. 7 and 16
18. limit 17 to (yr="1990 - 2006" and male and english language)
19. limit 18 to (case reports or editorial or letter)
20. 18 not 19
21. Impotence/
22. erecti\$.tw.
23. 21 or 22
24. RANDOMIZED CONTROLLED TRIAL.pt.
25. CONTROLLED CLINICAL TRIAL.pt.
26. RANDOMIZED CONTROLLED TRIALS.sh.
27. RANDOM ALLOCATION.sh.
28. DOUBLE BLIND METHOD.sh.
29. SINGLE-BLIND METHOD.sh.

30. or/24-29
31. (ANIMALS not HUMAN).sh.
32. 30 not 31
33. CLINICAL TRIAL.pt.
34. exp CLINICAL TRIALS/
35. (clin\$ adj25 trial\$).ti,ab.
36. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
37. PLACEBOS.sh.
38. placebo\$.ti,ab.
39. random\$.ti,ab.
40. versus.tw.
41. RESEARCH DESIGN.sh.
42. or/33-41
43. 42 not 31
44. 43 not 32
45. 32 or 44
46. 23 and 45
47. limit 46 to yr="1990 - 2008"
48. limit 47 to female
49. limit 47 to male
50. 47 not (48 not 49)
51. 20 not 50
52. limit 51 to english language

OID EMBASE Diagnostic Questions

1. Erectile Dysfunction/
2. erecti\$.tw.
3. 1 or 2
4. limit 3 to "diagnosis (sensitivity)"
5. routin\$.ti.
6. 3 and 5
7. or/4,6
8. follicle stimulating hormone/
9. (follicle stimulating hormone or fsh).tw.
10. Luteinizing Hormone/
11. (luteini?ing hormone or lh).tw.
12. Prolactin/
13. prolactin.tw.
14. Testosterone/
15. testosterone.tw.
16. or/8-15
17. 7 and 16
18. limit 17 to (yr="1990 - 2008" and male and english language)
19. limit 18 to (editorial or letter)
20. 18 not 19
21. Erectile Dysfunction/

22. erecti\$.tw.
23. 21 or 22
24. CLINICAL TRIAL.pt.
25. exp CLINICAL TRIALS/
26. (clin\$ adj25 trial\$.ti,ab.
27. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
28. PLACEBO.sh.
29. placebo\$.ti,ab.
30. random\$.ti,ab.
31. versus.tw.
32. METHODOLOGY.sh.
33. or/24-32
34. 23 and 33
35. limit 34 to yr="1990 - 2008"
36. limit 35 to female
37. limit 35 to male
38. 35 not (36 not 37)
39. 20 not 38

OID MEDLINE – Intervention questions

1. Impotence/
2. erecti\$.tw.
3. 1 or 2
4. RANDOMIZED CONTROLLED TRIAL.pt.
5. CONTROLLED CLINICAL TRIAL.pt.
6. RANDOMIZED CONTROLLED TRIALS.sh.
7. RANDOM ALLOCATION.sh.
8. DOUBLE BLIND METHOD.sh.
9. SINGLE-BLIND METHOD.sh.
10. or/4-9
11. (ANIMALS not HUMAN).sh.
12. 10 not 11
13. CLINICAL TRIAL.pt.
14. exp CLINICAL TRIALS/
15. (clin\$ adj25 trial\$.ti,ab.
16. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
17. PLACEBOS.sh.
18. placebo\$.ti,ab.
19. random\$.ti,ab.
20. versus.tw.
21. RESEARCH DESIGN.sh.
22. or/13-21
23. 22 not 11
24. 23 not 12
25. 12 or 24
26. 3 and 25

27. limit 26 to yr="1990 - 2008"
28. limit 27 to female
29. limit 27 to male
30. 27 not (28 not 29)
31. limit 30 to english language

OID MEDLINE – Intervention questions, Injectable medications

1. Injections/
2. inject\$.tw.
3. 1 or 2
4. Penis/
5. (peni\$ or intercav\$).tw.
6. or/4-5
7. 3 and 6
8. Papaverine/
9. Phentolamine/
10. Phenoxybenzamine/
11. Alprostadil/
12. Moxisylyte/
13. (papaverine or prostaglandin E1 or PgE1 or phentolamine or phenoxybenzamine or alprostadil or moxisylyte or thymoxamine or Opilon or Icavex or Trimix).tw.
14. or/8-13
15. 3 and 14
16. or/7,15
17. Impotence/
18. erectile dysfunction.tw.
19. or/17-18
20. 16 and 19
21. limit 20 to (yr="1990 - 2008" and male and english language)
22. limit 21 to (case reports or comment or editorial)
23. 21 not 22

OID EMBASE – Intervention questions

1. Erectile Dysfunction/
2. erecti\$.tw.
3. 1 or 2
4. CLINICAL TRIAL.pt.
5. exp CLINICAL TRIALS/
6. (clin\$ adj25 trial\$).ti,ab.
7. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj25 (blind\$ or mask\$)).ti,ab.
8. PLACEBO.sh.
9. placebo\$.ti,ab.
10. random\$.ti,ab.
11. versus.tw.
12. METHODOLOGY.sh.
13. or/4-12

14. 3 and 13
15. limit 14 to yr="1990 - 2008"
16. limit 15 to female
17. limit 15 to male
18. 15 not (16 not 17)
19. limit 18 to english language

OID EMBASE – Intervention questions – Injectable medications

1. Injection/
2. inject\$.tw.
3. 1 or 2
4. Penis/
5. (peni\$ or intercav\$).tw.
6. or/4-5
7. 3 and 6
8. Papaverine/
9. Phentolamine/
10. Phenoxybenzamine/
11. Prostaglandin E1/
12. Moxisylyte/
13. (papaverine or prostaglandin E1 or PgE1 or phentolamine or phenoxybenzamine or alprostadil or moxisylyte or thymoxamine or Opilon or Icavex or Trimix).tw.
14. or/8-13
15. 3 and 14
16. or/7,15
17. Erectile Dysfunction/
18. erectile dysfunction.tw.
19. or/17-18
20. 16 and 19
21. Phenoxybenzamine/ca [Intracavernous Drug Administration]
22. Papaverine/ca
23. Phentolamine/ca
24. Moxisylyte/ca
25. Prostaglandin E1/ca
26. or/21-25
27. 26 and 19
28. or/20,27
29. limit 28 to (yr="1990 - 2008" and male and english language)
30. limit 29 to (editorial or letter or note or short survey)
31. 29 not 30

OID AMED Intervention questions

1. erecti\$.mp.
2. impoten\$.mp.
3. exp sex disorders male/
4. or/1-3

5. exp clinical trials/
6. random\$.mp.
7. or/5-6
8. 4 and 7
9. limit 8 to yr="1990 - 2008"
10. limit 9 to english language

OVID CENTRAL Intervention questions

1. erecti\$.mp.
2. impoten\$.mp.
3. or/1-2
4. limit 2 to yr="1990 - 2008"

OVID PsycINFO Intervention questions

1. erecti\$.mp.
2. impoten\$.mp.
3. impotence/
4. or/1-3
5. exp treatment/
6. random\$.tw.
7. control\$.tw.
8. placebo\$.tw.
9. or/5-8
10. 4 and 9
11. limit 10 to yr="1990 - 2008"
12. limit 11 to female
13. limit 11 to male
14. 11 not (12 not 13)
15. limit 14 to english language

Scopus – Intervention questions

((TITLE-ABS-KEY(placebo) or TITLE-ABS-KEY(clin* W/25 trial*)) OR ((TITLE-ABS-KEY(random*) OR TITLE-ABS-KEY(doubl* w/25 blind*))) OR (TITLE-ABS-KEY(versus))) AND (TITLE-ABS-KEY(erecti*)) AND (LIMIT-TO(PUBYEAR,2006) OR LIMIT-TO(PUBYEAR,1990) OR LIMIT-TO(PUBYEAR,1994) OR LIMIT-TO(PUBYEAR,1998) OR LIMIT-TO(PUBYEAR,1995) OR LIMIT-TO(PUBYEAR,2000) OR LIMIT-TO(PUBYEAR,1992) OR LIMIT-TO(PUBYEAR,2005) OR LIMIT-TO(PUBYEAR,1999) OR LIMIT-TO(PUBYEAR,2001) OR LIMIT-TO(PUBYEAR,1996) OR LIMIT-TO(PUBYEAR,2004) OR LIMIT-TO(PUBYEAR,1991) OR LIMIT-TO(PUBYEAR,1993) OR LIMIT-TO(PUBYEAR,2002) OR LIMIT-TO(PUBYEAR,1997) OR LIMIT-TO(PUBYEAR,2003))

Vision loss or sleep apnea

Ovid MEDLINE

1. exp Sleep Apnea Syndromes/
2. Optic Neuropathy, Ischemic/
3. exp Vision Disorders/
4. or/1-3
5. (139755-83-2 or 224785-90-4).rn.
6. phosphodiesterase type 5 inhib\$.mp.
7. (PDE-5\$ or PDE inhibit\$).mp.
8. (sildenafil or vardenafil or tadalafil).mp.
9. or/5-8
10. 4 and 9

Embase

1. (139755-83-2 or 224785-90-4).rn.
2. phosphodiesterase type 5 inhib\$.mp.
3. (PDE-5\$ or PDE inhibit\$).mp.
4. (sildenafil or vardenafil or tadalafil).mp.
5. or/1-4
6. central sleep apnea syndrome/ or sleep apnea syndrome/
7. ischemic optic neuropathy/ or optic nerve infarction/
8. exp Visual Impairment/
9. or/6-8
10. 5 and 9

Fibrosis secondary to injectable medications

Ovid MEDLINE

1. Injections/
2. inject\$.tw.
3. 1 or 2
4. Penis/
5. (peni\$ or intercav\$).tw.
6. or/4-5
7. 3 and 6
8. Papaverine/
9. Phentolamine/
10. Phenoxybenzamine/
11. Alprostadil/
12. Moxisylyte/
13. (papaverine or prostaglandin E1 or PgE1 or phentolamine or phenoxybenzamine or alprostadil or moxisylyte or thymoxamine or Opilon or Icavex or Trimix).tw.
14. or/8-13
15. 3 and 14
16. or/7,15
17. Penile Induration/
18. Fibrosis/
19. fibro\$.tw.

20. or/17-19
21. 16 and 20
22. limit 21 to (yr="1980 - 2006" and english language)

Embase

1. Injections/
2. inject\$.tw.
3. 1 or 2
4. Penis/
5. (peni\$ or intercav\$).tw.
6. or/4-5
7. 3 and 6
8. Papaverine/
9. Phentolamine/
10. Phenoxybenzamine/
11. Alprostadil/
12. Moxisylyte/
13. (papaverine or prostaglandin E1 or PgE1 or phentolamine or phenoxybenzamine or alprostadil or moxisylyte or thymoxamine or Opilon or Icavex or Trimix).tw.
14. or/8-13
15. 3 and 14
16. or/7,15
17. Fibrosis/
18. Peyronie Disease/
19. fibro\$.tw.
20. or/17-19
21. 16 and 20
22. limit 21 to (yr="1980 - 2006" and english language)

Appendix B. Data Assessment, Data Abstraction and Quality Assessment Forms

Screening Forms

Level 1: Title and Abstract Screening

1. Is this a potentially relevant record addressing 1. the benefits or harms (note: only SRs examining Viagra studies for harms data to be included; all other drugs include original studies for harms) of a pharmaceutical treatment (oral, topical, intraurethral, injectable, or intracavernosal) for male erectile dysfunction? OR 2. the sensitivity or specificity of testosterone/LH/FSH/prolactin in identifying a glandular disorder as a cause of ED OR 3. the prevalence of a hormonal (testosterone/LH/FSH/prolactin) disorder in association with male erectile dysfunction?
 - Yes
 - No
 - Can't tell
2. Please indicate which of the following best describes the current record –
 - Original study
 - Narrative review
 - Systematic review/meta-analysis
 - Guideline
 - Comment/Opinion piece
 - Letter to the editor
 - Can't tell
3. Is this an English Language Record? (this question is optional)
 - Yes
 - No
 - Can't tell

Level 2: Full Text Relevance Screening

1. Which of the following best describes the attached record: (*please check all that apply*)
 - A study examining the measurement of testosterone and/or other androgen hormone, FSH, LH, Prolactin (but not GnRH, Inhibin, Activin, or Follistin) OR the sensitivity or specificity of hormones in ED screening/diagnosing OR prevalence of reversible hormonal disorders in males with erectile dysfunction
 - A study examining an oral medication in the treatment of [efficacy/effectiveness (for all drugs) and/or harm outcomes] in male erectile dysfunction in relevant a population (if yes; please indicate in the text box if this is a viagra monotherapy study)

- A systematic review of harms associated with Viagra
- A study examining an intramuscular injectable medication in the treatment of male erectile dysfunction
- A study of an injectable medication into the penis (intracavernosal) OR intraurethral pellet (alprostadil/MUSE, misoprostol, enprostil, arbabprostil, unoprostone) in the treatment of male erectile dysfunction
- A study examining a topical (patch or cream) or intranasal medication in the treatment of male erectile dysfunction
- None of the above (e.g., not relevant, animal study, etc.)
- Can't tell
- A study that examines any harm(s) (e.g., priapism; penile fibrosis/corporal fibrosis only) for injectable medications in males with ED (Note: treatment and/or f/u must be of ≥ 6 months in duration)
- A study that examines any harm(s) (e.g., priapism; penile fibrosis/corporal fibrosis only) for injectable medications in males with ED - treatment and/or f/u of less than 6 months in duration
- A study with treatment and/or f/u ≥ 6 months in duration that DOES NOT examine harm(s) for injectable medications in males with ED

2. Level of Evidence for this report:

- Systematic Review
- RCT parallel design, RCT cross-over, or RCT factorial design
- Controlled clinical trial (non-RCT)
- Multiple prospective cohort(s)
- Case-control
- Cross-sectional
- Before-and-after
- Single prospective cohort
- Single retrospective cohort
- Case series (non-comparative)
- Case study

- Cross-national ecological analysis
- Other (describe)
- Can't tell
- Not applicable (the study is considered to be not relevant)

3. This study meets relevancy requirements and is considered an included study:
Oral medication – only RCTs (Viagra systematic reviews including harms INCLUDED;
Viagra RCT effectiveness/efficacy included – EXCEPT in spinal cord population)

- Yes
- No
- Can't tell
- Not applicable (the study is deemed not relevant in Q#1)

4. This article should be retrieved to supplement introduction/background information for the report:

- Yes (indicate specific disorder etc.)

5. Additional Notes/Comments

Data Extraction Form

Summary Table- Randomized Controlled Trials

Author, (year)/ Funding source/ QA	Study design characteristics	Participant characteristics	Patient diagnosis details	Intervention	Outcome & measures
Author (year) {REF ID} Funding source:	N screened = N randomized = IG1, n = IG2, n = CG, n = ITT analysis used for primary outcome: Inclusion: Exclusion:	Age, mean (): Race: Co-morbidities, n (%): Previous ED treatment: Smoking status: Body weight: Other:	Concomitant medications, n (%): Duration of ED: Underlying disease, n (%): Psychogenic ED, n (%): Physiologic ED, n (%): Mixed ED, n (%): Other:	IG1: IG2: CG: IG1: Dose: Duration: Frequency: Compliance: IG2: Dose: Duration: Frequency: Compliance: CG: Dose: Duration: Frequency: Compliance: Run In period: Wash out period: Follow up duration:	Primary outcome (erectile function): Other outcomes assessed: Withdrawals/drop-outs/loss to followup, n (%): WDAE, n (%): TAE, n (%): SAE, n (%): Ascertainment of outcomes assessed: Other:

List of abbreviations: RCT=randomized control trial, CC=controlled clinical trials, ED=erectile dysfunction, NA=not applicable, IG=intervention group, CG=comparator/control group, HbA1C= haemoglobin, BMI=body mass index, wk=week(s), mo=month(s), yr=year(s), hr=hour (s), f/u=follow-up, M=male, IIEF= international index of erectile function, GAQ=global assessment question, ECG=electrocardiograms, ▲=increased, ▼=decreased, sign. =significant; vs.=versus, %=percent, max=maximum, kg=kilograms, lbs=pounds, ITT=intent-to-treat (Y = yes, N = no, NR = not reported), AE=adverse event, SAE=serious adverse event, TAE=total adverse event, grp=group, Hx: history, PgE₁: Prostaglandin E₁, IC= intracavernosal injection

Quality Assessment Forms

Randomized Controlled Trials (Jadad Scale)

1. Was the study described as randomized (including the use of words such as randomly, random, and randomization)?
 - Yes = 1
 - No = 0

2. The method used to generate the sequence of randomization was described and it was appropriate (table of random numbers, computer generated, etc)
 - Appropriate
 - Not appropriate

3. Was the study described as double blind?
 - Yes = 1
 - No = 0

4. The method of double blinding was described and was appropriate (identical placebo, active placebo, dummy, etc)?
 - Yes = 1
 - No = 0

5. Was there a description of withdrawals and dropouts, by treatment group?
 - Yes = 1
 - No = 0

Total Jadad Score: (i.e = 0 - 5)

Allocation Concealment:

1 = yes, 0 = no

A: Adequate

- Sequentially numbered, opaque, sealed envelopes (SNOSE)
- Pharmacy controlled
- Numbered or ordered containers
- Central randomization – e.g. by telephone to a trials office or other method which described elements convincing of concealment – e.g. a secure computer assisted method.

I: Inadequate

- Alternation
- Reference to case record numbers or to dates of birth

U: Unclear

- No mention of an allocation concealment approach at all
- An approach that does not fall into either adequate or inadequate allocation concealment

The Quality Assessment of Studies of Diagnostic Accuracy Included in Systematic Reviews (QUADAS)

- Q1: Was the spectrum of patients representative of the patients who will receive the test in practice? Yes/no
- Q2. Were selection criteria clearly described? Yes/no
- Q3. Is the reference standard likely to correctly classify the target condition? Yes/no
- Q4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests? Yes/no
- Q5. Did the whole sample or a random selection of the sample, receive verification using a reference standard? Yes/no
- Q6. Did patients receive the same reference standard regardless of the index test result? Yes/no
- Q7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)? Yes/no
- Q8. Was the execution of the index test described in sufficient detail to permit replication of the test? Yes/no
- Q9. Was the execution of the reference standard described in sufficient detail to permit its replication? Yes/no
- Q10. Were the index test results interpreted without knowledge of the results of the reference standard? Yes/no
- Q11. Were the reference standard results interpreted without knowledge of the results of the index test? Yes/no
- Q12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice? Yes/no
- Q13. Were uninterpretable/ intermediate test results reported? Yes/no
- Q14. Were withdrawals from the study explained? Yes/no

Appendix C. Evidence Tables

C1-Oral Sildenafil

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Abdel-Naser (2004) ¹</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 30</p> <p>IG1, n = 15 IG2, n = 15 CG, n = 12 (normal men)</p> <p>Intention to treat (ITT) analysis: NR</p> <p>Inclusion: men with psychogenic ED (no response to sildenafil citrate of up to 100 mg in more than one occasion within a one mo); also non-sildenafil treated pts with ED served as control</p> <p>Exclusion: penile anatomical defects, active peptic ulcer, bleeding dx, retinitis pigmentosa, major haematological renal or hepatic abnormalities; hx of stroke or recent MI; loss of libido; use of anihypertensives, nitrates, tranquilizers or drugs known to interfere with sildenafil citrate metabolism (e.g. cimetadine & ketoconazol)</p>	<p>Age, mean (sd): 42.5 (6.7) y, range 34-58 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 100% with Sildenafil, 100 mg</p> <p>Smoking status: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 100%</p> <p>Physiologic ED: 0</p> <p>Mixed ED: 0</p>	<p>IG1: sildenafil citrate (night 3) & placebo (nights 1,2 & 4) IG2: sildenafil citrate (night 4) & placebo (nights 1, 2, & 3) CG: placebo (all nights)</p> <p>IG1: Dose: 50 mg Duration: 4 nights Frequency: once, 1 hr before bedtime/ night Compliance (%): NR</p> <p>IG2: Dose: as IG Duration: 4 nights Frequency: as IG Compliance (%): NR</p> <p>CG: Dose: NA Duration: 4 nights Frequency: once/night Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: NPTR for basal condition, mean (sd) placebo nights vs. sildenafil night Number of events IG1 4.7 (1.4) vs. 6.7 (1.6) IG2: 3.8 (1.2) vs. 7 (1.2) Total event duration, hr: IG: 1.4 (0.2) vs. 2.1 (0.4) IG2: 1.3 (0.2) vs. 2.4 (0.2) Tip rigidity IG1: 39.7 (9.5) vs. 47.8 (10.4) IG2: 44.3 (10.3) vs. 57.6 (10.7) Base rigidity: IG1: 45.1 (8.8) vs. 57.3 (10.5) IG2: 49.4 (10.5) vs. 60.8 (11)</p> <p>Other outcomes assessed: base, tip RAU, and TAU (result suggestive of possible performance anxiety effect in this population); no result reported for CG</p> <p>Withdrawals/drop-outs/loss to f/u: NR WDAE: NR TAE, n (%): 3 (10), headache in 2 pts (6.7%), GI upset in 1 (3.3%) SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan nocturnal penile tumescence and rigidity (NPTR); RAU and TAU</p>

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<p>Albuquerque (2005) ²</p> <p>Funding source: Pfizer</p>	<p>N screened = 153 N randomized = 120</p> <p>IG, n = 61 CG, n = 59</p> <p>ITT analysis used for primary outcome: yes (n=120)</p> <p>Inclusion: men 18 y or older, with established ED of at least 6 mo duration, in a stable sexual relationship for 6 mo, and with hypertension that is being treated with at least 2 drugs. (Diuretics, alpha-blocker, beta blockers, ACE inhibitors or calcium blockers); baseline IIEF score of 25 or less</p> <p>Exclusion: Concurrent tx with nitrates, presence of genital deformity or sexual disturbance that precluded sexual intercourse, use of any form of ED tx within 4 wks, alcohol or drug abuse, presence of retinitis pigmentosa, major medical condition or inability to fill out log or comply with study</p>	<p>Age, mean (range): 30-81y</p> <p>Race: Brazilian</p> <p>Co-morbidities: None</p> <p>Previous ED treatment: None</p> <p>Smoking status n (%): 13 (21.3) vs. 15 (25.4)</p> <p>Body weight: NR</p>	<p>Concomitant medications: None</p> <p>Duration of ED, median (range): 2.0 (0.6 – 24) vs. 2.3 (0.6 –30)</p> <p>Underlying disease: hypertension (duration 0.6 -30 y)</p> <p>Psychogenic ED, n (%): 9 (14.8) vs. 7 (11.9)</p> <p>Physiologic ED, n (%): 11 (18) vs. 11 (18.6)</p> <p>Mixed ED, n (%): 41 (67.2) vs. 41 (69.5)</p> <p>Other, n (%): alcohol use 30 (49.2) vs. 30 (50.2)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50mg (adjusted to 25 or 100mg) Duration: 8wks Frequency: 1 hr before sexual intercourse Compliance n (%): 46 (75.4)</p> <p>CG: Dose: NA Duration: 8 wks Frequency: 1 hr before sexual intercourse Compliance n (%): 41 (69.5)</p> <p>Run In period: None Wash out period: 4 wks</p> <p>F/u duration: 2, 4 and 8 wks</p> <p>Other: % pts taking 25 mg: 6.6 vs. 5.1 50 mg: 39.3 vs. 74.6 100 mg: 54.1 vs. 20.3</p>	<p>Primary outcome results: IIFE, mean (sd): (mean baseline/Q=2) Q1: 4.2 (1.3) vs. 2.6 (1.5) Q3: 4 (1.3) vs. 2.6 (1.6) Q4: 4 (1.4) vs. 2.2 (1.6) Q5: 4.2 (1.2) vs. 2.6 (1.5) Q15: 3.6 (1.0) vs. 2.4 (1.1) Q6: 4.2 (1.3) vs. 3.4 (1.4) Q7: 4.2 (1.2) vs. 2.3 (1.4) GEQ, % improved: (87) vs. (37) Successful intercourse attempts wks 2, 4 and 8 (%): 54, 61, 73 vs. 13, 20, 29</p> <p>Other outcomes assessed: EDITS</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 22 (18.3)</p> <p>WDAE: tx interrupted 1 (1.4) vs. 2 (3.4) TAE, n (%): in 2% or more 35 (57.3) vs. 16 (27.1); including facial flushing 8 (13) vs. 2 (3.4); headache 7 (11.4) vs. 2 (3.4); rhinitis 6 (9.8) vs. 1 (1.7); dyspepsia 4 (6.5) vs. 0; dizziness= abdominal pain 2 (3.2) vs. 1 (1.7); paresthesia 1 (1.6) vs. 0; hypertension 1 (1.6) vs. 3 (5.1); chest pain 1 (1.6) vs. 2 (3.4); flue like syndrome= diarrhea 1 (1.6) vs. 2 (3.); AE in 82% vs. 40% of pts</p> <p>SAE: 3 (5) vs. 1 (1.7); CVA, pulmonary edema/heart failure, atrial fibrillation/arrhythmia, and one polytrauma due to MVA leading to death)</p> <p>Ascertainment of outcomes assessed: IIEF, patient logs, EDITIS, GEQ</p>

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<p>Althof (2006)³</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 553 (combined from two studies US, n=253; Brazil, Mexico, Australia and Japan n=300)</p> <p>IG, n = 274 CG, n = 279</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older with documented ED (score of 21 or less on IIEF)</p> <p>Exclusion: BP of 90 mmHg or less or 170/110 mmHg or more; sign cardiac dx; use of nitrates, nitric oxide donors, or ritonavir; more than 6 dosed of sildenafil within 6 mo prior to study entry</p>	<p>Age, mean (sd): 56 (11) vs. 55 (12) y</p> <p>Race: White 55.5%; Black 15%; Asian 5.5%; Other 23.5%</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 86 (16) vs. 85 (16) kg</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED, mean (sd): 4.4 (4.5) vs. 4.3 (4.4) y</p> <p>Underlying disease, n (%): Not specific</p> <p>Psychogenic ED, n (%): 44 (16) vs. 55 (20)</p> <p>Physiologic ED, n (%): 119 (43) vs. 113 (41)</p> <p>Mixed ED, n (%): 116 (41) vs. 106 (39)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: NR Duration: 12 wks Frequency: NR Compliance: NR</p> <p>CG: Dose: NA Duration: NR Frequency: NR Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wks (f/u intervals at 2, 4, 6, 8 wks)</p>	<p>Primary outcome results: IIEF, LS mean change from baseline (SE) EF: 11.0 (0.5) vs. 4.8 (0.5), p<0.001 OF: 2.5 (0.2) vs. .0 (0.2), p<0.001 SD: 1.3 (0.1) vs. 0.6 (0.1), p<0.001 IcS: 5.2 (0.2) vs. 2.9 (0.2), p<0.001 OS: 3.8 (0.2) vs. 1.7 (0.2), p<0.001 Successful sexual attempts, mean change %(sd): 59 (2.6) vs. 39 (42)</p> <p>GEQ, frequency of achieved erections at end of tx: 3.9 (1.5) vs. 2.7 (1.6), p<0.001</p> <p>Other outcomes assessed: SEAR sexual relationship domain (sign more improved in IG)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): 3 (1) vs. 1 (0.4) TAE, n (%): 129 (46) vs. 88 (32); included headache, flushing, dyspepsia, and rhinitis SAE, n (%): 1 (<1) vs. 1 (<1); one case of coronary artery disease in sildenafil grp and one case of urinary tract infection in placebo</p> <p>Ascertainment of outcomes assessed: SEAR; self-esteem, confidence and sexual relationship satisfaction; IIEF, GEQ, self reported event log</p>

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<p>Bank (2006) ⁴</p> <p>Funding source: Pfizer Inc. (educational grant)</p>	<p>N screened = NR N randomized = NR (n=35 completed the trial)</p> <p>IG1, n = 12 IG2, n = 10 CG, n = 13</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 25-75 y, in a stable relationship, and normal libido, IIEF-5 < 21, with current use of sildenafil (evaluated after the 2-4 wks run in period tx with 100 mg sildenafil); with vasculogenic ED</p> <p>Exclusion: use of lipid lowering agents, angiotensin converting enzyme inhibitors, anti-depressants or nitrates; hx of prostate cancer or pelvic/ low back surgery</p>	<p>Age, mean (SEM): 59.2 (1.9) vs. 58.7 (3.3) vs. 63.8 (2.1) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM type II, 2 (5) only in CG</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 3 (9%); one in each grp</p> <p>Body weight: NR</p> <p>Other: BMI, mean (SEM) 27.5 (1.5) vs. 29.7 (2.3) vs. 26.1 (0.9) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): vasculogenic</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p> <p>Other: lipid profiles reported, SBP; CBP; total cholesterol; LDL-c; HDL-c; TG, and CRP</p>	<p>IG1: Sildenafil + Atorvastatin IG2: Sildenafil + quinapril CG: Sildenafil + placebo</p> <p>IG1: Dose: 100 mg sildenafil + 40 mg atorvastatin Duration: 3 mo Frequency: sildenafil as instruction; atorvastatin once/d Compliance: NR</p> <p>IG2: Dose: 100 mg sildenafil + 10 mg quinapril Duration: 3 mo Frequency: as IG1 Compliance: NR</p> <p>CG: Dose: sildenafil as IG Duration: 3 mo Frequency: as IG Compliance: NR</p> <p>Run In period: 2-4 wks on 100 mg sildenafil Wash out period: NA</p> <p>F/u duration: 3 mo</p>	<p>Primary outcome results: Mean (SEM) baseline vs. post tx IIEF-5 IG1: 11.1 (1.5) vs. 16.7 (2.0) IG2: 9.9 (1.1) vs. 18.7 (2.2) CG: 10.2 (1.6) vs. 11.3 (2.1)</p> <p>IIEF-EF domain: IG1: 14.5 (2.2) vs. 20.8 (2.3) IG2: 13.8 (1.3) vs. 23.6 (2.3) CG: 12.8 (2.0) vs. 14.2 (2.5)</p> <p>N of intercourse attempts/3 mo, mean (SEM): IG1, 37.7 (12) vs. IG2, 22.5 (7.7) vs. IG3, 23.8 (13.9)</p> <p>Other outcomes assessed: NS differences between IG1/2 and CG for penile blood flow and vascular function, PSV, EDV, RI, and FMD; no differences for SBP, DBP, HDL-c and CRP, no correlation between IIEF scores and improvement on other measures</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF-5; Penile Doppler studies</p>

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<p>Bawa (2004) ⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 59 crossover design</p> <p>IG/ CG, n = 59</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Indian men with ED for 6 mo or longer</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 32.8 (18-60) y</p> <p>Race: Asian (India)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 23 (6-120) mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 50 mg Duration: 3 wks Frequency: NR Compliance (%): NR</p> <p>CG: Dose: N/A Duration: 3 wks Frequency: NR Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 1 y</p>	<p>Primary outcome (EF): IIEF score, mean (SEM) EF domain Baseline: 18.5 (0.7) post tx: 25.6 (0.7) vs. 22.1 (0.7), P<0.05 Intercourse satisfaction: Baseline 8.2 (0.4) post tx: 11.9 (0.4) vs. 10 (0.4), not sign OF: baseline: 7.3 (0.3) post tx: 8.8 (0.2) vs. 7.9 (0.3), p<0.05 SD: Baseline: 6.9 (0.1) post tx: 7.1 (0.1) vs. 6.9 (0.2), not sign OS: pre tx: 5.8 (0.2) post tx: 7.0 (0.2) vs. 6.4 (0.2), p<0.05 GAQ (% improved): 81.3% vs. 28.8% (P<0.001)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0 TAE: 4 (6.8%) vs. 3.4% including Headache 30.2%; Flushing: 43.5%; Dyspepsia: 18.8%; Dizziness: 7.5% SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; partner questionnaire</p>

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<p>Becher (2002) ⁶</p> <p>Funding source: Pfizer</p>	<p>N screened = 156 N randomized = 143</p> <p>IG, n = 72 CG, n = 71</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men with ED who were in a stable relationship with a female partner of at least 6 mo</p> <p>Exclusion: penile anatomical defects, primary diagnosis of another sexual disorder, SCI, any major psychiatric disorder not well controlled, poorly controlled DM, Hx of alcohol or substance abuse, major haematological, renal or hepatic abnormalities, hypotension or malignant hypertension, recent stroke or myocardial infraction or if they were receiving nitrated.</p>	<p>Age, mean (sd); 57.2 (11.5) vs. 56.7 (10.9) y</p> <p>Race, n (%): White Southern Latin 6 (8.3) vs. 7 (9.8) Hispanic: 66 (91.7) vs. 64 (90.2)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%):Current: 32 (44.4) vs.27 (38.0) Former: 28 (38.9) vs. 26 (36.6)</p> <p>Body weight, mean (sd): 84.2 (11.8) vs. 83.4 (14.2)</p>	<p>Concomitant medications, n (%): Any medication 51 (70.8) vs. 51 (71.8), with no sign difference between grps for use of any medication</p> <p>Duration of ED, mean (range): 3.5 (0.5-22.4) vs. 2.6 (0.5-20.5) y</p> <p>Underlying disease (diagnosis), n (%): Diabetes: 12 (16.6) vs. 13 (18.3) Hypertension: 23 (31.9) vs. 28 (43.6)</p> <p>Psychogenic ED: 44.3%</p> <p>Physiologic ED: 39.3%</p> <p>Mixed ED: 16.4%</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 25-50 and 100mg tablets Duration: 12 wks Frequency: 1h before planned sexual activity, up to once/d Compliance: 90%</p> <p>CG: Dose: NA (14 tablets/bottle as IG) Duration: 12 wks Frequency: as IG Compliance: 89%</p> <p>Run In period: 4 wks Wash out period: None</p> <p>F/u duration: 12 wks (2, 4, 8, and 12 wks)</p>	<p>Primary outcome results:IIEF mean (SE): % Change, Q3: 3.8 (0.17) (66.2) vs. 2.7 (0.18) (15.1) % Change Q4: 3.6 (0.18) (77.6) vs. 2.5 (0.18) (21.2) EF: 20.5 (0.6) vs. 15.9 (0.7) OF: 8.2 (0.35) vs. 7.0 (0.37) S-D: 7.68 (0.18) vs. 7.0 (0.19) GEQ, % with Improved erections: (77.3) vs. (33.8)</p> <p>Other outcomes assessed: all IIEF questions (1-15)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 3 (2) vs. 2 (3)</p> <p>WDAE, n (%): 7 (9.7) vs. 6 (8.5) discontinued treatment TAE, n (%): pts with AE 45 (59.1) vs. 21 (29.6) Flushing: 16 (22.2) vs. 3 (4.2); Headache: 17 (23.6) vs. 6 (8.4); Hypertension: 1 (1) vs. 3 (4); nasal congestion 2 (2.3) vs. 1 (1); tachycardia 3 (4) vs. 0 SAE: 2 (2.8) vs. 1 (1.4) died in due to MI</p> <p>Ascertainment of outcomes assessed: RigiScan test (nocturnal penile tumescence NPT), IIEF (q3 and 4) (investigator), GEAQ, self and partner reported event logs</p>

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<p>Boolell (1996) ⁷</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 12 (phase I: double blind, placebo controlled four way crossover trial; phase II: double blind, randomized placebo controlled two way cross over)</p> <p>IG1-3/CG (both phases), n = 12</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18-70 y, with penile ED of at least 6 mo, with no known organic cause by clinical examination and blood test</p> <p>Exclusion: pts with DM, hypertension or alcohol abuse</p>	<p>Age, range: 36-63 y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): IC papaverine 4 (30), three responders and one non responder</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>Phase I IG: single doese sildenafil + 2 hr visual stimulation 30 min post tx (VS) CG: placebo + VS</p> <p>Phase II IG: sildenafil + VS CG: placebo</p> <p>IG (phase I): Dose: 10, 25 or 50 mg Duration: NR Frequency: once/dose Compliance: 100%</p> <p>IG (phase II): Dose: 25 mg Duration: 7 d Frequency: once/d Compliance: 100%</p> <p>CG: Dose: NA Duration: Phase II= 7 d Frequency: phase phase II= once/d Compliance: 100%</p> <p>Run In period: NR Wash out period: phase I, 3 d between consecutive tx periods; 3 d between phases, phase II, at least 7 d F/u duration: 7 d</p>	<p>Primary outcome results:</p> <p>Phase I Duration of penile rigidity > 80%, mean (approximate values from figure): Base: < 4 vs. 8 vs. <12 vs. <2 min Tip: < 5 vs. <7 vs. < 8 vs. <2 min</p> <p>Phase II Erections of grade 3 or 4, mean: 1.6 vs. 0.5 N of erections phase I + phase II, mean (95% CI): IG vs. CG, p=0.005 6 (3.2-11.4) vs. 1.3 (0.5-2.7)</p> <p>Pts with improved erection, n/N (%): 10/12 (83) vs. 2/12 (16); p = 0.018</p> <p>Other outcomes assessed: frequency of erection and time of dosing; pulse rate, BP, laboratory safety data</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE, n (%): phase I: 2 (16) vs. 2 (16); phase II: 6 (50) vs. 5 (41) with headache, dyspepsia, pelvic musculoskeletal pain SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan (phase I); self diary, grading erection from 1=no erection to 4=max rigidity (phase II)</p>

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<p>Boulton (2001) ⁸</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 219</p> <p>IG, n = 110 CG, n = 109</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 37 or older; with diagnosed ED, and stable type II DM (≥ 2 y; HbA_{1c} <11%); also in stable heterosexual relationship for longer than 6 mo</p> <p>Exclusion: genital anatomical deformity; major psychiatric disorder; hx of alcoholism or substance abuse; ED resulting from SCI; MI, stroke, heart failure or unstable angina within previous 6 mo; hx of hypotension; nitrate tx; type I DM; HbA_{1c} $\geq 11\%$; recurrent hypoglycemic episodes; severe disabling autonomic neuropathy; diabetes secondary to pancreatic damage; Cushing's syndrome; acromegaly</p>	<p>Age, mean (range): 58 (range 38-80) vs. 59 (45-72) y</p> <p>Race (%): White 96; Black 2 vs. 0; Asian 2; other: 1 vs. 2</p> <p>Co-morbidities, %: Hypertension 40 vs. 52; Ischemic heart dx 6 v. 3; hypercholesterolemia 8 vs. 7</p> <p>HbA_{1c}, median, (range): 8.3 (5.1-12.1)</p> <p>Previous ED treatment: NR</p> <p>Smoking status (%): smokers 22 vs. 24</p> <p>Body weight, mean (range): 88 (60-146) kg</p>	<p>Concomitant medications: Insulin 32 vs. 37</p> <p>Duration of ED, mean (range): 4.6 (0.4-21) vs. 3.7 (0.7-11)</p> <p>Underlying disease: DM</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED, %: 100</p> <p>Mixed ED: NR</p> <p>Other: duration of DM, mean (range) = 10 (1-34) y</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG: Dose: 50 mg initially; could adjust to 25 or 100 mg Duration: 12 wk Frequency: NR Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: NR Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IIEF- Q3, mean (SEM): pre: 1.8; post 3.4 (0.2) vs. 1.9 (0.2) IIEF- Q3, mean (SEM): pre: 1.5; post: 3.4 (0.2) vs. 1.8 (0.2) IIEF- EF: pre: 10.4; post: 20.4 (1.2) vs. 11.5 (1.2) Successful intercourse, %: pre 13.8; post 58.8 vs. 14.4 GEQ, %: 65 vs. 11</p> <p>Other outcomes assessed: life satisfaction checklist; partner questionnaire</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE, %: 0 TAE: 65 vs. 11; pts with AE= 38% vs. 6.4%; including headache 18.2 vs. 4; flushing 15 vs. 0; dyspepsia 2 vs. 0.9; abnormal vision 5 vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, GEQ, life satisfaction checklist</p>

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<p>Cappelleri (2000)^{9 10}</p> <p>Companion Lewis (2001)</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 247</p> <p>IG, n = 124 CG, n = 123</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older; with documented diagnosis of ED for at least 6 mo; in stable relationship with female partner for longer than 6 mo</p> <p>Exclusion: hx of retinitis pigmentosa; uncontrolled psychiatric disorder, hyper/hypotension or DM; serious CVD (MI, stroke or arrhythmia within previous 6 mo); evidence of alcoholism or substance abuse within previous 12 mo; current use of nitrates; nitric oxide donor</p>	<p>Age, mean (range): IG1 58 (range 38-77) CG 60 (range 31-81)</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): Anti-inflammatory analgesic 98 (40) Antihypertensive 93 (38) Antidiabetic 49 (20) Vitamins 49 (20) Analgesic 30 (12) Diuretic 30 (12)</p> <p>Duration of ED, mean (range): 4 (0.4-17) y</p> <p>Underlying disease: Essential hypertension 83 (34) DM, Type II 49 (20) Hypercholesterolemia 37 (15) Hyperlipidemia 22 (9) Prostatic hyperplasia 30 (12)</p> <p>Psychogenic ED, n (%): 4 (3) vs. 6 (5)</p> <p>Physiologic ED, n (%): 102 (82) vs. 99 (81)</p> <p>Mixed ED, n (%): 36 (15)</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG: Dose: 50 mg, with option to titrate to 100 or 25 mg Duration: 12 wk Frequency: up to once/d, 1 dose 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: placebo, titration as IG Duration: 12 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA F/u duration: 12 wk</p>	<p>Primary outcome results: Mean response scores for questions 3 and 4 of IIEF- total, mean: pre: 9.5 vs. 9.6; post: 20 vs. 11 IIEF-EF, mean: pre: 1.7 vs. 1.6; post: 3.4 vs. 1.8 (Approximate mean values from figure): IIEF, Q3: pre: 1.8; post 3.7 vs. 2.2 IIEF, Q4: pre: 1.5; post 3.6 vs. 1.9 IIEF, Q7 (ICs): pre: 2.7; post: 3.9 vs. 2.2 GEQ-Q1, 2, %: 70 vs. 17 GEQ-Q3, least square mean: 3.5 vs. 1.8</p> <p>Other outcomes assessed: EDITS; partner satisfaction; positive correlation between self-assessment and IIEF-EF at baseline and post tx</p> <p>Withdrawals/drop-outs/loss to f/u: 7 (6) vs. 12 (10)</p> <p>WDAE, n (%): 2 (1.6) vs. 0 TAE: NR; pts with AE, n (%)=52 (42) vs. 20 (16); including flushing 17 (14) vs. 1 (1); headache 14 (11) vs. 1 (1); dyspepsia 5 (4) vs. 0; abnormal vision (blue tinge to vision, ▲ sensitivity to light, eye pain, & photophobia) 3 (2) vs. 0 SAE, n (%): 3 (2) vs. 3 (2); cause NR</p> <p>Ascertainment of outcomes assessed: IIEF, GEQ; ED self assessment scoring system</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Cavallini (2005) 11</p> <p>Funding source: Sigma Tau (Industrie Farmaceutiche Riunite)</p>	<p>N screened = 139 N randomized = 110</p> <p>IG1, n = 37 IG2, n = 40 CG, n = 33</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: Pts complaining of ED after having bilateral nerve- sparing radical retro pubic prostatectomy 6 mo or more before the study entry with completely functional erections before the prostatectomy and had not received adjuvant or neoadjuvant tx for prostate cancer or other ED txt, having undetectable PSA levels, involvement in a heterosexual relationship for at least 6 mo before surgery</p> <p>Exclusion: pts with Peyronie's dx, hormonal abnormalities, Myocardial or cerebral ischemia, major surgery, tobacco/alcohol use, DM, uncompensated hyper/hyoptension</p>	<p>Age, mean (sd): 63 (4) vs. 61 (4) vs. 60 (5) y</p> <p>Race (%): NR</p> <p>Co-morbidities, %: compensated hypertension 53 vs. 54 vs. 62; Hypercholesteremia 53 vs. 48 vs. 55 obesity 9 vs.7 vs. 10</p> <p>Previous ED treatment: None</p> <p>Smoking status, %: past smokers (56 vs. 56 vs. 55)</p> <p>Body weight: NR</p>	<p>Concomitant medications: gemfibrozil, simvastatin, cilazapril, enalapril, nifedipine, quinapril, losartan, lacidipine</p> <p>Duration of ED (yr): NR (mean time past surgery= 1 y)</p> <p>Underlying disease: prostate cancer/ prostatectomy</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Sildenafil + Carnitines (acetyl- and propionyl) IG2: Sildenafil + placebo CG: placebo</p> <p>IG1: Dose: 100 mg sildenafil + 2 g/d each carnitine Duration: 4 mo Frequency: once/d Compliance: NR</p> <p>IG2: Dose: 100 mg sildenafil Duration: 4 mo Frequency: once/d Compliance: NR</p> <p>CG: Dose: NR Duration: 4 mo Frequency: once/d Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 4 mo</p>	<p>Primary outcome results: IIEF, mean (sd), IG1 vs. IG2 vs. CG:</p> <p>IIEF, EF: pre: 13 (5) vs. 11 (4); post: 27 (5) vs. 22 (7) vs. 12 (4), p < 0.05 IIEF, ICs: pre: 3 (1); post: 9 (5) vs. 5 (3) vs. 3 (0.6), p < 0.05 IIEF, OF: pre: 3 (1); post: 9 (3) vs. 6 (3) vs. 3 (0.6), p < 0.05 IIEF, SD: pre: 7 (0.7) vs. 6 (0.8); post: 6 (0.6) vs. 7(0.6) vs. 6 (0.7), p => 0.05 General sexual well-being: pre: 3 (0.7) vs. 3 (0.9); post: 8.6 (2.0) vs. 5.4 (2.7) vs. 2.8 (0.7), p < 0.05</p> <p>Other outcomes assessed: Peak systolic and diastolic velocity</p> <p>Withdrawals/drop-outs/loss to f/u: 14 (13.5%) discontinued</p> <p>WDAE: None TAE, n (%): NR; AEs included headache 8 (25) vs. 9 (28) vs. 0; flushing 7 (22) vs. 8 (23) vs. 0; dizziness 3 (9) vs. 3 (9) vs. 0; nasal congestion 2 (6) vs. 2 (6) vs. 0; nausea 2 (6) vs. 2 (6) vs. 0; euphoria 2 (6) vs. 0 vs. 0; abdominal pain 0 vs. 0 vs. 1 (3) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF, Doppler effect</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Chen (2001) ¹²</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 236</p> <p>IG, n = 119 CG, n = 117</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 26-80 y; well-documented hx of ED for at least 6 mo; in stable heterosexual relationship for at least 6 mo</p> <p>Exclusion: genital anatomical abnormality or SCI; other coexisting sexual disorder; elevated serum PRL level or low T level; major psychiatric disorder or hx of alcohol or substance abuse; major hematologic, renal or hepatic dx; poorly controlled DM associated with untreated proliferative retinopathy; stroke or MI in last 6 mo; hypotension or any other sign CVD; hx of retinitis pigmentosa; taking drugs known to be causally associated with ED, androgen therapy, trazodone, nitrates or nitric oxide donor compounds; receiving any tx for ED</p>	<p>Age, mean (range): 61 (26-80) y</p> <p>Race (%): Asian 100%</p> <p>Co-morbidities: Benign prostatic hyperplasia 40 (34) vs. 44 (38) Visual disturbance 46 (39) vs. 37 (32) Essential hypertension 30 (25) vs. 40 (34) DM 26 (22) vs. 29 (25) Arthropathies and related disorders 16 (13) vs. 14 (12)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): current smoker: 27 (23) vs. 28 (24)</p> <p>Body weight, mean (range): 69 (46-98) kg</p>	<p>Concomitant medications, n (%): Antihypertensive 30 (25) vs. 43 (37) Antacid 52 (22) Antirheumatic/antigout 21 (18) Antidiabetic 38 (17) Hypnotic/sedative/anxiolytic 26 (11) Upper respiratory tract medication 33 (14) Vitamins 30 (13) Beta-adrenoceptor blocker 23 (10) Antibacterial 23 (10)</p> <p>Duration of ED, mean: 4 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 20 (8)</p> <p>Physiologic ED, n (%): 193 (82)</p> <p>Mixed ED, n (%): 23 (10)</p>	<p>IG: Sildenafil citrate CG: Placebo</p> <p>IG: Dose: 50 mg for first 2 wk; option to titrate to 100 mg or 25 mg Duration: 12 wk Frequency: once/d; 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IIEF, Q3, mean change from baseline: 1.9 vs. 0.7 IIEF, Q4 mean change from baseline: 2 vs. 0.9 IIEF-EF: pre: 14; post: 24 vs. 18 IIEF-ICs: pre: 5.3; post: 10 vs. 8 IIE-OF: pre: 5; post: 8 vs. 6 IIEF-SD: pre: 6; post: 7 vs. 6 IIEF-OS: pre: 4; post: 7 vs. 6 Successful intercourse, %: 62 vs. 30</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 10 (8) vs. 6 (5)</p> <p>WDAE, n (%): 1(<1) in IG; skin rash TAE, n (%): in at least 3 pts= 76 (64) vs. 58 (50); including: CV 34 (29) vs. 14 (12); flushing 30 (25) vs. 11 (9); palpitation 4 (3) vs. 2 (2); body as a whole 22 (19) vs. 11 (10); headache 8 (7) vs. 4 (3); abdominal pain 5 (4) vs. 0; chest pain 3 (2.5) vs. 0; respiratory system 15 (13) vs. 14 (12); nervous system 15 (13) vs. 9 (8); dizziness 9 (8) vs. 6 (5); musculoskeletal events 9 (3) vs. 3 (3); myalgia 3 (3) vs. 0; arthralgia 3 (3) vs. 2 (2); special senses 9 (8) vs. 2 (2); abnormal vision 3 (3) vs. 1 (0.9); skin appendages 7 (6) vs. 12 (10); fungal dermatitis 3 (3) vs. 2 (2) SAE, n (%): 4 (3) vs. 4 (3)</p> <p>Ascertainment of outcomes assessed: IIEF, pts filled diary</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Choi (2002) ¹³</p> <p>Funding source: Pfizer</p>	<p>N screened = 133 N randomized = 133</p> <p>IG, n = 66 CG, n = 67</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men with ED for at least 6 mo, in a stable heterosexual relationship for 6 mo or longer</p> <p>Exclusion: penile anatomical abnormalities; SCI, other co-existing sexual disorders, serum PRL levels > 3x upper limit to normal, low free T (> 0% below lower limit of normal), major psychiatric disorder, hx of alcohol or substance abuse; hx of haematological, renal, hepatic dx, MI; stroke, hypotension, retinitis pigmentosa, poorly condoled or causing proliferative retinopathy DM, use of drugs associated with androgen therapy, vacuum devices or other tx for ED.</p>	<p>Age, mean (range): 51 (28-78) vs. 51 (32-67) y</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): Eye disorders 21 (32) vs. 14 (21) Hypertension: 13 (20) vs. 10 (15) Hyperplasia of prostate: 11 (17) vs. 12 (18); DM: 10 (15) vs. 8 (12) GI disorders: 6 (9) vs. 5 (8)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): Smokers 25 (37.9) vs. 30 (44.8)</p> <p>Body weight, mean (range): 70 (52-102) vs. 71 (50-98)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): 5 vs. 5.6 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED n (%): 21 (32) vs. 24 (36)</p> <p>Physiologic ED: 31 (47) vs. 26 (39)</p> <p>Mixed ED: 14 (21) vs. 17 (25)</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 50 mg, option for titration at 2 wks to 100, or 25 mg Duration: 8 wks Frequency: once/d Compliance (%): 100</p> <p>CG: Dose: NA Duration: 8 wks Frequency: once/d Compliance (%): 97</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IIEF, mean score, IG vs. CG Q3: baseline=2.5; post tx: 4 vs. 3 Q4: baseline = 2; post tx: 4 vs. 2 EF domain: baseline=13; post tx: 23 vs. 15 IS: baseline= 6; post tx: 11 vs. 8 OF: baseline 5; post tx: 8 vs. 5 SD: baseline=6; post tx: 7 vs. 6 OS: baseline= 4; post tx: 7 vs. 5 GAQ, % yes: 81 vs. 28 Intercourse success, %: 62 vs. 26</p> <p>Other outcomes assessed: Event logs of sexual activity</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 2 (3)</p> <p>WDAE: 0</p> <p>TAE, n of events (%): 46 (70) vs. 25 (27); AE in at least 3 pts: CV=flushing 21 (32) vs. 3 (5); body as whole: 21 (32) vs. 9 (13); headache 17 (26) vs. 6 (9); Upper respiratory tract infection=nasal congestion: 5 (8) vs. 3 (4); digestive system events: 8 (12) vs. 9 (14); dyspepsia 3 (5) vs. 5 (8); special senses events: 10 (15) vs. 3 (5); abnormalities in colour vision: 4 (5) vs. 0; abnormal vision 3 (5) vs. 1 (2) SAE, n (%): 2 (3), in CG</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ, also event logs, 12 lead ECG, standard laboratory tests</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Choppin (2001) 14</p> <p>Funding source: Roche Bioscience</p>	<p>N screened = NR N randomized = 24</p> <p>IG1/IG2/CG, n = 24 (Latin-Square design)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: ED of continual duration \geq6 mo with no established organic cause</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 44 (18-65) y</p> <p>Race (%): black 41.7%, white 58.3%</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications:</p> <p>Duration of ED: at least 6 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Ro70-0004 (active α_{1A}-adrenoceptor) + VSS</p> <p>IG2: sildenafil + VSS</p> <p>CG: placebo + VSS</p> <p>IG1: Dose: 5 mg (oral) Duration: NA Frequency: single dose Compliance (%): NR</p> <p>IG2: Dose: 50 mg (oral) Duration: NA Frequency: as IG1 Compliance (%): NR</p> <p>CG: Dose: placebo (oral) Duration: NA Frequency: as IG Compliance (%): NR</p> <p>Run In period: NR Wash out period: 7 d</p> <p>F/u duration: 2.5 hrs post dosing</p> <p>Note: last tx was repeated at 4th visit</p>	<p>Primary outcome results: Duration of erection in 26 vs. 27 vs. 25 periods; for total of 20 pts):</p> <p>Base, >60% rigidity: 8.28 (3.7) vs. 22.64 (3.57) vs. 9.69 (3.71) min Tip, >60% rigidity: 5.52 (2.84) vs. 9.21 (2.75) vs. 5.33 (2.85) min</p> <p>Base, >80% rigidity: 0.45 (1.69) vs. 5.26 (1.63) vs. 0.67 (1.69) min Tip, >80% rigidity: 1.20 (1.20) vs. 3.18 (1.16) vs. 1.23 (1.21) min</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 4 (20)</p> <p>WDAE: NR TAE, n (%): any AE 2 (10) vs. 2 (9.1) vs. 1 (4.8); dizziness, hypotensive episode, GI disorder in IG1; dizziness, sedation and haematoma nose in IG2; an thrombophlebitis in CG SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan (30 min pre dose to 2.5 hrs post dose)</p>

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<p>Christiansen (2000) ¹⁵</p> <p>Funding source: Pfizer Ltd.</p>	<p>N screened = NR N randomized = 205</p> <p>IG, n = 99 CG, n = 106</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18-70 y with ED of psychogenic or mixed organic/psychogenic etiology for at least 3 mo; at least 1 grade 3 or 4 erection during 4 wk before screening or positive response to IC injection test (papaverine ≤40 mg or PgE₁ ≤20 µg)</p> <p>Exclusion: known vascular, neurological, endocrine or penile anatomical cause for ED; hx of major hematologic, renal or hepatic abnormality; stroke, subarachnoid haemorrhage, bleeding disorder or peptic ulceration; elevated serum PRL level; low serum T level; moderate to severe hyper/ hypotension; regular tx with nitrates, anticoagulants, major tranquilizers, estrogens or antiandrogens</p>	<p>Age, mean (sd): 53 (19-70) vs. 54 (21-70) y</p> <p>Race (%): NR</p> <p>Co-morbidities, %: Most frequent: Hypertension 14 Ischemic heart disease 12 Diabetes 7 Depression 5</p> <p>Previous ED treatment, n (%): IC injections 86 (42)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 4.8 (0.3-20) vs. 5.3 (0.3-23) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, %: 38 vs. 40%</p> <p>Physiologic ED: NR</p> <p>Mixed ED: 62 vs. 60</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG1: Dose: 10 or 25 mg, as determined during 16-wk tx phase prior to double-blind study Duration: 8 wk Frequency: up to once/d approximately 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: placebo Duration: 8 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 2 wk with placebo Wash out period: NA</p> <p>F/u duration (both on and off treatment): 8 wk</p> <p>Other: 16-wk open-label treatment phase after run-in period to adjust dosage</p>	<p>Primary outcome results: IIEF frequency of erections when sexually stimulated, mean change in score: ▲ 1.53 vs. ▼ 0.3 Question assessing frequency of erections lasting long enough: IG1 ▲ 1.72, CG ▼ 0.13 Mean number of grade 3 or 4 erections per wk: 1.5 vs. 0.6</p> <p>GAQ, % yes: 82 vs. 26</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 3 (3), all in IG1</p> <p>WDAE, n (%): 4 (3), no grp designation TAE: NR, most frequent AEs in IG vs. CG/ IG in 1 y open label, n (%): headache 6 (6) vs. 2 (2)/19 (10); dyspepsia. 5 (5) vs. 3 (3)/26 (14); flushing 7 (7) vs. 1 (1)/24 (13); abdominal pain 0 vs. 4 (4)/10 (5); diarrhoea 1 (1) vs. 0; nausea 1 (1) vs. 0/4 (2); back pain 2 (1) vs. 1 (1)/11 (6); asthenia 2 (2) vs. 0/3 (2); abnormal vision including colour hue or brightness perception 2 (2) vs. 0/4 (2); conjunctivitis 2 (2) vs. 0/4 (2) SAE: 24 no grp designation, including MI in open label phase</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ, Patient diary of grading erection (1=enlarged but not hard-4=full erection)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>DeBusk, (2004) 16</p> <p>Funding source: Pfizer Inc</p>	<p>N screened = 186 N randomized = 151</p> <p>IG, n = 75 (ITT=70) CG, n = 76 (ITT=72)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older with diagnosed ED (\leq 21 on Sexual Health Inventory), confirmed, and stable CAD for at least 4 wks</p> <p>Exclusion: currently using prescription for and/or taking nitrates, hypotension, uncontrolled hypertension, high cardiac risk, unstable angina, hypotrophic obstructive cardiomyopathy, moderate/severe aortic stenosis, concomitant TX with drugs that inhibit P450, commercial tx for ED, previously taken sildenafil</p>	<p>Age, mean (range): 61 (39-82) vs. 62 (41-80) y</p> <p>Race (%): more than 90% White</p> <p>Co-morbidities: CV conditions 100% (listed in full text); Hyperlipidemia 53 (72) vs. 49 (65); pure hypercholesterolemia 38 (51) vs. 38 (50); other also listed in full text</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): medication taken by more than 50% of pts= anti-inflammatory analgesics 133 (88); hyperlipidemia 131 (87); anti-hypertensives: 113 (75); Beta Blockers: 90 (60)</p> <p>Duration of ED, mean: 5 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 5 (7) vs. 3 (4)</p> <p>Physiologic ED, n (%): 36 (49) vs. 34 (45)</p> <p>Mixed ED, n (%): 33 (45) vs. 39 (51)</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 50 mg with option to titrate to 100 or 25 mg Duration: 12 wks Frequency: up to once/d (total dose=36) Compliance (%): 80</p> <p>CG: Dose: NA (titration as IG) Duration: 12 wks Frequency: up to once/d (total = 40) Compliance (%): 85</p> <p>Run In period: 2 wks Wash out period: NR</p> <p>F/u duration: 12 wks</p> <p>Other: final dose, n (%)= 25 mg: 3 (4) v. 0 50 mg: 16 (22) vs. 13 (17) 100 mg: 55 (74) vs. 63 (83)</p>	<p>Primary outcome results: IIEF- least square mean (SE) score: Q3, baseline=2; post tx: 3.5 vs. 2.7 Q4, baseline=1.6; post tx: 3.3 vs. 2.3</p> <p>GEQ, % of pts with improvement on: Erection: 59 vs. 28 Intercourse: 56 vs. 27 Intercourse success: 51 vs. 25</p> <p>Other outcomes assessed: IIEF, % of max possible score (all but SD improved in IG vs. CG, $p < 0.02$); EDITS scores; life satisfaction checklist scores</p> <p>Withdrawals/drop-outs/loss to f/u: 7 (10) vs. 9 (13); including lack of efficacy in 0 vs. 4 (6)</p> <p>WDAE, n (%): 1 (1.4) vs. 1 (1.3) TAE, %: 47 vs. 32; AE in more than 3% of pts, n (%)=headache 6 (8) vs. 1 (1); chest pain 4 (6) vs. 2 (3); hypertension 4 (6) vs. 1 (1); flushing 6 (8) vs. 0; dyspepsia 2 (3) vs. 4 (5); leg cramps 3 (4) vs. 0; respiratory tract infection 4 (5) vs. 2 (3); nasal congestion 2 (3) vs. 0; abnormal vision 1 (1) vs. 1 (1) SAE, n (%): 1 (1.4) vs. 2 (2.6), One chest pain in IG, and urinary tract infection, severe angina pectoris in CG</p> <p>Ascertainment of outcomes assessed: IIEF, EDITS; GEQ, and intercourse success rate by diary; life satisfaction check list</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Deveci (2004) ¹⁷</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 40</p> <p>IG, n= 20 CG, n= 20</p> <p>Intention to treat (ITT) analysis: NR</p> <p>Inclusion: NR</p> <p>Exclusion: presence of any contraindication for sildenafil use; hormonal disorders; performance concern; unsteady sexual partnership, past trial/use of oral sildenafil; chronic dx</p> <p>Data reported as IG vs. CG</p>	<p>Age, mean (range): 55 (25-65) y</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): DM 6 (15); hypertension 5 (12.5); benign prostatic hyperplasia 7(17.5); pts with 2 or more risk factors 4(10)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): current & past smokers 9 (22.5)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: more than 3 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil sublingual CG: placebo</p> <p>IG: Dose: 20 mg during sexual stimulation Duration: NR Frequency: NR Compliance (%): NR</p> <p>CG: Dose: NR Duration: as IG Frequency: as IG Compliance (%): NR</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Mean ▲ in IIEF-5: 1.75 (endpoint vs. baseline p=0.02) vs. 0.6 (endpoint vs. baseline p>0.05)</p> <p>Overall success rates, n (%): 13 (65) vs. 3 (15)</p> <p>Mean onset of erection: 15.5 vs. 30 min</p> <p>Mean duration of erection: 40 vs. 20 min</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE, n (%):NR; headache 2 (10) vs. 1 (5); flushing 2 (10) vs. 2 (10); sweating 2 (10) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: pts self reports; & IIEF-5 (5 item version of IIEF)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Diamond, LE (2005) ¹⁸</p> <p>Funding source: Palatin Technologies, Inc.</p>	<p>N screened = NR N randomized = 19 (cross over)</p> <p>IG1/ IG2/CG, n = 19</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 40-65 y, with diagnosed ED of at least 6 mo currently using viagra or levitra and having an adequate response to either of them</p> <p>Exclusion: ED caused by untreated endocrine dx, penile deformity, prostate cancer or prostatectomy, major hepatic, renal, CV, psychiatric or CNS dx, stroke, SCI</p>	<p>Age, mean (sd): 53 (6.7)</p> <p>Race (%): White 70, Black 10, Hispanic 20</p> <p>Co-morbidities, %: Diabetes 10, hypertension 20, hyperlipidemia 50, obesity 10</p> <p>Previous ED treatment: Viagra and levitra</p> <p>Smoking status: 50% (past/current)</p> <p>Body weight: 87 (13) kg</p> <p>Other: Total T level, mean: 436 (168) ng/dl</p>	<p>Concomitant medications:</p> <p>Duration of ED (yr): 5.0 (SD=5.4)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: IIEF mean score = 21.2 (6-29)</p>	<p>IG1: Sildenafil + PT141 IG2: Sildenafil + placebo CG: Placebo</p> <p>IG1: Dose: 25 mg+7.5 mg Duration: NR Frequency: NR Compliance: NR</p> <p>IG2: Dose: 25 mg Duration: NR Frequency: NR Compliance: NR</p> <p>CG: Dose: NA Duration: NR Frequency: NR Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p> <p>Other: Outcome assessments done on 3 visits 3-10 d apart and continuously monitored until 6 hrs after each dose</p>	<p>Primary outcome results: IG1 vs. IG2, mean (SE): Base rigidity => 60%: 112.9 (19.2) vs. 69.9 (14.3) min, p < 0.01</p> <p>Base rigidity => 80%: 61 (16) vs. 40 (10) min, p=>0.05</p> <p>Tip rigidity => 60%: 99.5 (16.6) vs. 40.6 (7.5) min, p < 0.001</p> <p>Tip rigidity => 80%: 48.6 (12.2) vs. 20.7 (4.8) min, p < 0.05</p> <p>Pts-assessed mean quality score of erection after sexual-visual stimulation (1-10) = 8.2 (0.41) vs. 6.8 (0.52), p < 0.05</p> <p>Rigidity parameters improved in IG1 vs. placebo (p < 0.05)</p> <p>Other outcomes assessed: tumescence activity levels</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: None TAE: more and new AE observed with combination tx; flushing one also had nausea 4 (21%) vs. 0 vs. 0; headaches 0 vs. 1 vs. 1 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan and questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Dinsmore, W (1999)¹⁹</p> <p>Funding source: NR</p>	<p>N screened = 127 N randomized = 111</p> <p>IG, n = 57 CG1, n = 54 CG2, n = 109 (<i>separate parallel study, no treatment, age matched, healthy subjects, single-visit data not included in this table</i>)</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men older than 18 with clinical diagnosis of ED of at least 6 mo, participated in a stable, heterosexual relationship for at least 6 mo and to forego self-injection programs</p> <p>Exclusion: advanced vascular, neurological, endocrine, or anatomic causes for ED, major hematologic, renal, or hepatic abnormalities, regular use of nitrates, hx of stroke in the past 6 mo. or currently active peptic ulceration, tx with any experimented drugs in the 3 mo. preceding the study</p>	<p>Age, mean (range): 56 (30-78) vs. 55 (29-89) y</p> <p>Race (%): NR</p> <p>Co-morbidities, %: hypertension IG 9 vs. 11; DM 7 vs. 7; ischemic heart disease 1 vs. 1</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED (%): 40 vs. 39 (CG1)</p> <p>Physiologic ED (%): 21 vs. 20</p> <p>Mixed ED (%): 39 vs. 37</p>	<p>IG: sildenafil (self-administered) CG: placebo CG2: no treatment</p> <p>IG: Dose: 25 mg (option to ▲ to 50 mg, max. 100 mg) Duration: 12 wks Frequency: 1-hr pre sexual activity but not > once daily Compliance: 87 %</p> <p>CG: Dose: NA (option to ▲ to 50 mg, max. 100 mg) Duration: 12 wks Frequency: 1-hr pre sexual activity but not > once daily Compliance (%): NR</p> <p>Run In period: 2-4 wks Wash out period: NR</p> <p>F/u duration (both on and off treatment): 12 wks + 2 wks = 14 wks</p>	<p>Primary outcome results: IIEF-Q1-15, range: pre (except Q11, and 12) \leq 2.52; post tx range 2.77-3.92 vs. 1.37-3.10, sign ▲ (p < 0.01)</p> <p>GEQ, % improved: 81% vs. 18% (p<0.0001) Grade 3 or 4 erection/mo, mean (event log): 6.9 vs. 2.4 (p<0.0001)</p> <p>Successful sexual intercourse attempts: 73% vs. vs. 30% (p<0.0001)</p> <p>Other outcomes assessed: all IIEF items</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 14 (13) including 3 in IG, and 11 in CG discontinued tx due to lack of efficacy</p> <p>WDAE: 0 TAE, n (%): 18 (30) vs. 3 (5.5) headache 7(12%) vs.1 0; flushing 5 (9) vs. 2 (4); dyspepsia 4(7) vs.1 (2); abnormal vision 2 (4) vs. 0</p> <p>SAE, n: nr</p> <p>Ascertainment of outcomes assessed: 15-item IIEF; GEQ; event log with of erection using a 5-point scale grading system (0 =no sexual activity; 1=almost never; 5=almost always) (added")</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Dunzendorfer (2002) ²⁰</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 77 (cross over)</p> <p>IG1, n = 44 IG2, n = 33 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts with ED, and low to non-response to 5 PDE inhibitors; with complaint of prostate disease</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 62 (34-77) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 100% with PDE-5 inhibitors; 4 wks screening drug program for low responders to (n=58), 3 hrs before sildenafil 100 mg intake (dose/ sexual activity): Midodrine 25 mg; Testosterone 250 mg/wk; Ginseng 900 mg; Yohimbine 15 mg; Akatinol 10 mg; Apomorphine 4 mg; Hydergin-S 8 mg; Prazosi 4 mg; DHE 5 mg</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): DM 4 (5); hypertension 17 (22); prostate dx 77 (100); mixed vasculogenic 77 (100)</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: A: Sildenafil/ B: Sildenafil + Dihydroergotamine (DHE) IG2: A: Sildenafil + DHE/ B: Sildenafil</p> <p>IG1: Dose: sildenafil 50 mg, titrated to 100 mg; DHE 5 mg Duration: NR Frequency: twice / wk Compliance: NR</p> <p>IG2: Dose: 50 mg (titration as IG1)+ 5 mg DHE Duration: NR Frequency: as IG1 Compliance: NR</p> <p>Run In period: 4 wks (see previous ED tx)</p> <p>Wash out period: 4 wks</p> <p>F/u duration: NR</p> <p>Other: Pts received tx A (IG1) or B (IG2) followed by a wash out period and then crossed over to B (IG1) or A (IG2) respectively</p>	<p>Primary outcome results: Mean IIEF Q3, 4, 5 and 6, range of mean scores per question, (SD range):</p> <p>Baseline (run in) = 1.1-1.8 (0.2-0.4) 50 mg sildenafil alone = 1.1-2.1 (0.2-0.4) 100 mg sildenafil = 1.5-2.1 (0.3-0.4) DHE alone = 1.3-2.2 (SD range 0.2-0.5) Combination 50 mg sildenafil + DHE = 2.9-3.2 (0.5-0.7) 100 mg sildenafil + DHE = 3.5-3.8 (.6-0.8)</p> <p>Other outcomes assessed: NO-cAMP (N1 oxide cyclic adenosine monophosphate), and cGMP (cyclic guanosine monophosphate) levels in corpora cavernosa; urodynamic profile</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE: NR TAE: NR (authors claim that combination tx reduced AE) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF, lab measures</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (1999) 21</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 16 (cross over)</p> <p>IG/CG = 16</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 18 or older, with ED of no known organic cause</p> <p>Exclusion: Hx of DM, untreated hypogonadism; tx with nitrates, antidepressants or tranquilizers. Concomitant sign.arterial disease; other tx for ED less than 2 wks prior to start of study</p>	<p>Age, mean (range): 35-68 (57) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 1.9 (0.25 – 8) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 0</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil CG: Placebo</p> <p>IG: Dose: 100 mg Duration: 2-5 hrs Frequency: twice Compliance (%): 100%</p> <p>CG: Dose: NA Duration: 2-5 hrs Frequency: twice Compliance (%): 100%</p> <p>Run In period: 2 wks Wash out period: 7 d</p> <p>F/u duration: f/u assessments at 2 and 4 hrs post dosing</p>	<p>Primary outcome results: Pts with grade 3 or 4 erection, n (%): IG only 13 (81.25)</p> <p>Duration of erection 2 hrs post dosing, mean: RigiScan, erections with > 60% rigidity at base: At 2 hrs post dosing: IG 2.5 min (responders = 4.1 min) At 4 hrs post dosing: IG responders = 2.2 min, for IG1 = 1.4 min Pts rated erection, grade 3 or 4: responders: At 2 hrs post dosing: 23.8 minutes At 4 hrs post dosing: IG responders 17.2 min</p> <p>Other outcomes assessed: None</p> <p>Withdrawals/drop-outs/loss to f/u: 0 WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan, self-rating scale</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (2001) 22</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 47 N randomized = 44 (crossover design)</p> <p>IG/CG, n = 44</p> <p>ITT analysis used for primary outcome: Yes (n=40)</p> <p>Inclusion: men 18-70 y; clinical diagnosis of ED of no established organic cause for longer than 6 mo; in stable relationship with female partner; have residual ED (at least one grade 3 or 4 erection) or positive response to papaverine or PGE₁ injection within 4 wk of study entry</p> <p>Exclusion: having 2 successive penetrative sexual intercourse acts per wk; hx of alcohol misuse; regular tx with nitrates, anticoagulants or acetylsalicylic acid within 2 wk; tx with antidepressants or major tranquilizers for psychoses or related conditions; continued use of other ED tx</p>	<p>Age, mean (range): grp: 53 (33-69) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 3 (0.5-10) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 100%</p> <p>Physiologic ED: 0</p> <p>Mixed ED: NR</p>	<p>IG1: sildenafil CG: placebo</p> <p>IG1: Dose: 25 mg with option to titrate to 50 mg and then 75 mg if necessary Duration: median 29 d (two 28 d tx periods) Frequency: 1 dose 30-60 min before sexual activity; max. 1/d Compliance: 91% took at least one dose</p> <p>CG: Dose: placebo (titration as IG) Duration: as IG Frequency: as IG Compliance: as IG</p> <p>Run In period: None Wash out period: None</p> <p>F/u duration: 10 wk (2 wks post last tx period)</p> <p>Other: 24 pts received sildenafil first, and 20 received placebo first; each period lasted for 28 d</p>	<p>Primary outcome results: Geometric mean number of grade 3 or 4 erections per wk: 4.2 vs. 1.4</p> <p>Erection of grade 3 or 4/ doses: 194 vs. 68</p> <p>Intercourse success/ dose, %: 62 vs. 12</p> <p>GEQ-Q1 (improved erection), % yes: 34 (94) vs. 9 (25) GEQ-Q2 (ease of use), %: 33 (94) vs. 13 (37)</p> <p>Other outcomes assessed: partners' assessment of quality of erections</p> <p>Withdrawals/drop-outs/loss to f/u: 5 (11)</p> <p>WDAE, n (%): 0 vs. 1 (<1) TAE, n (%): all reporting AE 23 (53) vs. 14 (33); tx related AE: headache 11 (26) vs. 0; flushing 4 (9) vs. 0; dyspepsia 3 (7) vs. 1 (2); arthralgia 3 (7) vs. 2 (5) SAE, n (%): 0 vs. 1 (<1) MI in second period</p> <p>Ascertainment of outcomes assessed: daily log of erection (grading system 1-4), and intercourse satisfaction</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (2002) 23</p> <p>Study a</p> <p>Funding source: NR</p>	<p>N screened = 17 N randomized = 17 (two-way crossover study)</p> <p>IG, CG, n = 17</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: age 35-70 y, clinical diagnosis ED, no organic cause for at least 6 mo</p> <p>Exclusion: hx of serious medical conditions (DM, untreated hypogonadism, sign arterial dx, migraine headaches, alcohol or substance abuse. Current tx with nitrates, antidepressants, tranquilizers or anticoagulants. Other therapies for ED (e.g. E₁ IC) discontinued 2 wks prior to start of study</p>	<p>Age, mean (range): 52yrs (37-70)</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 4 received prostaglandin, 2 yohimbine, 1 an investigational drug</p> <p>Smoking status: NR</p> <p>Body Weight: NR</p> <p>Other: other conditions, n (%); vasectomy 3 (17.6%), 1 unilateral orchidectomy, prostatitis 1 (5.8%), caricosities 1(5.8%)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 3.1 y (0.5-19)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil + 60 min visual sexual stimulation (VSS) CG: placebo + 60 min visual sexual stimulation</p> <p>IG: Dose: 50 mg Duration: NR Frequency: once Compliance (%): 100%</p> <p>CG: Dose: NA Duration: NR Frequency: once Compliance (%): 100%</p> <p>Run In period: NR Wash out period: 7 d</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Proportion of responders with rigidity > 60%, n (%): 14 (82) vs. 9 (53)</p> <p>Pts with grade 3 or 4 erection: 12 (71) vs. 6 (35)</p> <p>Time to onset of erections (median): 27 min (range 12-70) vs. 50 min</p> <p>The onset of erections occurred only after VSS; 8 (47%) responded to both active and placebo tx</p> <p>Other outcomes assessed: none</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1</p> <p>WDAE: 0 TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan; physical exam, patient report; standard laboratory tests</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (2002) 23</p> <p>Study b</p> <p>Funding source: NR</p>	<p>N screened = 16 N randomized = 16 (two-way crossover)</p> <p>IG/ CG, n = 16</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 35-70 yrs, clinical diagnosis ED, no organic cause for at least 6 mo</p> <p>Exclusion: hx of serious medical conditions (DM, untreated hypogonadism, sign arterial dx, migraine headaches, alcohol or substance abuse. Current tx with nitrates, antidepressants, tranquilizers or anticoagulants; other therapies for ED (IC injections) discontinued 2 wks prior to start of study.</p>	<p>Age, mean (range): 57 (35-68) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: none</p> <p>Smoking status: NR</p> <p>Body weight NR</p> <p>Other: pts conditions, n (%) vasectomy 7 (43.8), undescended right testicle 1 (6.3), prostatitis, redundant prepuce 1 (6.3), scrotal cyst 1 (6.3), hyperplasia of the prostate 1 (6.3)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (mean yrs, range): 1.9 (3-8.0) y</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil+ 60 min visual sexual stimulation (VSS) CG: placebo + 60 min VSS</p> <p>IG1: Dose: 100 mg Duration: NR Frequency: twice Compliance (%): 100%</p> <p>CG: Dose: NA Duration: NR Frequency: twice Compliance (%): 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: four assessment at 3 hrs and 5 hrs</p> <p>Other: pts received 4 tx (2 active and 2 placebo)</p>	<p>Primary outcome results: Proportion of responders with rigidity > 60%, n (%): 3 hrs post VSS: 12 (75) vs. 5 (31) 5 hrs post VSS: 13 (81) vs. 5 (31)</p> <p>Duration of erection, mean (SE): 3 hrs post VSS: 19.4 (4.1) vs. 3.9 (2.1) min 5 hrs post VSS: 17.2 (4.0) vs. 3.6 (2.0)</p> <p>Other outcomes assessed: none</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1 (6.3)</p> <p>WDAE: 0 TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan; physical exam patient report, standard laboratory tests</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (2005) 24</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 411 N randomized = 367</p> <p>IG1, n = 183 (first period) IG2, n = 184 (first period) CG, n = NA</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: Pts aged => 18 yr with documented ED of any aetiology and severity, in a steady relationship with the same female partner naïve to treatment for ED with drugs inhibiting PDE5</p> <p>Exclusion: Pts with endocrine dx, premature ejaculation, prostatectomy, pelvic surgery, penile deformity, sign renal or hepatic dx, CHF, Within 6 mo, MI, coronary artery bypass surgery, sudden cardiac arrest, SBP (< 90 - > 170 mmHg) or diastolic (< 50 - > 100 mmHg), malignant hypertension, retinitis pigmentosa, current tx with nitrates, cancer chemotherapy, HIV infection, substance/drug abuse in last 6 mo</p>	<p>Age, mean (sd): 54 (12) y</p> <p>Race (%): Caucasian 92, Black 4, Asian 3, other 1.3</p> <p>Co-morbidities, (%): Hyperlipidemia 11, coronary artery dx 6.5, hypertension 26.4, DM 9.5, depression 4</p> <p>Previous ED treatment: NR</p> <p>Smoking status, (%): current = 24</p> <p>Body weight: NR</p> <p>Other: current alcohol use (65%)</p>	<p>Concomitant medications: no other ED treatments</p> <p>Duration of ED: NR (pts with 1 y or more ED =74%)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 12%</p> <p>Physiologic ED: 28%</p> <p>Mixed ED: 60%</p> <p>Other: ED defined as consistent change in the quality of erection that adversely affects subject's satisfaction with sexual intercourse</p> <p>Other: Mean IIEF (EF): 14 (6); Severity of ED: severe (IIEF1-10): 31%, moderate (IIEF 11-16): 30%, mild (IIEF 17-30): 39%</p>	<p>IG1: Sildenafil IG2: Tadalafil</p> <p>IG1: Sildenafil Dose: 25-100 mg Duration: 12 wks Frequency: NR Compliance: NR</p> <p>IG2: Tadalafil Dose: 10-20 mg Duration: 12 wks Frequency: NR Compliance: NR</p> <p>Run In period: 4 wks Wash out period: 7-10 d</p> <p>F/u duration: before and after crossover 24 wks (2 periods of 12 wks)</p> <p>Other: Dose was titrated up and down between 25-100 for Sildenafil and 10-20 mg for Tadalafil</p>	<p>Primary outcome results: Mean least squares change from baseline for IIEF domains and 95% CI (IG2 vs. IG1): EF: 0.5 (-0.07, 1.1) OF: 0.3 (0.02, 0.5) SD: 0.2 (0.02, 0.6) Intercourse satisfaction: 0.17 (-0.1, 0.42)</p> <p>Mean change in IIEF questions: erection firmness, intercourse satisfaction and enjoyment, desire level, OS, erection confidence: tadalafil > sildenafil OS: 0.3 (0.02, 0.5) SEP, mean change from baseline: SEP-Q2: 36 vs. 39 SEP-Q3: 53 vs. 58</p> <p>Other outcomes assessed: mean scores of IIEF, drug preference</p> <p>Withdrawals/drop-outs/loss to f/u: IG1 (1st) and IG2 (2nd): n=42 IG1 (2nd) and IG2 (1st): n=39</p> <p>WDAE: IG1 (1st) and IG2 (2nd): n=4 IG1 (2nd) and IG2 (1st): n=7</p> <p>TAE, n (%): pts with 1 or more AE=125 (34) vs. 128 (35)</p> <p>SAE, n: 4 (2) vs.5 (3)</p> <p>Ascertainment of outcomes assessed: Questionnaires</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Fava (2006) ²⁵</p> <p>Funding source: Pfizer Inc. (conflict of interest for authors; paid by Pfizer, and other sources)</p>	<p>N screened = NR N randomized = 142</p> <p>IG1, n = 71 CG, n = 71</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older with ED diagnosed by Sexual Health Inventory for Men (SHIM) score of 21 or less, and diagnosed major depressive disorder (MDD) according to DSM-IV criteria in remission in stable relationship</p> <p>Exclusion: symptomatic for depression or anxiety despite tx; pts requiring tx with antipsychotics, mood stabilizers, other nonserotonergic antidepressant agents or lithium; use of nitrates or any commercially available for ED</p>	<p>Age, mean (range): 51 (27-74) y</p> <p>Race, %: White 86 vs. 92%; Black 6 vs. 3%; Asian 3 vs. 0%; other 6% in both grps</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (range): 92 (57-191) vs. 92 (60-138) kg</p>	<p>Concomitant medications, n (%): antidepressant therapy, selective SRI 133 (94); serotonin-norepinephrine reuptake inhibitor 10 (7); other antidepressant drugs 10 (7)</p> <p>Duration of ED, mean (range): 2.7 (0.1-14.2) vs. 2.2 (0.2-11.6) y</p> <p>Underlying disease, n (%): depression</p> <p>Psychogenic ED, n (%): 100%</p> <p>Physiologic ED: NA</p> <p>Mixed ED: NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg titrated to up to 100 or down to 25 mg based on efficacy and tolerance Duration: 6 wks Frequency: NR Compliance:</p> <p>CG: Dose: NA Duration: 6 wks Frequency: NR Compliance:</p> <p>Run In period: Wash out period:</p> <p>F/u duration: Other: mean dose taken/ mo= 13.6 vs. 11; 65% on 100 mg 34% on 50 mg and 1% on 25 mg sildenafil at end of study</p>	<p>Primary outcome results: IIEF mean score: Q3: baseline 2.4; post tx 3.9 vs. 3.1, p=0.003 Q4: baseline 2.1; post tx 3.7 vs. 2.8, P<0.001 GEQ- Q1, % improved: 70.6 vs. 28.8 GEQ-Q2, % improved: 72.1 vs. 27.7 GEQ-Q3, mean (SE) scale of 1-5: 2.5 (0.2) vs. 1.3 (0.2)</p> <p>Event log, mean (SE) N of events/ wk: N of sexual intercourse attempts: 2.6 (0.2) vs. 1.9 (0.2) N of successful attempts: 1.9 (0.2) vs. 0.6 (0.2) Successful attempts/ wk, % (95% CI): 71 (60 to 80) vs. 31 (22 to 43)</p> <p>Other outcomes assessed: All EDITS questions indicated tx success with sildenafil</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 9 (12.7) vs. 4 (5.6)</p> <p>WDAE: NR TAE, n (%): NR; all included headache 6 (9) in all; dyspepsia 6 (9) vs. 1 (1); anxiety 4 (6) vs. 3 (4); abnormal/ blurry vision 2 (3) vs. 0 SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: IIEF, EDITS, GEQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Fowler (2004) ²⁶</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 256 N randomized = 218</p> <p>IG, n = 104/ (102, 98% completed) CG, n = 113/ (n= 88, 78% completed)</p> <p>Intention to treat (ITT) analysis: yes</p> <p>Inclusion: men 18 yr or older, ED of at least 6 mo; diagnosis of multiple sclerosis (MS) of at least 1 yr (criteria not defined/ type of MS not defined), with residual disability level of 2-6 (ambulatory) based on Kurtzke Extended Disability Status Scale (EDSS)</p> <p>Exclusion: penile deformities; major haematological, renal or hepatic abnormalities, coexistence /sexual dx as primary cause; uncontrolled psychiatric condition; cardiovascular disorder; unknown hx of retinitis pigmentosa; use of nitrates, or corticosteroids (last 2 mo); nitric oxide donors</p>	<p>Age, mean: 46 y</p> <p>Race (%): NR</p> <p>Co-morbidities: 100% MS (mean duration 10.4 y)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Note: data reported for IG vs. CG</p>	<p>Concomitant medications: (used by > 10% of pts) analgesics; antibacterial; antidepressants; antihypertensive (> in CG); corticosteroids (> in IG); drugs affecting immune response, muscle relaxants; rheumatic diseases medication; vitamins</p> <p>Duration of ED: mean (range) 5.2 (0.7-23.1) vs. 6.1 (0.9-29) yr</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Sildenafil CG: placebo</p> <p>IG: Dose: 50 mg (32%); titrated up to 100 (64%), or down to 25 mg (4%) based on patient response & tolerability Duration: 12 wks Frequency: max once / d, 1 hr before sexual activity Compliance (%): NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks Note: this trial was followed by an open label period of 24-48 wks (n=206) & included those with non tx related AE; (50 mg sildenafil)</p>	<p>Primary outcome results: IIEF-Q1 (improvement in erection), % of pts: 90% vs. 24%, p<0.0001 Q2 (satisfactory erection for intercourse), % of pts: 92% of responders to Q1 Q3/Q4: IG better than CG, p<0.0001 Q9/ Q10: IG better than CG, p< 0.0001 Q11/ Q12: IG better than CG, p=0.0002 GEQ3, mean score: 4 vs. 2</p> <p>Other outcomes: quality of life, IG did better in 5/8 variables than CG, (sexual life 86% of pts vs. 22%)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 2 (2) vs. 25 (22)</p> <p>WDAE: 0 vs. 1% TAE (%): AE in more than 3% of pts in IG vs. CG/IG open label=66.3 vs. 43.4/73; headache 27 vs. 7/23; flushing 13 vs. 2/16; weakness 6 vs. 1/4; MS relapse 7 vs. 2/10; rhinitis 6 vs. 1/7; chromatopsia 4 vs. 0/4; dyspepsia 6 vs. 0/6 SAE, n (%): 3 (3) vs. 3 (3), urinary tract infection, worsening, & exacerbations of MS in IG; weakness, bone disorder, MI in CG</p> <p>Ascertainment of outcomes assessed: IIEF; GEQ, quality of life questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gentile (2004) ²⁷</p> <p>Funding source: Sigma-Tau, Italy</p>	<p>N screened = NR N randomized = 40</p> <p>IG, n = 20 CG, n = 20</p> <p>ITT analysis used for primary outcome: N</p> <p>Inclusion: men 18 or older, with ED, in a stable relationship of more than 6 mo; type 1 DM of at least 5 y or type 2 DM of at least 2 y (defined by National Diabetes Data Group), medical management of DM for 6 mo., HbA1C levels < 11%</p> <p>Exclusion: genital anatomical deformities, a primary dx of a sexual disorder other than ED, a poorly controlled major psychiatric disorder, a recent hx of major haematological, renal or hepatic abnormalities, MI, stroke, heart failure, unstable angina or hypotension, or tx with nitrates, HbA1C levels ≥ 11% (Complete list in full text article)</p>	<p>Age, mean (range): 64 (45-81) y</p> <p>Race (%): Caucasian 100 %</p> <p>Co-morbidities, %: hypertension 31 vs. 34; peripheral vascular dx 4 vs. 3; other 3 vs. 2</p> <p>HbA1C level, % (range): 8.6 (5.7-11.3) vs. 8.4 (5.6-10.9)</p> <p>Previous ED treatment: Viagra monotherapy in all</p> <p>Smoking status: smoker 32 vs. 29</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 5.7 (0.7-22) vs. 5.3 (0.6-19.5) y</p> <p>Underlying disease, %: DM type 1= 18 vs. 16; DM type 2= 82 vs. 84</p> <p>Organic ED, (%): 65 vs. 66</p> <p>Mixed ED, %: 35 vs. 34</p>	<p>IG: propionyl-L carnitine (PLC) + sildenafil CG: placebo PLC + sildenafil</p> <p>IG: Dose: 2 g PLC+ 50 mg sildenafil Duration: 24 wks Frequency: once/d + twice/wk Compliance: NR</p> <p>CG: Dose: 2 g (placebo) + 50 mg sildenafil Duration: 24 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 24 wks</p>	<p>Primary outcome results: IIEF-Q3, mean (sd): 4.3 (0.6) vs. 3 (0.7), p<0.01 IIEF-Q4, mean (sd): 3.9 (1) vs. 2.7(0.9), p<0.01 GEQ, (% yes): 68 vs. 23, p<0.01 Successful attempts of intercourse (Event logs), %: ▲ from 11% to 34% vs. ▲ 10% to 76%, p<0.01</p> <p>Other outcomes assessed: vascular evaluations [e.g. cavernosal artery; PSV, resistance index (RI)]</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: gastric pain 2 vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; GEQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gingell (2004) ²⁸</p> <p>Funding source: Pfizer</p>	<p>N screened = 17 N randomized = 16 (four way crossover trial)</p> <p>IG/ CG, n = 16</p> <p>ITT analysis used for primary outcome: yes (n=16)</p> <p>Inclusion: sildenafil naïve men 18 to 70 y and had been diagnosed with ED of no known organic cause for longer than 6 mo</p> <p>Exclusion: Men who had not experienced at least one erection of sufficient rigidity for penetrative intercourse in the previous 4 wks, or failed to give positive response to IC prostaglandin or papaverine at screening; hx of DM, untreated hypogonadism; sign arterial, renal or hepatic dx or used antidepressants, tranquilizers, nitrates, IC injections or any other tx for ED in 2 wks.</p>	<p>Age, mean (range): 55 (36-68) y</p> <p>Race, n (%): White 16 (94)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: None within last 2 wks.</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 83 (10) kg</p>	<p>Concomitant medications: None</p> <p>Duration of ED: ≥ 6 mo</p> <p>Underlying disease: None</p> <p>Psychogenic ED: None</p> <p>Physiologic ED: None</p> <p>Mixed ED: None</p>	<p>IG: Sildenafil (mix of both given at diff time periods) CG: Placebo</p> <p>IG: Dose: 100 mg Duration: three 14 hr inpatient stay in 4 wks Frequency: once/session (at one of either 12, 8, or 1 hr prior to VSS) Compliance: 100%</p> <p>CG: Dose: 3 tablets Duration: one 14 hr inpatient stay Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: 7 d</p> <p>F/u duration: 4 wks</p> <p>Other: pts were randomized into sequence grps (I-IV) and sildenafil or placebo administered test periods (A-D)</p>	<p>Primary outcome results: Duration of erections of ≥60% rigidity, mean for IG at 1, 8, 12 hr prior to VSS vs. CG: 26, 11, 8 vs. 3.4 min</p> <p>Duration of grade 3 or 4 erection, (hard enough, completely hard) at 1, 8, 12 hr: 33, 23, 16 vs. 7 min (75% reported grade 3 or 4 after 2 hrs)</p> <p>Other outcomes assessed: Proportion of sildenafil responders 1,8, 12 hrs, %: 69, 60, 31; 82% after 8 hrs, and 54% after 12 hrs</p> <p>Withdrawals/drop-outs/loss to f/u: 1 pts excluded (use of IC injection during trial)</p> <p>WDAE: None TAE: NR; most common, AEs at 1, 8, and 12 hrs pre VSS 27 vs. 1; AEs included headaches 12 vs. 0; flushing 9 vs. 0; diarrhea 1 vs. 0; dry mouth 1 vs. 0; GI disorder 1 vs. 1; respiratory tract infection 1 vs. 0; visual disturbances (chromatopsia) 2 vs. 0 Most common headache: 12 Facial Flushing: 9 CG n: Gastro 1 SAE: None</p> <p>Ascertainment of outcomes assessed: RigiScan; self-assessed duration of grade 3 or grade 4 erections:</p>

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<p>Glina (2001) ²⁹ Companion Glina (2002) ³⁰</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 245 (Parallel grp)</p> <p>IG, n = 124 CG, n = 121</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: Brazilian and Mexican men 18 or older with ED of broad-spectrum etiology ≥ 6 mo in a stable, heterosexual relationship for a duration of ≥ 6 mo.</p> <p>Exclusion: genital anatomical deformities; ED secondary to SCI, primary diagnosis of other sexual disorders; uncontrolled DM; hx of stroke, MI or sign. CV disease within previous 6 mo, hypotension or hypertension; alcoholism or substance abuse; receiving nitrates or nitric oxide</p>	<p>Age, mean (range): 58 (28-85) vs. 55 (27- 84)</p> <p>Race, n (%): Hispanic: 60 (48.4) vs. 57 (47.1); White 60 (48.4) vs. 58 (47.9); Other: 4 (3.2) vs. 6 (5)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: antihypertensives, insulin and antidiabetics, beta-adrenoreceptor blockers, hypnotics, sedatives, anxiolytics, anti-inflammatory analgesics, diuretics, hyperlipidemia tx</p> <p>Duration of ED, mean (range): 3.7 (0.5 – 25.6) vs. 3.4 (0.5 – 21.7) y</p> <p>Underlying disease (diagnosis); n (%): Hypertension 36 (29) vs. 29 (24); DM 30 (24) vs. 22 (18); Prostatic hyperplasia 6 (5) vs. 8 (7); Visual disturbance 5 (4) vs. 7 (5.8)</p> <p>Psychogenic ED; n (%): 25 (20.2) vs. 18 (14.9)</p> <p>Physiologic ED: Organic: 51 (41.2) vs. 50 (41.3)</p> <p>Mixed ED; n (%): 48 (38.7) vs. 53 (43.8)</p>	<p>IG: Sildenafil citrate CG: Placebo</p> <p>IG: Dose: 25, 50 or 100mg Duration: 12 wks Frequency: once daily 1 hr before sexual activity Compliance (%): 91</p> <p>CG: Dose: NA Duration: 12 wks Frequency: once daily 1 hr before sexual activity Compliance (%): 89</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF, mean (SE): Q3 (penetration): 3.93 (0.15) vs.2.56 (0.16) Q4 (maintained erections after penetration): 3.83 (0.15) vs. 2.33 (0.15) GEQ, % improved erection: 81% vs. 36% GEQ, % with successful intercourse: 71% vs. 32% % maximal domain score from graph³⁰: baseline (pre); post intervention IG vs. CG EF: pre 40; post 75 vs. 50 OF: pre 59; post 84 vs. 68 SD: pre 70; post 79 vs. 70 IS: pre 44; post 69 vs. 55 OS: pre 40; post 76 vs. 50</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 15 (12.1) vs. 16 (13.2)</p> <p>WDAE, n (%): 1 (0.8) vs. 0 TAE (%): 35% vs. 20%, flushing 11(8.9), vs. 0; headache 15 (12) vs. 6 (5); dyspepsia 9 (7) vs. 0; rash 5(4) vs. 0; dizziness 4(3) vs. 1(0.8); abnormal vision 4 (3.2) vs. 1 (0.8); rhinitis 3(2.4) vs. 1(0.8) SAE: 1 (<1) vs. 5 (4), no reasons provided</p> <p>Ascertainment of outcomes assessed: Q3 and Q4 and GEQ²⁹ 15 item IIEF questionnaire, and event log</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (1998)³¹ Companion³²</p> <p>Study a</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 532 (dose response)</p> <p>IG, n = 316 (completers: IG1, n = 96; IG2, n = 105; IG3, n = 101) CG, n = 216 (completers =199)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men in stable relationship 6 mo or longer, with ED confirmed by clinical exam and IC injection of vasoactive drug (31% of men), normal NPT, penile duplex ultrasonography, and endocrine testing</p> <p>Exclusion: penile deformities, another sexual disorder; SCI, major psychiatric dx; poorly controlled DM; peptic ulcer dx, hx or alcohol or substance abuse; hematologic, renal or hepatic abnormalities, recent stroke or MI in last 6 mo; nitrate therapy</p>	<p>Age, mean (range): 58 (24-87) vs. 57 (20-79) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 3.2 y</p> <p>Underlying disease (% of pts): hypertension 30 vs. 26; ischemic heart dx 8; hyperlipidemia 19 vs. 16; hx or radical prostatectomy 12 vs. 10; DM 13 vs. 15</p> <p>Psychogenic ED (%): 9 vs. 10</p> <p>Physiologic ED (%): 78 vs. 77</p> <p>Mixed ED (%): 13 (both grps)</p>	<p>IG1/3: Sildenafil- oral CG: placebo- oral</p> <p>IG1-3: Dose: 25 mg (IG1), 50 mg (IG2), 100 mg (IG3) Duration: 24 wk Frequency: once/d (one hr prior to sexual activity) Compliance: 97%</p> <p>CG: Dose: NA Duration: 24 wk Frequency: as IG Compliance: 99%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 24 wks</p>	<p>Primary outcome results: IIEF, Q3/ Q4 (similar values for both), mean (sd) score: Baseline: IG=CG 2 (0.2); Post tx: 3-4 (0.2) vs. 2 (0.2) IIEF-EF: increase in score with dose escalation, IG vs. CG p<0.001 Grade 3 or 4 erection, (%): 72, 80, 85 vs. 50% (80% of grade 3 and 94% of grade 4 erections resulted in intercourse; positive dose response) Improved erection (% of pts): 56, 77, 84 vs. 25, p< 0.001</p> <p>Other outcomes assessed: IIEF, Q6, 7, 8, 13 and 14 (> in IG); SD (no change)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%):IG=31 (10) [15 (15), 8 (7), 8 (7)] vs. CG =36 (17)</p> <p>WDAE: 4 (1) vs. 1 (<1) TAE, n (%): in 5% of pts or more IG 15 (15)/ 8 (7)/ 8 (7) vs. CG 36 (17); AE included headache 14-32 (14-30) vs. 14 (6); flushing 13-29 (13-27) vs. 3 (1); dyspepsia 3-17 (3-16) vs. 3 (1); rhinitis 1-12 (1-11) vs. 4 (2); visual disturbance 2-10 (2-9) vs. 1 (<1) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; ED validated questionnaire; self report event log (grading system)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (1998) 31</p> <p>Study b</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 329; (dose escalation + open label extension)</p> <p>IG, n = 163 CG, n = 166</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men in stable relationship 6 mo or longer, with ED confirmed by clinical exam and IC injection of vasoactive drug (31% of men), normal NPT, penile duplex ultrasonography, and endocrine testing</p> <p>Exclusion: penile deformities, another sexual disorder; SCI, major psychiatric dx; poorly controlled DM; peptic ulcer dx, hx or alcohol or substance abuse; hematologic, renal or hepatic abnormalities, recent stroke or MI in last 6 mo; nitrate therapy</p>	<p>Age, mean (range): 60 (26-79) vs. 59 (31-81) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 5 y</p> <p>Underlying disease (% of pts): hypertension 24 vs. 28; ischemic heart dx 15 vs. 8; hyperlipidemia 15 vs. 14; hx or radical prostatectomy 9 vs. 11; DM 8 vs. 11</p> <p>Psychogenic ED, n (%): 14 vs. 16</p> <p>Physiologic ED, n (%): 55 vs. 63)</p> <p>Mixed ED, n (%): 31 vs. 22</p>	<p>IG: Sildenafil -oral CG: placebo- oral</p> <p>IG: Dose: 50 mg (titrated at each f/u visit to double or 50% less based on the therapeutic response and AE) Duration: 12 wk Frequency: once/ d (one hr before sexual activity) Compliance: 94</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: 92</p> <p>Run In period: Wash out period:</p> <p>F/u duration: 12 wk (also at end of open label study of 32 wks)</p>	<p>Primary outcome results: IIEF, Q3/ Q4 mean (sd) score: Baseline (IG=CG): 2 (0.1)/ < 2 (0.1) post tx: 4 (0.1) vs. 2 (0.1)/ 4 (0.1) vs. 1.8 (0.1) IIEF-EF, mean score: 22 vs. 12, p<0.001 Successful attempts of sexual intercourse (%): 69 vs. 22 Mean n of successful attempts in last 4 wks: 6 vs. 1.5</p> <p>Improved erection, n (%): 101 (74) vs. 23 (19), p< 0.001</p> <p>Other outcomes assessed: IIEF, Q6, 7, 8, 13 and 14 (> in IG); SD (no change)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 9 (6) vs. 13 (8), open label (n=225)= 18 (8)</p> <p>WDAE, n (%): TAE, n (%): in 5% or more of all IG vs. CG/ IG open label: headache 30(18) vs. 14 (6)/ 28 (12); flushing 30 (18) vs. 1 (1)/ 22 (10); dyspepsia 9 (6) vs. 4 (2)/ 12 (5); rhinitis 8 (5) vs. 1(1)/ 4 (2); visual disturbance 4(2) vs. 1 (1)/ 9 (4) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; questionnaire for clinical assessment of ED, & tx outcomes; self report by event log; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (1998) 33</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 861</p> <p>Study I dose-response IG1, n = 316 CG1, n = 216</p> <p>Study II dose-escalation IG2, n = 163 CG2, n = 166</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men with ED of 6 mo or longer, in a stable relationship with a female partner for at least 6 mo</p> <p>Exclusion: penile anatomical defects, another sexual disorder; SCI; major psychiatric disorder, poorly controlled DM; peptic ulcer disease, hx of alcohol or substance abuse, major systemic abnormalities, recent stroke or MI; nitrate therapy</p>	<p>Age, mean: 58 (NR)</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: (n/grp) NR</p> <p>Duration of ED: NR, at least ≥ 6 mos.</p> <p>Underlying disease (%): 100 ED</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>Study I dose-response IG: oral sildenafil CG: oral placebo</p> <p>IG: Dose: 25 or 50 or 100 mg Duration: 12 wks Frequency: NR Compliance: NR</p> <p>CG: placebo (same as IG1)</p> <p>Study II dose-escalation: IG1: oral sildenafil CG: oral placebo</p> <p>IG1: Dose: 50 mg (dose could be doubled or reduced by 50% at f/u) Duration: 24 wks Frequency: NR Compliance: NR</p> <p>CG: placebo (same as IG1)</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: dose-response 12 wks dose-escalation 24 wks</p>	<p>Primary outcome results: IIEF, % increase from baseline in IG vs. CG: Q3, successful penetration Study I: 60 (25 mg), 84 (50 mg), 100 (100 mg) vs. CG 5 (p < 0.001); Study II, 95 vs. 10 (p < 0.001)</p> <p>Q4, maintaining erection Study I: 121 (25 mg), 133 (50 mg), 130 (100 mg) vs. 24 (p < 0.001); Study II: 140 vs. 13 (p < 0.001)</p> <p>All domains Study I & II: IG sign. higher with each dose vs. CG (p < 0.001)</p> <p>GEQ, % increase from baseline Study I: 56 (25 mg), 77 (50 mg), 84 (100 mg) vs. CG 25 (p < 0.001) Study II: 74 vs. 19 (p < 0.001)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR (AE in IG included headache, flushing, dyspepsia, transient visual disturbances) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; GEQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gómez (2002) ³⁴</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 159</p> <p>IG, n = 76 CG, n = 82</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: men 18 or older; with ED for 6 mo or longer; in stable relationship with female partner for at least 6 mo</p> <p>Exclusion: genital anatomic deformity; hyperprolactinemia; low free T level ;uncontrolled psychiatric disorders; alcoholism or substance abuse; hx of major hematological, renal or hepatic abnormality; uncontrolled DM; untreated proliferative diabetic retinopathy; hx of stroke, MI or CVD in last 6 mo; hypotension; known hx of retinitis pigmentosa; medication causally associated with ED; taking androgens, trazodone, nitrates (or nitric oxide donors); used vacuum devices, IC injection or any other ED tx</p>	<p>Age, mean (sd): 58 (11) vs. 55 (12) y</p> <p>Race, n (%): White 20 (13) Black 4 (2.5) Hispanic (mestizo) 123 (77) Other 11 (7)</p> <p>Co-morbidities: Hypotension 25 (33) vs. 17 (21) DM 13 (17) vs. 9 (11)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 3 (0.4-12) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 10 (13) vs. 16 (20)</p> <p>Physiologic ED, n (%): IG1 48 (63) vs. 44 (54)</p> <p>Mixed ED, n (%): 18 (24) vs. 22 (27)</p>	<p>IG: Sildenafil CG: placebo</p> <p>IG: Dose: 50 mg; titration to 25 or 100 mg Duration: 12 wk Frequency: NR Compliance (%): NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: NR Compliance (%): NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IIEF, change in mean score (approximate values from figure): Q3: 1.6 vs. 0.8 Q4: 1.8 vs. 0.8 EF: pre=13.6; post 22.1 vs. 18.4 OF: pre=6.9; post: 8.4 vs. 7.7 SD: pre=7; post 7.3 vs. 7.1 IC s: pre=7.4; post 10.8 vs. 9.4 OS: pre=4.6; post: 7.5 vs. 6.3 GAQ, % yes: 77 vs. 46 Successful intercourse attempts (last 4 wks), %: 65 vs. 35</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 12 (16) vs. 10 (12)</p> <p>WDAE, n (%): 1 syncope (1) vs. 0 TAE: pts with at least one AE=39 (51) vs. 27 (33); including headache 19 (25) vs. 10 (12); flushing 9 (12) vs. 6 (7); dyspepsia 5 (7) vs. 0; rhinitis 5 (7) vs. 1 (1); abnormal vision 5 (7) vs. 4 (5); conjunctivities 3 (4) vs. 0; diarrhea 3 (4) vs. 2 (2); chromatopsia 2 (3) vs. 0; palpitation 1 (1) vs. 2 (2); dizziness 0 vs. 3 (4); gastritis 0 vs. 2 (2); also laboratory abnormalities elevated blood urea nitrogen level in 4 (10) vs. 1 (1), elevated creatinine level in 3 (8) vs. 0; SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF (EF=1-5,15), event log on sexual function</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gopalakrishnan (2006)³⁵</p> <p>Funding source: Christian Medical College grant; Sun Pharmaceuticals provided the medication</p>	<p>N screened = 150 (40 were identified with ED) N randomized = 32 (randomized two way cross over)</p> <p>IG/CG, n = 32</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: married men with schizophrenia or delusional disorder on current tx; with ED</p> <p>Exclusion: regular use of nitrates, anticoagulants, or aspirin 2 wks prior to study entry; comorbid depressive syndrome; tx with antidepressants; alcohol or other substance dependence; hx of use of sildenafil citrated and continued use of other measures to improve ED</p>	<p>Age, mean (sd): 35.1 (5.5), range 24-45 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): paranoid schizophrenia 20 (62.5); catatonic schizophrenia 1 (3), undifferentiated schizophrenia 5 (16), delusional disorder 3 (9.3),</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: all pts on chlorpromazine equivalents dose 556.3 (198.6) range 200-1000 mg; mean dose of trihezyphenidyl 1.2 mg/d; 3 pts also on diazepam</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): as in comorbid conditions</p> <p>Psychogenic ED, n (%): 10%</p> <p>Physiologic ED, n (%): 0</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 25 mg titrated to 50 mg based on efficacy outcomes at 1st wk Duration: 2 wks Frequency: up to 1/d Compliance: 100%</p> <p>CG: Dose: NA Duration: 2 wks Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: none</p> <p>F/u duration: end of each 2 wks period</p>	<p>Primary outcome results: N of grade 3 or 4 erections, mean (sd) combined for two wks of tx: 6.52 (3.92) vs. 3.32 (3.5); P< 0.001</p> <p>duration of erection, mean (sd): 3.38 (2.25) vs. 2.20 (2.14) min, P<0.055</p> <p>Combined N of satisfactory intercourse attempts, mean (sd): 5.29 (3.84) vs. 2.45 (3.33); P<0.001</p> <p>Other outcomes assessed: tx interaction effects (NS)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1(3)</p> <p>WDAE, n (%): 0 TAE: 13 (41) vs. 3 (9.3) AEs, n (%): nasal congestion 4 (12.5) vs. 0; headache 3 (9.4) vs. 1 (3.1); loss of appetite 1 (3.1) vs. 0; retarded ejaculation 2 (6.3) vs. 1 (3.1); dyspeptic symptoms 1 (3.1) vs. 1 (3.1); giddiness 1 (3.1) vs. 0; rash 1 (3.1) vs. 0 SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: pts log</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Hartmann (1999) ³⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 315</p> <p>IG, n = 159 CG, n = 156</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older with documented diagnosis of ED for 6 mo or longer</p> <p>Exclusion: other sexual disorders, high serum PRL levels, low levels of free testosterone. Hx of renal, hepatic, haematological or bleeding disorders. Stroke or myocardial infarction \leq 6 mons, poorly controlled diabetes, retinitis pigmentosa, treatment with androgens, trazadone, nitrates, nitrogen oxide donors</p>	<p>Age, mean: IG1: 54 CG: 55</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): IG1: 5 CG: 5</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 50</p> <p>Physiologic ED, %: 46</p> <p>Mixed ED, %: 54 Unknown: 3 vs. 6%</p>	<p>IG: sildenafil CG: oral placebo</p> <p>IG1: Dose: 25 mg option to titration to 50 or 100 mg Duration: 26 wks Frequency: as needed Compliance (%): NR</p> <p>CG: Dose: NA Duration: 26 wks Frequency: as IG Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (both on and off treatment): NR</p> <p>Other: Final doses: 25 m: in 25% 50 mg in 26% 100 mg in 49%</p>	<p>Primary outcome results: IIEF, Q7, mean: pre= 2.0; post tx: 3.6 vs. 2 IIEF, Q3, and 4: as Q7 GEQ, % improved: 79% vs. 23%</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 13 (8) vs. 0</p> <p>WDAE, n (%): 8 (5) vs. 0 TAE: NR; most common AE reported headache, flushing, dyspepsia, rhinitis, respiratory tract infection (could not be extracted from table, bad scan); visual disturbances NR (1) vs. 0 SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF Q3, 4, 7, 13, and GEQ, Patient logbook</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Heiman (2007) 37</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 180</p> <p>IG, n = 86 CG, n = 94</p> <p>ITT analysis used for primary outcome: yes (n=85 vs. n=91)</p> <p>Inclusion: men 21 y or older with ED (score of 21 or less on Sexual Health Inventory for Men) and in stable relationship with female partner; with satisfactory sexual intercourse of 50% or less as reported by their female sexual partner</p> <p>Exclusion: couple with sign. dyspareunia or lifelong sexual dysfunction or men with more than six doses of any ED tx including PDE-5 inhibitor within 6 mo; use of nitrates, nitric oxide donors; medical or psychological conditions (i.e. CV, arthritis, hx of retinitis pigmentosa)</p>	<p>Age, mean (range): 58 (30-86) y</p> <p>Race: White 79%; Black 7%; Asian 2%; other 12.5%</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: current smokers 15% vs. 19% (43% never smoked)</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED, mean (range): 4.7 (0.2-21.6) vs. 6.1 (0.1-34.7) y</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED (%): 16 vs. 12</p> <p>Physiologic ED (%): 59 vs. 62</p> <p>Mixed ED (%): 24 vs. 27</p> <p>Other: IIEF baseline score, mean= 46.3 vs. 48.8; EF domain=13.2 vs. 12.6; OF domain= 5.6 vs. 5.5; SD domain=6.3 in both grps; IcS=6.7 vs. 6.1; OS=5; Q7=2.3 vs. 2.1</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: flexible dose 25, 50, and 100 mg Duration: 12 wks Frequency: as needed, 30 min to 1 hr prior to sexual activity Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 2 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF, change from baseline mean (SE): EF domain: 8.9 (1) vs. 3.4 (1) OF domain: 1.5 (0.4) vs. 0.9 (0.4) SD domain: 0.4 (0.2) vs. 0.1 (0.2) ICS domain: 2.1 (0.3) vs. 0.8 (0.3) OS domain: 2.1 (0.3) vs. 0.8 (0.3) Q7: 1.5 (0.2) vs. 0.3 (0.2) GEQ, % improved (95% CI): GEQ-1: 69 (57-79) vs. 25 (16-36) GEQ-2: 71 (60-80) vs. 30 (20-41)</p> <p>Other outcomes assessed: responses in partner; EDIT scores, SEAR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 21 (12)</p> <p>WDAE, n (%): 0 TAE, n (%): reported as tx related AE: 29 in 18 (21%) vs. 11 in 10 (11%) of pts; including one severe case of rhinitis in IG, and one severe headache in CG Most common AE: headache, vasodilatation, rhinitis, dyspepsia, and abnormal vision or chromatopsia (n=3 vs. 1) SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: EDITS; IIEF; Self-Esteem And Relationship (SEAR)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Herrmann (2006) ³⁸</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 16 (recruitment stopped; difficult recruitment due to concurrent release of vardenafil and tadalafil) N randomized = 12</p> <p>IG, n = 8 CG, n = 4</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with moderate to severe ED despite an adequate sildenafil trial, of max 100 mg (ED defined as IIEF score of 16 or less); with serum low density lipoprotein (LDL) cholesterol 100 mg/dL or higher</p> <p>Exclusion: hx of Psychogenic ED; severe endocrinopathy including diabetics with neuropathy, recent surgery including prostatectomy; acute</p>	<p>Age, mean (sd): 58 (13) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM 12% vs. 25%; elevated cholesterol 10 (83); hypertension 4 (33)</p> <p>Previous ED treatment:</p> <p>Smoking status: 38% vs. 75%</p> <p>Body weight: NR</p> <p>Other: LDL cholesterol 139 (19) vs. 146 (10) mg/dL; N of pts with DM is not consistently reported (text: n=2, 17% in total)</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: 4.2 (4.8) vs. 2.6 (2.9) y</p> <p>Underlying disease, n (%): as co-morbidities</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): all</p> <p>Mixed ED, n (%): NR</p> <p>Other: IIEF- EF domain at baseline, mean (sd) 10.2 (7.4) vs. 4 (3.6)</p>	<p>IG: Sildenafil + Atorvastatin CG: Sildenafil + placebo</p> <p>IG: Dose: Sildenafil 100 mg up to once/d; Atorvastatin 80 mg/d Duration: 12 wks Frequency: once /d (each medication) Compliance:</p> <p>CG: Dose: sildenafil as IG + Atorvastatin placebo tablets Duration: 12 wks Frequency: as IG Compliance:</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF, Q-15, mean (sd): Baseline 10.3 (7.4) vs. 4 (3.6) Post tx (12 wks): 18 (10.6) vs. 12.3 (12.4); influenced by single outlier increasing from 9 to 29; increase in post tx score excluding this pts = 4.3 (sildenafil grp ▲ by 7.8)</p> <p>IIEF-Q6: improved in 100% vs. 25%</p> <p>GAQ-1, % improved: 62.5% vs. 25% GAQ-2, % improved: 62.5% vs. 25% GAQ, % improved: 62.5% vs. 25%</p> <p>Other outcomes assessed: LDL cholesterol levels ▼ from 135 (19) to 78 (20) mg/dL, or 43% with Atorvastatin vs. from 146 (10) to 139 (24) in placebo</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; Blood analysis for lipid profile</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Hussain (2001) 39</p> <p>Funding source: Pfizer</p>	<p>N screened = 24 N randomized = 17 (crossover design)</p> <p>IG/CG, n = 24</p> <p>ITT analysis used for primary outcome: N</p> <p>Inclusion: Parkinson's (PD) disease or multiple system atrophy (MSA); resting and standing SBP 90-180 mm hg, and DBP 50-110 mm Hg, on tx if necessary</p> <p>Exclusion: no stable sexual partner; penile deformity; other sexual or psychological disorder; known hx of alcohol or drug dependence; DM; retinitis pigmentosa; hx of stroke or MI; sign cardiac hx; nitrate therapy; lipid abnormality; thyroid, renal, hepatic or hematologic dx</p>	<p>Age, median (range): PD 61 (48-68) MSA 54 (46-61) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease, n (%): PD 12 (97) MSA 6 (33)</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED, %: 100</p> <p>Mixed ED: 0</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG: Dose: 50 mg with option of titrate to 100 or 25 mg Duration: 10 wks Frequency: up to once/d, 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: placebo, titration option as IG Duration: 10 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: None</p> <p>F/u duration: 20 wk (cross over at 10 wks without washout)</p>	<p>Primary outcome results: (CG, n=16; IG n=14) IIEF-Q3, mean: 3 vs. 2 IIEF-Q4, mean: 4 vs. 1.4</p> <p>Quality of life questionnaire: Whole life, mean: 4.9 vs. 4.7 Sex life, mean: 4.2 vs. 2.2</p> <p>Other outcomes assessed: Partner questionnaire</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 8 (27) including one pts in PD due to lack of efficacy, pt chose to return to IC injections.</p> <p>WDAE: 3 (12.5) in (50% of MSA pts) TAE: NR; 3 events of orthostatic hypotension (fall in standing BP), feeling unwell and unable to stand in IG (MSA) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF, quality of life (0-5 for each questions)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Incrocci (2001) 40</p> <p>Funding source: Pfizer B.V., The Netherlands</p>	<p>N screened = 82 N randomized = 60 (cross-over)</p> <p>IG/ CG = 30</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men with progressive ED after 3-dimensional conformal external beam radiotherapy (3D-CRT) for prostate who agreed to perform sexual activity at least once/ wk; in a stable relationship</p> <p>Exclusion: hx of MI or CVA, prior radical prostatectomy; post-radiotherapy rise in PSA; use of nitrates or hormone therapy</p>	<p>Age, mean: 68 y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: None</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: PSA/micrograms, mean (range): 8.5 (1-227) litre</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): time from radiation to trial 39 (15-55) mo</p> <p>Underlying disease (%): Hypertension: 10%; DM 3%; Transurethral resection of the prostate: 18%</p> <p>Psychogenic ED: NA</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NA</p>	<p>IG: sildenafil CG: placebo</p> <p>IG1: Dose: 50 mg with option to increase to 100 at 2 wks, or decrease to 25 mg in case of AE Duration: 6 wks Frequency: at least 1/wk, up to 1/d Compliance (%): 100%</p> <p>CG: Dose: NA Duration: 6 wks Frequency: at least 1/wk, up to 1/d Compliance (%): 100%</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks (assessments at end of each 6 wks period)</p> <p>Other: 90% patients ▲ dose to 100 milligrams, 0% ▼ to 25 mg</p>	<p>Primary outcome results: IIEF baseline mean; post tx mean (sd) IG vs. CG</p> <p>Q1: 1.7; post 2.9 (1.6) vs. 1.8 (1.1) Q2: 1.5; post 2.8 (1.8) vs. 1.5 (1.1) Q3: 1.5; post 2.8 (1.7) vs. 1.6 (1.1) Q4: 1.3; post 2.6 (1.7) vs. 1.5 (1.0) Q5: 1.6; post 2.8 (1.1) vs. 1.8 (1.4) Q6: 1.2; post 2.8 (1.1) vs. 2.4 (1.0) Q7: 1.9; post 2.7 (1.6) vs. 1.9 (1.3) Q8: 1.6; post 2.8 (1.4) vs. 1.9 (1.1) Q10: 2.1; post 3.0 (1.6) vs. 2.4 (1.6) Q11: 2.8; post 3.0 (1.1) vs. 2.8 (1.2) Q12: 2.7; post 3.0 (1.0) vs. 2.6 (1.0) Q13: 2.3; post 3.0 (1.4) vs. 2.3 (1.2) Q14: 2.7; post 3.2 (1.4) vs. 2.8 (1.4) Q15: 2.1; post 3.0(1.1) vs. 2.4 (1.3) GEQ, % with improved: 45 vs. 8 Successful intercourse %: 55 vs. 18</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: AEs (%)= headache: 42 vs. 15; flushing: 13 vs. 2; myalgia 15 vs. 13; nasal congestion 22 vs. 12; dyspepsia 32 vs. 8; dizziness 17 vs. 10 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; GEQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Incrocci (2003) 41</p> <p>Funding source: Pfizer B.V.</p>	<p>N screened = NR N randomized = 60 (6 wk cross over); also open label phase</p> <p>IG, n = 30 CG, n = 30</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: progressive ED after 3 dimensional external beam radiotherapy for prostate cancer; normal EF before radiotherapy; in stable relationship</p> <p>Exclusion: use of nitrates</p>	<p>Age, mean (range): 68 (56-79) y</p> <p>Race (%): NR</p> <p>Co-morbidities: diabetes and/or hypertension 13%</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: Mean interval between completion of radiotherapy and study initiation = 39 mo (range 15-55)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NA</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: N</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil citrate orally CG: placebo orally</p> <p>IG: Dose: 50 mg for first 2 wk; option to increase to 100 mg for next 4 wk Duration: 6 wk Frequency: up to once/d, 1 hr before sexual activity at least once/ wk Compliance: NR</p> <p>CG: Dose: placebo Duration: 6 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: None</p> <p>F/u duration: 6 and 12 wks (last fu at 2 y)</p>	<p>Primary outcome results: Mean IIEF mean score (sd), IG vs. CG: Q1- pre: 2 (2); post: 3 (2) vs. 2 (1) Q2- pre: 2 (2); post: 3 (2) vs. 2 (1) Q3=Q4=Q5=Q7: pre: 2 (1); post: 3 (2) vs. 2 (1) Q6- pre: 1 (1); post: 3 (1) vs. 2 (1) Q9- pre: 2 (2); post: 3 (2) vs. 2 (1) Q10- pre: 2 (2); post: 3 (2) vs. 2.5 (2) Q11- pre: 3 (1); post: 3 (2) vs. 3 (1) Q12- pre: 3 (1); post: 3 (1) vs. 2.6 (1) Q13- pre: 2 (1); post: 3 (1) vs. 2 (1) Q14- pre: 3 (1); post: 3 (1) vs. 2.8 (1) Q15- pre: 2 (1); post: 3 (1) vs. 2.3 (1) GAQ1, %: 61 vs. NR GAQ2, %: 65 vs. NR</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: NR; % with AE (IG vs. CG/ IG open label): headache 42 vs. 15/17; flushing 13 vs. 2/11; myalgia 15 vs. 13/6; nasal congestion 22 vs. 12/11; dyspepsia 32 vs. 8/24; vision disturbances 17 vs. 8/13; dizziness 17 vs. 10/6 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, GEQ, 1 and 2</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kaplan (2007) ⁴²</p> <p>Funding source: Pfizer (conflict of interest reported)</p>	<p>N screened = N randomized = 62 (single center; open label)</p> <p>IG1, n = 21 IG2, n = 20 CG, n = 21</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men with self reported ED and untreated LUTS</p> <p>Exclusion: criteria complied with contraindication of both drugs</p>	<p>Age, mean (sd): 63.4 (7.6) y</p> <p>Race: NR</p> <p>Co-morbidities, %: DM 27.4; hypertension 25.8%; Ischemic heart disease 14.5</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: 24.8 (4.3) mo</p> <p>Underlying disease, n (%):</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: Sildenafil IG2: Alfuzosin CG: Sildenafil + Alfuzosin</p> <p>IG1: Dose: 25 mg Duration: 12 wks Frequency: one/d Compliance:</p> <p>IG2: Dose: 10 mg Duration: 12 wks Frequency: one/d Compliance: NR</p> <p>CG: Dose: combination of IG1 and IG2 doses Duration: 12 wks Frequency: one of each/d Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF mean (sd) Q3: baseline 2.2 (0.9); % improvement from baseline 41.7% vs. 27.3% vs. 65.2% Q4: baseline 2.3 (1.1); % improvement from baseline 59.1% vs. 33.3% vs. 68.2%</p> <p>EF domain: baseline 15.9 (3.2); post tx IG= 21.4 (5.7) vs. IG2=20.3 (5.2) vs. IG3=25.7 (4.9); % change from baseline: 49.7% vs. 16.7% vs. 58.6%</p> <p>Other outcomes assessed: IPSS; PVRU volume</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 7 (11)</p> <p>WDAE, n (%): total 7 (11); 2 (10) vs. 2 (10) vs. 3 (14) TAE: NR; AE flushing and dyspepsia in sildenafil grp vs. dizziness in Alfuzosin vs. dizziness in combination grp SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF-EF; International Prostate Symptom Score (IPSS); post-void residual urine (PVRU) volume</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Katz (2005) ⁴³</p> <p>Funding source: Pfizer</p>	<p>N screened = 202 N randomized = 137 (parallel design)</p> <p>IG, n = 63 CG, n = 74</p> <p>Intention to Treat (ITT): Yes (IG, n=60; CG n=72)</p> <p>Inclusion: men 18 y or older, with ED, (Sexual Health Inventory for Men score of 21 or greater), & documented evidence of stable coronary heart failure (CHF); naïve to sildenafil (discontinue at least by screening visit)</p> <p>Exclusion: hypotension, high cardiac risk, CHF secondary to hypertrophic cardiomyopathy; hx or myocarditis or implantable defibrillator firing 6 mo prior to entry; use of organic nitrates, drugs that inhibit cytochrome P450 (i.g. ritonavir) Data reported as IG vs. CG (unless otherwise indicated)</p>	<p>Age, mean (range): all, 60 (38-83) y</p> <p>Race (%): NR</p> <p>Co-morbidities: all pts had one or more conditions including diabetes, hypercholestrmia, hypertension, ischemic heart dx, past coronary bypass</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 22% in both grps; 19% vs. 33% were ex-smokers</p>	<p>Concomitant medications: ACE inhibitors; angiotension II receptor antagonist (29% vs. 15%); β blockers; loop diuretics, cardiac glycosides, oral anticoagulants, analgesics fro mild to moderate pain (11% vs. 22%)</p> <p>Duration of ED, mean (range): 5 (0.1-22) y</p> <p>Underlying disease: CHF, duration of 6 (0.27-31.7) vs. 4.8 (0.03-22.2) y</p> <p>Psychogenic ED, %: 2 vs. 1</p> <p>Physiologic ED, %: 57 vs. 56</p> <p>Mixed ED, %: 41 vs. 43</p>	<p>IG1: Sildenafil CG: placebo</p> <p>IG1: Dose: 50 mg, adjusted to 25 or 100 mg based on pts tolerability & efficacy Duration: 12 wk Frequency: NR Compliance (%): NR</p> <p>CG: Dose: NR Duration: as IG Frequency: NR Compliance (%): NR</p> <p>Run In period: 2 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: Baseline (mean); post tx (least square mean) scores: Q3 (improved erections): pre=1.7; post: 3.7 vs. 2.8 (p=0.0003); [74% of pts vs. 18% improved, (<0.002)] Q4 (improved intercourse), mean score: pre=1.4 post: 3.3 vs. 2.4 (p = 0.0012); [68% vs. 16% improved (p<0.002)] IIEF, EF: pre=33; post 71 vs. 53 IIEF Q9, 10: pre=45; post 77 vs. 67 IIEF Q11, 12: pre=61; post 69 vs. 63 IIEF, Q6, 8: pre= 35; post 69 vs. 55 IIEF, Q13, 14: pre=39; post: 79 vs. 58 Intercourse success (%): 53 vs. 20, Improved erection, %: 74 vs. 18 Improved intercourse, %: 68 vs. 16 Other outcomes assessed: IIEF Q 5-12; GEQ; life satisfaction check list; EDITS</p> <p>Withdrawals/drop-outs/loss to f/u: 20 (16) vs. 10 (14)</p> <p>WDAE: 2 (3) vs. 2 (3) TAE: (% of pts) 60% vs. 48% (headache 13% vs. 3%, also respiratory tract infection, asthenia, peripheral edema, rhinitis, back pain, rash, pain in both grps; vasodilatation; ▲ cough, neoplasm, chromatopsia only in IG) SAE: 3% vs. 5%</p> <p>Ascertainment of outcomes assessed: self administered IIEF; GEQ, EDITS</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kongkanand (2003) ⁴⁴</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 125</p> <p>IG, n = 63 CG, n = 62</p> <p>ITT analysis used for primary outcome: yes (n=125)</p> <p>Inclusion: men ED \geq 6 mo, stable heterosexual relationship \geq 6 mo.</p> <p>Exclusion: Genital deformities, SCI, co-existing sexual disorders, raised serum PRL levels or low free T level, major psychiatric disorder, hx of alcohol or substance abuse; major haematological, renal or hepatic dx, DM; poorly controlled or associated with untreated proliferative retinopathy; hx of stroke or MI \leq 6 mo; hypotension or other sign CV dx, hx of retinitis pigmentosa; taking drugs associated with ED; use of vacuum devices or other tx for ED.</p>	<p>Age, mean (range): 54 (31-76) vs. 56 (26-77)</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): Smokers: 11 (18) vs. 9 (15)</p> <p>Body weight, mean: 68 vs. 69, range 54-90 kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, n (%): \leq 2 y: 42 (67) vs. 35 (57); >2 to \leq 5 y: 15 (24) vs. 20 (32) > 5 y: 6 (10) vs. 7 (11)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 7 (11) vs. 6 (10)</p> <p>Physiologic ED, n (%): 41 (65) vs. 39 (63)</p> <p>Mixed ED, n (%): 15 (24) vs. 17 (27)</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG: Dose: initially 50 mg for 2 wks, then option to titrate up to 100 mg or down to 25 mg Duration: 12 wks (median= 84 d) Frequency: as needed Compliance (%): 92</p> <p>CG: Dose: NA Duration: 12 wks (median=83 d) Frequency: as needed Compliance (%): 84</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IIEF, Q3 frequency of penetrate, mean: baseline= 2; post tx: 4 vs. 3 IIEF, Q4, frequency of maintaining erection after penetration, mean: baseline=2; post tx: 4 vs. 3 IIEF, EF, mean: baseline=13; post tx: 22 vs. 17 IIEF, OF, mean: baseline=5, post tx: 8 vs. 5 IIEF, SD, mean: baseline=5, post tx: 7 vs. 6 IIEF, intercourse satisfaction, mean: baseline=6; post tx 11 vs. 9 Intercourse success, %: 66 vs. 32 GAQ, % yes: 82 vs. 36</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1 (2) in CG</p> <p>WDAE: 0 TAE, n (%): 19 (30) vs. 7 (11); including: flushing = 14%; headache = 6%; dizziness = 6%; laboratory abnormalities: included raised levels of eosinophils, total bilirubin, and blood urea nitrogen 1 (2) in IG; 4 sign laboratory abnormalities in n=2 in CG SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, pts event log, GAQ, physical exam</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Koulikov (2007) 45</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 82 N randomized = 60 (crossover)</p> <p>IG, n = 30 CG, n = 30</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men between 45 and 75 y and older with ED and various urological complaints (LUTS, ED and nephrolithiasis), and diagnosis of ADAM (direct Tb less than 0.7 gm/l were defined as hypogonadal)</p> <p>Exclusion: penile anatomical defects; uncontrolled medical illness or psychological disorders; pts with high cardiac risk (according to Princeton guideline); or regular or intermittently use of drugs that alter androgen metabolism or hx of PDE-5i</p>	<p>Age, mean (SEM): 63.3 (7.85), range 47-75 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): hypogonadal 27 (48), low total T in 13/27</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): various urological reasons</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg, titrated to 100 mg after 2 wks (if no improvement in EF with at least 3 pills) Duration: 1 mo Frequency: one pill 30-60 min before planned sexual activity up to once/d Compliance: NR</p> <p>CG: Dose: NA Duration: 1mo Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: at end of each tx period (each study period was 3 mo; washout and run in is not reported).</p>	<p>Primary outcome results: Improvement in EF, mean (SEM): 39 (1.9) vs. 52.7 (2)</p> <p>Improvement in IIEF-EF from baseline, mean (SEM): Normal men: 18.4 (3.6) Hypogonadal men: 6.7 (2.7) (no difference in baseline scores of EF between normal and hypogonadal men)</p> <p>Other outcomes assessed: FSH, LH, Total T, and Tb (numerical data NR)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 19 (63.3) vs. 12 (40)</p> <p>WDAE, n (%): 1 (3.3) vs. 1 (3.3) TAE, n (%): difficulty in controlling BP 0 vs. 1 (3.3); non-Q MI 1(3.3) before ingestion of first tablet vs. 0 SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: serum hormone analysis</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Levinson (2003) 46</p> <p>Funding source: Pfizer</p>	<p>N screened = 279 N randomized = 279</p> <p>IG, n = 128 CG, n = 126</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older with ED of at least 6 mo in duration; in a stable relationship</p> <p>Exclusion: penile abnormalities; SCI, concomitant tx with nitrates, endocrine anomalies; major haematological, renal, or hepatic dx, CV dx for less than 6 mo, poorly controlled DM, concomitant use of other ED therapies, hx of alcohol or substance abuse, major psychiatric disorder</p>	<p>Age, mean (range): 52 (26-75) vs. 52 (28-76)</p> <p>Race (%): Asian: 6 vs. 7; Black: 2 vs. 2 Mediterranean: 52, vs. 48 White: 40, vs. 42 (all from Egypt and South Africa)</p> <p>Co-morbidities (%): DM: 27; hypertension: 24; unspecified visual disorders: 14; hypercholesterolemia: 6</p> <p>Previous ED treatment: NR</p> <p>Smoking status (%): 20 vs. 29</p> <p>Body weight: NR</p>	<p>Concomitant medications, %: Antihypertensives: 24% Anitdiabetic drugs: 24% Anti-inflammatory agents: 15% Antibiotics: 11% Diuretics: 10% Drugs for hyperlipidemia: 8%</p> <p>Duration of ED, mean: 3.7 vs. 4.4 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED (%): 26 vs. 29</p> <p>Physiologic ED (%): 38 vs. 43</p> <p>Mixed ED (%): 37 vs. 29</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG: Dose: 50 mg, titrated to 100 or 25 mg Duration: 12 wks Frequency: up to once/d (total dose=41) Compliance (%): NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: up to once/d (total dose=33) Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: NR</p> <p>Other: pts information regarding dose of sildenafil used at the end of tx period, n: 25 mg: 7 vs. 1 50 mg: 32 vs. 5 100 mg: 86 vs. 114</p>	<p>Primary outcome results: Values are approximate (extracted from figure), mean: IIEF, Q3: baseline =2; post tx: 4 vs. 2.5 IIEF, Q4: baseline =2; post tx: 4 vs. 2 IIEF- Q7: baseline= 2; post tx: 4 vs. 2.3 GAQ, % yes: 74 vs. 27 Intercourse success, %: 69 vs. 28</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 15 (12) vs. 13 (10); including 0 vs. 4 (3) due to insufficient tx response</p> <p>WDAE, n (%): 3 (2) vs. 0 TAE, n (%): in at least 5%of pts= 63 (49) vs. 45 (36); including headache 26 (20) vs. 10 (8); dyspepsia 12 (9) vs. 1 (0.8); abnormal vision (chromotopsia) 10 (8) vs. 4 (3); flushing 8 (6) vs. 2 (2); rhinitis 7 (6) vs. 3 (2); flu syndrome) 5 (4) vs. 9 (7); CV events (including one re-infarction, and three pts with palpitations in IG and one hypertension in CG) 4 (3) vs. 1 (0.8) SAE: 3 (2) vs. 0; MI, accidental vertebral fracture, diverticulitis</p> <p>Ascertainment of outcomes assessed: physical exam, laboratory tests, questionnaires</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Lindsey (2002) 47</p> <p>Funding sources: Colorectal research fund, Pfizer</p>	<p>N screened = 43 N randomized = 32</p> <p>IG, n = 14 CG, n = 18 (n=10 crossed over to open label sildenafil after placebo)</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: male, postoperative with ED and colorectal cancer</p> <p>Exclusion: pre-operative ED, medical contraindication to sildenafil</p>	<p>Age, median (interquartile range): 59.5 (51.1–64.9) vs. 58.7 (49.4–67.5) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: 18 pts with total ED, 14 with partial</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR [time since surgery, median (IQR)= 5.6 (3.3-7.7) y]</p> <p>Underlying disease, n (%): proctectomy for rectal cancer 12 (37.5); proctectomy for Inflammatory Bowel Diseases 20 (62.5); stoma 11 (34.3)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: < age 65 50 mg; ≥ 65 y old pts 25 mg, max dose of 100 mg . Duration: 4 wks Frequency: NR Compliance (%): 100%</p> <p>CG: Dose: NA Duration: 4 wks Frequency: NR Compliance (%): 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 4 wks (duration of open label trial NR)</p> <p>Other: n=13, and n=11 were dosed up to 50, and 100 mg sildenafil respectively</p>	<p>Primary outcome results: IIEF total score, mean: Baseline: 26.7 vs. 29.5 Post tx: 57.4 vs. 34.5 (post open label: 67 vs. 39.7)</p> <p>GEQ, % with improved erection: 78.6% vs. 16.7%</p> <p>Other outcomes assessed: Subanalysis by disease grp and severity of impotence was performed on n=24 who receive sildenafil either as primary or crossover tx</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE, n (%): 7 (50) vs. 4 (22), most common AE facial flushing followed by headache (46%, and 64% of pts on 50 and 100 mg respectively experienced AE at end of open label) SAE: 0</p> <p>Ascertainment of outcomes assessed: GEQ, IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mahon (2005) ⁴⁸</p> <p>Funding source: Pfizer Inc. (study medication & placebo)</p>	<p>N screened = 41 N randomized = 16</p> <p>IG/CG, n = 16 (cross over)</p> <p>ITT analysis used for primary outcome: NR (analysis for n=13)</p> <p>Inclusion: men 18 y or older with ED and renal failure (on peritoneal dialysis)</p> <p>Exclusion: cerebro-vascular event within the last 6 mo, severe hepatic impairment, presence of penile anatomic deformities, severe cardiac dx, or concomitant nitrate therapy</p>	<p>Age, mean (range): 53 (26-74) y</p> <p>Race (%): White 46%; Black 46%; Indian 8%</p> <p>Co-morbidities: NR</p> <p>Smoking: 8% smoked</p> <p>Previous ED treatment: NR</p> <p>Other: n=1 heavy drinker; n=8 social drinker (<3 to 4 units/d)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 6 mo to 7 y</p> <p>Underlying disease: diabetes n=6 (46%); hypertensive (hypertensive nephropathy, diabetic nephropathy, focal segmental glomerulosclerosis, polycystic kidney disease) n=10 (77%)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil (1st then switched to placebo) CG: placebo (1st then switched to sildenafil)</p> <p>IG: Dose: 50 mg, titrated to 100 mg at wk 2 if no response was attained with the initial dose Duration: 4 wks Frequency: once/ d Compliance (%): 100%</p> <p>CG: Dose: 50 mg Duration: as IG Frequency: as IG Compliance (%): 100%</p> <p>Run In period: 4 wks Wash out period: none</p> <p>F/u duration: 12 wks (including the no treatment run-in period)</p>	<p>Primary outcome assessed: (some values extracted from figure and are approximate) IIEF-EF, mean score: pre: 6.7; post 20 vs. 12 IIEF-OF: pre: 3; post 6.5 vs. 3.8 IIEF- SD: pre: 5; post: 6.3 vs. 5.3 IIEF, ICs: pre: 2.8; post 9.8 vs. 5.7 OS: IG= 7 Q3 (ability to penetrate): post: 3.4 vs. 1.7 Q4 (maintaining erection): post: 3.2 vs. 1.6 GEQ, % improved: 75% vs. 28% PSV (20 min post PgE1 injection), median (range): 29.5 (7-66) m/s EDV (15 min post injection), median (range): 5 (0-13) m/s</p> <p>Other outcomes assessed: T levels, sex hormone binding globulin, PRL, luteinizing hormone, follicle stimulating hormone, HbA1C</p> <p>Withdrawals/drop-outs/loss to f/u: n=3 (1 died, reported unrelated to intervention)</p> <p>WDAE: 0 TAE: 1 headache in IG (no titration in this pts) SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: self administered IIEF; GEQ; Doppler ultrasound</p>

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<p>McVary (2007) ⁴⁹</p> <p>Funding source: Pfizer Inc. (two of the authors declare financial interest /relationship with Pfizer/ Lilly ICOS)</p>	<p>N screened = 683 N randomized = 370 (from 41 centres in US)</p> <p>IG, n = 189 CG, n = 181</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men at least 45 y with ED, score of 25 or less on IIEF-EF domain, and lower urinary tract syndromes (LUTS) associated with prostatic hyperplasia, I-PSS score of 12 or greater</p> <p>Exclusion: confirmed or suspected prostate malignancy; urinary tract dx; hypotension, hypertension, orthostatic hypotension or sign CV dx, use of nitrates; pts with hepatic or renal dysfunction, poorly controlled DM or hx of retinitis pigmentosa, use of antimuscarinics was prohibited</p>	<p>Age, mean (sd): 60 (8.7) vs. 60 (8.5) y</p> <p>Race: White 82%; Black 11.5%; Asian 2%; other 4%</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: 5.7 (<1-25) vs. 5.6 (<1-35) y</p> <p>Underlying disease %: LUTS, 100%</p> <p>Psychogenic ED, n (%): 5 (3) vs. 8 (4)</p> <p>Physiologic ED, n (%): 113 (60) vs. 97 (54)</p> <p>Mixed ED, n (%): 71 (38) vs. 75 (42)</p> <p>Other: baseline IIEF-EF score, mean (sd): 13.4 (6.8) vs. 13.2 (6.6)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg, titrated to 100 mg at 2 wks based on tolerability and efficacy (down to 50 mg if 100 mg was not tolerated, and discontinued if 50 mg was not tolerable) Duration: 12 wks Frequency: once/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: Wash out period:</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF-EF, mean IG vs. CG: Baseline= 13.4 vs. 13.2 12 wks: 23.5 vs. 15.9 IIEF-EF, LS mean change (95% CI): 9.17 (7.25, 11.09) vs. 1.86 (-0.03, 3.74)</p> <p>Other outcomes assessed: EDITS and SEAR questionnaire</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 21 (11) vs. 25 (13.8)</p> <p>WDAE, n (%): 10 (5) vs. 6 (3) TAE, n (%): 100 (53) vs. 78 (43); included headache, flushing dyspepsia and rhinitis in both grps SAE, n (%): 2 (1) vs. 3 (2); SAE included one case of moderated worsening of right knee arthralgia while on 100 mg sildenafil; and one case of severe acute cerebro-vascular stroke also on 100 mg sildenafil; no pts discontinued as result of SAE</p> <p>Ascertainment of outcomes assessed: IIEF; I-PSS; Qmax; SEAR; EDIT; BPHII and QOL</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Melnik (2005) ⁵⁰</p> <p>Funding source: NR</p>	<p>N screened = 287 N randomized = 30</p> <p>IG1, n = 10 IG2, n = 10 CG, n = 10</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 25-50 y, with exclusive diagnosis of non-organic, psychogenic (according to IDC-10) mild to moderate ED for at least 6 mo in duration; in a heterosexual relationship for at least 1 y</p> <p>Exclusion: clinical or psychiatric disease, primary sexual disorder, penile anatomic defects; use of medication known to interfere with sexual function; physical limitations for use of sildenafil citrate; patients with drug or alcohol use; smoking</p> <p>Data reported as IG1 n=8 vs. IG2 n=6 vs. CG n=8</p>	<p>Age, mean: 40 vs. 66 vs. 43 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: baseline IIEF</p>	<p>IG1: Sildenafil + grp psychotherapy IG2: Sildenafil CG: grp psychotherapy</p> <p>IG1/IG2: Dose: 50 mg Duration: 6 mo Frequency: on demand Compliance: NR</p> <p>CG: Dose: NA Duration: 6 mo Frequency: time limited Compliance: NR</p> <p>Run In period: Wash out period: NR</p> <p>F/u duration: immediately after tx at 6 mo, and 3 mo post intervention at 9 mo</p>	<p>Primary outcome results: IIEF (ED severity) at baseline, % of pts: Score 11-16: n: 5 vs. 4 vs. 5 Score 17-26: (mild ED) 3 vs. 2 vs. 3</p> <p>IIEF (ED severity) at 3 mo post tx, %: Score 11-16: 0 vs. 1 vs. 0 Score 17-26: 2 vs. 2 vs. 2 Score 26-30: 6 vs. 2 vs. 6 Severity of ED based on IIEF at 6 mo tx, %: Score 11-16: 0 vs. 1 vs. 0 Score 17-26: 4 vs. 3 vs. 2 Score 26-30: 4 vs. 2 vs. 6</p> <p>IIEF total score, mean: Pre: 41 vs. 46 vs. 43 Post (6 mo): 58 vs. 49 vs. 62 9 mo post: 62 vs. 53 vs. 63, sign.higher mean scores in IG2 vs. CG, p<0.05 Sign.differences between IG1 and CG in remission of symptoms (EF 26 or higher), p= 0.0002</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, %: 20 vs. 40 vs. 20</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; clinical interview</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Meuleman (2001) ⁵¹ Companion study ³⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 315</p> <p>IG, n = 159 CG, n = 156</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older, with clinical diagnosis of ED for at least mo; in stable relationship with female partner for more than 6 mo</p> <p>Exclusion: sign genital anatomical deformities (e.g. Peyronie's dx); primary diagnosis of other sexual disorders; hyperprolactinemia; hx of major haematological, renal or hepatic abnormalities; poorly controlled major psychiatric disorder; ED attributable to SCI; poorly controlled diabetes or untreated proliferative diabetic retinopathy; occurrence of CVD, stroke or MI within 6 mo before study; tx with anticoagulants, androgens, trazodone or nitrates</p>	<p>Age, mean (range): 55 (24-77) vs. 54 (23-82) y</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): Diabetes: 25 (16) vs. 24 (15); hypertension: 33 (21) vs. 30 (19); Ischemic heart dx 21 (13) vs. 10 (6); pelvic surgery 33 (21) vs. 27 (17)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 4.8 (1-35) vs. 5 (1-27) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 50 (32)</p> <p>Physiologic ED, n (%): 46 (29)</p> <p>Mixed ED, n (%): 60 (38) vs. 54 (35)</p> <p>Other types of ED, n (%): 0 vs. 3 (2)</p>	<p>IG: Sildenafil citrate CG: Placebo</p> <p>IG1: Dose: 25 mg titrated to 50 mg 100 mg at any of 5 times during tx period Duration: 28 wk Frequency: once daily, one hr before sexual activity Compliance: NR</p> <p>CG: Dose: Placebo Duration: 28 wk Frequency: once daily, one hr before sexual activity Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wks and 26 wks post tx</p>	<p>Primary outcome results:IIEF- at 12 wks (values very close to 26 wks result), mean (SEM) IIEF, Q3=Q4: pre=2 (2); Post 2 (0.2) vs. 4 (0.2) IIEF, EF: pre=12 (0.7); Post tx: 13 (0.7) vs. 21 (0.7) IIEF, OF: pre=6 (0.3); Post 6 (0.3) vs. 8 (0.3) IIEF, IS: pre=7 (0.4); Post: 8 (0.3) vs. 11 (0.4) IIEF, OS: pre=5 (0.2); post: 5 (0.2) vs. 7 (0.2) IIEF, SD: pre=6 (0.2); Post: 6 (0.2) vs. 7 (0.1)</p> <p>Other outcomes assessed: event log reports; partner satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u: 35 (22) vs.77 (49) stopped tx</p> <p>WDAE, n (%): 5 (3) vs. 1 (<1); headache (3) and colour tinge to vision, dizziness, diarrhoea, nausea, and intermittent stomach ache in IG, one headache in CG</p> <p>TAE, n (%): NR; most common: flushing, headache, dyspepsia, and rhinitis; abnormal vision in IG 2 (1), star vision, colour perception</p> <p>SAE, n (%): 8 (5) vs. 6 (4); two death in IG, one due to accident and one cardiac arrest 1 mo post last dose</p> <p>Ascertainment of outcomes assessed: IIEF; GAQ; diary log</p>

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<p>Montorsi (1999) 52</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 514</p> <p>IG1, n = 128 IG2, n = 132 IG3, n = 127 CG, n = 127</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, with at least 6 mo primary clinical diagnosis of ED</p> <p>Exclusion: SCI, hx of stroke or MI in the last 6 mo or longer, major hematologic, renal or hepatic abnormalities, receiving regular tx with nitrates; poorly controlled DM</p>	<p>Age, mean (range): 56 (19-77) y (slightly older in IG3, range 30-76)</p> <p>Race (%): NR</p> <p>Co-morbidities, n (range %): Genitourinary procedures: 57 (12-19%); Essential hypertension: 74 (11-17%); DM: 45 (7-10%); Genitourinary disease: IG1 = 3 (2%) IG2 = 6 (5%) IG3 = 13 (10%) CG = 5 (4%) Depression: 1-2%; Ischemic heart disease: 1-2%</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr) mean (range): 5 (0.5-30) y</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED, n (%): 129 (25)</p> <p>Physiologic ED: n (%): 166 (32)</p> <p>Mixed ED: 219 (42.5)</p>	<p>IG1/IG2/IG3: sildenafil CG: placebo</p> <p>IG1: Dose: 25 mg (IG1); 50 mg (IG2); 100 mg (IG3) Duration: 12 wks Frequency: up to once/d Compliance (%): NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: up to 1x/day Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration (both on and off treatment): mean 85 d</p>	<p>Primary outcome results: IIEF- EF, mean (values approximate extracted from graph): pre 13; Post IG 19 vs. 21 vs. 23 vs. CG 13 IIEF- Q3, mean score: IG1= 3.18; IG2= 3.65; IG3= 3.79 vs. CG= 2.17 (IG vs. CG p<0.0001) IIEF- Q4, mean score: IG1= 2.99; IG2= 3.40; IG3= 3.63 vs. CG= 1.96 (IG vs. CG p<0.0001) GEQ, % improved: IG1=67%; IG2=78%; IG3=86%; vs. CG=24% Successful intercourse attempt, mean/mo: range 4.4-5.8 vs. 1.6</p> <p>Other outcomes assessed: OF, intercourse satisfaction, OS (values NR; IG vs. CG p<0.0001; partner satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u: 6 (2) vs. 1 (<1%)</p> <p>WDAE, n (%): 6 (1.6) vs. 1(0.8) TAE, n (%): 63 (49), 80 (61), 92 (72) vs. 42 (33); most common AE (range % in IG vs. CG)= headache 17-20% vs. 4%; flushing 13-20% vs. 2%; dyspepsia 2-11% vs. 2%; altered vision 0-11% (n 15 pts) vs. 2%; back pain 0-8% vs. 2%; nausea 1-6% vs. 1% SAE: NR (one case of MI in IG2)</p> <p>Ascertainment of outcomes assessed: IIEF, GEQ, partner questions</p>

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<p>Montorsi (2000) 53</p> <p>Funding source: NR</p>	<p>N screened = 129 N randomized = 30 (cross-over design)</p> <p>IG/ CG, n = 30</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men with ED</p> <p>Exclusion: Depression; hx of sleep disorder; use of drugs affecting quality of sleep; hypogonadism; hx of low serum T, or hyperprolactinemia; MS; SCI; Parkinson's disease; hx of radical pelvic surgery; use of nitrates, complex (≥3 drugs) antihypertensive regimens, or drugs interfering with metabolic pathway of sildenafil; renal or hepatic failure</p>	<p>Age, mean (range): 58 (range 40-68) y</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): hypertension 12 (40) CAD 10 (33) DM 10 (33) Hyperlipidemia 10 (33)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): Current smoker 15 (50)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 8 (27)</p> <p>Physiologic ED, n (%): 22 (73)</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil CG: placebo</p> <p>IG1: Dose: 100 mg Duration: one night Frequency: once Compliance (%): 100</p> <p>CG: Dose: placebo Duration: one night Frequency: once Compliance (%): 100</p> <p>Run In period: 1 night adaptation with RigiScan™ attached but turned off</p> <p>Wash out period: none</p> <p>F/u duration: 3 d</p>	<p>Primary outcome results: Number of erectile episodes/ night, mean (SE): 3.8 (0.8) vs. 3.0 (0.5)</p> <p>Duration of erectile episodes, mean (sd): 46.1 (4.4) vs. 33.2 (5.2) min</p> <p>Duration of tip rigidity >60%: 17.5 (1.5) vs. 10.8 (1.7)</p> <p>RAU Tip: 90.5 (8.1) vs. 44.1 (7.8) Base: 101.8 (5.3) vs. 50.2 (4.2)</p> <p>TAU Tip: 55.8 (2.2) vs. 27.2 (1.8) Base: IG1 54.2 (3.1), CG 36.9 (2.2)</p> <p>Other outcomes assessed: None</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE, n (%): 2 (7) vs. 1(3) slight self resolving headache upon awakening SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

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<p>Nurnberg (2003) 54</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 117 N randomized = 90</p> <p>IG, n = 45 CG, n = 45</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 18-55; wit major depressive disorder in remission and tx with antidepressant for more than 12 wk (on stable dose for ≥4 wk);</p> <p>Exclusion: other than antidepressant-associated sexual dysfunction; SCI; uncontrolled psychiatric disorder or DM; proliferative retinopathy; alcohol or substance abuse; sign hematologic, renal or hepatic abnormality; stroke or MI within previous 6 mo; cardiac failure; unstable cardiac condition or arrhythmia; use of nitrates; BP lower than 90/50 or higher than 170/100 mm Hg; hyperprolactinemia, retinitis pigmentosa; investigational drug use within 3 mo; sexual dysfunction tx</p>	<p>Age, mean (sd): 45 (8) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: Antidepressant 100%</p> <p>Duration of ED: NR; pts with, n (%) ED= 37 (82) vs. 41 (91)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil citrate CG: placebo</p> <p>IG1: Dose: initially 50 mg; could increase to 100 mg Duration: 6 wk Frequency: once/d approximately 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: NA (titrated as IG) Duration: 6 wk Frequency: as IG Compliance: NR</p> <p>Run In period: None Wash out period: NA</p> <p>F/u duration: 6 wk</p>	<p>Primary outcome results: IIEF, mean score IG vs. CG (baseline IG-CG where different) IIEF, total: pre: 69-40; post 60 vs. 41 IIEF, Q3=Q4: pre: 3; post 4 vs. 3 IIEF, EF, pre: 18-17; post: 27 vs. 17 IIEF, OF: pre 6; post: 8 vs. 6 IIEF, SD: pre: 6; post: 7 vs. 6 IIEF, ICs pre: 6-7; post: 11 vs. 7 IIEF, OS: pre: 4-5; post: 7 vs. 5 ASEX, EF: pre 4; post 3 vs. 4 MGH-SFQ- EF: pre 4; post 3 vs. 5 Other outcomes assessed: see below</p> <p>Withdrawals/drop-outs/loss to f/u: 3 (7) vs. 10 (23)</p> <p>WDAE, n (%): 1 (2) vs. 1 (2), one acute panic and chest pain in IG, one suicidal gesture in CG TAE, %: NR; most common=40.5 vs. 10; AE in headache: 17 (41) vs. 4 (10); dyspepsia 2 (7) vs. 0; flushing 7 (17) vs. 1 (2); visual disturbances 5 (12) vs. 2 (5); nasal congestion 5 (12) vs. 1 (2); palpitations 2 (5) vs. 0; restlessness/anxiety 0 vs. 8 (20); insomnia 4 (10) vs. 2 (5) SAE: 0</p> <p>Ascertainment of outcomes assessed: Clinical Global Impression Scale -Sexual Function adapted (CGI-SF); Arizona Sexual Experience Scale (ASEX), Massachusetts General Hospital-Sexual Functioning Questionnaire (MGH-SFQ)</p>

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<p>O'Leary (2006) 55</p> <p>Funding source: Pfizer Inc. (financial interest and/ or other relationships with Pfizer existed for all authors)</p>	<p>N screened = 326 N randomized = 256</p> <p>IG, n = 129 CG, n = 127</p> <p>ITT analysis used for primary outcome: efficacy for all who took at least one dose and presented outcome data; safety for all who took at least one dose</p> <p>Inclusion: men 18 or older with documented ED (score of 21 or less on IIEF) with low self esteem determined by Self-Esteem subscale of the SEAR</p> <p>Exclusion: BP of 90 mmHg or less or 170/110 mmHg or more; sign cardiac dx; use of nitrates, nitric oxide donors, or ritonavir; more than 6 dosed of sildenafil within 6 mo prior to study entry</p>	<p>Age, mean (sd): 56 (12) vs. 55 (13) y</p> <p>Race: White 62%; Black 25%; Asian 2%; Other 11% (16 vs. 6)</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 92 (16) vs. 93 (18) kg</p> <p>Other: overall relationship subscale score, mean (sd)=44.4 (33.1) vs. 53.8 (29.8)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): not specific cause</p> <p>Psychogenic ED, n (%): 18 (14) vs. 15 (12)</p> <p>Physiologic ED, n (%): 61 (48) vs. 62 (50)</p> <p>Mixed ED, n (%): 49 (38) vs. 48 (38)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: flexible 25-100 mg Duration: 12 wks Frequency: up to once/d, 1 hr prior to sexual activity Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 2 wks Wash out period: NA</p> <p>F/u duration: 12 wks post dosing</p>	<p>Primary outcome results: IIEF, LS mean change from baseline: EF: 9.3 vs. 3.6, p<0.001 OF: 2.4 vs. 0.8, p<0.001 SD: 1.2 vs. 0.6, p<0.001 lcS: 4.0 vs. 2.2, p<0.001 OS: 2.1 vs. 3.1, p<0.001 Successful sexual attempts, mean change %(95% CI): 52% (44-60%) vs. 19% (11-27%)p<0.0001 GEQ, % (95% CI) more frequent erections allowing satisfactory intercourse: 3.6 (3.3-3.9) vs. 2.4 (2.1-2.7) p<0.0001</p> <p>Other outcomes assessed: sign correlation between SEAR component scores and IIER-EF domain scores, r range 0.34-0.69, p<0.0001; and other IIEF domain scores</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 23 (18) vs. 18 (14.4)</p> <p>WDAE, n (%): 0 TAE, n (%): NR; most common %: headache 10 vs. 2; rhinitis 6 vs. 0; vasodilatation 6 vs. 0; dyspepsia 6 vs. 1; chromatopsia, photophobia, dry mouth, and nausea 2 vs. 0; SAE, n (%): 0 vs. 1 death</p> <p>Ascertainment of outcomes assessed: IIEF domains; SEAR</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Olsson (2000) ⁵⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 351</p> <p>IG1, n = 90 IG2, n = 85 IG3, n = 81 CG, n = 95</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18-70 y with diagnosis of ED of at least 3 mo duration, who had at least a grade 3-4 (hard enough for penetration-fully rigid) erection at any time during 4 wks before entering the trial or positive response to papaverine (at least 40 mg) or PGE1 (at least 20 mg)</p> <p>Exclusion: Men with ED of organic causes; tx with nitrates, resting hypotension, uncontrolled hypertension, stroke, bleeding disorder, active peptic ulceration, taking anticoagulants, and a hx of a major haematological, renal, hepatic disorders</p>	<p>Age, mean (range): 52 (24-70) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): IG: 102 (40) CG: 41 (43)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 5 (0.2-40) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 153 (60) vs. 51 (54)</p> <p>Physiologic ED: 2 (1) vs. 0</p> <p>Mixed ED, n (%): 101 (39) vs. 44 (46)</p>	<p>IG1-3: sildenafil CG: placebo</p> <p>IG1-IG3: Dose: 10 mg (IG1), 25 mg (IG2), 50 mg (IG3) Duration: 4 wks Frequency: once/d Compliance: NR</p> <p>CG: Dose: NR Duration: 4 wks Frequency: once/d Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 wks</p>	<p>Primary outcome results: IG (1-2-3) vs. CG Mean N of grade 3-4 erections at wk 4, mean n: baseline: 2.1; post tx: 2.8 -3.0 - 3.6 vs. 1.8, p < 0.001 (IG vs. CG) GAQ, %: 64 -79 - 88 vs. 38, p < 0.001</p> <p>Mean Sexual Function Questionnaire (SFQ) scores =improved in IG vs. CG</p> <p>% Partners reporting improved erection: 64 -78 - 83 vs. 39, p < 0.001</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 7.8 - 8.2% vs. 13.6% vs. 9.5%</p> <p>WDAE, %: 2.2 -4.7- 8.6 vs. 4.2 TAE, %: 24.3 – 58.8 - 45 vs. 15% AE in at least 5% of pts, n (%): headache 12-20-16 (13-24-20) vs. 7 (7); dyspepsia 4-9-5 (4-11-6) vs. 3 (3); flushing 4-7-7 (4-8-9) vs. 0; myalgia 1-3-6 (1-4-7) vs. 1 (1); arthralgia 1-6-0 (1-7-0) vs. 1 (1); flue syndromes 0-5-2 (0-6-3) vs. 2 (2); other (NR) 1-0-2 (1-0-3) vs. 0</p> <p>SAE, n (%): n=3 (MI, renal cell carcinoma, epileptic crisis)</p> <p>Ascertainment of outcomes assessed: Questionnaire; GAQ; SFQ (15 question, of 14 d diary)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Olsson (2001) ⁵⁷</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 224</p> <p>IG, n = 136 CC, n = 88</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, with ED of at least 6 mo duration, in a stable relationship for more than 6 mo, clinical diagnosis of stable CVD treated for more than 6 mo with beta blockers and/or ACE inhibitors and/or calcium-channel blockers, written informed consent</p> <p>Exclusion: concomitant tx with nitrates in any form, genital anatomical deformities, any major psychiatric disorder, known hx of alcoholism or substance abuse, SCI, sign CV event (hx of stroke or MI, cardiac failure, unstable angina, life threatening arrhythmia) within 6 mo, major haematological, renal or hepatic abnormalities, poorly controlled DM; BP < 90/50 mmHg or >180/ 110 mmHg</p>	<p>Age, mean (range): 62 (42-77) vs. 62 (41-76) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: no sign differences between grps</p> <p>Duration of ED, mean: 4.6 y</p> <p>Underlying disease, n (%): hypertension: 109 (80) vs.78 (89); Previous MI 25 (18) vs. 18 (20); chronic ischemic heart disease 27 (20) vs. 13 (15); angina 24 (18) vs. 14 (16), Previous coronary bypass 21 (15) vs. 12 (14) Peripheral vascular disease 19 (14) vs. 8 (9)</p> <p>Psychogenic ED:</p> <p>Physiologic ED, %: 63 vs. 60</p> <p>Mixed ED: 36 vs. 40</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 50 mg with option to titration to 100 or 25 mg based on efficacy and tolerability Duration 12 wks Frequency: up to 1/d Compliance (%): 93%</p> <p>CG: Dose: NA Duration 12 wks Frequency: up to 1/d Compliance (%): 91%</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration (both on and off treatment): 12 wks</p> <p>Other: final doses, n (%): 25 mg: 2 (1) vs. 0 50 mg: 51 (38) vs. 9 (10) 100 mg: 83 (61) vs. 79 (90)</p>	<p>Primary outcome results: GEQ, % with improved erection: 71 vs. 24 IIEF, mean (SE): Q3: pre=2; post 3.7 vs. 2.2 Q4: pre=1.5; post 3.3 vs. 1.9</p> <p>IIEF Q3, and Q4: sign higher in IG than CG (p=0.0001)</p> <p>Other outcomes assessed: partner sexual satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u, (%): 4 vs. 3, due to insufficient clinical response</p> <p>WDAE, n (%): 0 vs. 1 (1) TAE: flushing 17 vs. 2; headache 15 vs. 1; dyspepsia 5 vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; GEQ; partner satisfaction questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Orr (2006) ⁵⁸</p> <p>Funding source: Pfizer Inc. Israel</p>	<p>N screened = 28 N randomized = 21 (cross over)</p> <p>IG/ CG, n = 21</p> <p>ITT analysis used for primary outcome:</p> <p>Inclusion: men age 18-60 y, with diagnosis of chronic post traumatic stress disorder (PTSD), and ED (score of less than 50 in IIEF, and less than 20 in IIEF-EF domain), in a stable relationship</p> <p>Exclusion: hx of alcoholism or substance dependence within the last 12 mo; genital or anatomical deformities; SCI; poorly controlled DM; hx of malignant hypertension, resting SBP > 180 mm Hg, hx of stroke or MI within the last 6 mo prior to study entry; predisposing to priapism; any other unstable medical conditions; use of nitrates, or nitric oxide in any form use of sildenafil more than once; tx with T; current use of any ED tx</p>	<p>Age, mean (sd): 44.5 (9.69) y, range 22-55 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): psychiatric conditions: current major depressive episode 47% (past episodes 29%); dysthymia 7%; current manic or hypomanic episode 4%; anxiety disorder: social phobia 39%; general anxiety disorder 61%, agoraphobia 61%; obsessive compulsive disorder 4%, psychotic symptoms reported in 38%</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): SSRIs 71%, tri-cyclic antidepressants 21%, other antidepressants 14%, anti-psychotics 25%, mood stabilizer 25%, and benzodiazepine 89%</p> <p>Duration of ED, mean (sd): 19.71 (10.21)</p> <p>Underlying disease, n (%): as in co-morbidities</p> <p>Psychogenic ED, n (%): 100%</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG1: Dose: 50-100 mg Duration: 4 wks Frequency: one pill 1 hr before sexual activity; total of 6 pills Compliance: NR</p> <p>CG: Dose: NA Duration: 4 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: no washout included</p> <p>F/u duration: Other: (pts were randomized to 2 grps, 1st grp started with 4 wks placebo, and 2nd grp started with 4 wks sildenafil)</p>	<p>Primary outcome results: IIEF, mean (sd) Total score: baseline 20 (12.32); post 45.19 (15.05) vs. 33.04 (12.99) EF: baseline 7.42 (5.3); post tx 18.57 (7.7) vs. 13.8 (5.3) SD: baseline 4.58 (2.23); post tx 4.95 (2.03) vs. 4.58 (1.8) OF: baseline 4.45 (3.74); post tx 5.59 (2.44) vs. 4.04 (2.15) lcS: baseline 4.39 (3.75); post tx 7.22 (1.92) vs. 6.20 (2.37) OS: baseline 3.37 (1.96); post tx 5.18 (2.55) vs. 4.20 (2.48)</p> <p>Other outcomes assessed: depression, subjective well being and PTSD symptoms score</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 6/27 (22) in placebo phase; 1/23 (4.3%) in sildenafil phase</p> <p>WDAE, n (%): NR TAE, n (%): NR, AEs included heartburn, decrease in appetite, constipation, diarrhea, nausea, vision blur, tinnitus, dizziness, headache, tiredness, backache, stomach ache, chest pain, hot flushes, rash, palpitation, sweating; no sign.between grps SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF domains; depression, subjective well being by SAS and ABS); PTSD symptom scores</p>

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<p>Padam-Nathan (1998) ⁵⁹</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized =</p> <p>IG, n = 163 CG, n = 166</p> <p>ITT analysis used for primary outcome: yes (last observation carried forward)</p> <p>Inclusion: men 18 or older, with ED of more than 6 mo, ED (ED aetiology determined at screening by medical hx, penile tumescence test, IC injection test, endocrine testing, and penile duplex ultrasonography)</p> <p>Exclusion: penile anatomical defects; SCI; other sexual disorders; low T; poorly controlled DM or untreated proliferative diabetic retinopathy; psychiatric dx; active peptic ulcer dx; hx of major haematological, renal, or hepatic abnormalities; recent hx of CV dx, stroke, or MI, or alcoholism; or substance abuse; tx with nitrates, androgens or trazodone</p>	<p>Age, mean (range): 60 (26-79) vs. 59 (31-81) y</p> <p>Race: NR</p> <p>Co-morbidities, (%): hypertension 24 vs. 28; Hyperlipidemia 15 vs. 15; ischemic heart dx 15 vs. 8; DM (any type) 8 vs. 11; depression 3 vs. 3; radical prostatectomy 9 vs. 11</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED, mean (range): 5 (0.5-26) y</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg (titrated to 100 mg, or 25 mg at 2 wks based on efficacy and tolerability); total 32 doses Duration: 12 wks (median=87 d) Frequency: up to one/d (approximately 1 hr before sexual activity) Compliance: NR</p> <p>CG: Dose: NA/ total of 29 doses Duration: 12 wks (median = 86 d) Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks no tx Wash out period: NR</p> <p>F/u duration: 12 wks</p> <p>Other: 23% of pts were on 50 mg; 74% on 100 mg at the end</p>	<p>Primary outcome results: GEQ, (% yes): 101/136 (74%) vs. 23/118 (16%), p<0.0001 Erection sufficient for intercourse, n (%): 94/137 (69) vs. 32/138 (23) Maintaining erection after penetration, n (%): 85/137 (62) vs. 22/138 (16) Maintaining erection on most occasions, n (%): 81/137 (59) vs. 21/138 (15) Successful intercourse, (%): 65% vs. 20%, p < 0.001 Frequency of successful intercourse attempts (n/mo): 5.9 vs. 1.5, p <0.0001</p> <p>Other outcomes assessed: partner assessment of sexual performance</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 9 (8) vs. 13 (6)</p> <p>WDAE, n (%): 1 (<1) vs. 2 (1) TAE, n (%): AE in at least 5% of pts= headache 30 (18) vs. 6 (4); flushing 30 (18) vs. 1 (1); dyspepsia 9 (6) vs. 4 (2); abnormal vision (▲ sensitivity or light or blurred vision) NR (3) vs. NR (1) SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: GEQ; pts log (sexual stimulation, and successful intercourse); optional two item partner questionnaire; IIEF (15 item version); AE by examiner</p>

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<p>Padma-Nathan (2003) ⁶⁰</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 228</p> <p>IG, n = 115 CG, n = 113</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: pts 18 or older with clinically documented ED at least 6 mo duration who had previously responded successfully to sildenafil treated minimum. of 2 mo, in a stable 100-mg sildenafil dose, established single-partner relationship; had to discontinue all medications for ED</p> <p>Exclusion: tx with nitrates or nitric oxide donors and those with hypotension (BP less than 90/50 mmHg), hypertension (PB more than 170/110 mmHg), MI, unstable angina, stroke, or symptomatic or clinically sign cardiac abnormalities in the past 3 mo</p>	<p>Age, mean (sd): 61(10) vs. 59(11)</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr, SD): 6.8(4.6) vs.7.2 (5.4)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED n (%): 3 (3) vs. 4 (4)</p> <p>Organic ED, n (%): IG 61 (53) vs. 66 (58)</p> <p>Mixed ED, n (%): 36 (31) vs. 29 (26)</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 100 mg Duration: 4 wks Frequency: up to once/d; as need Compliance: NR</p> <p>CG: Dose: NA Duration: 4 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: 2 wks</p> <p>F/u duration: 4 wks</p>	<p>Primary outcome results: IIEF: IG sign higher scores vs. CG for all domains p<0.001 (results provided in Figure 2) Sexual activity event log, mean time to onset of erection (min): 36.3 vs. 140.7 min. (sign, p<0.0001)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 4 (3.5) vs. 5 (4.4)</p> <p>WDAE: 2 (2) vs. 0 TAE: 41 vs. 18 in 29 (25%) vs. 15 (13%) of pts, most common AE, %: headache 6 vs.0; flushing 3.5 vs.0.9; respiratory tract infection 4.3 vs. 4.4; sinusitis 0 vs. 5 SAE: NR</p> <p>Ascertainment of outcomes assessed: Sexual activity event log: recorded at home time duration of sexual activity using a stopwatch. Other question: whether erection lasted long enough for successful intercourse. IIEF: questionnaire.</p>

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<p>Padma-Nathan, (1999) ³²</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 532</p> <p>IG, n = 316 CG, n = 216</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: ED</p> <p>Exclusion: penile anatomical deformities, hyperprolactinaemia or testosterone deficiency, stroke, MI, or sign. CVD in the previous 6 mo, poorly controlled DM or major psychiatric disorder, untreated proliferative diabetic retinopathy, major haematological, renal or hepatic abnormalities, active peptic ulcer dx, retinitis pigmentosa, concomitant tx with nitrates, nitric oxide donors, androgens or trazodone, hx of alcoholism or substance abuse</p>	<p>Age, mean (range): 58 (20-87)</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 3.2 y</p> <p>Underlying disease (%): NR</p> <p>Psychogenic ED (%): 9</p> <p>Organic ED (%): 77</p> <p>Mixed ED (%): 13</p>	<p>IG: sildenafil CG: placebo</p> <p>IG1: Dose: 25, 50 or 100 mg Duration: 6 mo Frequency: as need before sexual activity Compliance: NR</p> <p>CG: Dose: placebo Duration: 6 mo Frequency: as need before sexual Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 6 mo</p>	<p>Primary outcome results: Erections hard enough for sexual intercourse, mean %: 72 (25mg), 80 (50 mg), 85 (100mg) vs. CG 50 (p < 0.001) Number of erections, mean/mo: Grade 3= 2.1(25 mg), 2.4 (50 mg), 3.1 (100 mg) vs. CG 2.4 (p < 0.001); Grade 4=2.2 (25 mg), 4.2 (50 mg), 3.4 (100 mg) vs. CG 0.7 (p < 0.001) Successful intercourse (% , grade 3,4): grade 3 = 80 vs. NR grade 4 = 94 vs. NR</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE, n (%): 25 mg =1(1), 50 mg= 1 (1), 100 mg =2 (2) vs. CG= 1 (4)</p> <p>TAE, n (%): headache 25 mg =14(14), 50 mg= 23 (21), 100 mg= 32(30) vs. CG= 14 (6); flushing 25 mg= 13 (13), 50 mg= 29 (27), 100 mg 21 (20) vs. CG= 3 (1); Dyspepsia 25 mg= 3 (3), 50 mg= 12 (11), 100 mg= 17(16) vs. CG= 3 (1) Abnormal vision, 25 mg= 2(2), 50 mg =6 (6), 100 mg =10(9), CG= 1 (1) Rhinitis, 25 mg= 1(10), 50 mg =3 (3), 100 mg= 12(11), CG= 4 (2)</p> <p>SAE: NR</p> <p>Ascertainment of outcomes assessed: event log (4-point erection hardness scale and successful sexual intercourse attempts)</p>

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<p>Palmer (1999) ⁶¹</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = NR N randomized = 8 (crossover study)</p> <p>ITT analysis used for primary outcome: No</p> <p>IG/CG, n = 8</p> <p>Inclusion: men with ED and spina bifida</p> <p>Exclusion: NR</p>	<p>Age, range: 19-35 y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: sildenafil CG: placebo</p> <p>IGa/ IGb: Dose: a=25 mg; b=50 mg (one set for each dose; 5 tablets/ set) Duration: NR Frequency: 1/d Compliance (%): 100%</p> <p>CGa/ CGb: Dose: NA (two sets of tablets) Duration: NR Frequency: 1/d Compliance (%): 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Duration of erection, mean Baseline: 8.9 min Low dose: 17.9 vs. 10.4 min High dose: 25.6 vs. 13.5 min (improvement of 101% and 188% for IG a and b respectively)</p> <p>IIEF, high dose; low dose IG vs. CG mean score: Q1 baseline 2.1; post: 3.3; 4.4 vs. 2.5 (improvement of 57% and 110% for IG grps)</p> <p>Q15 baseline 2.3; post 3.0; 3.8 vs. 2.6 (improvement of 30% and 65% for IGa and b respectively)</p> <p>Erectile score: baseline 3.4; post 5.8, 6.9 vs. 3.7 (improvement of 71% and 103% for IG a and b respectively)</p> <p>Other outcomes assessed: None</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Palmer (2000) ⁶²</p> <p>Funding source: Pfizer, Inc</p>	<p>N screened = 17 N randomized = 17 (cross over)</p> <p>IG/CG, n = 17</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 18-35 with diagnosed spina bifida, and ED, medical clearance from primary care physician</p> <p>Exclusion: abnormal haematological evaluation, medical contraindications</p>	<p>Age, range: 19-35 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: Spina Bifida 100%</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1/2: sildenafil- oral CG: placebo- oral</p> <p>IG1/ IG2: Dose: 25 mg (IG1), 50 mg (IG2) Duration: NR Frequency: up to once/d, one hr before sexual activity; pts were given 4 sets of tablets (sildenafil 25 mg, 50 mg and two identical looking placebo tablet), 5 tablets/ set in a random order) Compliance: 88%</p> <p>CG1: Dose: NA Duration: NR Frequency: as IG Compliance: 88%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IIEF, mean score (values approximate from figure): Q3- baseline= <2.5 vs. <3; 12 wks: <3 vs. >3.5, p=0.001 (improvement in 35.7% vs. 19.9% of pts) Q4- baseline: <2; 12 wks: <2.5 vs. >3, p=0.001 (improvement in 68.4% vs. 26.5% of pts) Number of successful intercourse attempts (event log), %- baseline: 20; 12 wks 40 vs. >65, p=0.001 (improvement in 63% vs. 33% of pts) EF domain- baseline: <14; 12 wks: 15 vs. 20, p=0.001 GEQ, % improved: 66.6 vs. 28.6</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 4 (24)</p> <p>WDAE: 0 TAE, n (%): 5 (33) only with 25 mg including dyspepsia 1 (7); nausea 1 (7); headache, flushing and nasal congestion 1(7); urinary tract infection 1 (7), and haematological changes 1 (7) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, Q1 and 15, patient ratings of erection</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Perimenis (2004) ⁶³</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 30</p> <p>IG1, n = 15 IG2, n = 15 CG, n = NA</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: Men with clinically diagnosed ED and obstructive sleep apnea syndrome (OSAS)</p> <p>Exclusion: deformity in external genitals, taking nitrates, being treated for ED, hormonal deficiency, had not had a stable relationship for at least 6 mo</p>	<p>Age, mean (sd): 55.7 (3.6) vs. 56.4 (3.3)</p> <p>Race (%): NR</p> <p>Co-morbidities: DM (NR), atherosclerosis (NR), CAD (NR), hypertension (NR)</p> <p>% Pts with => 1 disease: n=11 (73%), in each arm</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): smokers 23 (77)</p> <p>Body weight: most pts were overweight</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 16.7 (7.6) vs. 15.7 (6.1) mo</p> <p>Underlying disease: OSAS (100%)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Continuous Positive Air Pressure (CPAP) IG2: Sildenafil</p> <p>IG1: Dose: NA Duration: 12 wks Frequency: nightly Compliance (%): NR</p> <p>IG2: Dose: 100 mg Duration: 12 wks Frequency: NR Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: Mean (sd) scores IG1 vs. IG2: IIEF total: pre=21.7 vs. 23.3; post = 27.3 (8.6) vs. 37.7 (10.5), p = 0.0025 IIEF-EF: pre=7 vs. 8; post 9 (3) vs. 13 (4) IIEF-OF: pre=3; post: 3 (1.6) vs. 5.5 (1.9) IIEF-SD: pre=7; post: 7 (1.4) vs. 7.7 (0.8) IIEF ICs: pre=3.3 vs. 3.7; post: 4.6 (1.7) vs. 6.4 (2) IIEF-OS: pre=2; post 2.9 (1.6) vs. 4.5 (2.3)</p> <p>pts satisfied with the treatment, n/N (%) = 3/15 (20) vs. 8/15 (53.3), p = 0.13 Successful attempts for intercourse, n/N (%) = 33/138 (23.9) vs. 97/180 (53.9), p = 0.001 Mean N of attempts per patient = 9.2 vs. 12, p = 0.005</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: 0 TAE: NR SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan, IIEF; pts diary questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Perimenis (2007) ⁶⁴</p> <p>Funding source: NR</p>	<p>N screened = N randomized = 40</p> <p>IG1, n = 20 IG2, n = 20 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED and sleep apnea (complete cessation of airflow for at least 10 s and hypopnea as the reduction in airflow by at least 50% for 10 s or more)</p> <p>Exclusion: genital deformity, use of nitrates; on tx with ED; hormonal deficiency, not in a stable relationship for at least 6 mo</p>	<p>Age, mean (range): 55.3 (42-64) vs. 55.5 (48-62) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: None</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: respiratory disturbance index (RDI) 9.9 (6-24) vs. 8.9 (6-25)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: 17.5 (6-36) vs. 18.7 (8-36) mo</p> <p>Underlying disease, n (%):NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: Sildenafil IG2: Continuous Positive Airway Pressure (CPAP) CG:</p> <p>IG1: Dose: 100 mg on demand, 1 hr prior to sexual activity Duration: 12 wks Frequency: once/d Compliance: NR</p> <p>IG2: Dose: NA Duration: 12 wks Frequency: during night time sleep Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks (every 4 wks)</p>	<p>Primary outcome results: Rate of successful intercourse attempts, per pts: 128/249 (51.4%) vs. 51/193 (26.9%) IIEF-EF, mean (sd): Baseline: 7.8 (1.2) vs. 7 (1.9) Post tx: 14.3 (5.0) vs. 10.8 (4.4), p = 0.025</p> <p>Other outcomes assessed: satisfaction with tx (better with sildenafil, 50% vs. 25%, p=0.007)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0</p> <p>WDAE, n (%): 0 TAE, n (%): NR SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: pts diary; IIEF, EDITS</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Pickering (2004) 65</p> <p>Funding source: Pfizer</p>	<p>N screened = 670 N randomized = 568</p> <p>IG, n = 281 CG, n = 287</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older with ED and hx of arterial hypertension treated with 2 or more different antihypertensive drugs, with stable dose for at least 4 wks; in stable relationship</p> <p>Exclusion: hypotension or uncontrolled hypertension, sign CV dx in previous 6 mo; current use of nitrates; past tx with sildenafil</p>	<p>Age, mean (sd): 59 (8) vs. 59 (9)</p> <p>Race: NR</p> <p>Co-morbidities: None</p> <p>Previous ED treatment: None</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: None</p> <p>Duration of ED, mean (sd): 4.6 (4.1) vs. 4.5 (4.6) y</p> <p>Underlying disease: Arterial hypertension</p> <p>Psychogenic ED, n (%): 23 (8.2) vs. 24 (8.5)</p> <p>Physiologic ED, (%): 145 (52) vs. 142 (50.2)</p> <p>Mixed ED, n (%): 111 (39.8) vs. 117 (41.3)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50mg (after 2 wks adjusted to 25 or 100 mg) Duration: 6 wks Frequency: before sexual intercourse Compliance (%): (94)</p> <p>CG: Dose: 1 tablet Duration: 6 wks Frequency: before sexual intercourse Compliance (%): (95)</p> <p>Run In period: 2 wks screening period Wash out period: None</p> <p>F/u duration (on and off treatment): Trial followed up by 6 wks open label phase where all participants received Sildenafil.</p>	<p>Primary outcome results: IIEF mean (sd) IG1 vs. CG Q3: pre= 3.6 (0.1) vs. 2.7 (0.1) Q4 (penetration): 3.6 (0.1) vs. 2.5 (0.1) GEA-Q1, % improved: 71 vs. 18 1: Improved erections: (71) vs. (18) GEA-Q2, %: 69 vs. 20 Intercourse success rate, %: 62 vs. 26</p> <p>Other outcomes assessed: EDITS: Patients who took sildenafil score higher mean scores on EDITS</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 7 (2.5) vs. 5 (2)</p> <p>WDAE, n (%): 4 (1.4) vs. 4 (1.4) TAE, n (%): 111 (39.9) vs. 73 (26) including headache 28 (10.1) vs. 10 (3.6); flushing 17 (6.1) vs. 1 (0.4); dyspepsia 15 (5.4) vs. 3 (1.1); dizziness 11 (4) vs. 1 (0.4); nasal congestion 7 (20.5) vs. 1 (0.4); abnormal vision 7 (2.5) vs. 0</p> <p>SAE: 2 (0.7) vs. 2 (0.7); including one due to MVA in CG</p> <p>Ascertainment of outcomes assessed: IIEF-Q3, and 4; GEA-Q1 and 2; pts event log</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Price (1998) ⁶⁶</p> <p>Funding source: Pfizer</p>	<p>N screened = NR N randomized = 21 (3 way cross over; two periods)</p> <p>IG1/IG2/CG, n = 21</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18-70 y with hx of DM type 1 or 2, for 5 y or more, ED of at least 6 mo (ED definition and diagnosis is described)</p> <p>Exclusion: sign ischemic heart dx or peripheral vascular dx, tx with antidepressants/tranquillizer, nitrates, anticoagulants, or salicylates in last 2 wks prior to study, hx of bleeding dx, severe untreated proliferative diabetic retinopathy, no ED tx in past 2 wks</p>	<p>Age, mean (range): 51 (42-65) y</p> <p>Race: NR</p> <p>Co-morbidities:</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, median (range): 3 (1-14) y</p> <p>Underlying disease: 100% DM, with mean duration of 11 (range 3-32) y; evidence of peripheral or autonomic neuropathy n=6 (28%)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NR</p>	<p>Phase I IG: single dose sildenafil + 90 min visual sexual stimulation (VS) CG: placebo</p> <p>Phase II IG: sildenafil CG: placebo</p> <p>IG phase I: Dose: 25 mg (IG1), 50 mg (IG2) Duration: NA Frequency: single dose Compliance: NR</p> <p>IG phase II: Dose: 25 mg (IG1), 50 mg (IG2) Duration: 10 d Frequency: once/d Compliance: NR</p> <p>CG phase I & phase II: Dose: NA Duration: as IG in respective phase Frequency: as IG Compliance: NR</p> <p>Run In period: 2 wks Wash out period: NR</p> <p>F/u duration: immediately post tx</p>	<p>Primary outcome results: Phase I, duration of erection with > 60% rigidity, mean (95% CI): Base: 5 (1.9-12.4) vs. 10.1 (4.2-23.1) vs. 2.8 (0.7-8.4) min Tip: 1.2 (0.2-3.8) vs. 2.2 (0.7-6) vs. 0.4 (-0.2-2.1) min</p> <p>Phase II (home study) N of erection sufficient for intercourse (grade 3 or 4), mean (95% CI): 1.3 (0.9-1.8) vs. 1.6 (1.1 -2.1) vs. 0.6 (0.4-0.9) % of pts with improved erection, n (%): 10 (50) in 25 mg vs. 2 (10) in placebo 11 (52%) in 50 mg vs. 2 (10) in placebo</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR; tx related AEs=8 vs. 8 vs. 3 including headache 4 vs. 0, myalgia 3 vs. 2, nausea 2 vs. 1, and dyspepsia 5 vs. 0 SAE: 1 (4.7) vs. 0; pneumococcal pneumonia with 25 mg dose</p> <p>Ascertainment of outcomes assessed: RigiScan (phase I); self report on grading system (phase II)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Randell (1999) ⁶⁷</p> <p>Funding source: study medications by Pfizer (author has served as paid consultant for Pfizer)</p>	<p>N screened = NR N randomized = 268</p> <p>IG, n = 136 CG, n = 132</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, medically documented ED for at least 6 mo, managed and stable DM (type 1 at least 5 y, type 2 at least 2 y); in a stable relationship for at least 6 mo</p> <p>Exclusion: penile anatomical deformities, primary diagnosis of sexual disorder other than ED; sign psychiatric dx; SCI, hx of major haematological, renal, or hepatic abnormalities; stroke or MI, in past 6 mo; active peptic ulcer; hypo/hypertension, diabetic retinopathy or severe autonomic neuropathy; hx of ketoacidosis in last 3 y; tx with nitrates or androgens</p>	<p>Age, mean (range): 57 (27-79) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): hypertension 139 (51); ischemic heart dx 70 (26)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): antihypertensive agents 141 (53); diuretics 33 (12); beta blockers 19 (7); antidepressant agents 13 (5)</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): DM type I = 50 (18); type II = 136 (50);</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED, (%): 256 (96)</p> <p>Mixed ED, n (%): 12 (4)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg (titrated up to 100, or down to 25 mg according to pts tolerability and efficacy) Duration: 12 wks Frequency: up to once/d (1 hr prior to sexual activity) Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk (no tx) Wash out period: NA</p> <p>F/u duration: 12 wks</p> <p>Other: pts receiving sildenafil 100 mg (high for placebo)= 126 (93%) vs. 127 (96%); 50 mg (medium) = 10 (7%) vs. 5 (4%); 25 mg (low) = 0 vs. 0</p>	<p>Primary outcome results: IIEF, Q1, 2, 3, 4 (baseline = 2), at 12 wk, mean (SE) for individual questions: 3 (0.2) vs. 2 (0.2); increase of 78% vs. 25%, P<0.001 IIEF, EF (Q5, 15): pre=1, post: individual questions, mean (SE): 3 (0.2) vs. 2 (0.2)</p> <p>Pts with at least 1 successful attempt at sexual intercourse: 61 (71/117) vs. 22 (25/114), p<0.001</p> <p>Other outcomes assessed: sexual satisfaction and OF; IIEF 11 & 12 (no change); efficacy variables for subgrp of DM pts</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 16 (6); IG 11 (8), vs. CG 5 (4)</p> <p>WDAE: 1 (<1) vs. 1 (<1); no detail TAE: AE in at least 3% of pts= 22 (16) vs. 5 (5); including: headache 15 (11) vs. 2 (2); dyspepsia 12 (9) vs. 0; respiratory tract disorder 8 (6) vs. 2 (2); CV 4 (3) vs. 6 (5); flushing 5 (4) vs. 0; abnormal vision 5 (4) vs. 1 (1) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF Q1, 2, 5-15 self report ability to achieve and maintain erection for sexual intercourse</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Safarinejad (2004) ⁶⁸</p> <p>Funding source: NR</p>	<p>N screened = 373 N randomized = 282</p> <p>IG, n = 144 CG, n = 138</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: pts 18 or older, with ED (NIH consensus), and DM longer than 6 mo; in a heterosexual stable relationship for at least 6 mo, and no tx for ED 4 wks prior to trial</p> <p>Exclusion: anatomical defects, another sexual disorder, major haematological, renal, hepatic, uncontrolled psychiatric disorder, tx with nitrates, androgens, CAD, hx of MI or stroke, peptic ulcer dx, poorly controlled DM, hx of drug/alcohol abuse, SCI, hypotension (resting < 90/50 mmHg) or hypertension (resting > 100 mmHg), proliferative retinopathy or autonomic neuropathy and hx of ketoacidosis</p>	<p>Age, mean (range): 46 (36-68) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR (none in 4 wks prior to trial)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: HbA1C, % = < 0.12</p>	<p>Concomitant medications, %: ACE inhibitors without diuretics 22; ACE inhibitors with diuretics 22.5, diuretics 12; β-blockers 4</p> <p>Duration of ED (yr): 3.6 (2.5-12)</p> <p>Underlying disease, %: DM type I =17; type II= 83</p> <p>Psychogenic ED: None</p> <p>Physiologic ED: 96%</p> <p>Mixed ED: 4%</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 100 mg Duration: 16 wks Frequency: once/d Compliance: NR</p> <p>CG: Dose: NR Duration: 16 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR F/u duration: 16 wks</p>	<p>Primary outcome results: IIEF-Q3, mean (SE): pre: 1.8 (0.2); post: 2.8 (0.2) vs. 2.2 (0.2), p < 0.002 (vs. baseline)</p> <p>IIEF-Q4, mean (SE): pre 1.7 (0.2); post: 2.9 (0.2) vs. 2.0 (0.2), p < 0.002 (vs. baseline)</p> <p>GEQ, n (%) with positive response: 68 (51) vs. 14 (11), p < 0.003</p> <p>Other outcomes assessed: Mean scores of IIEF 1,2,5-10,13-15 (improved with sildenafil, p <0.05)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 10 (7) vs. 10 (7)</p> <p>WDAE, n (%): 8 (6) vs. 0</p> <p>TAE: NR; most common AEs=22 vs. 1.4 (p < 0.001); AE included headache 29 (20) vs. 3 (2), flushing 27 (19) vs. 0; dyspnea 13 (9) vs. 3 (2); rhinitis 9 (6) vs. 0; CV events 10 (7) vs. 0; prolonged erection 1 (1.4)</p> <p>SAE: NR [CV events in sildenafil grp = four chest pain (two MI), two heart failures and four hypertensions]</p> <p>Ascertainment of outcomes assessed: Questionnaire</p>

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<p>Safarinejad (2006) ⁶⁹</p> <p>Funding source: not sponsored</p>	<p>N screened = 430 (486 entered a preliminary phase to emphasize the timing and instruction of sildenafil; responders were excluded) N randomized = 402</p> <p>IG1, n = 205 IG2, n = 197</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 y or older with ED; in a stable relationship, non-responders to sildenafil, and no tx of ED within the last 4 wks prior to entering the study</p> <p>Exclusion: penile anatomical defects, primary dx of another sexual disorder, use of psychotropic and antidepressant medications, poorly controlled DM, uncontrolled congestive or ischemic heart dx or renal or liver impairment, hx of alcohol or drug abuse, SCI, hx of prostate cancer, neurological dx causing ED</p>	<p>Age, mean (range): 41.5 (21-59) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM 44 (12); hyper-cholesterolemia 91 (24.6); hypertension 87 (23.5); Ischemic heart dx 52 (14)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: smokers 192 (52)</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED, mean (range): 2.8 (1.9-7) y</p> <p>Underlying disease, n (%): NS between grps: arteriogenic 132 (32.8); mixed vasculogenic 105 (26); veno-occlusive dysfunction 97 (24); corporeal fibrosis 8 (2)</p> <p>Psychogenic ED, n (%): 15 (7.3) vs. 13 (6.6)</p> <p>Physiologic ED, n (%): 374 (93)</p> <p>Mixed ED: NR</p>	<p>IG1: Sildenafil + Cabergoline IG2: Sildenafil + placebo</p> <p>IG1: Dose: sildenafil= 50 ▲ rapidly to 100 if not results were observed with the attempt; cabergoline= 0.5 mg ▲ by 0.25 biwklly up to 1 mg/wk Duration: 6 mo Frequency: sildenafil: pkg instructon up to 1/d; cabergoline: wkly Compliance: NR</p> <p>IG2: Dose: sildenafil as IG1+ placebo Duration: 6 mo Frequency: as cabergoline Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 mo</p>	<p>Primary outcome results: IIEF, LS mean (SE) scores: Q3: baseline 1.8 (0.2); post tx 3.3 (0.2) vs. 2 (0.2) Q4: baseline 1.7 (0.2); post tx 3.7 (0.2) vs. 2 (0.2) All other IIEF individual questions sign improved with cabergoline, p=0.04 IIEF- IcS domain mean score: baseline 10 vs. 11; post tx 15 vs. 10 Successful intercourse attempts (% with at least one success): 36% vs. 6%</p> <p>Other outcomes assessed: IVELT sign difference between tx grps (p=0.001)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 19 (9.3) vs. 13 (6.6)</p> <p>WDAE, n (%): 12 (5.9) vs. 2 (1) TAE, n (%): pts with AE 25 (12.2) vs. 4 (2) including nausea, headache, dizziness, somnolence SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF, Intra-vaginal ejaculatory latency time (IVELT) evaluation, serum T, and PRL levels</p>

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<p>Seibel (2002) ⁷⁰</p> <p>Funding source: NR</p>	<p>N screened = 226 N randomized = 48</p> <p>IG, n = 24 CG, n = 24</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men aged <70 yr; on hemodialysis for ≥6 mo; in stable relationship with female partner</p> <p>Exclusion: penile anatomic abnormality; cirrhosis; diabetes; angina; severe anemia; nitrate treatment; hx of recent (within previous 6 mo) stroke or myocardial infarction; illiteracy; current ED treatment</p>	<p>Age, mean (sd): 49 (10) vs. 46 (9)</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p> <p>Other: Duration of hemodialysis, mean (sd): 42 (31) vs. 36 (26) mo</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: Nr</p> <p>Mixed ED: NR</p> <p>Other: ED severity, n: Severe 2 vs. 3 Moderate 11 vs. 10 Mild-moderate 5 vs. 6 Mild 2 vs. 2</p>	<p>IG: sildenafil orally CG: placebo orally</p> <p>IG: Dose: 50 mg Duration: 1 mo Frequency: 1 dose 1 hr before sexual intercourse; max. 1/d; no drug when on hemodialysis Compliance (%): NR</p> <p>CG: Dose: placebo Duration: 1 mo Frequency: as IG Compliance (%): NR</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: 1 mo</p>	<p>Primary outcome results: IIEF -change from baseline (mean): Q3: 1.2 vs. 0.05 Q4: 1.4 vs. no change EF: 7.0 vs. 0.2 OF: 1.7 vs. 0.4 SD: 0.5 vs. 0.4 ICs: 2.6 vs. 0.7 OS: 2.3 vs. 0.6</p> <p>Other outcomes assessed: change in severity of ED;</p> <p>Withdrawals/drop-outs/loss to f/u: 4 (17) vs. 3 (13)</p> <p>WDAE: 0 TAW: 5 vs. 3; pts with AE =3 (13) vs. 3 (13); including headaches, facial flushing, dyspepsia vs. headaches and facial flushing SAE: 2 deaths in CG (neither associated with placebo ingestion or sexual intercourse)</p> <p>Ascertainment of outcomes assessed: IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Seidman (2001) 71 72</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 300 N randomized = 152</p> <p>IG, n = 74 CG, n = 78</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, with ED of at least 6 mo in duration, and in stable heterosexual relationship for > 6 mo, ED, DSM-IV (not defined) criteria for depressive disorder, 24-item Hamilton depression scale score \geq 12 at both screening interviews.</p> <p>Exclusion: other psychiatric disorder, substance abuse or dependence, current use of nitrates or antidepressant medication, abnormal serum hormone levels, hx of major hematologic renal or hepatic abnormalities, poorly controlled diabetes, retinitis pigmentosa, spinal cord injury, serious CV dx</p>	<p>Age, mean (sd): 57 (10) vs. 55 (12); range 25-81 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: baseline depression scores: Beck Depression inventory, mean, (sd): 15 (8) vs. 16 (7)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr (sd): 6 (6) vs. 5 (5) range 0.3-33 y</p> <p>Underlying disease: 1 radical prostatectomy</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: oral sildenafil CG: oral placebo</p> <p>IG: Dose: 50 mg with option to titrate up to 100 mg or down to 25 mg Duration: 12 wks Frequency: once/d Compliance (%): 87.8</p> <p>CG: Dose: NA Duration: 12 wks Frequency: once/d Compliance (%): 76.9</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wks</p> <p>Other: pts in dose grps at 12 wks, n (%): 100 mg: 57 (79) 50 mg: 14 (19) 25 mg: 1 () in IG, 73 (97) in CG.</p>	<p>Primary outcome results: Overall IIEF mean (SE) score: 23 (1.5) vs. 12 (1), p < 0.001 Ability to achieve erection; mean (SE): 4 (0.3) vs. 2 (0.2) Maintaining erection: 4 (0.3) vs.2 (0.2) CGI, improved erections, n (%): 60/66 (91) vs. 8/70 (11) Successful sexual intercourse, n (%): 59/66 (89) vs. 9/70 (13) % Pts responders = 73% vs. 14%</p> <p>Other outcomes assessed: Depressive symptoms, quality of life</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE:0 TAE, n (%): 43 (58) vs. 7 (9); AE in at least 5% of pts: headache 15 (20) vs. 5 (6); dyspepsia 11 (15) vs. 0; flushing 11 (15) vs. 1 (1); abnormal vision 6 (8) vs. 1 (1) SAE: NR</p> <p>Ascertainment of outcomes assessed: Clinical Global Impression Improvement (CGI); Self report questionnaires, Hamilton depression scale, Clinical Global Improvement scale, Beck Depression Inventory, IIEF, Life Satisfaction Checklist, physical exam</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
Shabsigh (1999) ⁷³ Funding source: NR	N screened = NR N randomized = 329 IG, n = 163 CG, n = 166 ITT analysis used for primary outcome: NR Inclusion: men with ED of 6 mo or longer Exclusion: NR	Age, mean: NR Race: NR Co-morbidities: NR Previous ED treatment: NR, all had tx for at least 6 mo prior to trial Smoking status: NR Body weight: NR	Concomitant medications: NR Duration of ED: NR Underlying disease (%): ED 100 Psychogenic ED (%): 15 Organic ED (%): 59 Mixed ED (%): 26	IG: sildenafil CG: placebo IG: Dose: 5 mg Duration: 12 wks Frequency: 1 hr before sexual activity Compliance: NR CG: Dose: placebo 5 mg Duration: 12 wks Frequency: 1 hr before sexual activity Compliance: NR Run In period: 2 wks (efficacy and toleration) Wash out period: NR F/u duration: 12 wk	Primary outcome results: IIEF, mean score: Q3: 3.9 vs. 2.3 (p < 0.001) Q4: 3.6 vs. 1.8 (p < 0.001) Other outcomes assessed: NA; aetiology of ED had no sign effect on outcome Withdrawals/drop-outs/loss to f/u: NR WDAE: NR TAE: NR SAE: NR Ascertainment of outcomes assessed: IIEF question 3 and 4 (/5)

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sharma (2006) 74</p> <p>Funding source: Zydus Cadila</p>	<p>N screened = NR N randomized = 32 (randomized cross over)</p> <p>IG/ CG, n = 32</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older and medically documented ED, who were renal transplant recipients with stable graft function in the last 6 mo; also in a stable relationship</p> <p>Exclusion: penile anatomic deformities, hx of recent stroke, MI, in last 6 mo, proliferative diabetic retinopathy, severe autonomic neuropathy, regular tx with nitrates/ androgens; SCI</p>	<p>Age, mean (sd): 40 (8)</p> <p>Race: NR</p> <p>Co-morbidities, n (%): chronic glomerulonephritis 14 (43); chronic interstitial nephritis 8 (25); diabetic nephropathy 7 (22); other basic diseases 3 (9.4)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: blood levels of hemoglobin, nitrogen, creatinine was reported</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): renal allograft</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg titrated up to 100 mg or down to 25 mg based on investigator's judgment of efficacy/ tolerability Duration: 8 wks Frequency: up to once/d Compliance: NR</p> <p>CG: Dose: NA Duration: 8 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: 2 wks</p> <p>F/u duration: end of each 8 wks study period</p> <p>Other: mean number of tablets= sildenafil 24.3 (3.3); placebo 23.8 (2.6)</p>	<p>Primary outcome results: IIEF, mean (sd): Q3: baseline 2.28 (0.72); post tx 3.9 (0.85) vs. 2.28 (0.73), P<0.001 Q4: baseline 2.09 (0.92); post 3.80 (0.66) vs. 2.15 (0.98), P<0.001 EF: baseline: 13 (3.3); post tx 22.3 (3.3) vs. 13.3 (3.43), P<0.001 OF: baseline 5.4 (1.8); post 10.4 (2.0) vs. 5.4 (1.77), P<0.001 SD: baseline 6.3 (1.4); post 6.65 (1.0) vs. 5.9 (1.99), P<0.32 IcS:baseline 5.1 (5.4); post 7.7 (1.4) vs. 5.4 (1.99), P<0.001 OS: baseline 4.8 (0.97); post 7.31 (0.9) vs. 5.1 (1.31), P<0.001 GEQ-1, % improved: 81.3% vs. 18.7%</p> <p>Other outcomes assessed: individual IIEF questions (Q13 placebo effect)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1 (<1)</p> <p>WDAE, n (%): 1 (<1) TAE, n (%): NR (AE included headache, flushing, generalized body ache, and typical bluish visual hallucination in IG) SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; diary card; laboratory blood analysis</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sharma (2006) 75</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 32 (cross over)</p> <p>IG/ CG, n = 32</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: renal transplant men with confirmed ED, and stable allograft function for the preceding 6 mo; in a stable relationship</p> <p>Exclusion: proliferative diabetic retinopathy or penile anatomic deformity; recent stroke</p>	<p>Age, mean: 40 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED, mean: 17 mo</p> <p>Underlying disease, n (%): renal surgery</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG: Dose: 50 mg Duration: 8 wks Frequency: 1 hr before sexual activity Compliance: NR</p> <p>CG: Dose: NA Duration: 8 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NA Wash out period: 2 wks</p> <p>F/u duration: 18 wks; evaluation at end of each 8 wks tx period</p>	<p>Primary outcome results: IIEF, scores: NR IG: improved in all questions (except SD domain), p<0.001 CG: ▲ only for Q13 (relationship satisfaction), p=0.03</p> <p>GAQ, % improved: 81.3% vs. 18.7%, p</=0.01</p> <p>Other outcomes assessed: concentration of ciclosporin assessed in n=5; serum creatinine level; blood urea nitrogen</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): 8 (25) vs. 2 (6.3) Headache 5 (15.6) vs. 2 (6.3); rhinorrhea and flushing 2 (6.3) vs. 0; blush visual hallucination 1(3.1) vs. 0 SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sommer (2007) 76</p> <p>Funding source: No outside support</p>	<p>N screened = NR N randomized = 112 (open label; also reported on n=18 non randomized who refused treatment)</p> <p>IG, n = 56 CG, n = 56</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 20-70 y with ED defined by IIEF –EF score of <26 for at least 6 mo in duration with mild to moderate, arteriogenic aetiology and responsive to ED treatments (PDE-5 or IC injection)</p> <p>Exclusion: penile anatomical abnormalities, primary hypoactive SD, ED of endocrine origin, radical pelvic surgery without erection, poorly controlled DM, or clinically sign. liver kidney, CV, or CNS disorders. Non responders to ED treatment (8 trials of sildenafil 100 mg, or 40 µg IC injection of PgE1), also pts with concurrent tx with nitrates, androgens or anticoagulants</p>	<p>Age, mean (range): 44.7 vs. 46.1 y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: BMI, mean (kg/m²)= 26.9 vs. 27.7</p> <p>ED severity at baseline, IIEF-EF: Severe=0 Moderate (11-16), 16 (29) vs. 20 (36) Mild to moderate (17-21) 28 (50) vs. 28 (50) Mild (22-25) 12 (21) vs. 8 (14)</p> <p>Peak flow velocity, men (sd): 25.8 (7.5) vs. 23.1 (6.9) cm/s</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 4.3 vs. 5.5 y</p> <p>Underlying disease (% of pts): NR</p> <p>Psychogenic ED (%): NR</p> <p>Physiologic ED (%): NR</p> <p>Mixed ED (%): NR</p>	<p>IG1: sildenafil IG2: sildenafil</p> <p>IG1-3: Dose: 50 mg Duration: 12 mo Frequency: every evening at bedtime Compliance: NR</p> <p>IG: Dose: 50 or 100 mg on demand for anticipated sexual activity Duration: 12 mo Frequency: NR Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NR</p> <p>F/u duration: 18 mo</p>	<p>Primary outcome results: % of pts with normal (at least 26) IIEF-EF at 12 mo: 32/48 (66.7%) [95% CI 51.6-79.6] vs. 33/49 (67.3%) [95% CI 52.5-80%]</p> <p>28/48 (58.3%) [95% CI 43.2-72.4%] vs. 4/49 (8.2%) [95% CI 2.3-19.6%] had normal EF domain scores 6 mo after completing the course of study</p> <p>Other outcomes assessed: PSV of cavernous arteries improved by 11.2 cm/s (95% CI 4.7-21.4; p=0.012) from 25.8 (7.5) to 37 (10.4) after 4 wks washout period (IG1); improved by 3.4 cm/s (95% CI –5.1-14.7; p=0.435)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 8 (14.3) vs. 7 (12.5)</p> <p>WDAE, n (%): 4 (7) vs. 4 (7) TAE, n (%): NR (AE included rhinitis in one man (IG1) vs. headache in 5, flushing in four, dyspepsia in four, and rhinitis in two (IG2) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Stuckey (2003) 77</p> <p>Funding source: Pfizer Inc, New York</p>	<p>N screened = 244 N randomized = 191</p> <p>IG, n = 97 CG, n = 94</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older with clinical dx of ED for at least 6 mo and controlled type 1 diabetes for longer than 1 y (HbA1c levels < 11%); in a stable heterosexual relationship</p> <p>Exclusion: penile anatomical deformities, major psychiatric disorder, hx of alcoholism, substance abuse, SCI, MI, stroke, heart failure, unstable angina, nitrate use; severe autonomic neuropathy, diabetes secondary to pancreatic damage; cushings syndrome or acromegaly</p>	<p>Age, mean (range): 47(25-69) y</p> <p>Race (%): White: 96 vs. 91; Black: 0 vs. 2; Asian: 4 vs. 7</p> <p>Co-morbidities: unspecified GI 6 (9) vs. 5 (8); unspecified disorders of eye: 21 (32) vs. 14 (21)</p> <p>HbA1C, % (range): 9 (6-13)</p> <p>Previous ED treatment, %: 28.4 vs. 20.4 including IC, and IU injections; pump; and sildenafil (reported dose only in IG, =28% used 50 mg, and 72% used 100 mg)</p> <p>Smoking status: Current 40 vs. 29</p> <p>Body weight, mean (range): 80 (56-118) vs. 77 (53-139) kg</p>	<p>Concomitant medications, %: Insulin: 100 (all pts) Oral antidiabetic: 3.2 vs. 2.1</p> <p>Duration of ED, mean (range): 5 (0.6-19) vs. 6 (0.7-27)</p> <p>Underlying disease, %: CVD= 34 vs. 39; hypertension= 30 vs. 33; Peripheral vascular dx: 1 vs. 5; DM 10 (15) vs. 8 (12)</p> <p>Psychogenic ED, %: 0 vs. 1</p> <p>Physiologic ED, %: 79 vs. 66</p> <p>Mixed ED, %: 21 vs. 33</p>	<p>IG: sildenafil citrate CG: placebo solution</p> <p>IG: Dose: 50 mg, option to titrate to 100 mg or 25 mg Duration: 12 wks Frequency: once/d Compliance (%): 88</p> <p>CG: Dose: NA (titration as IG) Duration: 12 wks Frequency: once/d Compliance (%): 82</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF Q3, improvement in mean scores from baseline, %: 36 vs. 20; post tx, mean (sd): 4 (0.5) vs. 3 (0.5)</p> <p>IIEF, Q4, improvement in mean score from baseline, %: 68 vs. 27; post tx, mean (sd): post tx: 3 (0.5) vs. 2 (0.5)</p> <p>GAQ, % yes: 66 vs. 29 Successful intercourse, %: 63 vs. 33</p> <p>Other outcomes assessed: subgroup analysis based on severity of ED for IIEF- OF; SD, intercourse satisfaction and OS (all values in figures); all sign better in IG vs. CG</p> <p>Withdrawals/drop-outs/loss to f/u: 8 (8) vs. 7 (7); including lack of efficacy: 2 (2) vs. 3 (3)</p> <p>WDAE, n (%): 1 (1) vs. 2 (2) TAE: 48.4 vs. 14 (n of AEs); including headache 20% vs. 7.5%; flushing 18% vs. 3%; dyspepsia 8% vs. 1%; visual disturbances 2% vs. 2% (headache, flushing and dyspepsia in >5% of pts) SAE, n (%): 0 vs. 1 (1)</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ; Questionnaires, personal diary logs</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Tan (2000) ⁷⁸ Tan (2002) ⁷⁹</p> <p>Funding source: Pfizer pharmaceuticals group (South East Asia Region)</p>	<p>N screened = NR N randomized = 254</p> <p>IG, n = 127 (final n=119) CG, n = 127 (final n=119)</p> <p>ITT analysis used for primary outcome: yes (n=16, 8 in each grp were excluded from analysis)</p> <p>Inclusion: men 26-78 with ED of at least 6 mo, in a stable heterosexual relationship for at least 6 mo</p> <p>Exclusion: genital anatomic abnormalities, SCI, co-existing sexual disorders, PRL levels 3 times higher than ULT, free T 20% below lower limit of normal in morning; hx of major psychiatric disorders, alcoholism, substance abuse, major hematologic, renal or hepatic abnormalities, stroke, MI, sign CVD for under 6 mo; hypotension, poorly controlled DM, retinopathy, retinitis pigmentosa, androgens, trazodone, nitrates or nitric oxide donor agents</p>	<p>Age, mean (range): 52 (31-78) vs. 51 (26-70)</p> <p>Race (%): 100 Asian</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): 36 (28) vs. 34 (27)</p> <p>Initial body weight, mean: 72 vs. 71 kg</p>	<p>Concomitant medications: Antidiabetic drugs 87 (34); antihypertensives 67 (26); lipid-lowering drugs 23 (9)</p> <p>Duration of ED, mean: 3.6 y</p> <p>Underlying disease, n (%): DM 91 (36); hypertension 61 (24); visual disturbance: 47 (19)</p> <p>Psychogenic ED, n (%): 15 (12) vs. 18 (14)</p> <p>Physiologic ED, n (%): 82 (65) vs. 78 (61)</p> <p>Mixed ED, n (%): 30 (24) vs. 31 (24)</p>	<p>IG: oral sildenafil CG: oral placebo</p> <p>IG1: Dose: 50 mg with option to titrate to 100 or 25 mg Duration: 12 wks Frequency: up to once/d Compliance (%): NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: up to once/d Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IIEF mean scores IG vs. CG: IIEF-Q3: 4.2 vs. 2.6 IIEF-Q4: 4.2 vs. 2.4 IIEF-EF: pre=13.3; post: 25 vs. 15.5 IIEF-OF: pre=5.6; post: 8.6 vs. 3.4 IIEF-SD: pre=7; post: 8 vs. 7 IIEF-IS: pre=6.7; post: 10.7 vs. 8.4 IIEF-OS: pre =4.5; post: 8.4 vs. 5.1 GAQ, % yes: 87 vs. 33 Intercourse success, %: 78 vs. 29.6</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 11 (4)</p> <p>WDAE, n (%): 1 (<1) vs. 1 (<1) TAE, n (%): 42 (33) vs. 29 (23), AE reported in at least 2 pts=body as a whole 18 (14) vs. 21 (17); CV events 13 (10) vs. 6 (5); respiratory system = nervous system events 7 (6) vs. 5 (4); digestive system events 5 (4) vs. 1 (0.8); special senses 5 (4) vs. 0; musculoskeletal events 4 (3) vs. 3 (2); laboratory abnormalities 2 vs. 3 SAE, n (%): 1 (<1) vs. 1 (<1); one severe angina pectoris 4 hr post medication with 100 mg sildenafil; one accidental hand injury in CG</p> <p>Ascertainment of outcomes assessed: IIEF, sexual activity & medication logs, GEQ, physical exam</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Tignol (2004) ⁸⁰</p> <p>Funding source: Pfizer Inc. (authors also supported by Pfizer)</p>	<p>N screened = 170 N randomized = 168</p> <p>IG, n = 83 CG, n = 85</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older, with ED, and in a stable relationship with a female partner for at least 6 mo</p> <p>Exclusion: major psychiatric disorder other than depression, ongoing major depressive disorder, reactive depression, hypotension, hypertension, stroke, MI, CVD, taking nitrates within 2 wks of entry</p>	<p>Age, mean (sd): 53 (10) y</p> <p>Race (%): White (100%)</p> <p>Co-morbidities, %: hypertension 10.8 vs. 16.5; DM 8.4 vs. 7.1</p> <p>Previous ED treatment: median duration: 89 (4-133) d vs. 86 (13-154) d</p> <p>Smoking status, %: present smoker 31.3 vs. 34.1</p> <p>Body weight: NR</p> <p>Other: mean (range) depression duration 4.8 (0-28.5) vs. 3.1 (0.2-20.5) y</p>	<p>Concomitant medications, %: antihypertensives = 13 vs. 14; diabetes drugs= 10 vs. 6</p> <p>Duration of ED: 4.3 (0.4-20.8) vs. 4.2 (0.3-32.9) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 51 (61) vs. 64 (75)</p> <p>Physiologic ED, n (%): 5 (6) vs. 2 (2.)</p> <p>Mixed ED, n (%): 27 (33) vs. 19 (22)</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: sildenafil Dose: 50 mg (flexible dosing) Duration: 12 wks Frequency: once/d Compliance (%): NR</p> <p>CG: placebo Dose: NR Duration: 12 wks Frequency: once/d Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF Q3: IG: NR vs. CG: NR, p < 0.0001 (improved in IG)</p> <p>IIEF Q3: IG: NR vs. CG: NR, p < 0.0001 (improved in IG) Successful intercourse attempts, % = 74 vs. 29, p = 0.0001 GAQ, % yes: 83 vs. 34</p> <p>Other outcomes assessed: mean IIEF scores for 5 other functional domains demonstrated in figures, mean Life Satisfaction Checklist (LSC) score</p> <p>Withdrawals/drop-outs/loss to f/u: 9 (11) vs. 10 (12)</p> <p>WDAE, n (%): 1 (1) vs. 0; also 3 (4) vs. 2 (2) temporarily discontinued or reduced dose TAE, n (%): 34 (41) vs. 14 (17); most common AEs were headache and flushing; abnormal vision in 2 (2) vs. 1 (1) including a change in colour vision (bluish tinge) in placebo SAE: NR</p> <p>Ascertainment of outcomes assessed: Questionnaires (IIEF, LSC, GEA)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Ugarte (2002) ⁸¹</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = 249 N randomized = 242</p> <p>IG1, n = 123 IG2, n = 119 CG, n = NA</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: men 18 or older, with mild to moderate ED for at least 6 mo; in stable sexual relationship with female partner</p> <p>Exclusion: psychological or social risk factor for entering the trial; genital /anatomic deformity impairing erection; ED due to another primary sexual disorder, SCI or radical prostatectomy, marked liver function abnormality, hx of gastro-duodenal ulceration, retinitis pigmentosa); use of investigational drugs in last 6 wk; or medications associated with ED unless prescribed 2 wk before study entry and no dosage adjustments anticipated; use of nitrates, nitric oxide donors or alpha blockers</p>	<p>Age, mean (range): 53.6 (25-75) vs. 55.2 (28-80) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (range): 79.9 (43-115) vs. 77.1 (51-155) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (range): 6 mo – 34 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 19 (15.4) vs. 17 (14)</p> <p>Physiologic ED, n (%): 42 (34) vs. 41 (34.5)</p> <p>Mixed ED, n (%): 62 (50) vs. 61 (51)</p>	<p>IG1: sildenafil citrate IG2: phentolamine</p> <p>IG1: Dose: 50 mg, titration option to 25 or 100 mg Duration: 8 wk Frequency: up to 1 dose/ d; 1 hr before sexual activity; max. 1/day Compliance (%): NR</p> <p>IG2: Dose: 40 mg Duration: 8 wk Frequency: up to 1 dose/ d; 30 minutes before sexual activity Compliance (%): NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 13 wk</p>	<p>Primary outcome results:IIEF domain scores, Least square mean score (sd): EF: pre= 16.3 vs. 15.4; post: (1-5,15): 27.2 (0.6) vs. 19.4 (0.7) OF (9,10): pre= 6.6 vs. 6; post: 9.3 (0.2) vs. 7.5 (0.2) SD (11,12): pre=6.8; post: 7.9 (0.1) vs. 7 (0.1) IC s (6-8): pre=8.2 vs. 7.9; post: 13.7 (0.3) vs. 1.3(0.3) OS (13,14): pre= 4.8 vs. 4.6; post: 8.5 (0.2) vs. 5.7 (0.2) GEQ, improved erection % yes: 95 vs. 51 GEQ, improved sexual ability % yes: 94.4 vs.46.4</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 29 (12)</p> <p>WDAE, n (%): 1 (<1) vs. 4 (3.4) TAE, n (%): 41 (33) vs. 49 (41), pts with at least 3% incidence of AE including headache 14 (11.4) vs. 6 (5); rhinitis 6 (5) vs. 15 (12.6); flushing 5 (4) vs. 3 (<1); tachycardia 1 (0.8) vs. 7 (5.9); nausea 1 (0.8) vs. 6 (5) SAE: 1 (0.8) vs.3 (2.5)</p> <p>Ascertainment of outcomes assessed: IIEF; EF and other domains; GEQ (two questions); event log of sexual function</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Webster (2004) 82</p> <p>Funding source: Grant from University of Alberta Hospital Foundation</p>	<p>N screened = 41 N randomized = 35 (cross over)</p> <p>IG/ CG, n = 35</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: pts with moderate to severe heart failure who had documented ED</p> <p>Exclusion: Pts with hypotension or SBP less than 80 mmHg; hx of myocardial ischemia, receiving psychotropic tx, hx of drug/alcohol abuse, abnormal ECG</p>	<p>Age, mean (SEM): 60 (2) y</p> <p>Race (%): NR</p> <p>Co-morbidities, %: ischemia 60; idiopathic 26; hypertension 69; DM 26</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, %: ACE inhibitors=β-blockers 94; diuretics 89; aspirin 66, coumadin=digoxin 63; Ca channel blocker 11</p> <p>Duration of ED: NR</p> <p>Underlying disease: CHF</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: Mean (SEM) IIEF score = 9(1)</p>	<p>IG: Sildenafil CG: Placebo</p> <p>IG1: Sildenafil Dose: 50 mg Duration: 6 wks Frequency: once/d Compliance: 100%</p> <p>CG: Placebo Dose: NR Duration: 6 wks Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: before and after crossover 12 wks</p>	<p>Primary outcome results: Mean (SE) IIEF score (IG1 vs. CG) before crossover at 6 wks = improved in IG1 (p < 0.001)</p> <p>Mean (SE) IIEF score (IG1 vs. CG) after crossover = improved in IG1 (p < 0.001)</p> <p>Overall response on IIEF scores before and after crossover (IG1-CG vs. CG-IG1) = NS (p=0.98)</p> <p>Other outcomes assessed: Mean scores of IIEF (shown in figure); no sign reduction of BP, or HR in IG</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: NR TAE: NR; arterial fibrillation in 2 (5.7); heart failure/dyspnea 1 (2.8), all during placebo phase SAE: 2 deaths (study personnel)</p> <p>Ascertainment of outcomes assessed: IIEF Questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Young (2002) ⁸³</p> <p>Funding source: Pfizer Inc.</p>	<p>N screened = blacks (B) 310, Hispanics (H) 257 N randomized = 443 (B, n =246, H, n = 197); open label, n = 191 (B=211; H=144)</p> <p>IG, n =223 (B= 124, H = 99) CG, n =220 (B= 122, H =98)</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: black American or Hispanic American, 18 or older; documented clinical diagnosis of ED for longer than 6 mo; in stable relationship</p> <p>Exclusion: previous txt with sildenafil for ED; other sexual disorders as primary dx; ▲ PRL levels or low free-T levels; uncontrolled DM; hx of stroke or MI within previous 6 mo; ED as consequence of SCI; concomitant use of nitrates, androgens or trazodone</p>	<p>Age, mean (sd): B= 53 (25-73) vs. 54 (23-81) H=55 (31-84) vs. 53 (22-75) y</p> <p>Race, n (%): black 246 (56), Hispanic 195 (44)</p> <p>Co-morbidities: % with ≥1 current medical condition B= 90; H= 90 vs. 86</p> <p>Previous ED treatment: NR</p> <p>Smoking status (%): current B= 38 vs. 31; H= 18 vs. 26</p> <p>Body weight, mean (range): B=95 (50-182) kg H= 85 (56-133) kg</p>	<p>Concomitant medications: % with any B= 86 vs. 87 H =80 vs. 75</p> <p>Duration of ED, mean (range): B= 4 (0.3-33) vs. 5.2 (0.3-30) H= 4 (0.2-43) vs.3 (0.2-20) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED (%): B=13; H 10 vs. 11</p> <p>Physiologic ED (%): B =56 vs. 54; H= 66 vs. 60</p> <p>Mixed ED (%): B 32 vs. 33; H 24 vs. 29</p> <p>Other: Severity of ED (%) Mild to moderate: B= 61 vs. 60, H= 46 vs. 62; Severe, B =31 vs. 30, H =39 vs. 26</p>	<p>IG: sildenafil CG: placebo</p> <p>IG: Dose: 50 mg, option to titrate to 100 or 25 mg Duration: 12 wk Frequency: up to. 1/d, one hr before sexual intercourse Compliance (%): NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: as IG Compliance (%): NR</p> <p>Run In period: None Wash out period: None</p> <p>F/u duration: 12 wk parallel (option to switch to opposite arm during the 12 wk parallel period)+ 12 wk of open-label tx extension (safety results shown)</p> <p>Other: results reported for 6 wks post intervention; n of pts who switched also reported</p>	<p>Primary outcome results: IG vs. CG, (B-H where not equal), mean score at 6 wks: IIEF, Q3: pre: 2.6-2.4; post: 4 vs. 3 IIEF, Q4: pre: 2; post 4 vs. 3 IIEF, EF: pre 14; post 23 vs. 18-16 IIEF, OF: pre 6; post: 8 vs. 6-7 IIEF, SD: pre 7; post 7 vs. 7-6 IIEF, ICs: pre: 6-7; post 11 vs. 9-8 IIEF, OS: pre 4-5; post 8 vs. 6 GEQ-Q1, %: B: 79 vs. 38; H: 82 vs. 30 GEQ-Q2, %: B: 81 vs. 36; H: 80 vs. 29 GEQ-Q3: B: 4 vs. 3; H: 3.5 vs. 2.5</p> <p>Other outcomes assessed: barriers to tx; subgrp ED severity; EDITS, EPQ</p> <p>Withdrawals/drop-outs/loss to f/u: B: 6 (5) vs. 10 (10); H: 13 (11) vs. 9 (9) Open label phase, B: 20 (9), H: 19 (13)</p> <p>WDAE, n (%): B=0; H: 2 (2) vs. 0 TAE, n (%): 12 wks, B: 18 (15) vs. 3 (3); H: 27 (22) vs. 11 (11); most common, % in IG/ pts switched to IG vs. CG: headache B: 11 vs. 2; H: 16/12 vs. 7; vasodilation B: 2 vs. 0; H: 7/9 vs. 2; rhinitis B: 2 vs. 0; H: 2/4 vs. 0; nausea B: 1 vs. 0, H: 2/1 vs. 0; dizziness B: 0; H: 3/1 vs. 0; abnormal vision B: 2 vs. 0, H: 2/1 vs. 0 SAE, n (%): 1 (<1) in IG (H)</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ; EDITS; erection problem question (EPQ)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Zinner (2007) ⁸⁴</p> <p>Funding source: Pfizer Inc. (conflict of interest: author has spoken for Pfizer)</p>	<p>N screened = N randomized = 48 (double cross over design- impact of food)</p> <p>IG/CG 1&2, n = 24 IG/CG 3&4, n = 24</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older in a stable relationship or 6 mo or longer taking 50 or 100 mg sildenafil; with IIEF of 25 or less and minimum 4 sexual attempts/ mo</p> <p>Exclusion: no response to sildenafil 100 mg; CVD in last 3 mo; current use or likely prescription of nitric oxide donors; use of an alpha-blocker; use of other ED tx; hx of retinitis pigmentosa; tx with ritonavir, or an investigational drug within 6 wks of screening; any known medical or psychological conditions; blood donation within 4 wks; drug or alcohol abuse; potential non-compliance</p>	<p>Age, mean (range): 57 (29-79) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): heart disease IG1&2= 4 (16.7) IG3&4 =1 (4.2)</p> <p>Previous ED treatment: 100% had been treated with sildenafil 50 or 100 mg</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: recreational drug use, n (%) IG1-2= 14 (58.3) IG3-4= 19 (79.2)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1-4: Sildenafil CG1-4: placebo</p> <p>IG1-4 (sildenafil): Dose: 100 mg Duration: 16 wks (4 wk s/ tx period) Frequency: 1 hr before meal (IG1); 30-60 min before sexual activity (IG2&4); during meal (IG3) Compliance:</p> <p>CG1-4 (placebo): Dose: NA Duration: 16 wks as IG Frequency: 30-60 min before coitus (IG1&3); 1 hr before meal (IG2); during meal (IG4) Compliance:</p> <p>Run In period: 1-2 wks (stopped sildenafil dosing) Wash out period: NR F/u duration: end of each tx period</p>	<p>Primary outcome results: IG1 vs. IG2 & IG3 vs. IG4 IIEF-EF change from baseline, mean: 11.4 vs. 11.4 & 11.2 vs. 11.2</p> <p>SEP-Q2 intercourse attempts: 93.9% vs. 91.8% & 91.4% vs. 92.6% SEP-Q3: 84.7% vs. 85.9% & 83.4% vs. 87.5%</p> <p>Time between dosing and intercourse attempt ▼ responses to SEP-3 (from max 92.8% at 1.5-2 hr to 81.6% when taken >10 hrs prior to coitus)</p> <p>Other outcomes assessed: mean interval between dosing and coitus in IG2 & IG4 =1.3 (0.6) & 1.1 (0.5) hr Intervals between dosing and coitus in IG1 & IG4= 4.8 (1.8) & 3.6 (1.9) hr No sign differences for EDITS responses or preference and satisfaction for any of the regiments</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): NR SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF; SEP- Q2 & 3; EDITS</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C2-Oral Vardenafil

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Carson (2004) ⁸⁵ ⁸⁶</p> <p>Companion Hatzichristou (2005) ⁸⁶</p> <p>Funding source: Bayer Corporation and GlaxoSmithKline</p>	<p>N screened = NR N randomized = 463</p> <p>IG, n = 233 CG, n = 230</p> <p>ITT analysis used for primary outcome: yes (N =454, n = 229 vs. n = 225)</p> <p>Inclusion: men 18 or older with ED, no response to 100 mg sildenafil indicated by at least 4/ 6 unsuccessful intercourse attempts; in heterosexual relationship for past 6 mo</p> <p>Exclusion: penile anatomical abnormalities; hypoactive SD; ED due to SCI or radical prostatectomy; retinitis pigmentosa; hepatitis B, C surface antigen or; unstable angina pectoris; MI, stroke, ischemia; DM; hypotension; use of anticoagulants, androgens, trazodone, antiandrogens, alpha1 antagonist, potent HIV protease inhibitor, nitrates, itraconazole, ketokonazole, erythromycin (more in full text)</p>	<p>Age, mean (range): 60 (29-83) vs. 59 (23-88) y</p> <p>Race, n (%): White: 404 (87); Asian: 18 (10); Hispanic: 14 (3); Black: 13 (3); Other: 5 (1)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: Sildenafil up to 100 mg</p> <p>BMI, mean (sd): 29 (4) vs. 28 (4) kg/m²</p> <p>Body weigh: NR Other: Severity of ED, Severe: 242 (52); moderate 164 (36); mild to moderate 9 (2); mild 8 (2)</p> <p>IIEF-EF domain= 9.3 vs. 9.7</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 5 (4) y</p> <p>Underlying disease, n (%): Hypertension 90 (39) vs. 92 (41) DM 78 (34) vs. 7 (25); Benign prostatic hyperplasia: 39 (17) vs. 40 (18); CAD 8 (3) vs. 11 (5)</p> <p>Psychogenic ED, n (%): 8 (3) vs. 20 (9)</p> <p>Physiologic ED, n (%): 148 (65) vs. 128 (57)</p> <p>Mixed ED, n (%): 3 (32% vs. 77 (34)</p>	<p>IG: vardenafil CG: Placebo</p> <p>IG: Dose: 10 mg (option to titrated to 5 or 20 mg at 4 and 8 wks) Duration: 12 wks Frequency: max 1/d Compliance: 99% [n=2 (<1%) did not complete]</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: 98%; [n=4 (2%) did not complete]</p> <p>Run In period: NR Wash out period: 24 hrs</p> <p>F/u duration: 12 wks + 24 hrs post final visit.</p> <p>Note: topical formulas were allowed in this study; investigational drugs within 30 days of screening therapy for ED within 7 d or vardenafil at any time prior to study.</p>	<p>Primary outcome results: IIEF-EF: baseline=<10 (severe ED); post tx pts with normal scores, n (%)=67 (31) vs. 12 (6)</p> <p>SEP- Q2, % yes, n (%): 0.25 hr post dosing= 57 (62) vs. 55 (30) >6 hr post dosing= 30 (77) vs. 18 (50)</p> <p>SEP-Q3, % yes, n (%): 0.25 hr post dosing= 57 (53) vs. 55 (12) >6 hr post dosing=30 (70) vs. 17 (24)</p> <p>GAQ, % yes: 61.6% vs. 15% 61.8% vs. 14.7% at LOCF, p<0.001)</p> <p>Other outcomes assessed: intercourse attempts data</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 25 (11) vs. 41 (18); including insufficient tx effect in 5 (2) vs. 17 (7)</p> <p>WDAE, n (%): 5 (2) vs. 3 (2) TAE, n (%): 40.7% vs. 22.6%; drug related in 2% or more=flushing 16 (7) vs. 2 (1); headache: 15 (6) vs. 4 (2); nasal congestion: 11 (5) vs. 1 (<1); dyspepsia: 8 (3) vs. 0; total mild AE= 55 (24) vs. 20 (9); total moderate AE= 34 (15) vs. 25 (11) SAE, n (%): 7 (3.0) vs. 3 (0.9)</p> <p>Outcome ascertainment: IIEF-EF; SEP, Q2 and 3; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Demir (2006) ⁸⁷</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 60</p> <p>IG, n = 39 CG, n = 21 (n=15 with no ED also served as ctrls, data not shown)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED (diagnose with color Doppler Ultrasound and IC injection of 60 mg papaverine) and functioning renal graft (serum creatinine level <2 mg/dL); in a stable relationship with a partner</p> <p>Exclusion: stroke, DM, MI, CHD, overt heart failure; sing penile anatomical deformities active peptic ulcer, chronic liver disease; sign hypo/hypertension; blood coagulation disorders; nitrate tx</p>	<p>Age, mean (sd): 48 (7.4) vs. 50 (7.1) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): immuno-suppressant tx: cycloporine (14+8) or JD506 (25+13); low dose prednisolone and ycophenolate mofetil</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): Renal transplant</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: 10 mg titrated to 20 mg based on efficacy measures Duration: 4 wks Frequency: up to once/d; 1 hr prior to sexual activity Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 4 wks</p>	<p>Primary outcome results: IIEF-EF, mean (sd): Baseline 12.8 (3.5) vs. 12.5 (3.7) Post tx 26.46 (2.4) vs. 13.27 (2.8) Tx effect, P<0.001</p> <p>ED Severity, baseline- post tx in IG: Severe: 3 -0 Moderate 17- 0 Mild to moderate: 9 – 2 Mild 10-4 None 0 – 32</p> <p>Other outcomes assessed: IIEF individual scores of Q1-5 and 15; serum T, FSH, and LH levels, not sign. between grps (data not provided)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE: NR TAE, n (%): 7 (18), including headache in 3, palpitation in one, flushing in two and dyspepsia in one SAE: NR</p> <p>Outcome ascertainment: self administered IIEF on renal transplant pts</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Edwards (2006) 88</p> <p>Funding source: NR</p>	<p>N screened = 288 N randomized = 260</p> <p>IG, n = 194 CG, n = 66</p> <p>ITT analysis used for primary outcome: yes (LOCF; n=254)</p> <p>Inclusion: men 18 or older with ED for at least 6 mo; no prior hx of PDE5i use</p> <p>Exclusion: unstable medical, psychiatric condition; substance abuse; hypoactive SD; SCI, surgical prostatectomy; hereditary degenerative retinal dx; hepatitis B surface angina, hepatitis C, HIV; liver disease; sign hematologic disease; active peptic ulceration; any cardiovascular condition; MI, stroke, serious arrhythmia within 6 mo of entry; uncontrolled hypo/hypertension; hx of malignancy within 5 y; use of nitrates or nitric oxide donors; androgens or any other investigational drug</p>	<p>Age, mean: 53.6 vs. 54.2</p> <p>Race: NR</p> <p>Co-morbidities, %: DM 27; hypertension 35; Hyperlipidemia 10 vs. 6</p> <p>Previous ED treatment:</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: BMI, mean 27.4 kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: 2 y</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, %: 16 vs. 23</p> <p>Physiologic ED, %: 29 vs. 24</p> <p>Mixed ED, %: 55 vs. 53</p> <p>Other: Baseline IIEF score: 13.6 Severity of ED, %: Severe 29% vs. 39%</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: flexible dose starting dose of 10 mg for 4 wks; adjusted to 5 or 20 mg for the next 8 wks Duration: 12 wks Frequency: NR Compliance: 99%</p> <p>CG: Dose: NA Duration: 12 wks Frequency: NR Compliance: 100%</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks (excluding the 4 wks run-in period)</p>	<p>Primary outcome results: IIEF-EF, mean: baseline moderate; post tx 23.5 vs. 15.8; increase on score of 8.8 in IG vs. CG (95% CI 6.4, 11.1; p<0.0001)</p> <p>SEP-2, %: baseline 48 vs. 46 12 wks: 85 vs. 65</p> <p>SEP-3, %: Baseline: 21 vs. 22 12 wks: 78 vs. 49</p> <p>GAQ, % improved: 83% vs. 38%, p<0.0001</p> <p>Other outcomes assessed: TSS, sign better score in IG vs. CG, p<0.0001</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 12 (6.7) vs. 4 (6.1)</p> <p>WDAE, n (%): 3 (1.5) vs. 1 (1.5); IG included MI, aortic bifurcation graft; CG muscle cramp</p> <p>TAE, n (%): NR; tx related occurring in 2% or more of pts, %: headache 5.2 vs. 0; flushing 7.3 vs. 0; Influenza 1 vs. 3</p> <p>SAE, n (%): 2 (1.0) vs. 0; aortic bifurcation graft and MI (MI occurred 5 d after last dose of 10 mg); no death occurred</p> <p>Outcome ascertainment: SEP- 2, 3; GAQ; IIEF-EF; Treatment Satisfaction Scale (TSS)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (2003) 89</p> <p>Funding source: Bayer Corporation</p>	<p>N screened = 452 N randomized = 452</p> <p>IG1, n = 153 (ITT = 149) IG2, n = 149 (ITT= 141) CG, n = 150 (ITT= 140)</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men older than 18 y, and clinical diagnosis of type 1 or type 2 DM, Ed of 6 mo or longer. HbA1c \geq12%.</p> <p>Exclusion: ED due to radical prostatectomy, hypoactive SD; SCI. MI, stroke, ischemia; sign arrhythmia; uncontrolled atrial tachyarrhythmia, unstable angina pectoris, liver dx, haematological dx or bleeding disorder, resting hypo/hypertension, retinitis pigmentosa, progressive retinopathy, autonomic neuropathy, migraine headaches; AE or dissatisfaction with Sildenafil; Nitrates, anti androgens, anti coagulant androgens, trazodone hypochloride not allowed</p>	<p>Age, mean (sd): 57 (NR) y</p> <p>Race n (%): White 350 (80); Black 41 (9); Hispanic 15 (8) Other 13 (3)</p> <p>Co-morbidities, n (%): Hypertension 231(53); depressive dx 45 (10)</p> <p>HbA1C levels, n (%): \leq 6 = 12 (3); > 6 to < 8= 192 (43) \geq 8.0 = 231 (53)</p> <p>Previous ED treatment n (%): Sildenafil 256 (58)</p> <p>Body weight: NR</p> <p>Other: Severity of ED n (%): Severe (<11)=240 (55); Moderate (11-16) 102 (23); Mild to Moderate (17-21): 68 (15); Mild (22-25): 26 (9); Normal (\geq 26): 3 (<1), only in IG2 & CG</p>	<p>Concomitant Medications, n (%): Beta Blockers 52 (12); Renin-angiotension system acting agents 210 (50); Calcium-channel blockers 45 (10); Serum lipid-reducing agents 146 (33); Diuretics 71 (16); Other antihypertensives 40 (9); Insulin 152 (35); Glucose-lowering drugs 318 (72)</p> <p>Duration of ED: 3.5 y</p> <p>Underlying disease: 88% type 2 diabetes and poor glycemic control</p> <p>Psychogenic ED: 2 (<1) only in IG1: 2 (1)</p> <p>Physiologic (organic) ED, n (%): 358 (81)</p> <p>Mixed ED: 77 (18)</p>	<p>IG1: vardenafil IG2: vardenafil CG: Placebo</p> <p>IG1: Dose: 10 mg Duration: 12 wks Frequency: as needed, no more than 1/day Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 12 wks Frequency: as needed, no more than 1/d Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as needed, no more than 1/d Compliance: NR</p> <p>Run In period: 4 wk unmedicated phase Wash out period: NR</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IG1 vs. IG2 vs. CG IIEF-EF, mean final score: 17 vs. 19 vs. 13 (change from baseline: 1.4 vs. 6 vs. 8) SEP-Q2, mean least square success rate (%): 61 vs. 64 vs. 36 (in severe ED= NR vs. 40 vs. 11; in mild ED= NR vs. 75 vs. 47) SEP-Q3, mean least square per pts (%): 49 vs. 54 vs. 23 (type I diabetes= 48 vs. 65 vs. 10; type II= 49 vs. 52 vs. 25) GAQ, proportion of men with improved erection: 54% vs. 72% vs. 13%</p> <p>Other outcomes assessed: Blood chemistries, ECG</p> <p>Withdrawals/drop-outs/loss to f/u: 73 (17)</p> <p>WDAE, n (%): 4 (3) vs. 5 (3) vs. 2 (1); headache, cutaneous flushing, rhinitis TAE, n (%): 7 (5) vs. 9 (6) vs. 6 (4) SAE, n: 3 (2) vs. 4 (3) vs. 4 (3); including chest pain, dyspnea, larynx edema, asthma (n=1); depression, hypesthesia, or moderate amnesia; no death occurred</p> <p>Outcome ascertainment: IIEF, SEP, Q2 and 3; GAQ, diary questions</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (2005) 90 91</p> <p>Companion study, by Fisher (2005)</p> <p>Funding source: Bayer HealthCare (conflict of interest for authors paid by Bayer Health Care)</p>	<p>N screened = NR N randomized = 229</p> <p>IG, n = 116 CG, n = 113</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men with ED of 6 mo or longer, previously treated for ED who had a stable heterosexual relationship for => 6 mo with a female partner without sexual disorder, Female Sexual Function Index (FSFI) > 26.55</p> <p>Exclusion: pts with unstable medical conditions, sign penile deformities, SCI, hx of prostatectomy, retinitis pigmentosa, unstable angina pectoris, MI, uncontrolled atrial fibrillation, taking nitrates or nitric oxide donors, anticoagulants, androgens, antiandrogens, indinavir, intraconazole, or erythromycin or any ED drug; female partner's having primary hypoactive sexual disorder measured by Female Sexual Function Index</p>	<p>Age, mean (sd): 58 (28-79) y</p> <p>Race (%): White: 85%, Black: 8%, Other: 7%</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: prior sildenafil in 81% vs. 91%</p> <p>BMI, mean: 29 kg/m²</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: Mean sexual intercourse activity: 6 during run in</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 4.7 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, %: 44.5%</p> <p>Physiologic ED, %: 5%</p> <p>Mixed ED, %: 50%</p>	<p>IG: vardenafil CG: placebo</p> <p>IG: Dose: starting dose 10 mg with option to titrate to 5 or 20 mg at 4 wks Duration: 12 wks Frequency: NR Compliance: NR</p> <p>CG: Dose: NR Duration: 12 wks Frequency: NR Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF-EF, mean score: baseline: 13; post tx 23 vs.13.5, p < 0.0001 (IG vs. CG)</p> <p>% Success rate of improved least squares mean on Sexual Encounter Profile: SEP-Q2, % yes: 80 vs. 47, p <0.0001 SEP- Q3, % yes: 68 vs. 28, p < 0.0001</p> <p>Mean Erection Quality Scale (EQS) score: 37 vs. 16, p < 0.0001 (IG vs. CG)</p> <p>Other outcomes assessed: Women's sexual function</p> <p>Withdrawals/drop-outs/loss to f/u: 1 (<1) vs. 0</p> <p>WDAE, n (%): 1 (<1) in IG; elevated creatinine TAE, n (%): drug related AEs in at least 2% of pts= 22% vs. 4%; including flushing 13 (11) vs. 0; nasal congestion 9 (8) vs. 0; headache 5 (4) vs. 3 (3); dyspepsia 4 (4) vs. 1 (<1) SAE, n (%): 1 (<1) vs. 0; unstable angina</p> <p>Outcome ascertainment: IIEF EF domain (Q1, 5, and 15); SEP Q2 and 3; Erection Quality Scale (EQS)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Hatzichristou (2004) ^{92 93}</p> <p>Funding source: Bayer Corporation, Bayer AG, GlaxoSmithKline</p>	<p>N screened = NR N randomized = 323</p> <p>IG1, n = 157 (ITT, n = 154) CG, n = 166 (ITT, n = 155)</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older with ED (NIH consensus), stable heterosexual relationship for 6 mo or longer, at least 50% of 4 or more attempts at sexual intercourse on 4 separate d during the 4 wk baseline period unsuccessful; answer 'no' to at least 1 diary question (IIEF)</p> <p>Exclusion: penile abnormalities, primary hypoactive SD, ED due to SCI; radical prostatectomy, unstable angina, poorly controlled DM, hypertension; liver or hematologic dx; use of organic nitrates, other nitric oxide donors, or potent CYP3A4; sildenafil use permitted except for unresponsiveness or WDAE in last 7 d prior to screening</p>	<p>Age, mean: 54 vs. 53 y</p> <p>Race (%): NR</p> <p>Co-morbidities, (%): hypertension 34 vs. 24; DM 16 vs. 20; hyperlipidemia 2 vs. 5; Cardiac dx 9 vs. 6; respiratory, thoracic</p> <p>Previous ED treatment, (%): Prior sildenafil use 54 vs. 50</p> <p>BMI, mean: 27 kg/m²</p> <p>Smoking status: Non smoker 61 % past smokers</p> <p>Body weight, mean: 81 vs. 82 kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 2 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, %: 21 vs. 22</p> <p>Physiologic ED, %: 37 vs. 42</p> <p>Mixed ED, %: 43 vs. 36</p>	<p>IG: Vardendafil (flexible dose) CG: placebo</p> <p>IG1: Dose: 10 mg titrated up or down if desired) Duration: 12 wks Frequency: as needed, no more than 1 dose/d Compliance: NR</p> <p>CG: Dose: placebo (titration as IG) Duration: 12 wks Frequency: as needed, no more than 1 dose/d Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wk</p> <p>Other: Titration data, n (%) At wk 4- down to 5 mg: 6 (4) vs. 0 At wk 4-up to 20 mg: 95 (61) vs. 136 (88) At wk 8- down to 5 or 10 mg: 7 (5) vs. 1 (<1) At wk 8- up to 20 mg: 20 (13) vs. 4 (3)</p>	<p>Primary outcome results: IIEF- EF, mean: Baseline=12.8; post tx: 24 vs. 16 SEP-Q2 (% yes): 84 vs. 53 SEP-Q3 (% yes): 74 vs. 34 GAQ; (% yes): 86 vs. 33</p> <p>Erection hardness mean (%): 63 vs. 23 OS (%): 65 vs. 28 Penis enlargement (%): 92 vs. 75 Successful ejaculation (%): 79 vs. 56 (all p<0.005)</p> <p>Other outcomes assessed: sub-grp by dose; depression; self confidence</p> <p>Withdrawals/drop-outs/loss to f/u: 22 (14) vs. 45 (29)</p> <p>WDAE, n (%): 5 (3) vs. 3 (2); tx emergent AEs only: abdominal pain, headache, dysphagia, pneumonia vs. accidental injury, vascular anomaly, ▲ CPK)</p> <p>TAE, %: pts with at least one AE = 45 vs. 27 (data provided for AE of 2 or more incidence= flushing, headache, rhinitis, flu syndrome, dyspepsia, back pain, CPK increase, dizziness, accidental injury, hypertension and QT interval prolonged); total n of AE= 94 vs. 50</p> <p>SAE: 4 (2.5) vs. 5 (3); cause NR</p> <p>Outcome ascertainment: IIEF, GAQ; SEP question 2 and 3; pts diary</p>

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<p>Hellstrom (2002) 94 95 96 97</p> <p>Funding source: Bayer Pharmaceutical & Bayer Inc.</p>	<p>N screened = 1311 N randomized = 805 (parallel grps)</p> <p>IG1: n= 193 IG2: n = 199 IG3: n = 188 CG: n = 182</p> <p>ITT analysis used for primary outcome: Yes (n=749; safety population: n=762)</p> <p>Inclusion: heterosexual men 18 y or older with ED, > 6 mo in duration; also with 50% or more failure rate in maintaining erection on at least 4 intercourse attempts on 4 separate d before tx</p> <p>Exclusion: Ed due to SCI, radical prostatectomy, retinitis pigmentosa, angina pectoris or poorly controlled DM; primary hypoactive SD, no response to sildenafil, hx of hepatitis B or C, & concomitant use of nitrates</p> <p>Note: Data reported as IG1 vs. IG2 vs. IG3 vs. CG</p>	<p>Age, range: 57-78 y (mean range per grp 57-58 y)</p> <p>Race, %: Caucasian 77 vs. 80 vs. 82 vs. 77</p> <p>Co-morbidities: hypertension, prostatic hyperplasia, diabetes type II, depression, prior MI, hyperlipidemia, obesity, all not sign. between grps</p> <p>Previous ED treatment sildenafil (%): 77 vs. 74 vs. 66 vs. 68 BMI, mean: 29 kg/m²</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 1st diagnosed: 3.6 vs. 3.6 vs. 4.2 vs. 2.9 y (1st noticed: 5.9 vs. 6 vs. 6.6 vs. 5.1 y)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, %: 7 vs. 7 vs. 7 vs. 9</p> <p>Physiologic ED, %: 61 vs. 59 vs. 60 vs. 54</p> <p>Mixed ED, %: 33 vs. 34 vs. 33 vs. 37</p> <p>Other: baseline IIEF score: 12.6 vs. 13.4 vs. 12.8 vs. 13.7</p>	<p>IG1-3: Vardenafil CG: placebo</p> <p>IG1-3: Dose: IG1 = 5 mg; IG2 = 10 mg; IG3= 20 mg Duration: 26 wks Frequency: once/ d Compliance (%): NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance (%): NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 26 wks (1 wk post last tx)</p>	<p>Primary outcomes: IIEF- mean score (LOCF), IG vs. CG: EF, Baseline=14; post tx: 18-22 vs. 15 IS (Intercourse satisfaction): 10 vs. 8 OS: 7 vs. 5</p> <p>SEP-Q2, % yes: Baseline: 43 vs. 45 vs. 41 vs. 46 Post tx: 66 vs. 76 vs. 81.1 vs. 52 SEP-Q3: Baseline=15; Post tx: 52-67 vs. 33</p> <p>GAQ, % yes: 65 vs. 80 vs. 85 vs. 28</p> <p>Other outcomes assessed: self reported erection hardness; satisfaction with intercourse, and OS</p> <p>Drop outs: n=297 (37%): 38% vs. 27% vs. 30% vs. 54% (non compliance, consent withdraw, insufficient tx effect, protocol violation, & lost to F/u) WDAE, n (%): 8 (4.1) vs. 7 (3.5) vs. 15 (7.9) vs. 4 (2.2) reasons reported only for IG=headache, abnormal liver function, nausea, and kidney calculus TAE: NR; AEs included headache, rhinitis, flushing, dyspepsia, accidental injury; all numerically more frequent in IG compare to CG SAE (%): 5 vs. 3 vs. 4 vs. 5 (one MI, no death)</p> <p>Outcome ascertainment: IIEF, GAQ, diaries, SEP, Q2 and 3</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Ishii (2006) ⁹⁸</p> <p>Funding source: Bayer Yakuhin Ltd.</p>	<p>N screened = 954 (enrolled) N randomized = 780</p> <p>IG1, n =340 IG2, n = 339 CG, n = 111</p> <p>ITT analysis used for primary outcome: yes (12 wks LOCF)</p> <p>Inclusion: men with ED (according to NIH Consensus statement) and DM > 3 y; currently under hypoglycemic drug tx or HbA_{1c} >6.5% at visit 1;</p> <p>Exclusion: penile deformities; substance abuse; major heart or liver disorders; SCI, MI, hx of hepatitis B, or C, HIV infection; cancer; hypo/hypertension; prostatectomy; retinitis pigmentosa; tx with; non respondent to PDE5i; ED tx within 7 d of trial entry (randomization); low T levels; elevated creatinine levels; tx with nitrates or nitric oxides (other criteria listed in detail in full report)</p>	<p>Age, mean (sd): 53 (7.7); range 26-64</p> <p>Race: Asian 100% (Japanese)</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: sildenafil 296 (37)</p> <p>Smoking status: NR</p> <p>Body weight, mean: 71.8 kg</p>	<p>Concomitant medications, n (%): Medication for DM</p> <p>Duration of ED: 5.4 y</p> <p>Underlying disease, n (%): DM</p> <p>Psychogenic ED, n (%): 0</p> <p>Physiologic ED, n (%): 720 (92.3)</p> <p>Mixed ED, n (%): 58 (7.7)</p> <p>Other: ED severity on EF domain score, n (%): < 11: 275 (35.4) 11-16: 231 (30) 17-21: 184 (23.8) 22-25: 79 (9.8)</p>	<p>IG1-2: Vardenafil CG: Placebo</p> <p>IG: Dose:20 mg (IG1), 10 mg (IG2) Duration: 12 wks Frequency: 1 hr prior to sexual activity up to 1/d Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks no ED tx Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF-EF, mean baseline: 13.7 12 wks LOCF, mean: 21.8 vs. 22.9 vs. 16.3 (more evident changes in pts, with baseline EF score of <11)</p> <p>SEP mean % (from graph): SEP- 2: Baseline 37.5 Post tx: 77 vs. 73 vs. 51</p> <p>SEP-3, Baseline: 12.5 Post tx: 63 vs. 60 vs. 29</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to F/u, n (%): 28 (8.4) vs. 11 (3.3) vs. 14 (13.2)</p> <p>WDAE, n (%): 9 (2.7) vs. 2 (0.6) vs. 2 (1.9)</p> <p>TAE, n (%): NR; AE in 2% or more palpitations in 7 (2) vs. 12 (4) vs. 2 (2); nasopharyngitis 17 (5) vs. 31 (9) vs. 6 (6); blood creatinine phosphokinase ▲ 1(<1) vs. 8 (2) vs. 3 (3); headache 20 (6) vs. 13 (4) vs. 2 (2); nasal congestion 6 (2) vs. 9 (3) vs. 0.; upper respiratory tract inflammation 6 (2) vs. 7 (2) vs. 2(2); hot flush 45 (13) vs. 32 (9) vs. 3 (3)</p> <p>SAE, %: 1 vs. 1 vs. 0 (detail NR)</p> <p>Outcome ascertainment: SEP-2, 3; IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Klotz (2001) ⁹⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 25 (cross over)</p> <p>IG1/IG2/CG, n = 25</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men, able to have an erection with visual stimulation; diagnosed with ED as per Cologne Evaluation Form for Erectile Dysfunction (KEED) and IIEF \leq 6 mo prior to study</p> <p>Exclusion: weak or no response to visual stimulation; no prior response to Sildenafil; ED of neurological or endocrine cause; anatomical abnormality (severe penile fibrosis); SCI, radical prostatectomy, retinitis pigmentosa, DM, any relevant comorbidities (not specified); major psychiatric illness; abnormal BP or heart rate or laboratory tests indicating AV-block] use of nitrites or nitrite oxide donors or user of any medication likely to interact with vardenafil.</p>	<p>Age, mean (sd): 34 (9), range 22-52 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight, mean (sd): 77 (7), range 64- 89 kg Broca index: 1 (0.1), range 0.9-1.1 kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1/ IG2: Vardenafil oral drinking solution + 20 min VS. (20 min post tx x 3) CG: placebo + 20 min VS. (20 min post tx x 3)</p> <p>IG1/IG2: Dose: 10 mg (IG1); 20 mg (IG2) Duration: N/A Frequency: once Compliance: 100%</p> <p>CG: Placebo Dose: NR Duration: N/A Frequency: once Compliance: 100%</p> <p>Run In period: NR Wash out period: 5 d Fasting overnight and 4 hr post initial dose</p> <p>F/u duration: immediately post tx</p>	<p>Primary outcome (EF): Duration of erection with 60% rigidity: Base: 54 (27) vs. 67 (39) vs. 31 (24) min Tip: 39 (26) vs. 45 (36) vs. 17 (20) min</p> <p>Duration of erection with >80% rigidity Base: 25 (25) vs. 31 (33) vs. 16 (19) min Tip: 9 (13) vs. 22 (30) vs. 7 (14) min</p> <p>Average event rigidity (%): Base: 64 (24) vs. 66 (20) vs. 53 (29) Tip: 47 (27) vs. 45 (23) vs. 32 (26)</p> <p>Circumference, mean (sd): Base= 8 (1); Tip = 7 (1) cm (similar in all 3 grps)</p> <p>Other outcomes assessed: duration of erection; pharmacokinetics; plasma concentration of vardenafil</p> <p>Withdrawals/drop-outs/loss to F/u: 5 (20); 3 not included in safety analysis</p> <p>WDAE: 0 TAE, n (%): 4 (18.2) vs. 2 (9.1) vs. 1 (4.5); including haematoma at the site of sampling IV cannula; headaches, moderate tiredness, nasal congestion, flush and nasal congestion SAE: 0</p> <p>Outcome ascertainment: RigiScan (15 s); measuring event rigidity of >20%</p>

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<p>Martin-Morales (2006) ¹⁰⁰</p> <p>Funding source: Química Farmacéutica Bayer</p>	<p>N screened = 159 N randomized = 121 (12 centres in Spain)</p> <p>IG, n = 64 CG, n = 65</p> <p>ITT analysis used for primary outcome: yes (n=61 vs. n=60)</p> <p>Inclusion: men 18-64 y with ED of at least 6 mo duration</p> <p>Exclusion: successful intercourse on more than 50% of attempts during the run in; T value lower than permitted (NR); IC injection of PgE1 in a few days before visit 1 with diagnostic intention; elevated liver enzymes and abnormal ECG</p>	<p>Age, mean (sd): 52.5 (8.6) y (age in severe ED pts 52.8 vs. 52.1 y)</p> <p>Race: White 100%</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): past or present smoker 89 (71.2); pack per y hx 44.9 (26.9) vs. 33.7 (21.0), p=0.019</p> <p>Body weight: 82.6 (12.1) kg</p> <p>BMI, man (sd): kg/m²</p> <p>Other: heavy alcohol consumption in 3 (2.4%)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p> <p>ED severity, n (%): by IIEF score, no ED 3 (2.5) Mild 52 (43) Moderate 36 (29.8) Sever 30 (24.8)</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: starting dose 10 mg, adjusted to 5 or 20 mg based on efficacy and tolerability Duration: 12 wks Frequency: NR Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: NR Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks (in addition to 4 wks run in)</p>	<p>Primary outcome results: Change in score from baseline to 12 wks, LS mean (sd): IIEF-EF: 10.9 (6.4) vs. 1.6 (7.7); difference -8.8 [95% CI -11.4; -6.1], p<0.001 IIEF-Q3, mean at 12 wks: 4.6 vs. 3.02 IIEF-Q4, mean at 12 wks: 4.34 vs. 2.69</p> <p>SEP, % of pts with positive response: SEP-Q2: 64.8% vs. 10.0% SEP-Q3: 62.7% vs. 0.7%</p> <p>GAQ, % improved: 73.8 vs. 25</p> <p>Other outcomes assessed: individual IIEF question scores</p> <p>Withdrawals/drop-outs/loss to F/u, n (%): 3 (4.7) vs. 5(7.7)</p> <p>WDAE, n (%): NR TAE, n (%): 18 (29.5) vs. 11 (17.2), p=0.138; including headache 8.2% vs. 0, flushing (IG only), nasopharyngitis 4.9% vs. 4.7%, flushing 8.2% vs. 0 SAE, n (%): 1 (1.6) vs. 1 (1.5); one case of intestinal obstruction in IG prior to randomization; non-cardiac chest pain in CG</p> <p>Outcome ascertainment: IIEF-EF; GAQ, SEP, 2-3; Rosenberg Self-Esteem scale, Johnson and McCoy scale Medical Outcome Short Form (SF-36) scale</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mazo (2006) ¹⁰¹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 135 (study also included n=30 healthy men, data not shown)</p> <p>IG, n = NR CG, n = NR</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED of at least 6 mo confirmed by pts hx and IIEF-EF domain; tx naïve; in a stable relationship</p> <p>Exclusion: tx with nitrates</p> <p>Note: all pts were examined with Doppler ultrasound of the penile arteries after IC injection of PgE1</p>	<p>Age, mean (sd): 51 (14.2)</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM 10 (6); hypertension 48 (29); CAD 20 (12.2), 10% vs. 14.5%; hyperlipidemia 56 (34.2); radical prostatectomy 15 (9)</p> <p>Previous ED treatment: none</p> <p>Smoking status: 27 (32.5) vs. 24 (29.3)</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): no specific cause</p> <p>Psychogenic ED, n (%): 42 (25.5)</p> <p>Physiologic ED, n (%): non-arterial 20 (12.1); arteriogenic 73 (44.3)</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: 20 mg Duration: NA Frequency: single doese Compliance: 100%</p> <p>CG: Dose: NA Duration: NA Frequency: once Compliance: 100%</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: NA (outcomes measured 1 hr post dosing)</p>	<p>Primary outcome results: No data assessed and reported</p> <p>Other outcomes assessed: % Increase of cavernosal arteries diameter, mean (sd) baseline 51 (26.5) vs. 51.1 (26.7) post tx 71.8 (22.1) vs. 51.6(27.2)</p> <p>Brachial artery flow mediated dilation: Baseline 9.7 (5.4) vs. 10.6 (5.6) Post tx 13 (4.4) vs. 10.7(5.6); Also reported analysis of outcomes for ED etiology subgroup with greater FMD values in pts with arteriogenic ED, non-sign</p> <p>Withdrawals/drop-outs/loss to F/u, n (%): 0</p> <p>WDAE, n (%): NR TAE, n (%): NR SAE, n (%): NR</p> <p>Outcome ascertainment: no ED outcome measures used; FMD by Ultrasound</p>

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<p>Montorsi, F (2004) ¹⁰²</p> <p>Funding source: Bayer Corporation, Pharmaceutical Division</p>	<p>N screened = NR N randomized = 732</p> <p>IG1, n = 237 IG2, n = 248 CG, n = 247</p> <p>ITT analysis used for primary outcome: yes (ITT: n=708; safety: n=724)</p> <p>Inclusion: men 18 or older, with ED of 6 mo or longer; with 50% or more failure in 4 attempts of intercourse during the run in period</p> <p>Exclusion: penile abnormality; hypoactive SD; uncontrolled DM; radical prostatectomy or malignancy; SCI; chronic haematological, liver dx; retinitis pigmentosa; unstable angina pectoris; atrial tachyarrhythmia; MI, or stroke ≤ 6 mo; use of nitrates, anticoagulants, androgens, anti-androgens, trazodone, selected CYP3A4 inhibitors, alpha blockers/ other ED; hx of unresponsiveness/AE to other PDE5 inhibitors</p>	<p>Age, mean (range): 56 (22-81) y</p> <p>Race, n (%): Caucasian: 603 (83); Black: 22 (3); Hispanic: 13 (2); Asian: 9 (1)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): Sildenafil 521 (72)</p> <p>BMI, mean: 27 kg/m²</p> <p>Smoking status, n (%): 385 (53)</p> <p>Body weight: NR</p> <p>Other: Severity of ED, n (%): Normal (≥26)= 9 (2%); Mild (22-25)= 63 (9%); Mild-moderate (17-21)= 149 (21); Moderate (11-16)= 205 (28); Severe (≤ 10)=280 (39)</p>	<p>Concomitant medications: Drugs acting on renin-angiotensin system: 22% Lipid reducing agents: 17% Calcium channel blockers: 9% Beta-blockers: 9%</p> <p>Duration of ED, mean: 4 y</p> <p>Underlying disease, %: hypertension 30; lipid disorders 17; DM 17; prostatic neoplasms/hypertrophy 13</p> <p>Psychogenic ED: 310 (43%)</p> <p>Physiologic ED: 118 (16%)</p> <p>Mixed ED: 295 (41%)</p>	<p>IG1: Vardenafil oral IG2: Vardenafil oral CG: Placebo oral</p> <p>IG1: Dose: 10 mg Duration: 4 wks Frequency: 1/d Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 4 wks Frequency: 1/d Compliance: NR</p> <p>CG: Placebo Dose: NA Duration: 4 wks Frequency: 1/d Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 4 wks</p>	<p>Primary outcome results: Onset of adequate erections At ≥ 25 min, (% yes): 50 vs. 53 vs. 26 At 10 min post intake in subgrps, %: Mild/moderate ED: 40 vs. 34 vs. 23 Moderate ED: 21 vs. 20 vs. 10 Severe ED: 6 vs. 12 vs. 8 IIEF, mean (sd) score, IG vs. CG: IIEF- EF: baseline= 13.4 (NR); post tx: 21 (8) vs. 14 (0.6) IIEF-IS: 10 (3) vs. 7 (0.4) IIEF-OS: 7 (3) vs. 5 (0.4) SEP-Q2, % yes: 71 vs. 73 vs. 46 SEP-Q3, % yes: IG 75-77 vs. CG 45-47</p> <p>Other outcomes assessed: SEP-3 in various time intervals post tx; elapsed time to adequate erection</p> <p>Withdrawals/drop-outs/loss to F/u, n (%): 9 (4) vs. 6 (2) vs. 14 (6) WDAE, n (%): 0 vs. 0 vs. 1 (<1) TAE (%): NR; most common AE in ≥ 2% of pts = headache 7 vs. 12 vs. 1; flushing 6 vs. 9 vs. < 1; nasal congestion 2 vs. 4 vs. < 1; nausea <1 vs. 2 vs. 0; dyspepsia 2 vs. 1 vs. 0; abdominal pain <1 vs. 2 vs. 0 SAE, n: 0 vs. 5 (2) vs. 1 (<1); one patient in IG2 experienced two SAEs; IG included 1 skin ulcer, 1 reflux dx, 1 MI, 1 syncope + encephalitis; CG one pneumonia</p> <p>Outcome ascertainment: IIEF domains; SEP-Q2 and 3</p>

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<p>Nagao (2004) ¹⁰³</p> <p>Funding source: Bayer Yakuhin Ltd</p>	<p>N screened = 375 N randomized = 283</p> <p>IG1, n = 67 IG2, n = 75 IG3, n = 66 CG, n = 71</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 20-70 y, with ED for 6 mo or longer, willing to attempt at least 4 sexual intercourse during 4 wk run-in period, with no sign cardiac dx</p> <p>Exclusion: any medical, psychiatric, substance abuse disorder; any major clinically sign dx or condition; abnormal hormone profile; use of nitrates or nitric oxide donors, beta blockers; erythromycin, ketoconazole, anti-coagulants; antiandrogens, traxodone, investigational drugs in the previous 3 mo; sildenafil or other ED tx within 7 d; hypersensitivity to sildenafil or to ≥ 3 other drugs; unresponsiveness to sildenafil</p>	<p>Age, mean (range): 52 (21-70) y</p> <p>Race (%): all Asian (Japanese)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): Sildenafil IG= 25 (12) vs. CG=4 (6)</p> <p>Smoking status: NR</p> <p>Body weight, mean: 68 kg</p> <p>Other: IIEF-EF Baseline score: mean (sd) 13.7 (5)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean range: 2- 3 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 183 (88) vs. 62 (87)</p> <p>Physiologic ED, n (%): 10 (5) vs. 4 (6)</p> <p>Mixed ED, n (%): 10 (5) vs. 5 (7)</p>	<p>IG1-IG3: Oral vardenafil CG: Placebo</p> <p>IG1-3: Dose: 5 mg (IG1); 10 mg (IG2); 20 mg (IG3) Duration: 12 wks Frequency: as required, no more than once/d Compliance (%): NR</p> <p>CG: Dose: 20 mg Duration: 12 wks Frequency: as required, no more than once/d Compliance (%): NR</p> <p>Run In period: 4 wk unmedicated Wash out period: NR</p> <p>F/u duration: 12 wks, every 4 wks for AE</p>	<p>Primary outcome results: Least square mean IG1- 2-3 vs. CG: IIEF Q3: baseline= 3; post: 4.1- 4.5- 4.6 vs. 3.2 IIEF Q4: baseline = 2; post: 3.5- 4.2- 4.3 vs. 2.3 IIEF EF: baseline= 13.7; post: 22.4- 25.6- 25.9 vs. 16.7 GAQ, % yes: 73, 85.3, 86.4 vs. 35.2 Successful intercourse, % yes, baseline vs. tx grp= IG1: 64 vs. 13; IG2: 79 vs. 8; IG3: 80 vs. 10; CG: 33 vs. 9</p> <p>Other outcomes assessed: Fugl-Meyer quality of life questionnaire</p> <p>Withdrawals/drop-outs/loss to F/u: 7 (10) vs. 9 (12) vs. 6 (9) vs. 15 (21)</p> <p>WDAE, n (%): 2 (3) vs. 2 (2.7) vs. 3 (4.5) vs. 4 (6)</p> <p>TAE, n (%): Per-patient incidence 39 (57) vs. 47 (63) vs. 49 (74) vs. 37 (52); most frequently reported IG vs. CG: flushing 60 (28) vs. 6 (4); headache 21 (10) vs. 6 (4); rhinitis 14 (7) vs. 0</p> <p>SAE: NR</p> <p>Outcome ascertainment: IIEF- Q3 & 4; GAQ; pts diary of sexual intercourse; Fugl-Meyer quality of life questionnaire</p>

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<p>Nehra (2005) ¹⁰⁴ ¹⁰⁵</p> <p>Companion Brock (2003) ¹⁰⁵</p> <p>Funding source: Bayer Pharmaceuticals Corp & Bayer Inc.</p>	<p>N screened = 567 N randomized = 440</p> <p>IG1, n = 146 (ITT, n = 135) IG2, n = 149 (ITT, n = 145) CG, n = 145 (ITT, n = 134)</p> <p>ITT analysis for primary outcome: Yes</p> <p>Inclusion: men 18 or older, with ED due to nerve sparing-radical retro pubic prostatectomy, between 0.5 and 5 y prior to screening; localized tumours allowed; 4 attempts at sexual intercourse on 4 separate d with a 50% or higher chance of failure</p> <p>Exclusion: unstable CV; Gleason tumour score \geq 8, hx of unresponsiveness to sildenafil due to lack of efficacy or sign. side effects leading to discontinuation, hypoactive SD, low serum T, DM; prostate cancer.</p>	<p>Age, mean: 60 y</p> <p>Race, (%): White 99 vs. 87 vs. 93</p> <p>Co-morbidities, n (%): depressive disorder1 (<1) vs. 8 (6) vs. 10 (7); acute MI 12 (3); hypertension 130 (30); prostate hyperplasia 11 (3); hypercholesterolemia 91 (21); vasectomy 44 (10)</p> <p>Previous ED treatment, n (%): 338 (77)</p> <p>BMI, mean: 28 kg/m²</p> <p>Smoking status, (%): 46-55% previously smoked</p> <p>Body weight: NR</p> <p>Other: IIEF EF score, mean: pre-operation =23; baseline =9</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 1.7 y (post surgery)</p> <p>Underlying disease: nerve sparing radial retro pubic prostatectomy (Mean Gleason tumour=6)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NR</p> <p>Other: neurovascular bundle sparing: n (% bilateral): 112 (76) vs. 101 (72) vs. 99 (71)</p>	<p>IG1: Oral Vardenafil IG2: Oral Vardenafil CG: placebo</p> <p>IG1/IG2: Dose: 10 mg (IG1), 20 mg (IG2) Duration: 12 wks Frequency: as needed but no more than 1x/day Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk tx free Wash out period: NA F/u duration: 12 wks</p>	<p>Primary outcome results: Last observation carried forward, mean IIEF- -Intercourse satisfaction, mean: Baseline, all =5; post tx: 8 vs. 7 vs. 5 IIEF-OF, mean: Baseline, all=5; post tx: 6 vs. 6 vs. 5 IIEF-OS: Baseline, all=5; post tx: 6 vs. 6 vs. 5 Hardness of erection, (mean per pts satisfaction rate %): 28 vs. 24 vs. 8 IIEF-EF score: Baseline, all =9; post tx 15 vs. 15 vs. 9 Mild-moderate ED: 26 vs. 25 vs. 16 Moderate ED: 23 vs. 19 vs. 13 Severe ED: 11 vs. 13 vs. 7 SEP-Q2, mean per pts success rate (%): baseline 21 vs. 18 vs. 14 Post tx: 47 vs. 48 vs. 22 SEP-Q3, mean per pts success rates (%): baseline 7 vs. 7 vs. 6; post tx 37 vs. 34 vs. 10 GAQ, % yes: 59 vs. 65 vs. 13 Other outcomes assessed: NA Withdrawals/drop-outs/loss to f/u: NR WDAE, (%): 4 vs. 3 vs. < 1% TAE, (%): Tx emergent AEs 57 vs. 65 vs. 40; including headache 16 vs. 22 vs. 4; Vasodilation 19 vs. 21 vs. 0; Rhinitis 16 vs. 20 vs. 6; Sinusitis 6 vs. 7 vs. 1; dyspepsia 4 vs. 5 vs. 0; nausea 1 vs. 5 vs. <1 SAE: 1 (<1%) vs. 3 (2%) vs. 1 (<1%) cause NR</p> <p>Outcome ascertainment: IIEF; GAQ; SEP-Q2, and 2</p>

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<p>Porst (2001) ¹⁰⁶ ¹⁰⁷</p> <p>Companion study ¹⁰⁷</p> <p>Funding source: Bayer</p>	<p>N screened = NR N randomized = 601 (data reported for n=590, pts who took at least one dose of study medication)</p> <p>IG1, n = 147 IG2, n = 141 IG3, n = 150 CG, n = 152</p> <p>ITT analysis used for primary outcome: Y (n=580)</p> <p>Inclusion: age 21-70 y; in stable heterosexual relationship with ED for at least 6 mo;</p> <p>Exclusion: DM; SCI; radical prostatectomy; sign CAD; hx of hepatitis B and/or C; hypogonadal T levels; thyroid stimulating hormone level <0.28 mU/L; prior nonresponse to sildenafil No other ED tx, or nitrates were permitted</p> <p>Companion study reports on additional analysis in ITT population (n=580), for subgroups of various age and prior sildenafil use</p>	<p>Age, mean (sd): 53 (11) vs. 52 (11) vs. 52 (12) vs. 52 (11) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): Sildenafil 74 (51) vs. 67 (50) vs. 72 (49) vs. 72 (49)</p> <p>Smoking status: NR</p> <p>Body weight (sd): 83 (16) vs. 85 (14) vs. 84 (14) vs. 85 (15) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 3 (3) vs. 3 (4) vs. 3 (4) vs. 3 (3) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 163 (27)</p> <p>Physiologic ED, n (%): 178 (30)</p> <p>Mixed ED, n (%): 245 (41)</p> <p>Other: Severity IIEF domain score, n (%): >25 (none)= 21 (4); 18-25 (mild)= 156 (26); 11-17 (moderate)= 204 (34); <11 (severe)= 195 (32)</p>	<p>IG1-3: vardenafil hydrochloride orally CG: placebo orally</p> <p>IG1-3: Dose: 5 (IG1), 10 (IG2) or 20 (IG3) mg Duration: 12 wk Frequency: once 1 hr before intercourse; max 1/d Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 13 wk Other: 11 (2%) did not take medication</p>	<p>Primary outcome results: Mean change from baseline (sd): IIEF-Q3: 1.2 (1.7) vs. 1.3 (1.5) vs. 1.5 (1.7) vs. 0.2 (1.7) IIEF-Q4: 1.4 (1.7) vs. 1.5 (2.0) vs. 1.7 (2.0) vs. 0.5 (1.7) IIEF- EF: 5.7 vs. 8 vs. 9 vs. 1.6 IIEF-IcS: 2.9 vs. 3.5 vs. 3.6 vs. 1 IIEF-OF: 1.9 vs. 1.6 vs. 1.8 vs. 0 IIEF-OS: 2.1 vs. 2.6 vs. 2.8 vs. 0.8 IIEF-SD: 0.5 vs. 0.4 vs. 0.6 vs. 0</p> <p>GAQ, % improved: 66 vs. 76 vs. 80 vs. 30, IG vs. CG p<0.001</p> <p>% of successful intercourse, mean %: baseline: 28.9 vs. 26.1 vs. 24.2 vs. 23.7 post tx: 71.1 vs. 70.9 vs. 74.6 vs. 39.5, IG vs. CG p<0.001</p> <p>Other outcomes assessed: Fugl-Meyer Quality of Life Questionnaire</p> <p>Withdrawals/drop-outs/loss to f/u: 10 (0.2)</p> <p>WDAE: 7 (5) vs. 2 (1) vs. 1 (0.7) vs. 2 (1) (Not specified) TAE, n (%): pts with one or more AE 40 (27) vs. 38 (27) vs. 62 (41) vs. 14 (9); including headache, flushing, dyspepsia, rhinitis SAE, n (%): 4 (3) vs. 1 (<1) vs. 2 (1) vs. 4 (3) Not specified</p> <p>Outcome ascertainment: IIEF; SEP; GAQ; Fugl-Meyer QoL; pts diary</p>

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<p>Porst (2006) ¹⁰⁸</p> <p>Funding source: NR</p>	<p>N screened = 483 N randomized = 383 (International 31 centres)</p> <p>IG, n = 194 CG, n = 189</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, with ED > 6 mo IIEF-EF score >5 or lower than 26, who failed on at least 50% of intercourse attempts</p> <p>Exclusion: penile abnormalities; hypoactive sexual dysfunction; surgical prostatectomy; retinitis pigmentosa; hx of hepatitis B surface antigen, hepatitis C, hepatic impairment, haematological disease; MI, stroke or serious arrhythmia in last 6 mo; uncontrolled atrial fibrillation, or DM; hypo/hypertension; heart failure; use of nitrates or nitric acid donors, antiandrogens, androgens, alpha blockers, anticoagulants; vardenafil in last 30 d; ED tx within 7 d</p>	<p>Age, mean (sd): 54.8 (9.3) vs. 56.6 (10.1) y</p> <p>Race: White 75%; Hispanic 11%; Black 8%; Asian 7%; other <1%</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment, %: sildenafil 33%; tadalafil 28%; vardenafil 10%</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: BMI, mean (sd): 28 (4.7) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED, mean (sd): since diagnosed 4.0 (3.2) vs. 3.9 (3.1) y</p> <p>Underlying disease, n (%): no specific cause</p> <p>Psychogenic ED, n (%): 42 (11)</p> <p>Physiologic ED, n (%): 165 (44)</p> <p>Mixed ED, n (%): 168 (45)</p> <p>Other: -ED severity, n (%): Mild 32 (9) Mild/moderate: 90 (24) Severe 134 (36) -IIEF-EF at baseline, mean (sd): 13.3 (5.5)</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: starting dose 10 mg adjusted to 5, 10, or 20 mg; initial dose of 10 mg, titrated to 5 or 20 mg at wk 2 Duration: 10 wks Frequency: 8 hr before sexual activity Compliance:</p> <p>CG: Dose: NA Duration: 10 wks Frequency: as IG Compliance:</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 10 wks</p> <p>Other: Dose titration to 20 mg, %: 75 vs. 94</p>	<p>Primary outcome results: IIEF-EF, LS mean at 10 wks: 22.8 vs. 14.9</p> <p>Success rate wk 2-6/ wk 0-10, LS mean, %: SEP-2: 81 vs. 51/ 79 vs. 50 SEP-3: 69 vs. 34/ 65 vs. 31</p> <p>GAQ, %: 77 vs. 27</p> <p>Other outcomes assessed: EQS superior scores IG vs. CG, p<0.001; primary efficacy data analysed for wk 2-10 (after dose titration)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 17 (9) vs. 30 (16)</p> <p>WDAE, n (%): 1 (<1) vs. 1 (<1) TAE, %: pts with any tx emergent AE 39% vs. 22% SAE, n (%): 8 (4) vs. 0; included flushing, headache, hypoaesthesia, hypotension, muscle cramp, arthralgia, back pain, diarrhoea, intervertebral disc protrusion and lethargy</p> <p>Outcome ascertainment: IIEF-EF; GAQ; SEP,2/3;Global Confidence Question (GCQ); Erection Quality Scale (EQS); SEP2, 3</p>

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<p>Rosen (2006) ¹⁰⁹</p> <p>Funding source: Bayer, and GlaxoSmithKline</p>	<p>N screened = 488 N randomized = 280</p> <p>IG1, n = 137 CG, n = 143</p> <p>ITT analysis used for primary outcome: yes (also LOCF)</p> <p>Inclusion: men 18 or older with ED for 6 mo or longer; with diagnosed but untreated mild major depressive disorder; who were not in psychotherapy or taking antidepressants; in a stable heterosexual relationship for more than 6 mo with 50% or more failure rate on at least 4 attempts of sexual intercourse</p> <p>Exclusion: men medically unstable; hx of substance abuse, serious suicidal or homicidal risk, bipolar, schizophrenia, delusional, panic, or personality disorder, posttraumatic stress; penile anatomical abnormalities, primary hypoactive SD; SCI; or prior non-response to sildenafil.</p>	<p>Age, mean (sd): 54 (10) vs. 52 (12)</p> <p>Race, (%): Caucasian 75; Black 8; Asian 2; Hispanic <1; American Indian <1</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, %: Sildenafil 59</p> <p>BMI, mean (sd): 28 (4) vs. 27 (4) kg/m²</p> <p>Smoking status, %: 51</p> <p>Body weight mean (sd): 85 (15) kg (overweight)</p>	<p>Concomitant medications: None</p> <p>Duration of ED, mean (sd): ≥6mo 3.5 (4)</p> <p>Underlying disease, %: Depression 100; DM 15; vvascular hypertensive 29; elevated cholesterol 12</p> <p>Psychogenic ED, n (%): 32 (24) vs. 49 (37)</p> <p>Physiologic ED: 25 (19) vs. 15 (11)</p> <p>Mixed ED, n (%): 75 (57) vs. 69 (52)</p> <p>Other, n (%): 12% with elevated cholesterol</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG1: Dose: 10 mg (titrated to 5 or 20 mg at 4, or 8 wks) Duration: 12 wks Frequency: once/d Compliance, n (%): 118 (86)</p> <p>CG: Dose: NA (titration as IG) Duration: 12 wks Frequency: Once/d Compliance n, (%): 111 (78)</p> <p>Run In period: 4wk Wash out period: None</p> <p>F/u duration (on and off treatment): wk 4, 8, 12</p>	<p>Primary outcome results: IIEF Score, least square mean (LSM): IIEF-EF LS mean improved from baseline: 10 vs. 2, p<0.0001 Intercourse satisfaction: 10.9 vs. 7.8 OF: 7.7 vs. 5.9 OS: 7.1 vs. 4.9 SD: 7.3 vs. 6.4 Erectile hardness: 55.2 vs. 25</p> <p>SEP-Q2: 76.7 vs. 52.4, p<0.0001 SEP-3: 66.4 vs. 38.1, p<0.0001</p> <p>GAQ, % improved: (LOCF): 83% vs. 30%; p<0.0001</p> <p>Other outcomes assessed: Remission of depressive symptoms</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 10 (7) vs. 29(20); including Insufficient therapeutic effect: 2 (1) vs. 10 (7)</p> <p>WDAE, n (%): 4 (3) vs. 2 (1); reason NR TAE, n (%): NR; AE in at least 2% of pts included headache: 15 (11) vs. 1 (1); flushing: 9 (7) vs. 1 (1); nasal congestion: 4 (3) vs. 0; insomnia: 0 vs. 4 (3) SAE: NR (no death occurred)</p> <p>Outcome ascertainment: IIEF domains, SEP-2/3;GAQ; Hamilton Depression rating scale (HAM-D) score, Rosenberg self-esteem scale.</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Stark (2001) ¹¹⁰</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 21 (3 way cross over)</p> <p>IG1, n = 21 IG2 randomized = 21 CG randomized = 21</p> <p>ITT analysis used for primary outcome: NR/ or no</p> <p>Inclusion: men 18-60 y, normal body weight, mild to moderate ED for ≥ 6 mo or longer. Able to respond positively to visual sexual stimuli 4 wks.</p> <p>Exclusion: penile anatomical deformity, SCI, prostatectomy, neurological or endocrine causes of ED, major psychiatric illness, retinitis pigmentosa, DM, extreme hypo or hypertension, medications that might interact with PDE5 inhibitors (nitrates), intolerance to medications, hypersensitivity and/or allergic reactions, excessive alcohol consumption, past failure to respond to Sildenafil</p>	<p>Age, mean (sd): 45 (10) y</p> <p>Race (%): 100% Caucasian</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 83 (10) kg</p> <p>Other: Mean Broca Index = 1 (0.09)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR:</p>	<p>IG1: oral vardenafil hydrochloride solution IG2: oral vardenafil hydrochloride solution CG: oral placebo solution</p> <p>IG1/ IG2: Dose: 20 mg (IG1); 40 mg (IG2) Duration: 24 hrs Frequency: once Compliance: 100%</p> <p>CG: Dose: NR Duration: 24hrs Frequency: 1x Compliance: 99%</p> <p>Run In period: NR Wash out period: 5 d</p> <p>F/u duration: NR</p>	<p>Primary outcome (EF): Base, % event rigidity, mean (sd): 59 (26) vs. 70 (17) vs. 42 (24) Base, average event tumescence, mean (sd): 10 (4) vs. 11 (3) vs. 8 (4) Tip, % Event rigidity, mean (sd): 50 (24) vs. 58 (19) vs. 34 (23) Tip, average event tumescence, mean (sd): 9 (4) vs. 9 (2) vs. 7 (4)</p> <p>Duration of erections with Rigidity >60% 58 vs. 64 vs. 14 min Mean individual ▲ in duration: 43 vs. 49 vs. NR (IG vs. CG, p <0.001) Duration of erections with Rigidity >80% 30 vs. 40 vs. 6 min pts with at least one erection: 18 (86) vs. 20 (95) vs. 16 (76)</p> <p>Other outcomes assessed: pharmacokinetic results</p> <p>Withdrawals/drop-outs/loss to f/u, n: 3 withdrew and were replaced</p> <p>WDAE: 0 TAE, n (%): 10 (48) vs. 14 (61) vs. 10 (48); including headache, flushing, nasal congestion, visual disturbance (1 event, 35 min post tx with 40 mg), in total 66 AE in 18 (85%) of patients SAE: 0</p> <p>Outcome ascertainment: RigiScan device, venous blood samples, pts interview/self report</p>

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<p>Stief (2004) ¹¹¹</p> <p>Funding source: Bayer Vital GmbH, Leverkusen</p>	<p>N screened = NR N randomized = 1020 (n=755 completed 1st 12 mo; data provided for n=566 who continued 2nd 12 mo extension period)</p> <p>IG1, n = 272 IG2, n = 294 CG, n = NA</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older with ED (NIH Consensus Statement definition) in a steady heterosexual relationship for 6 mo or longer, had to complete the 1st 12-mo tx to be eligible to enter 2nd 12-mo tx period</p> <p>Exclusion: penile abnormalities, primary hypoactive SD, SCI-related ED, retinitis pigmentosa, angina pectoris, uncontrolled DM, resting hypo/hypertension, prior radical prostatectomy, prior use of vardenafil/sildenafil with poor tolerance or unresponsiveness within 6 mo</p>	<p>Age, mean (sd): 55 (22-89) y</p> <p>Race (%): White (91), Black (4), others (5)</p> <p>Co-morbidities: hypertension (33%), diabetes (16%), prostate hyperplasia (18%)</p> <p>Previous ED treatment: Previous viagra use % = 56 vs. 65</p> <p>BMI, mean (sd): 27 (4) vs. 28 (4) kg/m²</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 2 (3) vs. 2 (4) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 17%</p> <p>Physiologic ED: 45%</p> <p>Mixed ED: 36%</p>	<p>IG1: Vardenafil IG2: Vardenafil</p> <p>IG1: Dose: 10 mg Duration: 24 mo Frequency: once/d Compliance: 85%</p> <p>IG2: Dose: 20 mg Duration: 24 mo Frequency: once/d Compliance: 84%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 2 y</p>	<p>Primary outcome results: Last observation carried forward (IG1 vs. IG2) IIEF-EF score, mean (sd): Baseline: 13 (5) vs. 14 (6) Post tx: 25 (7) vs. 26 (6)</p> <p>SEP-Q2, mean % with yes response: Baseline: 48 vs. 43; Post tx: 92 vs. 94 SEP-Q3 mean % with yes response: Baseline: 16 vs. 17; Post tx: 87 vs. 89</p> <p>GAQ, % yes: 90 vs. 92% (sildenafil naïve 90.9 vs. 89.3; Sildenafil experienced 90.1 vs. 93.7)</p> <p>Other outcomes assessed: The Fugl-Meyer Life Satisfaction Checklist items 'sexual life' and 'sexual satisfaction'</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 41 (15) vs. 46 (16)</p> <p>WDAE, n (%): 5 (2) vs. 6 (2) TAE, n (%): NR; AEs=headache in 16 vs. 20%; flushing in 14 vs. 20%; rhinitis in 10 vs. 14%; nausea 2 vs. 2%; dyspepsia 4 vs. 9%; sinusitis 1 vs. 2%; conjunctivitis 2 vs. 1%; visual symptoms 5 (2) vs. 8 (3) SAE, n (%): 21 (8) vs. 13 (4); death 1 (0.4) vs. 3 (1) (unknown if the deaths are included in the 34 SAE)</p> <p>Outcome ascertainment: IIEF; SEP question 2, 3, Fugl-Meyer Life Satisfaction Checklist; and CESD scale</p>

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<p>Valiquette, (2005) ^{112 113}</p> <p>Funding source: GlaxoSmithKline, King of Prussia, Pa, and Bayer Healthcare Pharmaceutical Division</p>	<p>N screened = 600 (773 originally approached for 4 wk run-in) N randomized = 523</p> <p>IG1, n = 260 (ITT, n = 255) CG, n = 263 (ITT, n = 254)</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older, heterosexual relationship, ED of 6 mo or longer (NIH Consensus Statement), no prior use of Vardenafil. At least 50% of sexual intercourse attempts during the 4 wk run in phase; IIEF-EF score ≤ 26 and ≥ 5, positive 1st time response to 10 mg challenge.</p> <p>Exclusion: evidence of unstable or chronic medical, psychiatric or substance abuse, penile abnormality, primary hypoactive SD, SCI, hx of radical prostatectomy, retinitis pigmentosa, unstable angina pectoris, hx of MI, stroke or life-threatening arrhythmia in last 6 mo (complete list can be found in full text article)</p>	<p>Age, mean (sd): 53.2 (11) vs. 54.5 (11) y</p> <p>Race (%): White 75; Asian 12; Black 5; Hispanic 4; Other <1</p> <p>Co-morbidities: Hypertension: 155 (30); DM 72 (14); Benign prostatic hyperplasia 69 (14); Dyslipidemia 82 (16)</p> <p>Previous ED treatment, n (%): sildenafil 337 (64); tadalafil 104 (20)</p> <p>BMI mean (sd): 27 (4) kg/m²</p> <p>Body Weight: NR Other: IIEF-EF score, mean (sd)= 15 (5); severity of ED (%): no attempts (≤ 5)= 1; severe 23; moderate 35; mild-moderate 30; mild 7; no ED (>25) < 1</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 6 (5); range 1-29 vs. 1-41 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: n (%): 82 (16)</p> <p>Physiologic ED: n (%): 219 (42)</p> <p>Mixed ED: n (%): 208 (40)</p>	<p>IG: Vardenafil CG: placebo</p> <p>IG: Dose: 10 mg Duration: 12 wks Frequency: as needed, no more than once/ d Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk run in period followed by 1 wk open label challenge phase Wash out period: NR</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF-EF score, least square mean (se): 24 (0.4) vs. 16 (0.4) IIEF-EF score equal or more than 26, (% of pts): 50 vs. 16</p> <p>SEP2-, (% yes): Baseline: 56 vs. 53 Post tx: 83 vs. 56</p> <p>SEP-Q3, (% yes): Baseline: 22 vs. 21 Post tx: 77 vs. 42</p> <p>GAQ, (% yes) according to last observation carried forward: 81 vs. 32</p> <p>Other outcomes assessed: median # of doses/ pts= 32 vs. 20</p> <p>Withdrawals/drop-outs/lo to f/u, n (%): 76 (30) vs. 43 (17)</p> <p>WDAE, n: 2 (0.8) vs. 4 (2) TAE, n (%): any event 72 (28) vs. 40 (15); including headache 13 (5) vs. 5 (2); flushing 14 (5) vs. 2 (0.8), dyspepsia 6 (2) vs. 1 (0.4) SAE, n: 2 (0.8) vs. 0; facial palsy, appendicitis</p> <p>Outcome ascertainment: SEP, Question 2 and 3; IIEF-EF, and GAQ</p>

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<p>van Ahlen (2005) ¹¹⁴</p> <p>Funding source: NR(5/6 authors are employees of Galxo-SmithKline/Bayer producers of vardenafil)</p>	<p>N screened = NR N randomized = 388 (98 primary care sites in Germany)</p> <p>IG, n = 193 (ITT=178) CG, n = 195 (ITT= 176)</p> <p>ITT analysis used: yes (last observation carried forward)</p> <p>Inclusion: men 18 or older with ED of 6 mo or longer; arterial hypertension controlled with 1 or more medication; able to maintain 4 wk ED tx free (at least 4 intercourses)</p> <p>Exclusion: prior use of PED5 inhibitors; penile anatomical abnormalities; hypoactive SD; ED due to SCI or radical prostatectomy; retinitis pigmentosa; hepatitis B, C surface antigen or; unstable angina pectoris; MI, stroke, ischemia; DM; hypotension; use of anticoagulants, androgens, trazodone, antiandrogens, alpha1 antagonist, potent HIV protease inhibitor, nitrates, ketokonazole, erythromycin (more in full text)</p>	<p>Age, mean (range): IG1: mean 56 (range 22-78) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI, mean: 28 vs. 27 kg/m²</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 88 (14) vs. 86 (12) kg</p>	<p>Concomitant medications, n (%): Antihypertensive medications: Diuretics: 24 (13) vs. 15 (8); Beta-blockers: 81 (42) vs. 82 (43); Calcium channel blockers: 36 (19) vs. 28 (15); Reninangiotensin acting agents: 136 (71) vs. 133 (70) Mean number of antihypertensives per patient: 1.5 vs. 1.4</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease, (%): Hypertension 100 vs. 99</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Vardenafil CG: placebo</p> <p>IG: Dose: starting 10 mg (5 mg in pts 65 or older) one step titration to 5 or 20 mg at 4 & 8 wks Duration: 12 wks Frequency: 1/ d Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: 1/ d Compliance: NR</p> <p>Run In period: 4 wks tx free Wash out period: 4 wks ED tx free</p> <p>F/u duration: 12 wks (4, 8, and 12 wks measures)</p> <p>Other: Allowed a single dose per day (No use of nitrate or concurrent ED therapy ≤ 7 d of study or any investigational drugs < 30 d prior to screening; no use of alpha-blockers permitted)</p>	<p>Primary outcome results: SEP-Q2, % yes: 83 vs. 58, p< 0.0001 SEP- Q3, % yes: 67 vs. 35, p < 0.0001</p> <p>IIEF-EF, mean score: baseline = 14 vs. 14.5; post tx= 25 vs. 18, p< 0.0001 (unaffected by the class of antihypertensive used)</p> <p>GAQ, % yes: 80 vs. 40, p < 0.0001</p> <p>Other outcomes assessed: association of tx with clinical measures of BP, or HR</p> <p>Withdrawals/drop-outs/loss to f/u: 34 (8.7)</p> <p>WDAE, n (%): 4 (2) vs. 2 (1) TAE, (%): 21.2% vs. 16.4%; including headache: 6 (3) vs. 1 (0.5); flushing: 3 (2) vs. 1 (0.5) SAE, n (%): 6 (3) vs. 2 (1); no detail provided</p> <p>Outcome ascertainment: IIEF-EF, sum score of Q 1, 5 and 15, SEP question 2 and 3; and GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
Ziegler (2006) 115	<p>N screened = NR N randomized = 318 (82 sites in Germany)</p> <p>IG, n = 163 CG, n = 155 ITT analysis used for primary outcome: yes (IG n=153, CG n=149)</p> <p>Inclusion: men 18 or older with ED (by NIH Consensus statement); established DM type I; PDE5i naïve Exclusion: penile abnormalities; hx or SCI, hepatitis B, C; MI; heart or liver conditions (explicitly reported); hypo/hypertension; uncontrolled DM; hx of malignancy within past 5 y or serum creatinine levels > 2.5 mg/dL (pts were prohibited to take nitrates while in the trial); tx with anticoagulant drugs (except anti-platelets); androgens, alpha1-antagonists, potent HIV protease inhibitors, anti mycotic agents itraconazole and ketoconazole, and erythromycin; other ED tx within 7 d of trial entry</p>	<p>Age, mean (sd): 50.3 (9.7) y</p> <p>Race: NR</p> <p>Co-morbidities (%): CV 157 (51.8); nervous system 94 (31); eyes 90 (29.7); endocrine/metabolic 83 (27.4); musculoskeletal system 49 (16.2); urinary tract 46 (15.2); other including allergies 28 (9.3)</p> <p>Previous ED treatment: NR Smoking status: NR</p> <p>Body weight, mean (sd): 85.8 (13.4) kg</p> <p>Other: BMI, mean (sd): 27.2 (3.8) vs. 26.9 (3.4) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): DM</p> <p>Psychogenic ED, n (%): NA</p> <p>Physiologic ED, n (%): all, 100%</p> <p>Mixed ED, n (%): NR</p> <p>Other: Glycemic control, good (HbA_{1c} 7% or less) in 43 vs. 51%; moderate (HbA_{1c} 7-8%) in 58 vs. 47%; poor (HbA_{1c} >8%) 53 vs. 51%</p>	<p>IG: Vardenafil CG: Placebo</p> <p>IG: Dose: flexible dose starting with 10 mg (5 mg for pts 65 or older) titrated to 20 mg Duration: 12 wks Frequency: on demand 1 hr prior to intercourse, up to 1/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks no tx Wash out period: NA</p> <p>F/u duration: 12 wks</p> <p>Dosing at 12 wks: 87.7% on 20 mg vardenafil; 10.8% on 10 mg, and 1.5% on 5 mg</p>	<p>Primary outcome results: IIEF domains change in score from baseline, mean (sd): EF: 7.79 (7.9) vs. 2.05 (5.8); improvements unaffected by level of glycemic control IcS: 3.43 (3.6) vs. 0.72(2.45) OF: 1.99 (2.6) vs. 0.30 (2.7) SD: 0.67 (1.5) vs. 0.09 (1.4) OS: 2.32 (2.6) vs. 0.52 (2.0) SEP-2, mean % (sd); Baseline: 41 (38) vs. 47 (40) Post tx: 71 (35) vs. 52 (38) SEP-2, mean % (from graph): Baseline: 13 vs. 18 Post tx: 50 vs. 28</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 16 (5.3) with no efficacy evaluation at baseline or post tx</p> <p>WDAE, n (%): 3 (1.8) vs. 2 (1.3) TAE, n (%): 29.4 vs. 20.6; AE in 2% or more pts n= 14 vs. n= 8; headache 5 (3.1) vs. 0; flushing 4 (2.5) vs. 0; bronchitis 3 (1.84) vs. 4 (2.6); nasopharyngitis 2 (1.2) vs. 4 (2.96) SAE, n (%): 7 (4.6) vs. 3 (2), cause NR</p> <p>Outcome ascertainment: IIEF-EF; SEP2, and 3</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA_{1c}=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C3-Oral Tadalafil

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Aversa (2007) 116</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 20 (22 eligible at level II screening)</p> <p>IG1/IG2, n = 20 CG, n = NA</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 y or older with at least 3 mo hx of ED of any severity or etiology</p> <p>Exclusion: tx with nitrates, cancer chemotherapy or anti-androgens; CHF; hyper-homocysteinemia or other conditions or drugs impairing endothelium-dependent vaso-relaxation; (pts with past use of commercially available PDE-5i; and concurrent active drugs were not excluded)</p> <p>Data reported for organic vs. relational vs. Psychogenic pts</p>	<p>Age, mean (sd): 54 (8) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): hyper-cholesterolemia 6 (30); DM type II 4 (20); hypertension 4 (20); smoking 4 (20); Psychogenic 2 (10)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): smokers 4 (20)</p> <p>Body weight: NR</p> <p>Other: BMI, mean (sd) 25.4 (3.6) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): see co-morbidities</p> <p>Psychogenic ED, n (%): 2 (10)</p> <p>Physiologic ED, n (%): 18 (90)</p> <p>Mixed ED, n (%): NR</p> <p>Other: semi structured interview for erectile dysfunction (SIEDY) score, median (quintile)= organic 3.93 (0-9); relational 2.53 (0-9); Psychogenic 3.33 (0-5)</p>	<p>IG1: Tadalafil on demand (OD) IG2: Tadalafil on schedule alternated days (AD)</p> <p>IG1: Dose: 20 mg Duration: Frequency: 4 wks Compliance:</p> <p>IG2: Dose: 20 mg Duration: 4 wks Frequency: OD Compliance:</p> <p>Run In period: 4 wks Wash out period: 2 wks</p> <p>F/u duration: 6 time point measurements at baseline and end of each tx period, and 2 wks after last dosing; SIEDY not measured at end point</p>	<p>Primary outcome results: Sexual intercourse/mo: 5.9 (0.4) vs. 6.0 (0.7) N of pills/ mo: 6.0 (1.9) vs. 15.2 (0.6), p<0.05 PSV (cm/s): Baseline: 9.3 (0.3) vs. 9.5 (0.4) Post tx: 10.4 (0.9) vs. 13.2 (0.1) FMD, %, mean (sd) Baseline: 3.3 (0.6) vs. 1.2 (0.6) Post tx: 2.1 (0.9) vs. 8.3 (0.3) Systolic pressure (variation in mmHg): -6.1 (2.2) vs. -4.0 (1.3) Diastolic pressure (variation in mmHg): -3.3 (1.3) vs. -2.3 (1.2)</p> <p>Other outcomes assessed: endothelial markers (VCAM; ICAM; ET-1; CRP; insulin); insulin levels ▲ sign in OD (IG1) compare to IG2</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): 0 TAE, n (%): 2 (10); headache, back pain, pain and myalgia (no report of abnormal vision or priapism) SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: blood flow measures by laboratory analysis; sexual measures by pts logs/interviews</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Carrier (2005) 117</p> <p>Funding source: NR (conflict of interest reported as Eli Lilly, or ICOS CO employed some investigators)</p>	<p>N screened = 283 N randomized = 253</p> <p>IG1, n = 103 IG2, n = 100 CG, n = 50</p> <p>ITT analysis used for primary outcome: yes,</p> <p>Inclusion: men 18 or older, with at least a 3 mo hx of ED (organic, psychogenic or mix) in a monogamous relationship, and no ED tx for at least 4 wk prior to randomization</p> <p>Exclusion: hx of radical prostatectomy or other pelvic surgery with subsequent failure to achieve erections, presence of clinically sign penile deformity, renal insufficiency, angina, unstable angina in last 6 mo, hx of MI, coronary artery bypass graft surgery or precutaneous coronary intervention within 90 d, HIV, current tx with nitrates, cancer chemotherapy or antiandrogens, or prior non-response to tx with sildenafil</p>	<p>Age, mean (sd): 59 (9) vs. 58 (11) vs. 59(10) y Race: 95% Caucasian</p> <p>Co-morbidities, (%): hypertension 23 vs. 32 vs. 18, arthritis 23 vs. 24 vs. 20; DM 23 vs. 24 vs. 16; allergic reaction 22 vs. 13 vs. 16; prostate dx 19 vs. 16 vs. 26; hypercholesteremia 13 vs. 18 vs. 8; hyperlipidemia 11 vs. 8 vs. 12, back pain 12 vs. 12 vs. 4, hernia 6 vs. 7 vs. 12; headache 7 vs. 5 vs. 10; pain 11 vs. 8 vs. 10</p> <p>Previous ED treatment, %: sildenafil 68 vs. 54 vs. 62</p> <p>Smoking status, %: 12 vs. 21 vs. 22</p> <p>Body weight, mean (sd): 90 (15) vs. 88(10) vs. 84 (12) kg</p>	<p>Concomitant medications: for hypertension CAD, cardiac arrhythmias, congestive heart failure, hyperlipidemia, and DM, n (%)= 101 (98) vs. 28 (56) vs. 62 (62)</p> <p>Note: list of medications is provided in the full text article</p> <p>Duration of ED, n (%): 1 yr or more= 92 (92) vs. 92 (89) vs. 45 (90)</p> <p>Underlying disease, %: prostatic disorder 19 vs. 16 vs. 26</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: most commonly present</p> <p>Mixed ED: NR</p>	<p>IG1: Tadalafil IG2: Tadalafil CG: placebo</p> <p>IG1: Dose: 20 mg Duration: 12 wks (three 4 wk periods, Frequency: once /d Compliance: NR</p> <p>IG2: Dose: 10 mg Duration: 12 wks Frequency: once/ d Compliance: NR</p> <p>CG: Dose: NR Duration: same as IG Frequency: same as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: Change in IG1 vs. IG2 vs. CG, mean (SE) IIEF EF domain (1-30): 8 (0.8) vs. 6.6 (0.8) vs. -0.9 (1.1) IIEF intercourse satisfaction (0-15): 3.2 (0.3) vs. 2.2 (0.3) vs. 0.4 (0.4) Successful penetration (SEP-Q2): 21.3 (3.6) vs. 21.3 (3.8) vs. -6.4 (4.1) Successful intercourse (SEP-Q3): 29 (3.7) vs. 32.8 (3.7) vs. 4.9 (4.3)</p> <p>End point Improved erection (GAQ), n (%): 79 (79) vs. 69 (67) vs. 11 (22)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: n=34 (4 vs. 14 vs. 6) Note: pts without both baseline and post-baseline data were excluded from analysis, 3 vs. 4 vs. 1</p> <p>WDAE: n=5 (IG1 n=3, IG2 n=2) TAE, n (%): AE in >= 5%= 94 (94) vs. 84 (82) vs. 31 (62) (% with dyspepsia: 22 vs. 10 vs. 2; headache: 17 vs. 15 vs. 8; infection: 11 vs. 19 vs. 22; pain: 8 vs. 10 vs. 2; back pain: 7 v. 5 vs. 2; vasodilatation 6 vs. 4 vs. 4; flu syndrome: 5 vs. 8 vs. 10; accidental injury: 5 vs. 1 vs. 4; rhinitis: 4 vs. 6 vs. 4; myalgia 4 vs. 5 vs. 4 SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF; SEP Q2 & 3 and GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Carson (2005) 118</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 241 N randomized = 195</p> <p>IG, n = 146 CG, n = 49</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older, with ED of at least 3-mo duration; in stable heterosexual relationship</p> <p>Exclusion: serious CV condition (e.g. MI, unstable angina, sign.ECG conduction deficit) within 90 days before screening; nitrate tx; congestive heart failure of New York Heart Association Class 2 or above; stroke in previous 6 mo; SBP >100 mm Hg or <90 mm Hg; DBP >100 mm Hg or <50 mm Hg; hx of radical prostatectomy or other pelvic surgery with subsequent failure to achieve an erection; prior ineffective txt with sildenafil</p>	<p>Age, mean (sd): 60 (11) vs. 60 (10)</p> <p>Race (%): White: 119 (82) vs. 43 (88); African descent: 23 (16) vs. 6 (12); Hispanic: 3 (2) vs. 0; Asian: 1 (0.7) vs. 0</p> <p>Co-morbidities, n (%): Coronary artery disease: 15 (10) vs. 0; DM 32 (22) vs. 8 (16); Hyperlipidemia: 152 (36) vs. 19 (39); Hypertension: 59 (40) vs. 21 (43); Prostatic cancer: 17 (11) vs. 4 (8)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 24 (16.) vs. 8 (16.)</p> <p>Body weight: NR</p>	<p>Concomitant medications: More than one: 126 (86) vs. 40 (82); none 20 (14) vs. 9 (18)</p> <p>Duration of ED, range: 025 or less-1 y or more [≥0.25 to <0.5 y: 3 (2) vs. 0 ≥0.5 to <1.0 y: 11 (8) vs. 2 (4); ≥1 y: 132 (90) vs. 47 (96)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 4 (3) vs. 2 (4)</p> <p>Physiologic ED, n (%): 119 (82) vs. 41 (84)</p> <p>Mixed ED, n (%): 23 (16) vs. 6 (12)</p>	<p>IG: tadalafil orally CG: placebo orally</p> <p>IG1: Dose: 20 mg Duration: 12 wk Frequency: 1 dose before sexual activity; max. 1/d Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: 1 dose before sexual activity; max. 1/d Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IG vs. CG, mean change (SE) IIEF EF: 7 (0.8) vs. -0.2 (1), p<0.001 IIEF -Q3 (ability to penetrate): 1 (0.2) vs. 0.1 (0.3), p <0.001 IIEF-Q4 (maintaining erection): 1 (0.2) vs. 0 (0.2), p < 0.001 Intercourse satisfaction: 3 (0.3) vs. -0.2 (0.5), p <0.001 OS: 2 (0.3) vs. -0.3 (0.3), p<0.001 SEP- Q2 ability to penetrate (% yes): 26 (3) vs. 2 (4.2), p<0.001 SEP-Q3 OS (% yes): 34 (3) vs. 5 (4), p<0.001</p> <p>Other outcomes assessed: partner SEP2 and 3</p> <p>Withdrawals/drop-outs/loss to f/u: 48 (IG1 30 [20.5%], CG 18 [36.7%])</p> <p>WDAE, n: 9 (5.5% vs. 2%) TAE: NR (AEs included headache in 9%, dyspepsia 5%, myalgia 3%; reported mild or moderate in 90% of cases) SAE: 4; 3 (2%, carotid artery bruit, esophageal spasm, brain neoplasm) vs. 1 (2%, angina pectoris)</p> <p>Ascertainment of outcomes assessed: IIEF- SEP; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Chen, KK (2004) 119</p> <p>Funding source: NR</p>	<p>N screened = 222 N randomized = 196</p> <p>IG, n = 65 IG2, n = 65 CG, n = 66</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men at least 21 yrs, in a monogamous relationship, at least 3 mo hx of ED of any origin</p> <p>Exclusion: hx of radical prostatectomy or other pelvic surgery with subsequent ED, insufficiency in past 6 mo, hepatobiliary dx, angina occurring during sexual intercourse in last 6 mo, hx of MI, coronary artery bypass graft surgery, or percutaneous coronary intervention within 90 d prior to 1st visit, hx of HIV infection or current infection with any sexually transmitted dx, tx with nitrates, cancer chemotherapy, or anti-androgens, and prior no response to tx with sildenafil citrate</p>	<p>Age, mean (sd): 59 (11.8) vs. 60.4 (11.5) vs. 60.2 (12.9) yr Race (%): NR</p> <p>Co-morbidities, n (%): prostatic dx 20 (31) vs. 25 (39) vs. 25 (38) hypertension 11 (17) vs. 22 (34) vs. 19 (29); CAD (NR); hyperlipidemia 8 (12) vs. 5 (8) vs. 5 (8), and DM 11 (17) vs. 20 (31) vs. 16 (25)</p> <p>Previous ED treatment, n (%): sildenafil 29 (45) vs. 39 (60) vs. 31 (47)</p> <p>Smoking status, n (%): 22 (34) vs. 24 (37) vs. 25 (38)</p> <p>Body weight: NR</p>	<p>Concomitant medications: medication for hypertension (20% vs. 37% vs. 36%), CAD; cardiac arrhythmias; congestive heart failure; hyperlipidemia; DM (14% vs. 25% vs. 18%)</p> <p>Duration of ED, n (%): > 1yr 59 (91) vs. 58 (89) vs. 61 (92)</p> <p>Underlying disease: prostatic disorder; hypertension (17% vs. 34% vs. 29%); DM (17) vs. 31% vs. 24%); hyperlipidemia</p> <p>Psychogenic ED (%): 6 vs. 9 vs. 11</p> <p>Physiologic ED (%): 71 vs. 69 vs. 65</p> <p>Mixed ED (%): 23 vs. 22 vs. 24</p>	<p>IG1: Tadalafil 10 mg IG2: Tadalafil 20 mg CG: Placebo</p> <p>IG1: Dose: 10 mg Duration: 12 wks Frequency: as needed, max 1/d Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 12 wk Frequency: as needed, max 1/d Compliance: NR</p> <p>CG: Dose: NR Duration: 12 wk Frequency: as needed, max 1/d Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: mean change in score from baseline; overall p value in IG1 vs. IG2 vs. CG: IIEF (1-30): 8 vs. 8 vs. 2.6; p<0.001 [IIEF (intercourse satisfaction domain): sign. ▲ in IG1 and IG2 vs. placebo % of pts with normal IIEF score at end point: 42 vs. 63 vs. 20 SEP (Q2): 34 vs. 35, vs. 10; p<0.001 SEP (Q3): 48, vs. 50, vs. 15; p<0.001 GAQ, % of pts improved erections at endpoint (%): 92 vs. 85 vs. 55 (p<0.001 for overall and pair wise comparison)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): n=13 (7); 4 (6) vs. 3 (5) vs. 6 (9) (personal, sponsor or physician decision to withdraw, n=4 vs. 2 vs. 2)</p> <p>WDAE, n (%): n=3 (1.5); IG2 1 (1.5) elevated serum transaminases vs. CG 2 (3), deafness and MI TAE, n (%): incidence in >/=5%= 37 (57) vs. 46 (71) vs. 29 (44); AE included back pain, dyspepsia, myalgia, infection, rhinitis, dizziness, headache, ▲ cough, arthritis, pharyngitis SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF at 4, 8 and 12 wks; SEP Q2 & 3 post each intercourse; GAQ at final visit</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Choi (2006) ¹²⁰</p> <p>Funding source: Lilly Research Laboratories</p>	<p>N screened = N randomized = 121 (multi center in Korea)</p> <p>IG, n = 80 CG, n = 41</p> <p>ITT analysis used for primary outcome: yes (LOCF)</p> <p>Inclusion: men 18 or older, in a monogamous relationship, with ED of at least 3 mo in duration; caused by Psychogenic, organic or mixed etiology</p> <p>Exclusion: hx of radical prostatectomy or other pelvic surgery with subsequent failure to achieve erection; sign renal insufficiency within last 6 mo; sign hepatobiliary disease; angina during sexual intercourse in the last 6 mo of study entry; hx of MI or coronary artery bypass graft or precutaneous coronary intervention within 90 d of study entry; HIV</p>	<p>Age, mean (range): 51.4 (24.7-74.4) y</p> <p>Race: 100% Asian</p> <p>Co-morbidities, n (%): benign prostatic hyperplasia 16 (20) vs. 9 (22); DM 16 (20) vs. 5 (12.2); hypertension 12 (15) vs. 5 (12.2); hyperlipidemia 5 (6.3) vs. 4 (9.8)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean: 70.7 kg</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR; pts with ED of at least 1 y 71 (88.8) vs. 39 (95.1)</p> <p>Underlying disease, n (%): no specific condition</p> <p>Psychogenic ED, n (%): 15 (18.8) vs. 10 (24.4)</p> <p>Physiologic ED, n (%): 56 (70) vs. 27 (65.9)</p> <p>Mixed ED, n (%): 9 (11.3) vs. 4 (19.5)</p> <p>Other: ED severity, n (%): Mild 33 (41.3) vs. 17 (41.5) Moderate 33 (41.3) vs. 16 (39) Severe 14 (17.5) vs. 8 (19.5)</p>	<p>IG: Tadalafil CG: Placebo</p> <p>IG: Dose: 20 mg Duration: 12 wks Frequency: on demand, up to once/d (no restriction on food or timing) Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance:</p> <p>Run In period: 4 wks Wash out period:</p> <p>F/u duration:</p>	<p>Primary outcome results: Change from baseline, mean: IIEF-EF: 7.8 vs. 0.1, p<0.001 EF by ED severity: Mild 4.8 (n=32) vs. -1.6 (n=17) Moderate 8.6 (32) vs. -0.8 (n=16) Severe 12.7(n=14) vs. 5.3 (n=8)</p> <p>IIEF-Q3: 0.9 vs. -0.2, p<0.001 IIEF-Q4: 1.6 vs. 0.2, <0.001 IIEF-IS: 4.4 vs. 1.5, p<0.001 IIEF-OS: 2.6 vs. 0.7, p<0.001</p> <p>SEP-2, %: 17.1 vs. 0.5, p<0.001 SEP-3, %: 53.6 vs. 10.1, p<0.001</p> <p>GAQ-1, %: 80 vs. 43.9 GAQ-2, %: 80 vs. 43.9</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 6 (7.5) vs. 0</p> <p>WDAE, n (%): 1 (1.3) vs. 0 TAE, n (%): 38 (47.5) vs. 11 (26.8) Headache, flushing eye pain (only in IG), arthralgia, palpitations, myalgia, pharyngitis, naso-pharyngitis, gastritis somnolence SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: IIEF, SEP, GAQ</p>

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<p>De Rose (2005) 121</p> <p>Funding source: NR</p>	<p>N screened = 134 N randomized = 120</p> <p>IG, n = 60 CG, n = 60</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: at least 3-mo hx of ED; in a monogamous relationship</p> <p>Exclusion: failure to achieve erection after pelvic surgery; clinically sign. penile deformity; penile implant; stroke within previous 6 mo; spinal cord trauma within previous 6 mo; clinically sign. renal or hepatic insufficiency; treatment with nitrates, antiandrogens or cancer chemotherapy</p>	<p>Age, mean (range): 46 (25-66) vs. 46, (29-63) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): Smoker: 16 (35) vs. 18 (39)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 5 (10) vs. 6 (13)</p> <p>Physiologic ED, n (%): 24 (52) vs. 22 (48)</p> <p>Mixed ED, n (%): 17 (38) vs. 18 (39)</p> <p>Other: baseline IIEF, n (%): mild 18 (40) vs. 19 (41); moderate 12 (25) vs. 11 (24); severe 17 (35) in both grps</p>	<p>IG1: tadalafil oral CG: placebo oral</p> <p>IG1: Dose: 20 mg Duration: 3 mo Frequency: twice/wk Compliance: 98.3%</p> <p>CG: Dose: placebo Duration: 3 mo Frequency: as IG Compliance: 96.7%</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 3 mo</p>	<p>Primary outcome results: Mean change in IIEF EF: 12 vs. 3</p> <p>Mean absolute change in positive response to SEP (%yes) SEP-Q1- (erection): 36 vs. 14 SEP-Q2 (penetration): 34 vs. 12 SEP-Q3 (intercourse completion): 57 vs. 11 SEP-Q4 (hardness of erection): 72 vs. 3 SEP-Q5 (sexual experience): 77 vs. 5</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n: 3 (1 vs. 2)</p> <p>WDAE: 0 TAE, n of pts with at least one AE: 14 vs. 5, included headache 6 vs.3; flushing 4 vs. 0; dyspepsia 2 vs. 2; myalgia and back pain 2 vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, SEP</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Eardley (2004) 122</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 237 N randomized = 220</p> <p>IG1 screened = NR IG1 randomized = 168</p> <p>IG2 screened = NA IG2 randomized = NA</p> <p>CG screened = NR CG randomized = 52</p> <p>Inclusion: age ≥18 yr; at least 3-mo hx of mild to severe ED; in stable heterosexual relationship</p> <p>Exclusion: hx of radical prostatectomy (except for bilateral nerve-sparing) or other pelvic surgery, with subsequent failure to achieve erection; hx of ineffective treatment with sildenafil; unstable cardiovascular disease (e.g. unstable angina, recent myocardial infarction or stroke, poorly controlled hypertension, and New York Heart Association Class II and above congestive heart failure); evidence of clinically sign. renal insufficiency or hepatic insufficiency (e.g. active symptomatic hepatobiliary disease or jaundice); treatment with nitrates, antiandrogens or chemotherapy</p>	<p>Age, mean (sd): IG1 53.6 (range 26-78), CG 52.9 (range 29-73)</p> <p>Race (%): White: IG1 167 (99.4%), CG 52 (100%)</p> <p>Co-morbidities (unrelated to disease): Hypertension: IG1 42 (25.0%), CG 10 (19.2%) Diabetes: IG1 20 (11.9%), CG 5 (9.6%) Alcohol user: IG1 82 (48.8%), CG 30 (57.7%)</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: Sildenafil: IG1 81 (48.2%), CG 26 (50.0%)</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: Smoker: IG1 39 (23.2%), CG 16 (30.8%)</p> <p>Initial body weight: IG1 84.5 kg (range 41-150), CG 83.2 kg (range 60-118)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): 0.25-0.5: IG1 15 (8.9%), CG 7 (13.5%) 0.5-1: IG1 14 (8.3%), CG 7 (13.5%) ≥1: IG1 139 (82.7%), CG 38 (73.1%)</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED: IG1 30.4%, CG 26.9%</p> <p>Physiologic ED: IG1 37.5%, CG 32.7%</p> <p>Mixed ED: IG1 32.1%, CG 40.4%</p> <p>Other: Mild ED: IG1 56 (33.3%), CG 16 (30.8%) Moderate ED: IG1 41 (24.4%), CG 13 (25.0%) Severe ED: IG1 68 (40.5%), CG 21 (40.4%)</p>	<p>IG1: tadalafil orally IG2: NA CG: placebo orally</p> <p>IG1: Dose: 20 mg Duration: 12 wk Frequency: as needed (max 1/day) Compliance (%): NR</p> <p>IG2: NA Dose: Duration: Frequency: Compliance (%):</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: as needed (max 1/day) Compliance (%): NR</p> <p>Run In period: 4 wk</p> <p>Wash out period: NA</p> <p>F/u duration (both on and off treatment): 12 wk</p> <p>Other: No</p>	<p>Primary outcome results: Change in EF domain of IIEF and in positive response to questions 2 (“Were you able to insert your penis into your partner’s vagina?”) and 3 (“Did your erection last long enough for you to have successful intercourse?”) of Sexual Encounter Profile (SEP) diary Mean change in IIEF EF IG1 11.1 (SD 27.2), CG 0.4 (SD 6.6) Mean absolute change in positive response to SEP Q2: IG1 41.0%, CG 7.3% Q3: IG1 56.5%, CG 10.8%</p> <p>List (narrative) other outcomes assessed: Change in other IIEF domains; positive response to SEP questions 4 and 5; positive response to GAQ (“Has the treatment you have been taking during this study improved your erections?” and “If yes, has the treatment improved your ability to engage in sexual activity?”)</p> <p>AE (in ≥2% of patients in IG1): Headache: IG1 30 (17.9%), CG 3 (5.8%). Dyspepsia: IG1 22 (13.1%), CG 0. Flushing: IG1 8 (4.8%), CG 1 (1.9%). Back pain: IG1 6 (3.6%), CG 0. Pain in limb: IG1 6 (3.6%), CG 0. Myalgia: IG1 4 (2.4%), CG 1 (1.9%).</p> <p>ITT analysis used for primary outcome? Y</p> <p>Withdrawals/drop-outs/loss to f/u [N and/or %]: 25 (IG1 16, CG 9)</p> <p>WDAE (N and/or %): IG1 5 (3.0%), CG 1 (1.9%)</p> <p>TAE: NR</p> <p>SAE: IG1 3, CG 1; none judged to be related to study drug</p> <p>Ascertainment of outcomes assessed: NA</p>

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<p>Eardley (2005) 24</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 411 N randomized = 367</p> <p>IG1, n = 183 (first period) IG2, n = 184 (first period) CG, n = NA</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: Pts aged => 18 yrs with documented ED of any aetiology and severity, in a steady relationship with the same female partner naïve to treatment for ED with drugs inhibiting PDE5</p> <p>Exclusion: Pts with endocrine dx, premature ejaculation, prostatectomy, pelvic surgery, penile deformity, sign renal or hepatic dx, CHF, Within 6 mo, MI, coronary artery bypass surgery, sudden cardiac arrest, sign. arrhythmia, SBP (< 90 - > 170 mmHg) or diastolic (< 50 - > 100 mmHg), malignant hypertension, retinitis pigmentosa, current tx with nitrates, cancer chemotherapy, HIV infection, substance/drug abuse in last 6 mo</p>	<p>Age, mean (sd): 54 (12) y</p> <p>Race (%): Caucasian 92, Black 4, Asian 3, other 1.3</p> <p>Co-morbidities, (%): hyperlipidemia 11, coronary artery dx 6.5, hypertension 26.4, DM 9.5, depression 4</p> <p>Previous ED treatment: NR</p> <p>Smoking status, (%): current = 24</p> <p>Body weight: NR</p> <p>Other: current alcohol use (65%)</p>	<p>Concomitant medications: no other ED treatments</p> <p>Duration of ED: NR (pts with 1 y or more ED =74%)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 12%</p> <p>Physiologic ED: 28%</p> <p>Mixed ED: 60%</p> <p>Other: ED defined as consistent change in the quality of erection that adversely affects subject's satisfaction with sexual intercourse</p> <p>Other: Mean IIEF (EF): 14 (6); Severity of ED: severe (IIEF1-10): 31%, moderate (IIEF 11-16): 30%, mild (IIEF 17-30): 39%</p>	<p>IG1: Sildenafil IG2: Tadalafil</p> <p>IG1: Sildenafil Dose: 25-100 mg Duration: 12 wks Frequency: NR Compliance: NR</p> <p>IG2: Tadalafil Dose: 10-20 mg Duration: 12 wks Frequency: NR Compliance: NR</p> <p>Run In period: 4 wks Wash out period: 7-10 d</p> <p>F/u duration: before and after crossover 24 wks (2 periods of 12 wks)</p> <p>Other: Dose was titrated up and down between 25-100 for Sildenafil and 10-20 mg for Tadalafil</p>	<p>Primary outcome results: Mean least squares change from baseline for IIEF domains and 95% CI (IG2 vs. IG1): EF: 0.5 (-0.07, 1.1) OF: 0.3 (0.02, 0.5) SD: 0.2 (0.02, 0.6) Intercourse satisfaction: 0.17 (-0.1, 0.42) Mean change in IIEF questions: erection firmness, intercourse satisfaction and enjoyment, desire level, OS, erection confidence: tadalafil > sildenafil OS: 0.3 (0.02, 0.5) SEP, mean change from baseline: SEP-Q2: 36 vs. 39 SEP-Q3: 53 vs. 58</p> <p>Other outcomes assessed: mean scores of IIEF, drug preference</p> <p>Withdrawals/drop-outs/loss to f/u: IG1 (1st) and IG2 (2nd): n=42 IG1 (2nd) and IG2 (1st): n=39</p> <p>WDAE: IG1 (1st) and IG2 (2nd): n=4 IG1 (2nd) and IG2 (1st): n=7 TAE, n (%): pts with 1 or more AE=125 (34) vs. 128 (35) SAE, n: 4 vs.5</p> <p>Ascertainment of outcomes assessed: Questionnaires</p>

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<p>Govier F (2003) 123</p> <p>Funding source: NR (correspondence: Eli Lilly and Company)</p>	<p>N screened = NR N randomized = 215 (cross over)</p> <p>IG1, n = 109 (Tadalafil - Sildenafil)</p> <p>IG2, n = 106 (Sildenafil - Tadalafil) CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men with ED for => 3 mo, aged 18-65 yrs, in heterosexual relationship who had never received tadalafil or sildenafil</p> <p>Exclusion: Pts treated with nitrates, recent hx of MI or coronary revascularization, <= 6 mo hx of unstable angina, ED secondary to endocrine disorders, pelvic surgery, stroke or SCI within the last 6 mo, retinitis pigmentosa, HIV infection</p>	<p>Age, mean (sd): 50 (11) y</p> <p>Race (%): White 87, African 9, Hispanic 3</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: No tadalafil; sildenafil (15.3%)</p> <p>Smoking status: 23% current smokers</p> <p>Body weight: 90 (19.0) kg</p> <p>Other: height, mean (sd) = 179 (7) cm</p>	<p>Concomitant medications: CVD or diabetes (n = 54)</p> <p>Duration of ED, %: 75% with hx of 1 y or longer</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 18%</p> <p>Physiologic ED: 39%</p> <p>Mixed ED: 42%</p> <p>Other: severity of ED (based on clinical judgement) = mild (12%), moderate (60%), severe (27.5%)</p>	<p>IG1: tadalafil IG2: sildenafil CG: NA</p> <p>IG1: tadalafil Dose: 20 mg Duration: 4 wks Frequency: once/d Compliance: NR</p> <p>IG2: sildenafil Dose: 50 mg Duration: 4 wks Frequency: once/d Compliance: NR</p> <p>Run In period: 1 wk Wash out period: 1-2 wks</p> <p>F/u duration: 10 wks (per treatment = 4 wks)</p>	<p>Primary outcome (EF): Treatment Preference Question ('which treatment did you prefer?') =</p> <p>N (%) pts preferring tadalafil (over sildenafil) vs. N (%) pts preferring sildenafil (over tadalafil) = 126 (66.3%) vs. 64 (33.7%), p < 0.001</p> <p>Total N of attempts at sexual intercourse = IG1: 2334 vs. IG2: 2233, p = NR</p> <p>Other outcomes assessed: AE</p> <p>Withdrawals/drop-outs/loss to f/u: n=24 (11.2%), n=11 (lost to f/u)</p> <p>WDAE, n: 2 (each pt in IG1 vs. IG2) TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: questionnaires</p>

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<p>Guo (2006) ¹²⁴</p> <p>Funding source: Eli Lilly and Company</p>	<p>N screened = 399 N randomized = 367</p> <p>IG1, n = 125 IG2, n = 120 CG, n = 122</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older in monogamous relationship, at least 3 mo hx of ED, with Psychogenic, organic or mixed cause</p> <p>Exclusion: hx of radical prostatectomy; or other pelvic surgery with subsequent failure to achieve erection; renal insufficiency, hepatobiliary disease, unstable angina within the last 6 mo; hx of MI; coronary artery bypass graft surgery, or precutaneous coronary intervention within 90 d prior to 1st visit; hx of HIV infection; tx with nitrates, cancer chemotherapy, or antiandrogens (discretionary criteria was ineffective tx with sildenafil)</p>	<p>Age, mean (range): 52 (24-82) y</p> <p>Race: East/South-eastern 100%</p> <p>Co-morbidities, n (%): hypertension 77 (21); DM 42 (11.4); benign prostatic hyperplasia 14 (3.8); hyperlipidemia 9 (2.5)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>BMI, mean (range): 24.8 (15.6-50.4) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: pts with ED of 1 y or longer 341 (92.9)</p> <p>Underlying disease, n (%): no specific cause</p> <p>Psychogenic ED, n (%): 59 (16.1)</p> <p>Physiologic ED, n (%): 107 (29.2)</p> <p>Mixed ED, n (%): 201 (54.8)</p> <p>Other: IIEF severity, n (%) Normal 3 (0.8) Mild 23 (6.3) Mild/moderate 93 (25.3) Moderate 135 (36.8) Sever 113 (30.8)</p> <p>IIEF-EF baseline, mean: 13.6 vs. 13.6 vs. 14</p>	<p>IG1:Tadalafil low dose IG2: Tadalafil high dose CG: Placebo</p> <p>IG1: Dose: 10 mg Duration: 12 wks Frequency: on demand up to once/d Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 12 wks Frequency: as IG1 Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: Change in mean from baseline:</p> <p>IIEF-EF: 8.1 vs. 8.7 vs. 2.4 IIEF-Q3: 1.4 vs. 1.5 vs. 0.4 IIEF-Q4: 1.4 vs. 1.6 vs. 0.5 SEP-2, % yes: 33.5 vs. 34.8 vs. 7.7 SEP-3, % yes: 50.0 vs. 56.4 vs. 18.3 GAQ, %: 80.9 vs. 85.7 vs. 43.9</p> <p>Other outcomes assessed: IIEF-EF based on severity of ED (% of pts in each grp), mean change in score: Mild (31 vs. 28 vs. 34) 24 vs. 23.5 vs. 21.9 Moderate (34.2 vs. 35.2 vs. 37.7) 22.3 vs. 23.0 vs. 15.6 Severe (30 vs. 30.4 vs. 30.2) 18.1 vs. 21.6 vs. 10.7</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 10 (8.3) vs. 12 (9.6) vs. 8 (6.6)</p> <p>WDAE, n (%): 2 (1.7) vs. 2 (1.6) vs. 1 (0.8)</p> <p>TAE, n (%): in 2% or more 18 (15) vs. 17 (13.6) vs. 4 (3.3) including headache, back pain, dizziness, dyspepsia, chest pain, cough</p> <p>SAE, n (%): 1 death in IG2</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ, SEP</p>

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<p>Incrocci (2006) 125</p> <p>Funding source: Lilly Icos</p>	<p>N screened = 632 medical records screened; 358 invited</p> <p>N randomized = 60 (cross over trial)</p> <p>IG1/ CG, n = 30/grp depending on the order of tx randomization (IG1 tadalafil first, CG placebo first)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: pts with histological proven prostate carcinoma treated by 3DCR at least 12 mo before study</p> <p>Exclusion: excluded prior to surgery: tx with chemotherapy or anti androgens, or hx of metastases; use of nitrates, CVD, coronary artery bypass graft within 90 d of entry, stroke, SCI within 6 mo of entry</p>	<p>Age, mean (range): 69 (53-84) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): hypertension 17 (28); DM 2 (3); both 3 (5)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight:</p> <p>Other: tumor stages, and differentiation grade PSA, mean (range) 13.9 (1-86) µ/L</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: NR (calculated from mean age at radiation-mean age at entry =4 y)</p> <p>Underlying disease, n (%): prostate carcinoma radiation tx</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Tadalafil CG: Placebo</p> <p>IG: Dose: 20 mg Duration: 6 wks Frequency: on demand, at least once/wk, up to once/d (no restriction on alcohol or food) Compliance: 100%</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: 100%</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 12 wks; outcomes assessed at end each tx period</p>	<p>Primary outcome results: Mean (sd), tadalafil vs. placebo</p> <p>-IIEF- EF, baseline: 8.4 (3.1): Post tx: 17.7 (9.9) vs. 9.5 (5.9), p</p> <p>-IIEF-OF, baseline: 6.7 (3.0) Post tx: 7.4 (3.1) vs. 4.9 (3.5)</p> <p>-IIEF-SD, baseline: 8.0 (1.9) Post tx: 8.7 (1.7) vs. 7.9 (1.9)</p> <p>-IIEF-IS baseline: 5.9 (1.9) Post tx: 8.2 (3.5) vs. 5.6 (2.3)</p> <p>-IIEF-OS, baseline: 4.3 (2.4) Post tx: 6.5 (3.0) vs. 4.4 (2.6)</p> <p>SEP-2, %: 47 vs. 19, p<0.0001 SEP-3, %: 46 vs. 12</p> <p>GAQ, %: 67 vs. 20 Successful intercourse, %: 48 vs. 9</p> <p>Other outcomes assessed:</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0</p> <p>WDAE, n (%): 0 TAE, n: 56 vs. 10 AE included headache, flushing, and dyspepsia sign more in IG; myalgia, nasal congestion, back pain, dizziness not sign between grps SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: IIEF, SEP</p>

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<p>McMahon (2005) 126</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 152 N randomized = 140</p> <p>IG1, n = 93 CG, n = 47</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: ≥18 yr; in monogamous relationship with female partner; at least 3-mo hx of ED</p> <p>Exclusion: premature ejaculation; penile implant; penile deformity; ED due to untreated endocrine condition; radical prostatectomy; pelvic surgery; sign central nervous system injury within 6 mo of screening; clinically sign renal insufficiency within previous 6 mo, hepatobiliary dx or uncontrolled DM; unstable angina; MI, coronary artery bypass grafting or percutaneous coronary arterial intervention within 90 days of screening; prior sildenafil treatment failure (for complete list of exclusions refer to full text article)</p>	<p>Age, mean (sd): IG1 58 (9), CG 61 (7) y</p> <p>Race (%): 98% white in both grps</p> <p>Co-morbidities, n (%): hypertension: 15 (32) vs. 26 (28) hypercholesterolemia: 7 (15) vs. 17 (18) hyperlipidemia: 8 (17) vs. 12 (13) dyspepsia: 6 (13) vs. 12 (13); DM: 8 (17) vs. 9 (10)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 1 yr (96% of pts)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 2 (4) vs. 10 (11)</p> <p>Physiologic ED: 21 (45) vs. 37 (40)</p> <p>Mixed ED: 24 (51) vs. 46 (50)</p> <p>Other: No</p>	<p>IG: tadalafil orally CG: placebo</p> <p>IG: Dose: 20 mg Duration: 6 mo (24-26 wk) Frequency: 1 dose before sexual activity; max 1/d Compliance: NR</p> <p>CG: Dose: placebo Duration: 6 mo (24-26 wk) Frequency: 1 dose before sexual activity; max 1/d Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 24-26 wk + 96 h</p>	<p>Primary outcome results:IG vs. CG, mean change from baseline: IIEF EF: 6.8 vs. 1.6 IIEF- intercourse satisfaction (range 0-15): 2.6 vs. -0.1, p <0.001 IIEF OS (range 2-10): 2.5 vs. 2 GAQ, end point (%): 78 vs. 13 SEP, mean absolute change from baseline in positive response (%): SEP-Q2: 26.5 vs. -7.5 SEP-Q3: 40 vs. 0.9</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 15 vs. 4</p> <p>WDAE, n: 4 (headache 2, dyspepsia 2) vs. 0 TAE, n of events: 142 vs. 39 (AEs reported: most common) included headache in 40 (43) vs. 4 (9); dyspepsia 20 (22) vs. 0; back pain 15 (16) vs. 7 (15); surgical procedure 15 (16) vs. 8 (17); infection 13 (14) vs. 5 (11); pain 11 (12) vs. 3 (7); accidental injury 10 (11) vs. 7 (15); diarrhea 9 (10) vs. 4 (9); myalgia 9 (10) vs. 1 (2); other included arthralgia, vasodilatation, abdominal pain, cough, flu symptoms, gout, nausea (n of events NR) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF- SEP, and GAQ questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>McMahon (2005) 127</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 145 (cross over)</p> <p>IG1/IG2, n = 145 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: heterosexual men age 18 or older with ED of 3 mo or longer; with 50% or greater failure rate in maintaining an erection sufficient for completion of sexual intercourse on at least four occasions during the 4 wk run in period</p> <p>Exclusion: penis anatomic abnormalities, hx of radical prostatectomy, ED due to SCI, severe chronic liver dx, renal failure, retinitis pigmentosa, unstable angina pectoris, uncontrolled atrial tachyarrhythmia or any MI, stroke, electrocardiography ischemia or life-threatening cardiac arrhythmia in last 6 mo</p>	<p>Age, mean: 57.6 vs. 57.3 mo</p> <p>Race (%): NR</p> <p>Co-morbidities, n: Diabetes 18 vs. 15, CAD 9 vs. 7; hypertension 22 vs. 21; peripheral vascular disease 4 vs. 2; hyperlipidemia 24 vs. 26; obesity 12 vs. 10</p> <p>Previous ED treatment, n (%): sildenafil in 94 (65), responders 61 (5)</p> <p>Smoking status, n (%): 43 (30)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 21 vs. 22 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 18 (12)</p> <p>Physiologic ED, n (%): 86 (59)</p> <p>Mixed ED: 41 (28)</p> <p>Other: baseline IIEF (ED domain) score, 15 vs. 14; baseline severity of ED in all pts, n (%): mild 23 (16); mild-moderate 33 (23); moderate 56 (39); severe 33 (23)</p>	<p>IG1: Tadalafil 10 mg IG2: Tadalafil 20 mg on demand</p> <p>IG1: Dose: 10 mg Duration: 12 wks Frequency: daily Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 12 wks Frequency: on demand, 2-3 hrs before sexual activity Compliance: NR</p> <p>Run In period: 4 wks Wash out period: 2 wks</p> <p>F/u duration: 12 wks after each intervention regimens</p>	<p>Primary outcome results: IIEF EF domain scores both grps: 26 vs. 23 (p<0.001 vs. baseline, p<0.05 for IG1 vs. IG2) SEP-Q2, mean rate (%): baseline= 36, at 12 wks 73 vs. 85 (p<0.001 vs. baseline, IG1 vs. IG2, p<0.05) SEP-Q3-, mean rate (%): baseline = 30; at 12 wks 80 vs. 67 (p<0.001 vs. baseline, IG1 vs. IG2, p<0.05) Return to normal IIEF score (>26), % of respondents: 73 vs. 57 (p<0.05) GAQ, proportion of yes responses: 88% vs. 73% (p<0.05)</p> <p>Other outcomes assessed: tx preference; severity of AE</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: total n=6 (4%), 4 vs. 2 TAE, n (%): incidence of >2%=35 (24) vs. 41 (28) headache 6 (8) vs. 12 (17); dyspepsia 8 (11) vs. 9 (13); facial flushing 6 (8), vs. 7 (10); nasal congestion 6 (8) vs. 5 (7.1); backache 5 (7) vs. 3 (4); myalgia 3 (4) vs. 3 (4); dizziness 1(1) vs. 2 (3) SAE: n=4 MI, 2 in each tx arms</p> <p>Ascertainment of outcomes assessed: IIEF ED domain; SEP (Q 2 and 3); GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>McVary (2007) 128</p> <p>Funding source: Lilly ICOS L.L.C.</p>	<p>N screened = 479 N randomized = 281 (65% ED pts)</p> <p>IG, n = 138 CG, n = 133</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 45 y or older with hx of LUTS secondary to BPH of 6 mo</p> <p>Exclusion: PSA > 10 ng/ml; hx of any pelvic surgery; neurological condition affecting bladder function; recent LUTS; hx of urethral obstruction; intravesical obstruction 2nd to the prostate median lobe; prostate cancer; PVR 200 ml or more; certain CVD; unstable angina; recent MI; poorly controlled BP or DM; sign renal or hepatic insufficiency; stroke or SCI; use of nitrates, chemotherapy, antiandrogens or potent cytochrome P450 3A4 inhibitor</p>	<p>Age, mean (range): 62 (45-82.4) y</p> <p>Race: White 81%; Black 9.6%; Hispanic 6.8%; Other 2.5</p> <p>Co-morbidities, n (%): LUTS</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: mean baseline I-PSS score post placebo run in=17.9 (range 3-53)</p>	<p>Concomitant medications, n (%): pts agreed not to use any other BPH medication during the study; alpha-blocker tx 24%</p> <p>Duration of ED: reported as pts with ED of 1 y or longer 61.6% vs. 52.1%</p> <p>Underlying disease, n (%): LUTS</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p> <p>Note: reported pts with ED: 99 (71.1%) in Tadalafil vs. 84 (59.2%) in placebo</p>	<p>IG: Tadalafil CG: Placebo</p> <p>IG: Dose: 5 mg; titrated to 20 mg at 6 wks Duration: 12 wks Frequency: Compliance: 100% of all pts with data (3% NR)</p> <p>CG: Dose: NA Duration: 12 wks Frequency: as IG Compliance: as IG</p> <p>Run In period: 4 wks single blind placebo Wash out period: NA</p> <p>F/u duration: 16 wks</p>	<p>Primary outcome results: IIEF-EF: Baseline mean: 13.7 vs. 14.3</p> <p>Change from baseline (post run in), mean (SE) 6 wks: 6.0 (0.9) vs. 0.6 (0.9) 12 wks: 7.7 (0.9) vs. 1.4 (1.0)</p> <p>Other outcomes assessed: change from baseline in I-PSS score, mean (95% CI)= 1.7 (0.5, 2.9) at 6 wks and 2.1 (0.9, 3.3) at 12 wks; more pts in IG improved in this score compare to CG (49% vs. 6.4%, p=0.03)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 30 (10.67); 18 (6.8%) in first period, 12 (4.5%) in second period (wk 6-12)</p> <p>WDAE, n (%): 5 (3.6) vs. 2 (1.4) TAE, n (%): NR; AEs were ▲ erection; dyspepsia back pain, headache, nasopharyngitis, upper respiratory tract infection all more in IG SAE, n (%): 0 vs. 1 (0.7)</p> <p>Ascertainment of outcomes assessed: IIEF-EF; I-PSS; GAQ (post hoc analysis to examine changes at 6 and 12 wks vs. visit 2 before the placebo run in)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mirone (2005) 129 130</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 4568 N randomized = 4262 (crossover design)</p> <p>IG1/ IG2, n= 4262 CG, n = NA</p> <p>ITT analysis used for primary outcome: y</p> <p>Inclusion: age ≥18; at least 3-mo hx of ED of any severity or etiology; must have same female partner during study</p> <p>Exclusion: treatment with nitrates, cancer chemotherapy or anti-androgens; symptomatic congestive heart failure</p>	<p>Age, mean (sd): 55 (11) y</p> <p>Race (%): white 97%, African descent 0.7%, western Asian 0.1%, Hispanic 0.1%, east/southeast Asian 0.1%, other 0.2%</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: another phosphodiesterase type 5, 2513; other ED treatment, 316</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR pts with < 1 yr 14.8%, ≥1 yr 85.2%</p> <p>Underlying disease (%): cardiovascular dx 32.9; (hypertension in 27), DM 18, hyperlipidemia 12.5, LUTS 9.5, depression 5.2, bilateral-nerve-sparing prostatectomy 3.8</p> <p>Psychogenic ED: 18.1%</p> <p>Physiologic ED: 34.5%</p> <p>Mixed ED: 47.5%</p>	<p>IG1: tadalafil orally IG2: tadalafil orally</p> <p>IG1: Dose: 20 mg Duration: 5-6 wk Frequency: on demand before sexual activity (max. 1/d) Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: 5-6 wk Frequency: 3 times/wk Compliance: NR</p> <p>Run In period: 3-4 wk Wash out period: 1 wk</p> <p>F/u duration: on treatment: 10-12 wk; after treatment: at least 2 wk</p> <p>Other: n=2108 assigned to on-demand first, followed by set dosage; n=2154 vice versa</p>	<p>Primary outcome results: IIEF, mean score, IG1 vs. IG2: EF: pre=14.3; post: 24.6 vs. 24.8 (% with scores ≥26 =60% vs. 62%) IC s: pre= 6.9; post 11.6 vs. 11.5 OF: pre=2.9; post: 8.3 vs. 8.4 OS: pre= 4.5; post: 7.8 vs. 7.9 SD: pre=6.7; post 7.5 vs. 7.5</p> <p>SEP (% of pts with positive response): Q1: 68.7; post 91.4 vs. 92.8 Q2: pre=47.8; post: 84.1 vs. 85.6 Q3: pre=21; post: 73 vs. 74 Q4: pre= 6.5; post: 62.9 vs. 65.4 Q5: pre=5.7; post 60.3 vs. 62.8</p> <p>Other outcomes assessed: Subjects' treatment preference</p> <p>Withdrawals/drop-outs/loss to f/u: 535</p> <p>WDAE: 4.8% (detail NR) TAE: 926 (22) vs. 1078 (25), AE with at least 2% incidence included headache: 311 (7) vs. 329 (8); dyspepsia: 258 (6) vs. 299 (7); back pain: 110 (3) vs. 125 (3); flushing: 95 (2) vs. 123 (3); myalgia: 88 (2) vs. 128 (3); upper abdominal pain: 64 (1) vs. 74 (2); AE in at least 0.4% in extension phase also reported (headache, dyspepsia, back pain) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, Sexual Encounter Profile (SEP) diary</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Montorsi (2004) 131</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 351 N randomized = 303</p> <p>IG, n = 201 CG, n = 102</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: bilateral nerve-sparing retro pubic radical prostatectomy 12-48 mo before screening; 65 or younger at time of surgery; postoperative prostate cancer pathological stage pT3 or less; development of ED after surgery</p> <p>Exclusion: ED due to other causes; clinically sign penile deformity; other prior pelvic surgery; penile implant; clinically sign renal or active, symptomatic hepatic dx; uncontrolled diabetes; unstable CV condition; nitrate therapy; detectable PSA level; prior or planned radiation or hormonal therapy for prostate cancer, hx of HIV infection; sign CNS injury</p>	<p>Age, mean (sd): 60 (5) y</p> <p>Race, n (%): White: 186 (93) vs. 95 (93)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: severity of ED, n (%): Mild 51 (25) vs. 27 (27); moderate 44 (22) vs. 22 (22); severe 106 (23) vs. 53 (52)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: tadalafil -oral CG: placebo -oral</p> <p>IG1: Dose: 20 mg Duration: 12 wk Frequency: 1 dose before sexual activity (max. 1/d) Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: 1 dose before sexual activity (max. 1/d) Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: IG vs. CG Change in IIEF EF, mean (SEM): 5 (0.5) vs. 1 (0.6), p<0.001 SEP- Q2, mean (SEM) absolute change in positive response: 22% (2.4) vs. 9% (2.5) SEP- Q3: 23% (2.3) vs. 4% (2.3) GAQ: NR</p> <p>Other outcomes assessed: Mean ED Inventory of Treatment Satisfaction scores; ED outcomes also reported for subgrp of pts</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 66 (33), n=40 vs. n=26</p> <p>WDAE, %: 5.5 vs. 2 TAE, n (%): 13 (65) vs. 16 (16); headache 42 (21) vs. 6 (6); dyspepsia 27 (13) vs. 1 (1); myalgia 13 (7) vs. 0; pack pain 9 (5) vs. 6 (6); nasal congestion 9 (5) vs. 1 (1); fatigue 7 (4) vs. 1 (1); flushing 7 (4) vs. 0; sinus congestion 5 (3) vs. 0; cough 4 (2) vs. 1 (1); gastroesophageal reflux dx 4 (2) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF- SEP questionnaire Other: a priori subgrp of n=201 with postoperative penile tumescence 50% or greater positive response to SEP-Q1</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Nagao (2006) ¹³²</p> <p>Funding source: Lilly Research Laboratories</p>	<p>N screened = 382 N randomized = 343 (34 Centres in Japan)</p> <p>IG1, n = 85 IG2=IG3, n = 86/ grp CG, n = 86</p> <p>ITT analysis used for primary outcome: yes (LOCF)</p> <p>Inclusion: men 20 or older with ED of at least 3 mo in duration</p> <p>Exclusion: ED due to primary sexual disorders, hx of radical prostatectomy, pelvic surgery, penile implantation or clinically sign penile deformity; renal insufficiency, HIV infection, CHD, recent hx of MI or coronary artery bypass, malignant hypertension; stroke, angina, or serious arrhythmia, severe hepatobiliary disease; tx with nitrates, alpha-blockers, cancer chemotherapy, or antiandrogens, hx of sign CNS injuries, past unresponsiveness to sildenafil</p>	<p>Age, mean: 55.1 y</p> <p>Race: 100% Asian</p> <p>Co-morbidities, n (%): hypertension 66 (25.7); DM 53 (20.6); benign prostatic hyperplasia 35 (13.6); hyperlipidemia 34 (13.2)</p> <p>Previous ED treatment: sildenafil tx 194 (56.3)</p> <p>Smoking status: 136 (39.7)</p> <p>Body weight, mean: 68.8 kg</p> <p>Other: alcohol consumption 259 (75.5)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: pts with ED of at least 1 y 303 (88.3)</p> <p>Underlying disease, n (%): no specific condition</p> <p>Psychogenic ED, n (%): 98 (28.6)</p> <p>Physiologic ED, n (%): 111 (32.4)</p> <p>Mixed ED, n (%): 134 (39.1)</p> <p>Other: ED severity, n (%): Mild 128 (37.3) Moderate 83 (24.2) Severe 132 (38.5)</p>	<p>IG1-3: Tadalafil (various doses) CG: Placebo</p> <p>IG1-3: Dose: 5 mg (IG1), 10 mg (IG2), 20 mg (IG3) Duration: 12 wks Frequency: as needed, up to one tablet/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IIEF-EF, mean baseline score: 13.9 Post tx: 21.0 vs. 23.2 vs. 23.5 vs. 16.0 IIEF-EF, LS mean by ED severity: Mild: 26.6 vs. 26.0 vs. 25.3 vs. 21.1 Moderate: 22.7 vs. 24 vs. 23.0 vs. 15.5 Severe: 15.8 vs. 20.2 vs. 21.9 vs. 11.2</p> <p>SEP-2 mean % Baseline (from graph): 45 Post tx: 71.2 vs. 81.3 vs. 84.1 vs. 53.6 SEP-3 mean per pts%: Baseline (graph): 15 Post tx: 51.7 vs. 64.6 vs. 69.4 vs. 27.8</p> <p>GAQ, %: 76.5 vs. 81.4 vs. 83.7 vs. 31.4</p> <p>Other outcomes assessed: SEP-2/3 post hoc analysis for ED severity grps</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 8 (9.4) vs. 7 (8) vs. 7 (8) vs. 19 (22); total IG vs. CG 22 (8.6) vs. 19 (22)</p> <p>WDAE, n (%): 3 (1.2) vs. 0 TAE, n (%): pts with 3% or more AE 104 (40.5) vs. 24 (86) Ocular hyperemia 3 (3.5) only in IG3 SAE, n (%): 3 (1.2) vs. 0 including acute prostatitis and pyelonephritis (IG2); mental disorder (IG3); uretral calculus (IG1)</p> <p>Ascertainment of outcomes assessed: IIEF, SEP, GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Porst (2003) ¹³³</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = NR N randomized = 348</p> <p>IG, n = 175 CG, n = 173</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: men 18 or older, minimum 3 mo ED (defined as consistent change in the quality of erection adversely affecting the pts satisfaction with intercourse), in a stable monogamous relationship</p> <p>Exclusion: penile implants or clinically sign penile deformities, failure to achieve erection after radical prostatectomy or pelvis surgery, hx of stroke or spinal cord trauma in the past 6 mo, unstable cardiac disease, and concomitant antiandrogen use or chemotherapy</p>	<p>Age, mean (sd): 57 (NR), range: IG 22-80, CG 28-87 yr</p> <p>Race (%): White 93 vs. 95; African 8 vs. 2; Hispanic 4 vs. 7; other 1 vs. 0</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: current smoker 25% vs. 23</p> <p>Body weight: NR</p> <p>Other: alcohol use 57% vs. 61%</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): more than 1 y (in majority of pts)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, %: 13 vs. 18</p> <p>Physiologic ED, %: 45 vs. 53</p> <p>Mixed ED, %: 42% vs. 36%</p> <p>Other: severity of ED (IG vs. CG) mild 70% vs. 69%, moderate 45% vs. 43%, severe 60% vs. 61% (based on erectile domain of IIEF)</p>	<p>IG1: Tadalafil CG: Placebo</p> <p>IG1: Dose: 4 x 20 mg Duration: 8 wks (two 4 wk period, intercourse 24 hrs and 36 hrs after each dose in 1st and 2nd period respectively) Frequency: twice/ 4 wks Compliance: 98%</p> <p>CG: Dose: placebo Duration: same as IG Frequency: same as IG Compliance: 99.5%</p> <p>Run In period: Wash out period: 8-10 d between two doses in each 4 wk period</p> <p>F/u duration: 8 wks</p>	<p>Primary outcome results: Successful intercourse attempts, n (%): 24 hr: 120/227 (53) vs. 72/247 (29.), p<0.001 36 hr: 132/223 (59) vs. 60/212 (28), p<0.001</p> <p>Patients with successful intercourse attempts, (%): 24 hr: 61 vs. 37, p<0.001 36 hr 64 vs. 35, p<0.001</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: n=21</p> <p>WDAE, n (%): n=4, 3 (2) vs. 1 (0.5) TAE, n (%): 89 vs. 2; Headache 14 (8) vs. 2 (1), p=0.003, Flushing 10 (6) vs. 0, p=0.002 Dyspepsia 59 (34) vs. 0, p=0.004 Myalgia 6 (3) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: Pts self report on Sexual Encounter Profile (SEP-Q3)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rajfer (2006) ¹³⁴</p> <p>Funding source: Lilly ICOS LLS.</p>	<p>N screened = 314 N randomized = 287(15 US Centres)</p> <p>IG1, n = 96 IG2, n = 97 CG, n = 94</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 y or older, with ED at least 3 mo in duration caused by psychological, organic or mixed factors</p> <p>Exclusion: ED due to premature ejaculation or untreated endocrine disease, radical prostatectomy or pelvic surgery; penile implant or penile deformity; clinically sign renal or hepatic insufficiency; unstable angina; MI; coronary artery intervention; hx of heart problems; SBP > 170 or <90 mmHg, DBP >100 or <50 mmHg; hx of stroke, SCI; HIV infection</p>	<p>Age, mean (range): 60 (25.5-82.3) y</p> <p>Race: Caucasian 86%; Hispanic 5.6%; African decent 5.6%; Western Asian 1%; Other 1%</p> <p>Co-morbidities, n (%): CAD 30 (10.4); depression 22 (7.6); DM 40 (14); hyper-lipidemia 64(22.3); hypertension 123 (42.8)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: ED severity at baseline, % by IIEF: mild 35%; moderate 26%; sever 39%.</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: 96.3% with ED of 12 mo or longer</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 5 (5) vs. 2 (2) vs. 5 (5)</p> <p>Physiologic ED, n (%): 67 (70) vs. 67 (69) vs. 62 (66)</p> <p>Mixed ED, n (%): 24 (25) vs. 28 (29) vs. 27 (29)</p> <p>Other: baseline ED defined as: consistent change in erection quality adversely affecting satisfaction with sexual intercourse)</p>	<p>IG1:Tadalafil low dose IG2:Tadalafil high dose CG: placebo</p> <p>IG1: Dose: 2.5 mg Duration: 24 wks Frequency: once/d Compliance: 94.8%*</p> <p>IG2: Dose: 5 mg Duration: 24 wks Frequency: once/d Compliance: 94.8%*</p> <p>CG: Dose: Duration: 24 wks Frequency: once/d Compliance: 94.8%*</p> <p>Run In period: 4 wks Wash out period:</p> <p>F/u duration:</p> <p>*Note: compliance met if >70% of doses were administered</p>	<p>Primary outcome results: IIEF-EF, mean baseline: 13.4 (1-28) all pts at 24 wks: 19.1 vs. 20.8 vs. 14.6 In mild ED: 24.3 vs. 26.2 vs. 20.8 In moderate ED: 21 vs. 21.9 vs. 14.3 In sever ED: 13.8 vs. 15.5 vs. 8.9 SEP-2, %: All pts at 24 wks: 65.3 vs. 70.7 vs. 51.1 Mild ED: 90.0 vs. 91.9 vs. 79.9 Moderate ED: 74.8 vs. 82.2 vs. 55.7 Severe ED: 38.9 vs. 44.9 vs. 20.1 SEP-3, %: All pts at 24 wks: 50.0 vs. 56.9 vs. 31.3 Mild ED: 72.5 vs. 82.2 vs. 56.7 Moderate ED: 56.3 vs. 61.3 vs. 27.3 Severe ED: 27.4 vs. 32.6 vs. 9.2 GAQ-1, % yes: 62.8 vs. 72.8 vs. 26.1 GAQ-2, % yes: 58.5 vs. 70.7 vs. 23.9</p> <p>Other outcomes assessed: IIEF, IS domain; IIEF Q3, 4</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 15 (15.6) vs. 16 (16.5) vs. 18(19)</p> <p>WDAE, n (%): 6(6.3) vs. 4(4.1) vs. 2(2.1) TAE, n (%): AE occurring in 3% or more 40 (42) vs. 35 (36) vs. 22 (23) SAE: pts with >/=1 SAE 2 vs. 3 vs. 2 including MI, fractures, an road traffic accident</p> <p>Ascertainment of outcomes assessed: IIEF-EF; SEP-2, 3;GAQ; PAIRS</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rodriguez (2006)¹³⁵</p> <p>Funding source: NR (medication was not provided to pts)</p>	<p>N screened = NR N randomized = 132 (open label randomized)</p> <p>IG1-6, n = 22 per grp (each grp randomized to particular sequence in which they took the three tx)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older, with heterosexual relations, mild to moderate ED of at least 6 mo in duration; naïve to PDE-5i</p> <p>Exclusion: hx of MI; or unstable angina; resting SBP >170 or <90; or DBP >110; retinitis pigmentosa or hx of hepatitis B or C; tx with androgens, cytochrome P-450-3 A4 inhibitors, or alpha blockers</p>	<p>Age, mean (sd): NR</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: sildenafil IG2: vardenafil IG3: tadalafil</p> <p>IG1: Dose: 100 mg Duration: 45-60 d Frequency: at least 6 doses Compliance: NR</p> <p>IG2: Dose: 20 mg Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>IG3: Dose: 20 mg Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>Run In period: NR Wash out period: 7 d</p> <p>F/u duration: 3 mo (f/u at end of each tx period)</p>	<p>Primary outcome results: IIEF, median (percentile 10-90) Baseline: 17 (11-23) Sildenafil post tx: 29 (25-30) Vardenafil post tx: 28 (23.10-30) Tadalafil post tx: 30 (25-30) (baseline vs. post tx, p<0.0001)</p> <p>Other outcomes assessed: tx preference: Sildenafil 25 (28%) vardenafil 18 (20%) tadalafil 47 (52.22)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 42 (31.8)</p> <p>WDAE, n (%): 5 (3.8) vs. 5 (3.8) vs. 2 (1.5) [pts stating they would not continue after study due to AE: 7(5.3%) vs. 2 (1.5%) vs. 4 (3)]</p> <p>TAE: NR AE reported, %: headache 11 vs. 12 vs. 9; flushing 8 vs. 3.3 vs. 4.4; dyspepsia 4.4 vs. 5.5 vs. 2.3; myalgia 0 vs. 0 vs. 4.4; nasal congestion 1.1 vs. 1.1 vs. 2.2; tachycardia 4.4 vs. 1.1 vs. 2.2; vision disorders 4.4 vs. 3.3 vs. 3.3</p> <p>SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF, EDITS</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rosano (2005) 136</p> <p>Funding source: Pfizer</p>	<p>N screened = 49 N randomized = 32 (Parallel double-blinded)</p> <p>IG, n = 16 CG, n = 16</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men aged 59-71 y, with presence of more than 2 risk factors for coronary artery dx (CAD) regardless the degree of their ED;</p> <p>Exclusion: clinically sign findings on physical exam or presence of know clinically sign dx that would prejudice the completion of the study or contraindicate tadalafil assumptions; Recent acute MI, primary valvular, congenital heart dx; myocardial, pericardial or endocardial dx; congestive heart failure</p>	<p>Age, mean (sd): 65 (6) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Blood glucose, mean (sd): sub grp (n=8) with type 2 diabetes 7 (0.5) HbA1C</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²); mean (sd): 25.4 (3.2)</p> <p>Smoking status, n (%): 10 (31)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): Diabetes: 8 (25) Hypertension: 9 (28)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: only 16 (50%) had presence of ED</p>	<p>IG: Tadalafil (TAD) CG: Placebo</p> <p>IG1: Dose: 20mg Duration: 4 wks Frequency: every other d Compliance: 100%</p> <p>CG: Dose: Duration: 4 wks Frequency: every other d Compliance: 100%</p> <p>Run In period: 4wks Wash out period: None</p> <p>F/u duration: Baseline, end of each treatment, 2 wks after last tx</p>	<p>Primary outcome results: IG vs. CG, mean (sd) GAQ, (yes %) in IG, n=9; CG, n = 7: 8 (88) vs. 1 (14)</p> <p>Brachial artery diameter, baseline to 4 and 6 wks: basal-1, basal 2, nitroglycerine & hyperemia (mm): no sign change from baseline in either grps</p> <p>FMD, %: (sign ▲ from baseline in IG only)= 4 (0.6) to 9 (0.3) vs. 4 (0.6) to 4 (0.9)</p> <p>Other outcomes assessed: endothelial marker, mean (sd): Serum nitrogen oxides 38 (12) to 53 (12) vs. 36.5 (12) to 39 (8) μmol/l; endothelin-1: sign ▼ from baseline - 12% vs. 20% p/ml Nitrite levels, (sign ▲ from baseline in IG only) 38% vs. 7%</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: None TAE, n (%): IG, 2 (12) Dyspepsia, headache, back pain, pain, myalgia, spontaneous erection nasal congestion and infection SAE: None</p> <p>Ascertainment of outcomes assessed: GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rosen (2004) ¹³⁷</p> <p>Funding source: NR (Eli Lilly and company, and ICOS corporation were involved in editorial and critical review of manuscript)</p>	<p>N screened = NR N randomized = 233</p> <p>IG, n = 74 IG2, n = 75 CG, n = 74</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: heterosexual men age 21 or older, with hx of ED for 3 mo or longer who were not using any other ED therapy during the study</p> <p>Exclusion: ED caused by untreated endocrine disorders, hx of penile implant or sign penile deformities, hx of radical prostatectomy, hepatic, renal, cardiovascular, or central nervous system disorders/injuries, treatment with nitrates, cancer chemotherapy or antiandrogens, current infection with any sexually transmitted disease, hx of drug, alcohol, or substance abuse within the past 6 mo, previous use of tadalafil</p>	<p>Age, mean (sd): 58 (11) vs. 59 (12) vs. 59 (11) yr</p> <p>Race (%): White 87; African decent, 7; Asian, 2; Hispanic, 4</p> <p>Co-morbidities, n (%): Hypertension, 24 (32) vs. 25 (33) vs. 35 (47) DM, 20 (27) vs. 23 (31) vs. 17 (23) Depression, 5 (67) vs. 11 (15) vs. 5 (7) Hyperlipidemia, 3 (4) vs. 4 (5) vs. 7 (10)</p> <p>Previous ED treatment, n (%): sildenafil 7 (10) vs. 5 (7) vs. 7 (10)</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 94 (17) vs. 92 (18) vs. 91 (17) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, n (%): 3 mo or longer: 3 (4) vs. 0 vs. 1 (1) 6 mo or longer: 5 (7) vs. 8 (11) vs. 4 (5) 1 yr or longer: 66 (89) vs. 67 (89) vs. 69 (93)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Tadalafil low dose-oral IG2: Tadalafil high dose-oral CG: placebo</p> <p>IG1: Dose: 10 mg (total=292 doses) Duration: 4-5 wks Frequency: 4 doses once every 8-10 d Compliance: NR</p> <p>IG2: Dose: 20 mg (total=300 doses) Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>CG: Dose: Placebo (total=284 doses) Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 28 d no tx Wash out period: NR</p> <p>F/u duration: 30 min after dosing</p>	<p>Primary outcome results: SEP (Q3) yes response (mean %) - at 30 min: 25 vs. 34 vs. 18, (IG1 vs. CG p=0.054, IG2 vs. CG p=0.002) - at 16 min: 9 vs. 47 (16) vs. 22 (8) , (IG1 vs. CG p=0.05, IG2 vs. CG 0.012)</p> <p>Other outcomes assessed: minimum time to effect; post hoc analysis for dosing and ED severity</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 2 (2.7) vs. 1 (1.3) vs. 6 (8.1)</p> <p>WDAE, n (%): 1(1) vs. 1 (1) vs. 2 (3) TAE, n (%): incidence in 11 (15) vs. 13 (17) vs. 1 (1); AE included headache, 3 (4) vs. 6 (8) vs. 0; Myalgia 3 (4) vs. 1 (1) vs. 0; Dyspepsia = nausea = vasodilation 1 (1) vs. 2 (3) vs. 0 Back pain, 2 (3) vs. 0 vs. 1 (1) SAE: NR</p> <p>Ascertainment of outcomes assessed: SEP (Q3) and patient diary</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sáenz de TeJada (2002) 138</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = NR N randomized = 216</p> <p>IG1, n = 73 IG2, n = 72 CG, n = 71</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older; clinical diagnosis of type 1 or 2 DM; mild to severe ED for ≥3 mo; in stable monogamous relationship with female partner</p> <p>Exclusion: pts with HbA1C > 13% recent hx of diabetic ketoacidosis; hypoglycaemia requiring assistance; angina during intercourse, unstable angina, dx of coronary artery dx, poorly controlled BP (for complete list of exclusion criteria refer to full text)</p>	<p>Age, mean (sd): 55.7 (9) y</p> <p>Race, n (%): White 215 (99.5); Black 1 (0.5)</p> <p>Co-morbidities, n (%): type I diabetes IG1 = CG 8 (11.3) vs. IG2 4 (5.6); type II DM 65 (89) vs. 68 (94.4) vs. 63 (88.7) Hypertension 80 (37); hypercholesterolemia 38 (18); micro-vascular complications in all grps 48 (22.2)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, (%): insulin only 36 vs. 28 vs. 45; oral only 44 vs. 54 vs. 41; mix 12 vs. 8 vs. 10</p> <p>Duration of ED, n (%): > 1y: 201 (93)</p> <p>Underlying disease: diabetes; hypertension</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: all</p> <p>Mixed ED: NR</p> <p>Other: IIEF score overall, mean (sd)= 12.2 (6.2) Other: subgroup defined based on HbA1C levels: poor (>9.5%)= 40 (18.5), fair (7-9.5%)= 136 (63), good (<7%)= 40 (18.5)</p>	<p>IG1: Tadalafil oral CG: placebo oral</p> <p>IG1: Dose: 10 (IG1) or 20 (IG2) mg Duration: 12 wk Frequency: 1 dose before anticipated sexual activity; max. 1/d Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: 1 dose before anticipated sexual activity; max. 1/d Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 13-14 wk</p>	<p>Primary outcome results: IG1 vs. IG2 vs. CG Change (▲) in mean EF domain of IIEF: 6.4, vs. 7.3 vs. 0.1 (% of pts with more than 5 positive points in IIEF EF domain: 44% vs. 56% vs. 13%, p <0.001) Change (▲) in mean % of “yes” response: SEP-Q2: 22 vs. 23 vs. - 4.1 SEP-Q3: 28 vs. 29 vs. 2 GAQ, proportion of positive responses, (%): 56 vs. 64 vs. 25, p < 0.001</p> <p>Other outcomes assessed: IIEFQ 3 and 4; OS, and OF (all sign post tx, values NR)</p> <p>Withdrawals/drop-outs/loss to f/u: 25</p> <p>WDAE: 6 (3%); 5 in IG and 1 in CG; 2 MI one in each grp; moderate myalgia, pain, headache & flushing TAE, n (%): AE in > 3% of pts= 29 (40) vs. 32 (44) vs. 22 (31); dyspepsia 8 (11) vs. 8 (11) vs. 0; headache 9 (10) vs. 6 (8) vs. 2 (3), myalgia 4 (6) vs. 3 (4) vs. 1 (1), flu symptoms, IG=CG 3(4), back pain 1 (1) vs. 4 (6) vs. 1 (1), flushing 2 (3) vs. 3 (4) vs. 0 SAE: 2 (MI) (1 in either grp; however, patient in IG1 never took study drug)</p> <p>Ascertainment of outcomes assessed: IIEF, SEP, GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Saylan (2006) ¹³⁹</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 139 N randomized = 132 (Egypt and Turkey)</p> <p>IG, n = 101 CG, n = 31</p> <p>ITT analysis used for primary outcome: yes (LOCF)</p> <p>Inclusion: men at least 18 y, with ED of at least 3 mo in duration and any kind of severity and etiology</p> <p>Exclusion: ED caused by premature ejaculation or untreated endocrine disease, or after pelvic surgery or pts receiving nitrates, antiandrogens or chemotherapy, sign penile deformity or penile implant, clinically sign renal or hepatic insufficiency, poorly controlled DM; stroke, MI, or SCI, unstable cardiovascular disease; prior ineffective tx with sildenafil (physician discretion)</p>	<p>Age, mean (range): 48.7 (26.6-67.7) vs. 51.7 (27.8-66.1) y</p> <p>Race: Caucasians</p> <p>Co-morbidities, n (%): DM 21 (20.8) vs. 8 (25.8); hypertension 10 (9.9) vs. 7 (22.6); benign prostatic hyperplasia 4 (4.0) vs. 2 (6.5); hypercholesterolemia 3 (3.0) vs. 1 (3.2); hyperlipidemia 1 (1.0) vs. 2 (6.5) UTI 1 (1.0) vs. 2 (6.5)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 25.6 vs. 32.3%</p> <p>Body weight: 82.35 kg</p> <p>Other: alcohol consumption <7%</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: <6 mo: 14% >=6 mo: 10 vs. 22.6% >= 1 y: 75.2 vs. 64.5%</p> <p>Underlying disease, n (%): no specific condition</p> <p>Psychogenic ED, n (%): 11 (10.9) vs. 2 (6.5)</p> <p>Physiologic ED, n (%): 31 (30.7) vs. 9 (29)</p> <p>Mixed ED, n (%): 59 (58.4) vs. 20 (64.5)</p> <p>Other: ED severity, n (%): Mild 35 (34.7) vs. 11 (35.5) Moderate 38 (37.6) vs. 12 (38.7) Sever 28 (27.7) vs. 8 (25.8)</p>	<p>IG: Tadalafil CG: Placebo</p> <p>IG: Dose: 20 mg Duration: 12 wks Frequency: on demand, up to once/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks (3 visits)</p>	<p>Primary outcome results: Mean change from baseline (SE): IIEF-EF: 9.3 (0.8) vs. 2.3 (1.6) -By ED severity: Mild: 6.3 (n=32) vs. 0.2 (n=9) Moderate: 8.2 (n=37) vs. 0.3 (n=11) Severe: 14.8 (n=27) vs. 7.5 (n=8)</p> <p>IIEF-Q3: 1.5 (0.2) vs. 0.2 (0.3) IIEF-Q4: 2.0 (0.2) vs. 0.8 (0.3) IIEF-IS: 4.8 (0.3) vs. 2.3 (0.7) IIEF-OS: 3.6 (0.3) vs. 1.1 (0.6)</p> <p>SEP-2, %: 34.5 (4.1) vs. -4.6 (8.1) SEP-3, %: 52.2 (3.8) vs. 16.8 (7.8)</p> <p>GAQ-1, %: 81.2 vs. 41.9 GAQ-2, %: 76.2 vs. 41.9</p> <p>Other outcomes assessed: SEP Q4-5 Withdrawals/drop-outs/loss to f/u, n (%): 17 (16.8) vs. 6 (19.4)</p> <p>WDAE, n (%): 4 (3.9) vs. 0 TAE, n (%): NR Most commonly reported, %: Headache 16.8 vs. 9.7; back pain 6.9 vs. 0; dyspepsia 2 vs. 6.5 SAE, n (%): 1 (1) vs. 0 (death cardiac arrest in a pts with multiple diseases)</p> <p>Ascertainment of outcomes assessed: IIEF, SEP, GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Seftel (2004) ¹⁴⁰</p> <p>Funding source: Lilly ICO LLC</p>	<p>N screened = 239 N randomized = 207</p> <p>IG1, n = 159 CG, n = 48</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older; at least 3-mo hx of mild to severe ED; stable relationship with female partner</p> <p>Exclusion: clinically sign penile deformity or penile implant; recent hx of stroke of SCI; hx of unstable CV dx in last 90 d; SBP >170 mm Hg or <90 mm Hg, or DPB>100 mm Hg or <50 mm Hg; clinically sign renal or hepatic insufficiency; failure to achieve erection after radical prostatectomy or pelvic surgery; tx with nitrates, antiandrogens or chemotherapy; prior ineffective tx with sildenafil</p>	<p>Age, mean (sd):</p> <p>Race, n (%): White: 151 (73) African descent: 26 (16); 26 (16); Asian: 3 (1); Other: 1 (0.6)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, n (%): ≥1 y in duration 148 (93) vs. 47 (98)</p> <p>Underlying disease: hypertension 75 (36); bbenign prostatic hyperplasia 58 (28); diabetes 36 (17); hyperlipidemia 37 (18); depression 13 (6); CAD 10 (0.5); peripheral vascular disease 1 (2)</p> <p>Psychogenic ED, n (%): 16 (10) vs. 4 (8)</p> <p>Physiologic ED, n (%): 94 (59) vs. 24 (50)</p> <p>Mixed ED, n (%): 49 (31) vs. 20 (42)</p> <p>Other: baseline severity of ED= mild 43 (27) vs. 15 (31); moderate 42 (26) vs. 12 (25); severe 69 (43) vs. 20 (41)</p>	<p>IG: Tadalafil oral CG: placebo oral</p> <p>IG: Dose: 20 mg Duration: 12 wk Frequency: 1 dose before sexual intercourse (max. 1/day) Compliance: NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: same as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: Change in IIEF, mean (sd): IIEF-EF: 9.3 (0.6) vs. 0.3 (0.9) Intercourse satisfaction: 4 (0.3) vs. 0.8 (0.4), OS: 3 (0.2) vs. 0 (0.3)</p> <p>Mean (sd) absolute change in positive response: SEP-Q2: 31.6% (2.5) vs. 2% (5.5) SEP-Q3: 43.6% (2.7) vs. 3.5% (4.2) SEP- Q4: 44 (3) vs. 6 (3)</p> <p>GAQ (improved erection), mean (sd) at 12 wk: 125 (83) vs. 9 (20)</p> <p>-Sign improvement in all IG vs. CG, p <0.001</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 31 (23 vs. 8)</p> <p>WDAE: 9; 8 (5.0%) vs. 1 (2) TAE: NR (AE (%)=headache: 16 vs. 6; back pain: 9 vs. 0; dyspepsia 8 vs. 0) SAE, n: 2 (chest pain) vs. 0</p> <p>Ascertainment of outcomes assessed: IIEF- SEP (Q2 and 3)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Skoumal (2004) 141</p> <p>Funding source: Eli Lilly and Company</p>	<p>N screened = NR N randomized = 409</p> <p>IG1, n = 305 CG, n = 104</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: men 18 or older, with at least 3-mo hx of mild to severe ED; same female partner throughout study</p> <p>Exclusion: ED due to premature ejaculation or untreated endocrine dx; failure to achieve erection after pelvic surgery, including radical prostatectomy (except bilateral nerve-sparing); sign penile deformity or penile implant; clinically sign renal or hepatic insufficiency; poorly controlled diabetes; unstable CA dx; recent hx of sign CNS injury; hx of HIV infection; exclusion of pts with prior ineffective tx with sildenafil was at discretion of investigators</p>	<p>Age, mean (95% confidence interval): 52 (51-53) vs. 52 (49-54) y</p> <p>Race (%): NR</p> <p>Co-morbidities, n (%): hypertension 98 (32) vs. 31 (30); Diabetes 43 (14) vs. 9 (9); Prostatic hyperplasia/hypertrophy 19 (6) vs. 11 (11); hypercholesterolemia 31 (10) vs. 9 (9); hyperlipidemia: 16 (5) vs. 3 (3)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: less than 0.25 y - equal or more than 1 y (majority, 78 vs. 80% with 1 y or longer)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 46 (15) vs. 19 (18)</p> <p>Physiologic ED, n (%): 89 (29) vs. 29 (28)</p> <p>Mixed ED, n (%): 170 (56) vs. 56 (54)</p> <p>Other: baseline IIEF EF severity class, n (%)= mild 145 (48) vs. 49 (47); moderate 89 (29) vs. 31 (30); severe 71 (23) vs. 24 (23)</p>	<p>IG1: Tadalafil (Cialis^(R)) oral CG: placebo- oral</p> <p>IG1: Dose: 20 mg Duration: 12 wk Frequency: as needed (max. 1/day) Compliance (%): NR</p> <p>CG: Dose: placebo Duration: 12 wk Frequency: as needed (max. 1/day) Compliance (%): NR</p> <p>Run In period: 4 wk</p> <p>Wash out period: NA</p> <p>F/u duration: 12 wk</p>	<p>Primary outcome results: Mean change in IIEF score (and 95% confidence interval) EF: 10 (9-10.6) vs. 1.4 (0.1-2.8) Intercourse satisfaction: 5 (4.4-5.1) vs. 1.4 (0.8-2.1) OF: 2 (1.9-2.6) vs. 0.2 (-0.4-0.8) SD: 1 (0.9-1.3) vs. 0 (-0.3-0.4) OS: 4 (3.4-4.0) vs. 0.7 (0.2-1.2) Mean absolute change SEP-Q2 (yes): approx. 2% vs. 35% SEP-Q3: IG1 approx. 53%, CG approx. 13% GAQ-1: 86% vs. 33% GAQ-2: 97% vs. 94%</p> <p>Other outcomes assessed: ED Inventory of Treatment Satisfaction scores</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 23 (6)</p> <p>WDAE: 1 vs. 0 TAE, n (%): >= 2 events= 55 (18) vs. 3 (3); headache, back pain in 10 vs. 3%; flushing, influenza, and nasal congestion only in IG (9%) SAE: 2 (pulmonary embolism, subarachnoid hemorrhage) vs. 0</p> <p>Ascertainment of outcomes assessed: IIEF ED domain, SEP (Q2, and 3); GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Staab (2004) ¹⁴²</p> <p>Funding source: Eli Lilly and Company</p>	<p>N screened = NR N randomized = 212</p> <p>IG, n = 171 (2 mg =42, 5 mg= 44, 10 mg= 42, 25 mg =43) CG, n= 41</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older; with ED for 3 mo or longer; in stable, monogamous, heterosexual relationship</p> <p>Exclusion: ED due to untreated endocrine disorder; hx of radical prostatectomy, with failure to achieve any erection; pelvic surgery; sign penile curvature; prior unsuccessful tx with phosphodiesterase type 5 inhibitors; hx of human immunodeficiency virus infection; poorly controlled diabetes; clinically sign hepatic, renal, cardiovascular or central nervous system dx during prior 6 mo</p>	<p>Age, mean (sd): 58 (10) y</p> <p>Race, n (%): White 194 (92), African descent 10 (5), Asian 7 (3), other 1 (0.5)</p> <p>Co-morbidities, n (%): currently active cardiovascular condition 85 (40), hx of cardiovascular condition 8 (4), diabetes 44 (21)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): Current smoker 40 (19)</p> <p>Body weight, mean (sd): 87 (14.5) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: ED severity: mild 93 (44%); moderate 52 (25%); severe 67 (31%); no sign difference between IG</p>	<p>IG1: tadalafil -oral CG: placebo -oral</p> <p>IG1: Dose: 2, 5, 10 or 25 mg Duration: 8 wk Frequency: max. 1/day (1 dose before sexual intercourse) Compliance: NR</p> <p>CG: Dose: placebo Duration: 8 wk Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wk Wash out period: NA</p> <p>F/u duration: 8 wk</p>	<p>Primary outcome results: IG (only reported for 25 mg grp) vs. CG: IIEF Q3, approximate % with score of 5: 75% vs. 20% IIEF Q4, approximate % with score of 5: 62% vs. 10% IIEF EF, mean score: 24 vs. 14</p> <p>SEP Q3 - % positive response: 82% vs. 52% SEP Q4 - % positive response: 78% vs. 40%</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n: 10</p> <p>WDAE, n: 2 TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF questions 3 and 4: scored from 0 (no intercourse) to 5 (best performance) IIEF EF domain: sum of scores for questions 1-5 and 15</p> <p>Other: results are shown in probability tables</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Von Keitz (2004) 143</p> <p>Funding source: Lilly ICOS LLC</p>	<p>N screened = 299 N randomized = 219 (cross over drug preference)</p> <p>IG1, n = 105 IG2, n = 114 CG, n = NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men 18-65, with ED for at least 3 mo (consistent change in the quality of erection that adversely affected the patient's satisfaction with sexual intercourse), in heterosexual relationship; also pts non-responsive to previous tx with sildenafil</p> <p>Exclusion: Pts treated with nitrates, recent hx of MI or coronary revascularization (within 90 d), rapid ejaculation, 6 mo or longer hx of unstable angina, ED secondary to endocrine disorders, pelvic surgery, stroke or SCI within the last 6 mo, retinitis pigmentosa, HIV infection</p>	<p>Age, mean (sd): 52.5 (9.3) y</p> <p>Race (%): White 89, African 7, Hispanic 2, Asian 2</p> <p>Co-morbidities, (%): hypertension 26, DM 17, depression 4, CAD 3</p> <p>Previous ED treatment: sildenafil (66%)</p> <p>Smoking status, (%): current smokers = 29</p> <p>Body weight: NR</p>	<p>Concomitant medications: CVD or diabetes (n = 54)</p> <p>Duration of ED (yr): => 1 yr (94%)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 7%</p> <p>Physiologic ED: 42%</p> <p>Mixed ED: 51%</p> <p>Other: severity of ED (based on clinical judgement; %) = mild (18%), moderate (56%), severe (26%)</p>	<p>IG1: Tadalafil+ Tadalafil instruction 1st; Sildenafil + sildenafil instruction 2nd</p> <p>IG2: Sildenafil+ Sildenafil instruction 1st; Tadalafil + Sildenafil instruction 2nd</p> <p>IG1: Dose: 20 mg Duration: 12 wks/ period Frequency: once/d Compliance: NR</p> <p>IG2: Dose: 50 mg Duration: 12 wks/period Frequency: once/d Compliance: NR</p> <p>Run In period: 1 wk Wash out period: 1-2 wks (1st washout), 96 hrs 92nd washout post 24 wks prior to 12 wks extension period) F/u duration: 38 wks (2 x12 wks tx + 1-2 wks washout + 96 hrs no tx at end +12 wks extension Other: preference of dosing instructions also in two additional arms (n=36)</p>	<p>Primary outcome (EF): No ED outcomes reported</p> <p>N (%) pts preferring tadalafil (over sildenafil) vs. N (%) pts preferring sildenafil (over tadalafil) = 132 (73) vs. 49 (27), p < 0.001</p> <p>Other outcomes assessed: treatment preference by subgroups, AE</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 24 (23) vs. 28 (25); including total withdrawals 17 (16) vs. 21 (18); lost to f/u 7 (7) vs. 7 (6)</p> <p>WDAE, n (%): 4 (4) vs. 3 (3) TAE, n (%): pts with 2 or more AE = 73 (70) vs. 57 (50); AE included headache 26 (12) vs. 17 (8); dyspepsia 14 (6) vs. 10 (5); back pain 9 (4) vs. 4 (2); myalgia 9 (4) vs. 1 (0.5); flushing 6 (3) vs. 8 (4); nasal congestion 6 (3) vs. 10 (5); influenza-like illness 3 (1) vs. 7 (3) SAE: NR</p> <p>Ascertainment of outcomes assessed: questionnaires to determine pts preference of tx</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Yip (2006) ¹⁴⁴</p> <p>Funding source: Lilly Research Laboratories</p>	<p>N screened = N randomized = 242 (17 centres across China)</p> <p>IG1, n = 159 CG, n = 83</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older with ED of at least 3 mo in duration of Psychogenic, organic or mixed causes</p> <p>Exclusion: ED caused by premature ejaculation, or untreated endocrine disease; pelvic surgery, including radical prostatectomy; penile deformity, or penile implant, renal or hepatic insufficiency, uncontrolled DM, unstable CVD, hx of central nervous system injury, HIV infection (discretionary criteria: prior ineffective tx with sildenafil)</p>	<p>Age, mean (range): 54 (28-78) y</p> <p>Race: East/Southeast Asian 97%</p> <p>Co-morbidities, n (%): DM 31%; hypertension 30%; benign prostatic hyperplasia 22.9% vs. 17.6; hypercholesterolemia 6% vs. 11%</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: 70.3 (9.4) vs. 68.6 (9.5) kg</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: pts with ED longer than 1 y, n (%) 131 (82.4) vs. 76 (91.6)</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 22 (13.8) vs. 19 (22.9)</p> <p>Physiologic ED, n (%): 94 (59.1) vs. 54 (65.1)</p> <p>Mixed ED, n (%): 43 (27) vs. 10 (12)</p> <p>ED severity, n (%): severe 26%; moderate 33%; mild 41%</p> <p>Baseline IIEF-EF, mean: 14.9 vs. 14.8</p>	<p>IG: Tadalafil CG: placebo</p> <p>IG1: Dose: 20 mg Duration: 12 wks Frequency: on demand, up to once/d Compliance: NR</p> <p>CG: Dose: NA Duration: 12 wks Frequency: on demand, up to once/d Compliance:</p> <p>Run In period: 4 wks Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: Change in mean from baseline:</p> <p>IIEF-EF: 8.5 vs. 2.1, P<0.001 IIEF-Q3: 1.3 vs. 0.2, P<0.001 IIEF-Q4: 1.7 vs. 0.5, P<0.001 SEP-2, % yes: 30.1 vs. -1.2, P<0.001 SEP-3, % yes: 46.7 vs. 8.9, P<0.001</p> <p>GAQ-1, % improved: 86.2 vs. 30.1 GAQ-2, % improved: 80.5 vs. 28.9</p> <p>Other outcomes assessed: IIEF-EF based on severity of ED (% of pts in each grp), mean change in score: Mild (39% vs. 42%) 5.3 vs. -0.3 Moderate (35% vs. 30) 9.1 vs. 2.7 Severe (25.8% vs. 26.5%) 12.5 vs. 5.2</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 12 (5) [5 (3) vs. 7 (8)]</p> <p>WDAE, n (%): 2 (<1) vs. 1 (<1) TAE, n (%): AE in 3% or more 46 (28.9) vs. 6 (7.2); included headache, back pain, dizziness, dyspepsia, and myalgia SAE, n (%): 3 (1.8) vs. 1 (1.2) including a worsening of CAD, fractures and dengue fever in IG; DM & sepsis in CG</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ, SEP</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Young (2005) ¹⁴⁵</p> <p>Funding source: Lilly ICOS LLC (Bothell, Wash and Indianapolis)</p>	<p>N screened = NR N randomized = 483 (phase III) IG1, n = 161 IG2, n = 161 CC, n = 161</p> <p>Note: pts further sub-divided for efficacy analyses at 24 hr post dosing (n= 80) & 36 hr (n= 81) for all grps ITT analysis used for primary outcome: y</p> <p>Inclusion: at least 18 y of age, reported minimum of 3 mo hx of ED</p> <p>Exclusion: clinically sign. penile deformities or penile implants, a recent hx of stroke or spinal cord trauma, unstable cardiovascular status (e.g. unstable angina, myocardial infarction, or myocardial revascularization within 90 days), use of nitrates, cancer chemotherapy, or antiandrogens, failure to achieve erection following radical prostatectomy or pelvic surgery.</p>	<p>Age, mean (range): 57.4 (33-82) vs.58 (26-75) vs. 58(37-78) y</p> <p>Race (%): Caucasian 80 vs. 87 vs. 83; African descent 10 vs. 8 vs. 14; Hispanic 8 vs. 5 vs. 2; other 2 vs. 0.6 vs. 2</p> <p>Co-morbidities, (%): DM 8 (11) vs. 11 (7) vs.15 (9); hypertension 64 (40) vs. 64(40) vs. 60 (37); coronary artery disease 5 (3) vs. 8(5) vs. (5)</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): current smoker 27(17) vs. 26 (16) vs. 21(13)</p> <p>Body weight: NR</p>	<p>Concomitant medications: testosterone (total = 22 pts) during post baseline period</p> <p>Duration of ED: 3 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 16 (10) vs. 14 (9) vs.16 (10)</p> <p>Organic ED, n (%): 109 (68) vs. 115 (71) vs.100 (62)</p> <p>Mixed ED, n (%): 36 (22) vs. 32 (20) vs. 45 (28)</p>	<p>IG: tadalafil, 10 mg, oral IG2: tadalafil, 20 mg, oral CG: oral placebo IG Dose: 10 mg Duration: 4-6 wks Frequency: 4 diff. times at 24 or 36 hrs post dosing, 7 d between each dose Compliance: NR IG2 Dose: 20 mg Duration: 4-6 wks Frequency: as IG1 Compliance: NR CG: Dose: placebo Duration: 4-6 wks Frequency: as IG Compliance: NR</p> <p>Run in period: 4 wks + 2-4 wks equilibration phase</p> <p>Wash out period: 7 d F/u duration: 4-6 wks for efficacy 6 mos open-label active medication extension – results NR)</p>	<p>Primary outcome results: SEP3, mean per pt % “yes” responses, % change): 24-hrs IG (55.8%, ▲ 25.5%, p = 0.038), IG2 (67.3%, ▲ 46.3%, p < 0.001) sign superior vs. CG (41.8%, ▲9.4%) 36-hrs IG (56.2%, ▲ 23.9%, p< 0.001), IG2 (61.9%, ▲28.7%, p<0.001) sign successful vs. CG (32.8%, ▲1.9%) Other outcomes assessed: SEP-Q1, 2,4,5</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 23 (4.8%)</p> <p>WDAE (%): IG= 2, vs. CG= 0.6</p> <p>TAE n (%): AE in 2% or more= 37 (23) vs. 55 (34) vs. 9 (5.6); AE included headache 9 (6) vs. 17 (11) vs. 1 (0.6); back pain 11 (7) vs. 10 (6) vs. 1 (1); dyspepsia 6 (4) vs. 8 (5) vs. 1 (0.6); nasopharyngitis 8 (5) vs. 5 (3) vs. 5 (3); nasal congestion 3 (2) vs. 6 (4) vs. 0; upper respiratory tract infection 4 (3) vs. 5 (3) vs. 3 (2); myalgia 2 (1) vs. 5 (3) vs. 0; influenza 2(1) vs. 4 (3) vs. 3 (2). SAE: n=3, 1 death in IG2; 2 (NR) in CG</p> <p>Ascertainment of outcomes assessed: SEP3: “Did your erection last long enough for you to have successful intercourse?” [yes/no]</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

F4-Apomorphine (sublingual)

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Dula (2000) ¹⁴⁶</p> <p>Funding source: TAP Holdings Inc.</p>	<p>N screened = NR N randomized = 569</p> <p>IG1, n = 242 IG2, n = 119 IG3, n = 89 CC, n = 119</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: age 21-73; in stable heterosexual relationship for ≥6 mo; failed to achieve and maintain firm erections for satisfactory intercourse in ≥50% of attempts in last 3 mo</p> <p>Exclusion: MS; SCI; Parkinson's disease; hypogonadism; hyperprolactinemia; uncontrolled diabetes or hypertension; radical prostatectomy; major penile deformity or penile prosthesis; ED tx in preceding 3 mo; hx of drug or alcohol abuse within past 2 yr; AIDS or positive HIV test; hx of cancer; allergy to opiates; partner breast-feeding, pregnant or with hx of major affective disorder (IG1 vs. IG2 vs. IG3 vs. CG)</p>	<p>Age, mean (range): 55 (21-72) vs. 55 (37-71) vs. 55 (26-73) vs. 56 (25-71) y</p> <p>Race,(range %): White 90-92%; African-American 1-7%; other 2-7%</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: % of pts with one or more of following hypertension 29%; diabetes 6%; benign prostatic hyperplasia 16%; CAD 12%</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: ED severity, (%): severe 35%; moderate 37%; mild 28% (determined by IIEF)</p>	<p>IG1/2/3: apomorphine - sublingually CG: placebo-sublingually</p> <p>IG1/2/3: Dose: IG1=2, 4, 5, 6 mg (dose optimizing grp); IG2= 5 mg; IG3=6 mg Duration: 8 wk (4 wk, dose adjustment + 4 wks steady dose for IG1) Frequency: wk 1-4: 2-5 doses/wk; wk 5-8: ≥2 doses/wk Compliance: NR</p> <p>CG: Dose: placebo Duration: 8 wk Frequency: wk 1-4: 2-5 doses/wk; wk 5-8: ≥2 doses/wk Compliance: NR</p> <p>Run In period: None Wash out period: NA</p> <p>F/u duration: 8 wk</p>	<p>Primary outcome results: Erection firm enough for intercourse, (%): Baseline: 26 vs. 21 vs. 28 vs. 24 Post tx: 53 vs. 53 vs. 53 vs. 35 (▲ in %=27 vs. 32 vs. 25 vs. 11) Attempts resulting in erection firm enough for intercourse, (%): Baseline: 26 vs. 21 vs. 26 vs. 23 Post tx: 50 vs. 51 vs. 50 vs. 33 (▲ in %=24 vs. 34 v. 30 vs. 10)</p> <p>Other outcomes assessed: Partner rated erection; time to erection</p> <p>Withdrawals/drop-outs/loss to f/u: IG 111 (25), CG 14 (12)</p> <p>WDAE: 25 (10) vs. 8 (7) vs. 8 (9) vs. 1 (1) TAE: NR AE in 10% or more of pts, (%), [1st 4 wks; 2nd 4 wks]: nausea [25; 12] vs. [34; 12] vs. [44; 17] vs. [3; 0]; headaches [16; 6] vs. [12; 2] vs. [19; 6] vs. [10; 4] vs. [0; 0]; sweating [10; 5] vs. [10; 0] vs. [16; 1] vs. [1; 0]; yawning [10; 3] vs. [14; 0] vs. [16; 0] vs. [6; 0]; somnolence [7; 2] vs. [15; 4] vs. [11; 0]; [2; 1] Note: AE data reported for n=197 vs. n=94 vs. n=70 vs. n=105) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; partners brief Sexual Functional Inventory</p>

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<p>Dula (2001) ¹⁴⁷</p> <p>Study a</p> <p>Funding source: TAP Pharmaceuticals Inc.</p>	<p>N screened = NR N randomized = 194 (cross over)</p> <p>IG/CG, n = 194</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: male with ED 3 mo or longer, in stable sexual relationship 6 mo or longer; controlled diabetes, hypertension, benign prostate hypertrophy, and CAD</p> <p>Exclusion: unable to achieve at least 55% base rigidity for 10 min on at least once/ two nights; sign neurological dx, endocrine, genito/urinary or psychiatric dx, HIV, AIDS, cancer in remission; drug abuse, hypersensitivity to morphine, recent tx for ED, use of metoclopramide Introduction of or dose changes in anxiolytics, serotonin reuptake inhibitors, beta-blockers, thiazide diuretics, alpha-methyl dopa, clonidine; penile fibrosis; severe pyronie's dx, or prior penile prosthesis</p>	<p>Age, mean (range): 56.7 (27-72) y</p> <p>Race n (%): Caucasian: 166 (86) African-American: 13 (7) Hispanic: 13 (7) Other: 2 (1)</p> <p>Co-morbidities, n (%): Hypertension: 85 (44) Diabetes: 30 (16) Benign prostatic hypotrophy: 49 (25) CAD: 19 (10) None: 79 (41)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight mean, (range): 179 (155-198) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: severity of ED, n (%)= severe 62 (32), moderate 56 (29), mild 52 (27), none 1 (0.5), not specified 23 (12)</p>	<p>IG: sublingual formulation of apomorphine CG: placebo formulation</p> <p>IG: Dose: 3 mg Duration: 4 wks Frequency: minimum twice /wk with at least 8 hr in between doses Compliance: 84%</p> <p>CG: Dose: NA Duration: 4 wks Frequency: as IG Compliance: 84%</p> <p>Run In period: 2-4 wks Wash out period: 24-96 hrs</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Percentage attempts resulting in erection firm enough for intercourse IG1: 46.9% CG: 32.3% IG1 significantly superior to CG across all severities of ED</p> <p>Other outcomes assessed: Time to erection</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE, n (%): AE reported by 5% or more of pts= 61/185 (33) vs. 24/177 (14); including: nausea 13 (7) vs. 2 (1); yawning 15 (8) vs. 1 (0.6); dizziness 12 (7), vs. 6 (3); somnolence 9 (5) vs. 3 (2), headache 4 (2) vs. 8 (5); vasodilatation 4 (2) vs. 4 (2) SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan, home diaries, Brief Sexual Function Inventory, IIEF</p>

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<p>Dula (2001) ¹⁴⁷</p> <p>Study b</p> <p>Funding source: TAP Pharmaceuticals Inc.</p>	<p>N screened = NR N randomized = 102 (cross over)</p> <p>IG1/IG2, n = 102</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: male with ED 3 mo or longer, in stable sexual relationship 6 mo or longer; controlled diabetes, hypertension, benign prostate hypertrophy, and CAD</p> <p>Exclusion: unable to achieve at least 55% base rigidity for 10 min on at least once/ 2 nights; sign neurological dx, endocrine, genito/urinary or psychiatric dx, HIV, AIDS, cancer in remission; drug abuse, hypersensitivity to morphine, recent tx for ED, use of metoclopramide Introduction of or dose changes in anxiolytics, serotonin reuptake inhibitors, beta-blockers, thiazide diuretics, alpha-methyl dopa, clonidine; penile fibrosis; severe pyronie's dx, or prior penile prosthesis</p>	<p>Age, mean (range): 57 (32-71) y</p> <p>Race n (%): Caucasian: 87 (85) African-American: 9 (9) Hispanic: 5 (5) Other: 1 (1)</p> <p>Co-morbidities, n (%): hypertension: 35 (34) Diabetes: 12 (12) Benign prostatic hypertrophy: 20 (20) Coronary artery disease: 12 (12) None: 46 (45)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (range): 178 (155 – 199) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: severity of ED, n (%)= severe 32 (31); moderate 35 (34); mild 20 (20); not specified 15 (14)</p>	<p>IG1: apomorphine-sublingual IG2: apomorphine-sublingual</p> <p>IG1: Dose: 3 mg Duration: 4 wks Frequency: minimum twice /wk with at least 8 hr in between doses Compliance: 78%</p> <p>IG2: Dose: 4 mg Duration: 4wks Frequency: as IG1 Compliance: 78%</p> <p>Run In period: 2-4 wks Wash out period: 24-96 hrs</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Percentage of attempts resulting in erection firm enough for intercourse 49% vs. 50%</p> <p>Other outcomes assessed: Proportion of attempts culminating in successful intercourse</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE, n (%): AE reported by 5% or more of pts= 23/90 (26) vs. 51/92 (55); included nausea 3 (3) vs. 13 (14); yawning 8 (9) vs. 12 (13); dizziness 2 (2) vs. 5 (5); somnolence 5 (6) vs. 9 (10); headache 4 (4) vs. 6 (7); vasodilatation 1 (1) vs. 6 (7) SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan, pts diaries, IIEF, Brief Sexual Function Inventory</p>

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<p>Eardley (2004) 148</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 139 (cross over open label)</p> <p>IG1, n = 66 (sildenafil - apomorphine) IG2, n = 65 (apomorphine - sildenafil) CG randomized = NA</p> <p>ITT analysis used for primary outcome: Yes (n=118)</p> <p>Inclusion: male pts with ED (Sexual Health Inventory-Male score <= 21) aged > 18 yrs, in a stable relationship</p> <p>Exclusion: pts taking concomitant nitrates, hypersensitivity to morphine, previous treatment for ED, concurrent dosing with the inhibitor of the CYP3A4 enzyme system, unstable CVD, hx of retinitis pigmentosa, and other major hepatic renal or haematological abnormalities</p>	<p>Age, mean (range): 57.6 (39-77) vs. 54.7 (28-82) y</p> <p>Race: White 92%; other 8%</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: None</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 86 (17) vs. 87 (16) kg</p> <p>Other: mean height= 177 vs. 175 cm</p>	<p>Concomitant medications: None</p> <p>Duration of ED, mean (range): 4.7 (0.2-25) vs. 3.3 (0.2-17) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: sildenafil (1st period)/ apomorphine (2nd) IG2: apomorphine (1st)/ sildenafil (2nd)</p> <p>IG1: Dose: NR Duration: 8 wks (given in 1st or 2nd period) Frequency: NR Compliance: n=5 pts did not take sildenafil</p> <p>IG2: Dose: NR Duration: 8 wks (given in 1st or 2nd period) Frequency: NR Compliance: n=8 pts did not take apomorphine</p> <p>Run In period: 2 wks Wash out period: 2 wks</p> <p>F/u duration: 8 wks for each drug; chronological = 18 wks (2 periods and wash out period combined)</p>	<p>Primary outcome results: Sildenafil vs. apomorphine, adjusted mean (95% CI): IIEF-EF score: Post tx: 25 (24-27) vs. 16 (14-17) Tx 9.3 (7.6-11) OS: Post tx: 8.5 (8- 9) vs. 6 (5.4-6.3) Tx difference: 2.7 (2- 3) EDITS 'successful intercourse attempts (% of pts): Post tx: 75 (69, 81) vs. 35 (29- 41) Tx difference: 40 (33, 46.5) EDTS, total score: Post tx: 82.5 (78-87) vs. 47 (42-52) Tx difference: 36 (30-41)</p> <p>Other outcomes assessed: OF, sexual desire;</p> <p>Withdrawals/drop-outs/loss to f/u: n = 21</p> <p>WDAE, n (%): 5 (8); including n=2 (sildenafil), MI; postural hypotension, dizziness, & shortness of breath; n=3 (apomorphine), suspected MI; headache and blurred vision; nausea) TAE: 110 (in n=62) vs. 53 (in n=42) SAE: n=5, suspected MI, Dupuytren's contracture (apomorphine) vs. deterioration of an arthritic shoulder and MI, atrial fibrillation (sildenafil), one atrial fibrillation 30 d post end of tx</p> <p>Ascertainment of outcomes assessed: IIEF, EDITS</p>

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<p>Gontero (2005) 149</p> <p>Funding source: NR</p>	<p>N screened = 154 N randomized = 130</p> <p>IG, n = 65 CG, n = 65</p> <p>ITT analysis used for primary outcome: no</p> <p>Inclusion: diabetic men (type I and II) with hx of ED, lasting at least 3 mo. for which never received treatment</p> <p>Exclusion: any major psychiatric disorder, absence of stable partner, penile deformities, concomitant presence of a neurological disease (other than diabetes)</p>	<p>Age, mean (sd): IG 56.58(10.25), CG 56.05(9.65)</p> <p>Race (%): NR</p> <p>Co-morbidities: ischemic heart disease 17 vs. 21; nitrates 5 vs. 7; hypertension 44 vs. 38; cholesterol (> 200) 22 vs. 21</p> <p>Blood glucose, mean (sd): 8 (2) vs. 8(1.7) HbA1C</p> <p>Previous ED treatment: NA</p> <p>Smoking status (%): 34% vs. 38</p> <p>Body weight: NR</p> <p>Other: diabetes (%): type I= 15 vs. 15; type II (insulin)= 47 vs. 41</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean. (sd): 25 (26) vs. 23(19) mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: duration of diabetes, mean (sd): 12 (9) vs. 11 (8) y; Baseline IIEF-ER, mean (sd): responders=13 (6) vs. 13 (5); non-responders 13 (6) vs. 13 (6); pts with Erection grade 3 or higher, (%): responders 73 vs. 67; non-responders= 40 vs. 38</p>	<p>IG: apomorphine SL, oral CG: placebo, oral</p> <p>IG: Dose: 3 mg Duration: 4 wks Frequency: X1, 15 min before sexual intercourse, max= once in 8-hr period Compliance (%): non-responders= 45%; responders= 10% did not take all tablets</p> <p>CG: Dose: 3 mg Duration: 4 wks Frequency: as IG Compliance (%): non-responders= 50%; responders= 12% did not take all tablets</p> <p>Run In period: NA Wash out period: NA</p> <p>F/u duration: NA</p>	<p>Primary outcome results: IIEF- EF domain: 13.8(6) vs. 13.2 (6) IIEF- Q3 (erection sufficient for intercourse): 2 (1) vs. 2 (1) IIEF-Q4 (ability to maintain erection): 2 (1) vs. 2 (1) = no sign. differences for all variables p > 0.05 IIEF-GEQ: affirmation responses 25 %, vs. 21% (P=0.65)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: 9% vs. 5% (nausea) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF-questionnaire; GEQ, 1 item (yes or no), IIEF-EF domain was considered sign. if improved by 5 point</p>

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<p>Hagemann (2003) ¹⁵⁰</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 12</p> <p>IG, n = 6 CG, n = 6</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men with ED based on documentation of less than 50% successful attempts to attain and/or maintain an erection firm enough for intercourse with partner for a min of 90 d prior to study or if no attempts were made</p> <p>Exclusion: Men without ED</p>	<p>Age, mean (range): 35 (24-41) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): 6 (50)</p> <p>Body weight, mean (range): 82 (65-93) kg,</p> <p>Other: consumed alcohol, n (%)= 9 (75)</p>	<p>Concomitant medications: None</p> <p>Duration of ED: Min 90 d prior to study</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Apomorphine SL CG: Placebo</p> <p>IG: Dose: 4 mg Duration: 70 min Frequency: during Positron emission tomography (PET) procedures Compliance: 100%</p> <p>CG: Dose: placebo Duration: 70 min Frequency: as IG Compliance: 100%</p> <p>Run In period: None Wash out period: None</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IG vs. CG n (%) RigiScan positive response 4 (67) vs. 0 (0)</p> <p>Other outcomes assessed: PET scan: ▲ cerebral activity post administration of apomorphine, associated with penile rigidity.</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: None TAE, n (%): 0 vs. 2 (33) headache SAE: None</p> <p>Ascertainment of outcomes assessed: RigiScan monitoring penile rigidity during all PET procedures. (40%=positive response, below 40%=non-responsive) PET scan, 4 were performed in each pts following a 30 s video</p>

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<p>Lammers (2002) 151</p> <p>Funding source: NR</p>	<p>N screened = 68 N randomized = 43 (4 way cross over)</p> <p>IG1-4, n = 43 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED of \geq 6mo, moderate to severe, in a stable monogamous heterosexual relationship, provided informed consent, informed partners of study participation</p> <p>Exclusion: ED caused by untreated endocrine dx, postural hypotension or uncontrolled hypotension, sign. penile pathology, hx of sign. hepatic or renal dx, CAD, nervous system dx, radical prostatectomy, uncontrolled psychiatric condition, known intolerance to study medications, concomitant use of organic nitrates, regular use of sympathetic-CNS depressors, blood donations (pts with ∇ of $>$30% SBP, or DBP or \blacktriangle of $>$30% HR after in office drug administration were withdrawn)</p>	<p>Age, range: 40-75 y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: many had used sildenafil, (and other study medications)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (mo): \geq 6 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: phentolamine + apomorphine IG2: phentolamin + papaverine IG3: phentolamine + papaverine + apomorphine IG4: sildenafil</p> <p>IG1: Dose: 40 mg + 6 mg Duration: NA Frequency: once (in office)</p> <p>IG2: Dose: 40 mg +150 mg Duration: NA Frequency: as IG1</p> <p>IG3: 40 mg+150 mg +6 mg Duration: NA Frequency: as IG1</p> <p>IG4: Dose: 100 mg (not blinded) Duration: NA Frequency: as IG1 Compliance (all): 100%</p> <p>Run In period: 4 wks placebo Wash out period: NA F/u duration: 60 min post tx</p>	<p>Primary outcome results: SEP, mean \blacktriangle from baseline: 1.9 vs. 1.6 vs. 1.7 vs. 1.8</p> <p>Successful vaginal penetrations, mean proportion: Baseline: 0.13 Post tx: 0.5 vs. 0.4 vs. 0.5 vs. 0.4 GAQ (1-5), mean score: 2.9 vs. 2.9 vs. 2.9 vs. 2.5</p> <p>Rigidity by VAS (baseline = 17): 45 vs. 44 vs. 45 vs. 46</p> <p>Other outcomes assessed: Tx preference, duration and satisfaction; vaginal intercourse leading to orgasm</p> <p>Withdrawals/drop-outs/loss to f/u: 1</p> <p>WDAE: 0 TAE: 150 (in 19 pts) including CV events 2 (5) in IG3, and 2 (5%) in IG4 Most frequent AEs: rhinitis 4 (10) vs. 2 (5) vs. 6 (15) vs. 3 (8); headache 2 (5) vs. 1 (2) vs. 1(2) vs. 3 (8); dyspepsia 2 (5) only in IG3; nausea 2 (5) only in IG2 SAE: 1 hospitalization for right nephrectomy, (grp NR)</p> <p>Ascertainment of outcomes assessed: SEP; visual analogue scale of 0-100 (VAS), GAE, reports of AE</p>

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<p>Perimenis (2004) ¹⁵²</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 40</p> <p>IG1, n = 20 (apomorphine-sildenafil) IG2, n = 20 (sildenafil-apomorphine) CG, n = NA</p> <p>ITT analysis used for primary outcome? NR</p> <p>Inclusion: male outpatients with non-arteriogenic ED (repeated PSV 25 cm/s or higher), with a stable relationship of 6 mo or longer, age 18-80 yrs</p> <p>Exclusion: penile or testicular deformity, SCI, severe neurological dx, hormonal deficiency, severe BP abnormality or hx of retinitis pigmentosa, tx with vacuum devices, IC injections, testosterone or nitrates</p>	<p>Age, mean: 56. y, 95% CI= 53.9, 57.6</p> <p>Race: NR</p> <p>Co-morbidities, (%): DM (17.5), hypertension (50), Ischemic cardiac disease (12.5), dyslipidaemia (37.5)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: smokers (95%)</p> <p>Body weight: NR</p> <p>Other: mean IIEF-5 score = 17, 95%CI: 16.1, 18.4; mean PSV: 31.5 cm/s, 95% CI: 28.8, 33.1</p>	<p>Concomitant medications: pts were receiving medications to control comorbidities during trial (not specified)</p> <p>Duration of ED, mean: 9.2 mo, 95%CI: 7.1, 11.3</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: non-arteriogenic 100%</p> <p>Mixed ED: NR</p>	<p>IG1: apomorphine IG2: sildenafil</p> <p>IG1: apomorphine Dose: 2-3 mg Duration: 6 wks (given in 1st or 2nd period) Frequency: once/d Compliance: NR</p> <p>IG2: sildenafil Dose: 50-100 mg Duration: 6 wks (given in 1st or 2nd period) Frequency: once/d Compliance: NR</p> <p>Run In period: NR Wash out period: 1 wk F/u duration: 6 wks for each drug; chronological = 13 wks (1st, 2nd periods, and wash out period combined)</p> <p>Other: for apomorphine and sildenafil the dose was titrated 2-3 mg and 50-100 mg respectively if the patient was not satisfied with the effectiveness</p>	<p>Primary outcome results: of successful intercourse attempts, n/N (%) = IG1: 326/520 (63%) IG2: 373/510 (73%), p < 0.0004 (two periods combined)</p> <p>Other outcomes assessed: tx satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Questionnaires</p> <p>Other: the pts' response to 2 mg apomorphine & 50 mg sildenafil was age-related (p < 0.05), but not related to ED duration, PSV, or IIEF score</p>

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<p>Perimenis (2004) ¹⁵³</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 43</p> <p>IG1 randomized = 24 (apomorphine 1st period; sildenafil 2nd) IG2 randomized = 19 (sildenafil 1st, apomorphine 2nd) CG randomized = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: male outpatients with ED with a stable relationship of 6 mo or longer, repeated PSV lower than 25 cm/s</p> <p>Exclusion: penile or testicular deformity, SCI, hormonal deficiency, severe blood pressure abnormality or hx of retinitis pigmentosa, tx with vacuum devices, IC injections, T or nitrates tx</p>	<p>Age, mean (sd): 59.2, 95%CI: 57.3, 61.2</p> <p>Race (%): NR</p> <p>Co-morbidities, (%): DM (17), hypertension (47), CVD (9), respiratory obstruction (5), transurethral prostatectomy (5), depression (2), heart failure (2)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: smokers (95%)</p> <p>Body weight: NR</p> <p>Other: mean IIEF-5 score = 7.9, 95%CI: 7.07-8.74; mean penile PSV: 20.7 cm/s, 95%CI: 19.5, 21.9</p>	<p>Concomitant medications: pts were receiving medications to control co-morbidities during trial</p> <p>Duration of ED, mean: 19.3 mo, 95%CI: 13.1, 25.4</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: arteriogenic 100%</p> <p>Mixed ED: NR</p>	<p>IG1: apomorphine IG2: sildenafil</p> <p>IG1: Dose: 2-3 mg Duration: 6 wks (given in 1st or 2nd period) Frequency: once/d Compliance: NR</p> <p>IG2: Dose: 50-100 mg Duration: 6 wks (given in 1st or 2nd period) Frequency: once/d Compliance: NR</p> <p>Run In period: NR Wash out period: 1 wk</p> <p>F/u duration: chronological = 13 wks (1st, 2nd periods, and wash out period combined)</p> <p>Other: for apomorphine and sildenafil the dose was titrated 2-3 mg and 50-100 mg respectively if not satisfied</p>	<p>Primary outcome results: Apomorphine vs. sildenafil of successful intercourse attempts, n/N (%) 1st + 2nd period= 189/588 (32%) vs. 375/589 (64%), p < 0.01 1st period= 31.3% vs. 62.6% 2nd period= 32.9% vs. 64.8% n/N (%) of successful intercourse attempts=</p> <p>Other outcomes assessed: satisfaction with tx</p> <p>Withdrawals/drop-outs/loss to f/u: n=2 (apomorphine)</p> <p>WDAE: n=2 (apomorphine) due to repeated nausea, syncope episode (in a pt who consumed alcohol) TAE: apomorphine: 6 (14%) including nausea, headache, dizziness and syncope vs. sildenafil: 3 (7%) including headache, dyspepsia SAE: NR</p> <p>Ascertainment of outcomes assessed: Questionnaires (event log)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Porst (2007) ¹⁵⁴</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 131 (cross over)</p> <p>IG1, IG2 n = 131 (1:1 to either arms: IG1sildenafil then apomorphine n=68 vs. IG2 apomorphine then sildenafil, n=63) CG: NA</p> <p>ITT analysis used for primary outcome: yes (n=116)</p> <p>Inclusion: men with ED, IIEF-5 of 21 or lower, in stable relationship</p> <p>Exclusion: hypersensitivity or any components of study medication or to opiates, major genital deformities leading to difficulties in performing intercourse, serious CV conditions, ED tx known to induce side effects, alcohol or drug abuse within last 30 d also excluded</p>	<p>Age, mean (sd): 53 (12) y, range 22-77 y</p> <p>Race: White 98% Black 1%; other 1%</p> <p>Co-morbidities, n (%): hypertension 27.9%; DM 9.3%; dyslipidemia 7%; CAD 4.6%;</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: 85 (11.7) kg</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED, mean (range): 4.2 (0.2-30.6) vs. 3.5 (0.1-13.8) y</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 18 (26.5) vs. 23 (37.7)</p> <p>Physiologic ED, n (%): 19 (27.9) vs. 17 (27.9)</p> <p>Mixed ED, n (%): 31 (45.6) vs. 21 (34.4)</p>	<p>IG1: Sildenafil IG2: Apomorphine</p> <p>IG1: Dose: initial 50 mg (adjusted to 25-100 based on efficacy and tolerability after 4 wks; 55% titrated up and 5% titrated down) Duration: 8 wks Frequency: on demand Compliance: see dropouts</p> <p>IG2: Dose: initial 2 mg (adjusted to 2-3 after 4 wks; 88% of pts titrated up) Duration: 8 wks Frequency: as IG Compliance: as IG</p> <p>Run In period: 2 wks Wash out period: 2 wks</p> <p>F/u duration: f/u measures at end of each 8 wks tx period</p>	<p>Primary outcome results: IIEF, mean sum score: EF: 23.6 vs. 12.8, P<0.0001 IS: 12 vs. 9.2, P<0.0001 OS: 8.2 vs. 5.7, P<0.0001</p> <p>Individual IIEF questions mean difference from baseline (sd): Q2: 1.9 (1.5) vs. 0.6 (1.3) Q3: 1.8 (1.5) vs. 0.7 (1.2) Q4: 1.8 (1.6) vs. 0.6 (1.2) Successful intercourse attempts: 62.7% vs. 28.3% GEQ, % improved: 88.7% vs. 43.1%</p> <p>Other outcomes assessed: adjusted mean tx difference between grps</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 11 (8.4) did not complete the study; 15 (11) excluded from analysis; 8 completed one phase</p> <p>WDAE, n (%): 1 (0.8) TAE, n: 65 vs. 35; pts with AE= 45 (35.7) vs. 27 (21.8) most common were headache, flushing, dyspepsia and rhinitis vs. headache and nausea SAE, n (%): 2 (1.6) vs. 1 (0.8); including 1 death</p> <p>Ascertainment of outcomes assessed: IIEF, EDITS and GEQ, Q1 and Q2</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>von Keitz (2002) 155</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 507 IG1, n = 254 CG, n = 253 ITT analysis used for primary outcome: Y</p> <p>Inclusion: heterosexual; in stable health; aged 18-70; hx of ED; some intrinsic penile function; in stable sexual relationship for ≥6 mo Exclusion: MS, or SCI; hypogonadism; serum T < 8.3 nmol/L; uncontrolled diabetes; HbA_{1C} >10%; episode of ketoacidosis in last 3 mo; radical prostatectomy; penile prosthesis; penile deformity; pelvic surgery; uncontrolled hyper or hypotension; MI within last 6 mo; unstable angina; any major CV impairment; hx of drug of alcohol abuse; positive HIV or hepatitis B surface antigen; cancer with dx-free interval <5 yr; ED medication within last 2 wk prior to randomization; hx of allergic reaction to opiates</p>	<p>Age, mean (range): 55 (22-70) y</p> <p>Race (%): white 99</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, (%): used at least one medication, 63 vs. 51</p> <p>Duration of ED: NR</p> <p>Underlying disease, (%): Hypertension 24 vs. 19 CAD 1 vs. 10 Diabetes 10 vs. 8 Benign prostatic hyperplasia 5.5 vs. 6</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: apomorphine SL-sublingually CG: placebo sublingually</p> <p>IG: Dose: 2 mg initially, ▲ by 1 mg at 2 and 4 wk (forced dose escalation regimen) Duration: 8 wk Frequency: once/ 8 hrs 1/8 hrs Compliance: NR</p> <p>CG: Dose: placebo Duration: 8 wk Frequency: as IG Compliance: NR</p> <p>Run In period: None Wash out period: NA</p> <p>F/u duration: 8 wk</p>	<p>Primary outcome results: Erections sufficient for intercourse (%): 62 vs. 55 (p=0.021)</p> <p>Successful attempts resulting in sexual intercourse (%): Overall: 38 vs. 28 3 mg apomorphine vs. CG: 35 vs. 26</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 33 (13) vs. 33 (13)</p> <p>WDAE, n (%): 12 (5) vs. 4 (2) TAE: 400 (in n=158) vs. 131 (in n= 62) SAE: 9 in n=6; 3 events considered related to study drug: IG1: syncope and vomiting in n=1 CG: angina pectoris of moderate intensity in n=1</p> <p>Ascertainment of outcomes assessed: diary card</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁ IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA_{1C}=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y=yes, N=no, NR=not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C5-Intracavernous Injection Trials

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Allen (1992) ¹⁵⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 7 Cross over design</p> <p>IG1/IG2/IG3, n = 7 CC, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with organic ED, abnormal nocturnal penile tumescence</p> <p>Exclusion: NR</p>	<p>Age, mean (sd): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: Effective Papaverine + phentolamine IC ≥1 mo before</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 7 (100%)</p> <p>Mixed ED: 0</p>	<p>IG1: Papaverine + Phentolamine IG2: Papaverine + Phentolamine + PgE₁ IG3: Papaverine + PgE₁</p> <p>IG1: Dose: Papaverine 30 mg/ml + phentolamine 5 mg/ml IG2: Dose: a + PgE₁ 5 µg/ml IG3: Dose: Papaverine 30 mg/ml + PgE₁ 5 µg/ml Frequency: two injections/d (a+ either b or c) Compliance, all: 86%</p> <p>Run In period: NR Wash out period: time to de-tumescence to be (<5 mm from baseline) at each test d; 1 wk between two test d, NR</p> <p>F/u duration: NA tumescence between injections</p>	<p>Primary outcome results: Duration: mean valued longer than a in IG3 (p=0.002), and trimix (p=0.001)</p> <p>Mean max rigidity: both combination of PgE1 better than (no sign)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 1 drop-out, post single intervention of 2 injections</p> <p>WDAE: NR TAE: NR (no pain observed) SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan for penile rigidity Erection duration timed: started when > 80% of max and stopped < 80% for ≥ 20 min</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Aversa (1996) 157</p> <p>A: (single-blind trial)</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 24 (cross over)</p> <p>IG1/IG2, n = 24 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts 20-45 yrs with non-organic ED => 6 mo duration (inability to achieve or maintain adequate erection for successful coitus), normal testicular size, no concomitant disease, no recent hx of drug abuse, normal cella turcica roentgenograms, normal results of neurological, vascular and clinical chemistry (3h glucose tolerance, liver and renal function tests), and normal basal serum levels (PRL < 25 ng/ml, testosterone > 653 nmol/l)</p> <p>Exclusion: NR</p>	<p>Age, range: NR (20-45) yrs (based on total sample from 2 separate trials (study a and b))</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: n=18 (total in 2 separate trials)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): => 6 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 100%</p> <p>Physiologic ED: None</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 IG2: PgE1 + phentolamine</p> <p>IG1: Dose: 20 µg/ml Duration: NA Frequency: once Compliance: NR</p> <p>IG2: Dose: 20 µg/ml (PgE1) 0.5 µg/ml (phentolamine) Duration: NA Frequency: once Compliance: NR</p> <p>Run In period: 12 hr (no smoke, no coffee) Wash out period: 7 d</p> <p>F/u duration: 7 d (assessments done 15 min after the injections)</p>	<p>Primary outcome results: N (%) pts with full response (IG1 vs. IG2) = 5 (21%) vs. 13 (54%), p < 0.05</p> <p>N (%) pts with partial response (IG1 vs. IG2) = 10 (42%) vs. 8 (33%), p = NR</p> <p>% pts with a valid-for-intromission erection (IG1 vs. IG2) = 63% vs. 87%, p < 0.05</p> <p>Mean duration of erection (IG1 vs. IG2) = 112 (7.9) vs. 130 (8.5), p = NR</p> <p>Other outcomes assessed: level of anxiety</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: mild to moderate discomfort in 21%; prolonged erection in 2: 1 IG1 (4%); 1 in IG2 (4%) Note: % of pts reported for combined data, n=34 SAE: NR</p> <p>Ascertainment of outcomes assessed: questionnaires; axial rigidity by tonometer, and radial rigidity by RigiScan</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Aversa (1996) ¹⁵⁷</p> <p>B:(single-blind trial)</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 10 (cross over)</p> <p>IG1/ IG2, n= 10 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts 20-45 y with non-organic ED => 6 mo duration (inability to achieve or maintain adequate erection for successful coitus), normal testicular size, no concomitant disease, no recent hx of drug abuse, normal cella turcica roentgenograms, normal results of neurological, vascular and clinical chemistry (3h glucose tolerance, liver and renal function tests), and normal basal serum levels (PRL < 25 ng/ml, testosterone > 653 nmol/l)</p> <p>Exclusion: NR</p>	<p>Age, range: (20-45) y (based on total sample from 2 separate trials)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: n=18 (total in 2 separate trials)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): => 6 mo</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED: 100%</p> <p>Physiologic ED: None</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 IG2: PgE1 + phentolamine</p> <p>IG1: Dose: 25 µg/ml Duration: 7 d Frequency: NR Compliance: NR</p> <p>IG2: Dose: 25 µg/ml (PgE1) 0.5 µg/ml (phentolamine) Duration: 7 d Frequency: NR Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 7 d (assessments done 15 min after the injections)</p>	<p>Primary outcome results: N (%) pts with full response (IG1 vs. IG2) = 3 (30%) vs. 6 (60%), p < 0.05</p> <p>N (%) pts with partial response (IG1 vs. IG2) = 3 (30%) vs. 3 (30%), p = NR</p> <p>% pts with a valid-for-intromission erection (IG1 vs. IG2) = 60% vs. 90%, p < 0.05</p> <p>Mean duration of erection (IG1 vs. IG2) = 115 (8.5) vs. 135 (10.5), p = NR</p> <p>Other outcomes assessed: level of anxiety</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: questionnaires</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Baum (2000) ¹⁵⁸</p> <p>Funding source: Upjohn Pharmaceutical Company</p>	<p>N screened = 50 N randomized = 50 (parallel)</p> <p>IG, n= 25 CG, n= 25</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: psychogenic ED, assessed by preservation of full, rigid morning or nocturnal erection and rigid erection with self-stimulation or masturbation</p> <p>Exclusion: endocrin cause of ED</p> <p>Data reported for IG vs. CG</p>	<p>Age, mean: 49.6 vs. 50.1</p> <p>Race (%): 64% White; 32% Black; 2% Hispanic; 2% Oriental</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment (n): IG1 vs. CG None 22 vs. 24 Oral medications 2 vs. 1 Vacuum or other device 1 vs. 0</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 3.5 vs. 4.4 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 50 (100%)</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Low dose PgE1 + information + instructional video CG: standard sex therapy</p> <p>IG: Dose: 2.5-5.0 µg (initial 2.5 µg + 2.5 µg after 60 min if erection <75% of pts normal erection, Optimum dose:produced erection lasting 60 min or more with rigidity adequate for intercourse) Duration: 12 wks Frequency: up to 3x/wk with at least 24 hr between doses Compliance: 52 %</p> <p>CG: Dose: up to 12 Duration: NR Frequency: 1x/wk Compliance: 64</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: assessment at wks 4,8,12</p>	<p>Primary outcome results:IG vs. CG Improvement in obtain un-aid erection: 47% vs. 58% Duration of erection: 35 vs. 10 min sex situations producing erection: 63% vs. 82% Extremely satisfied with treatment: 69% vs. 75% Improvement in Sexual Life Quality Questionnaire Subscale: 74 vs. 71 points Frequency of intercourse: 20.5 vs. 20</p> <p>Other outcomes assessed: Prediction of ability to perform 6 mo in future, cost comparison of treatment arms</p> <p>Withdrawals/drop-outs/loss to f/u: 12 (48%) vs. 9 (36%)</p> <p>WDAE: 0 TAE: penile bleeding & pain, n=1 in IG, n=1 report of ecchymosis also in IG SAE: NR</p> <p>Ascertainment of outcomes assessed: Sexual Life Quality Questionnaire (SLQQ), RigiScan device</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Bechara (1996) ¹⁵⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 32 (crossover design)</p> <p>IG1/IG2, n = 32</p> <p>CG randomized = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: lack of response to 2 consecutive tests with papaverine plus phentolamine</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 61 (26-71) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): 2.56, range 0.5-4.25</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE₁ + visual and manual stimulation IG2: Trimix + visual and manual sexual stimulation CG: NA</p> <p>IG1: Dose: 40 µg Duration: NR Frequency: 1 dose Compliance: NR</p> <p>IG2: Dose: 17.64 mg papaverine, 0.58 mg phentolamine, 5.8 µg PgE₁ Duration: NR Frequency: 1 dose Compliance: NR</p> <p>Run In period: NR Wash out period: ≥ 1 wk</p> <p>F/u duration: NR</p>	<p>Primary outcome results: examiner assessment of response on 5-point scale from E0 (no tumescence) to E5 (full rigidity) 15 min after injection Grade 4 or 5 erection IG1: 7 (22%) IG2: 16 (50%)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 15</p> <p>WDAE: NR</p> <p>TAE: NR (Pain 41% vs. 12.5%) SAE: NR</p> <p>Ascertainment of outcomes assessed: NR</p> <p>Other: NA</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Bechara (1997) ¹⁶⁰</p> <p>Funding source: drugs by Farmacica</p>	<p>N screened = NR N randomized = 60 (cross over design)</p> <p>IG/CG = 60 (randomized into 6 grps, details of these grps NR)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts with hx of ED longer than 6 mo</p> <p>Exclusion: major neurological impairment secondary to SCI or radical pelvic surgery; previous use of self injected vasoactive drugs, or previous pharmacological erection test</p>	<p>Age, mean (range): 58 (22-6-78) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NA</p> <p>Smoking status: NR</p> <p>Body Weight NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: More than 6 mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Papaverine + phentolamine; IG2: PgE1 CG: placebo</p> <p>IG1: Dose: 30 mg/ml papaverine + 0.5 mg/ml phentolamine (1 ml solution) Duration: NA Frequency: once/ wkl Compliance: 100%</p> <p>IG2: Dose: 30 µg/ml prostaglandine (1 ml solution) Duration: NA Frequency: once/ wkl Compliance: 100%</p> <p>CG: Dose: placebo: 1 ml isotonic sodium chloride solution Duration: NA Frequency: once/ wkl Compliance: 100%</p> <p>Run In period: NR Wash out period: 1 wk</p> <p>F/u duration: NR Other: Data provided for 3 intervention type</p>	<p>Primary outcome results: Erection response (IG1 vs. IG2 vs. CG) [N erectile response (%)]:</p> <p>Grade 4: 20 (33) vs. 16 (27) vs. 0 Grade 5: 14 (23) vs. 14 (23) vs. 0 Grade 4+5: 34 (56) vs.30 (50) vs. 0</p> <p>Other outcomes assessed: Systemic effects: No effects were noted</p> <p>Withdrawals/drop-outs/loss to f/u: n=0</p> <p>WDAE: n=0 TAE: Total pts with AE: NR Prolonged erection lasting more than 3 hr, n (%): 11 (18) vs. 9 (15) vs. 0 Pain: 9 (15) vs. 21 (35) vs. 0 SAE: NR</p> <p>Ascertainment of outcomes assessed: Manual & visual sexual stimulation at 10, 20 and 30 min post injection-erectile responses classified as E0 = no tumefaction to E5=full rigidity (E4-5= positive, E0-3 = negative)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Buvat (1998) ¹⁶¹</p> <p>Funding source: Schwarz Pharma A.G., Mannheim, Germany</p>	<p>N screened = 186 N randomized = 156</p> <p>IG1, n= 81 IG2, n= 75 CG, n= NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Age 18-70 y; with ED of 6 mo or longer in duration</p> <p>Exclusion: Drug/alcohol addiction; presence of other severe disease (e.g. unstable angina, MI) within 3 mo before study start; urological pathology responsible for ED (e.g. hypospadias); ED of hormonal origin; concomitant treatment with other vasoactive agents; hx of Peyronie's disease' anatomical deformation of penis</p>	<p>Age, mean (sd): 53.7 (10.8) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 4.5 (5.2) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 73 (46%)</p> <p>Physiologic ED: 41 (26%)</p> <p>Mixed ED, n (%): 43 (28%)</p> <p>Other: NA</p>	<p>IG1: moxisylyte chlorhydrate IG2: PgE1 (alprostadil α-cyclodextrin)</p> <p>IG1: Dose: 10–20 mg Duration: 6 wk Frequency: up to 6 injections/ 6 wks Compliance: NR</p> <p>IG2: Dose: 10–20 µg Duration: 6 wk Frequency: up to 6 injections/ 6 wks Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 wk</p>	<p>Primary outcome results: IG 1 vs. IG2 Penile buckling test with axial loading force of 1 kg, (clinic): ≥ 1 positive test: 32 (40%) vs. 56 (75%) Occurrence of rigid erection after self-injection, (home): ≥1 positive test: 37/61 (61%) vs. 58/68 (85%)</p> <p>Other outcomes assessed: positive buckling test by subgroups of psychogenic s. physiologic vs. mixed Successful injections; patient & partner opinion of tx</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE NR TAE:IG1 vs. IG2, (%): Pain during injection: clinic 15 vs. 15; home 13 vs. 25 Pain during erection: clinic 3 vs. 35; home 17 vs. 24 Pain after erection: clinic 0 vs. 5; home 7 vs. 19 Bleeding: clinic 3 vs. 5; home 3 vs. 15 Erection > 2 hr: clinic 0 vs. 2; home 5 vs. 4 Dizziness/hypotension: home 8 vs.1 SAE: 0</p> <p>Ascertainment of outcomes assessed: NA</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Colli (1996) 162</p> <p>Funding source:</p>	<p>N screened = NR N randomized = 45 (cross over)</p> <p>IG1-3/ CG, n= 45</p> <p>ITT analysis used for primary outcome? No</p> <p>Inclusion: Men aged 18-65 yrs with ED of probable vascular, neurological and/or psychological origin of => 6 mo duration</p> <p>Exclusion: penile anatomical deformation, priapism or corporeal fibrosis, endocrine ED (serum testosterone < 120 ng/dl and PRL > 20 ng/ml), sickle cell anemia, hematologic diseases, systematic or psychiatric dx of recent onset, uncontrolled DM (fasting blood sugar > 300 mg/dl), uncontrolled hypertension (systolic > 150 and diastolic > 100 mmHg), hypotension (systolic < 100 mmHg), smokers (> 40 cigarettes/d), present use of PgE1</p>	<p>Age, mean (sd): NR (NR); 20% (< 40 yrs), 33.3% (40-49 yrs), 37.7% (50-59 yrs), 8.8% (=> 60 yrs)</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): <= 1 yr (22.2%) 1-2 yrs (31.1%) 2-5 yrs (22.2%) 5-10 yrs (20%) > 10 yrs (4.4%)</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): diabetes 2 (4.4%)</p> <p>Psychogenic ED: 24 (53.3%)</p> <p>Physiologic ED: vascular 12 (26.6%), neurologic 2 (4.4%)</p> <p>Mixed ED: Mixed 5 (11.1%)</p>	<p>IG1-3: PgE1 (alprostadil) CG: placebo</p> <p>IG1: PgE1 Dose: 5 µg (IG1), 10 µg (IG2), 20 µg (IG3) Duration: NA Frequency: one/wk Compliance (%): NR</p> <p>CG: placebo Dose: NR Duration: NA Frequency: one/wk Compliance (%): NR</p> <p>Run In period: NR Wash out period: 1 wk F/u duration: NR (assessments done 5-120 min after injection)</p>	<p>Primary outcome results: IG1 vs. IG2 vs. IG3 vs. CG 'Full' erection as assessed by clinical manual palpation (n): 12 vs. 23 vs. 4 vs. 0, p < 0.001 (likelihood ratio test for the treatment effect) 'No' erection as assessed by clinical manual palpation (n): 11 vs. 5 vs. 2 vs. 41, p < 0.001 (likelihood ratio test for the treatment effect) 'Excellent' erection- pts assessment (n): 5 vs. 9 vs. NR, vs. 0, p < 0.001 (likelihood ratio test for the treatment effect) 'Full' erection (70% or more rigidity at tip or base for 10 min), n: 17 vs. 25 vs. 7 vs. 0, p < 0.001 (likelihood ratio test for rigidity)</p> <p>Other outcomes assessed: latency of erection</p> <p>Withdrawals/drop-outs/loss to f/u NR WDAE: NR TAE: NR; AE reported as treatment-related n=3 (IG2) vs. n=1 (IG1) SAE: NR</p> <p>Ascertainment of outcomes assessed: manual palpation; RigiScan, questionnaires</p>

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<p>Costa (1993) ¹⁶³</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized =64 (cross over design: this grp received 3 single dose of active intervention a, b, c, & placebo</p> <p>IG1/2/3/CG, n = 64</p> <p>Inclusion: Diagnosis of ED</p> <p>ITT analysis used for primary outcome? No</p> <p>Exclusion: Peyronie's disease; endocrine impotence; cardiac; renal; hepatic; ventilatory failure; systolic BP < 100 mm/Hg; neoplasm</p> <p>*Note: only values of IG3 is reported for outcome, since very similar to all other doses</p>	<p>Age, mean (range): 30 (20-50) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: IG2=32</p> <p>Physiologic ED: Neurogenic 12 (34%)</p> <p>Mixed ED: NR</p> <p>Other: neither psychogenic or hormonal in 50%</p>	<p>IG1-3: Moxisylyte in 3 dosages, tourniquet at penis base CG: Placebo (Lyophilized Mannitol) IC (tourniquet used)</p> <p>IG1/IG2/IG3: Dose: 10, 20 and 30 mg (2 ml volume) Duration: NA Frequency: single</p> <p>CG: Dose: 2 ml placebo Duration: NA Frequency: single</p> <p>Compliance all: 95% (n=61)</p> <p>Run In period: 1 mo Wash out period: 7-15 d</p> <p>F/u duration: 2 wks post last IC</p>	<p>Primary outcome results:IG3* vs. CG (Max at 15 min for all parameters) Penile length/ circumference, mean (SE): At 0 min: 113 (3) vs. 113 (3) mm/ 93 (2) vs. 91(2) mm At 30 min post tx: 135 (3) vs. 133 (3) mm/ 110 (3) vs. 98 (3) mm Erection sufficient for intercourse, n (%): 53 (87) vs. 17 (28) Duration of erection, mean (range): 2 hrs (50 min – 4 hr)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: N=3</p> <p>WDAE: NR TAE, n (%): mild pain during injection 4(5); hypotension + nausea 1 (1.4); prolonged erection (24h) 1 (1.4); faintness + normal BP 2 (2.8); drowsiness with all dose 1(1.4); sharp pain at injection1 (1.4); Hot flushes 1 (1.4); Rhinorrhea 4 (5) SAE: 1 sustained erection (24h) 10cc aspirated at 6hr to avoid priapism</p> <p>Ascertainment of outcomes assessed: Patient & clinician evaluated erection rigidity/ parameters</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Dinsmore (1999) 164</p> <p>Funding source: Senetek plc</p>	<p>IG screened = 236 IG randomized = 171 (parallel)</p> <p>IG1/ CG, n= 107 (ITT) IG2/ CG, n = 29 (ITT)</p> <p>ITT analysis used for primary outcome: Yes (per protocol analysis also reported)</p> <p>Inclusion: en 18 y or older, with ED of 1 y or longer in duration in stable heterosexual relationship</p> <p>Exclusion: overt psychogenic aetiology, ability to perform intercourse without medication or physical aid, hypoactive sexual dx, nocturnal or early morning erections, systemic dx, sickle-cell trait or dx; surgery, hormonal imbalance requiring treatment (except diabetes mellitus), angina pectoris, uncompensated congestive heart failure, hx of drug abuse (other exclusion lists could be found in the article)</p> <p>Note: Dose assessment phase: vasoactive intestinal polypeptide given by auto injector IC</p>	<p>Age, mean (range): 56.5 (25-81) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment (n): IC PgE-1 n=96; papaverine/PM n=64; Other (yohimbine, vacuum devices) n=19</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED (%): 61% (arteriogenic 16%; DM 16%; neurogenic 16%; venous leakage 13%) Other 2%</p> <p>Mixed ED: 37%</p>	<p>IG: vasoactive intestinal polypeptide (VIP) + phentolamine meyslate (PM)</p> <p>IG1/IG2: Dose: 25 µg VIP, + 1mg (G1) or 2 mg (G2) phentolamine (dose of MP was established for each pts in the initial non-randomized dose assessment phase) in .35 mL volume Duration: 6 o Frequency: 10 injections in 6mo Compliance (96.5%) (n/grp): 136/141</p> <p>CG: Dose: 35 mL solution Duration: as IG Frequency: two injections in 6 mo Compliance: as IG</p> <p>Run In period: NR Wash out period: at least 36hrs between injections</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Erection suitable for intercourse (% of injections): IG1 75% vs. CG 12% IG2 66% vs. CG 18% Duration of erection, median in all grps: 56 min (range from 26 min in pts with venous leakage to 92 min in min in neurogenic pts) OS with drug (%) 88% (108/136) Satisfaction with auto-injector (%) 92% (111/136 participants)</p> <p>Other outcomes assessed: response of patients previously treated with one or more alternative therapies</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): n=35 (30 never used injections and were removed)</p> <p>WDAE, n (%): 6 (4) TAE: reported for dose assessment + RCT phase: % of injections with at least one AE 65 vs. 68 vs. 27 (flushing 47 vs. 50 vs. 9; bruising in less than 8% of injections and pain experienced only on injection in 8% in CG alone; priapism in n=1 IG1 equal to 0.1% of 962 injections); AE experienced in 91% vs. 93% vs. 65% of pts SAE: 0</p> <p>Ascertainment of outcomes assessed: Diary entries, F/u questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Earle (1990) ¹⁶⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 205 crossover design (1 & 2)</p> <p>IG1/IG2, n = 205</p> <p>CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED, (also included low testosterone men)</p> <p>Exclusion: NR</p> <p>Data reported for n=129 who completed the 1st injection</p>	<p>Age, mean range: 52-59 y</p> <p>Co-morbidities: Alcohol >420 gm/wk: 20</p> <p>Blood glucose: ▲ glucose in diabetics n=6, & normal glucose n=15</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 18 smokers 55 ex-smokers</p> <p>Body weight: NR</p>	<p>Concomitant medications: 80/129 (33 on hypotensive/ cardio-active medication)</p> <p>Duration of ED: NR</p> <p>Underlying disease: Low testosterone (<11nmol/L) n=11</p> <p>Psychogenic ED: Affective psychosis 1</p> <p>Physiologic ED: n=80 Vascular 51; Lower back injury: 2; Diabetes 26; Bowel tumor resection: 1</p> <p>Mixed ED: NR</p> <p>Other: also other causes of ED, idiopathic n=35</p>	<p>IG1: PgE₁, Compressed base, massaged penis</p> <p>IG2: Papaverine, Compressed base, massaged penis</p> <p>IG1: Dose: 5 µg Duration: 5-10 s Frequency: once every mo for 2 mo Compliance: 83% for 1st injection; 100/129 (78%) for 2nd injection</p> <p>IG2: Dose: 18 mg Duration: as a Frequency: as a Compliance: as IG a</p> <p>Run In period: NR Wash out period: 1 mo</p> <p>F/u duration: 10-20 min post injection</p>	<p>Primary outcome results:Quality of erection, n (%): IG1 vs. IG2 No response: 0 vs. 5 (39) Partial erection: 95 (74) vs. 107 (83) Full erection: 34 (26) vs. 17 (13) (chi-square = 6.26, p<0.025) Attempts to intercourse on intervention, a vs. b Successful intercourse (4 wks): 40 (31%) vs. 43 (33%), chi-square = 0.077, (p > 0.05)</p> <p>Other outcomes assessed: self reported observations</p> <p>Withdrawals/drop-outs/loss to f/u: 76 (37% post initial IC); 29 (22%) dropout following 2nd intervention</p> <p>WDAE: NR TAE: NR [AE Pain during injection: IG1: 11 (8.5%) IG2 6 (4.7%) Prolonged erection: < 8 hrs: 1in IG2 (no event in IG1)]</p> <p>SAE: NR</p> <p>Ascertainment of outcomes assessed: patient report</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>EI-Saleh (1995) ¹⁶⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 16 (cross over)</p> <p>IG1/IG2/IG3, n = 16</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: Use of PGE1 to obtain erection suitable for intercourse</p> <p>Exclusion: NR</p> <p>Result of this study is presented in graphs. The data could not be extracted for this table.</p>	<p>Age, mean (sd): 59 (7.7) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 82.73 (11.29), kg</p>	<p>Concomitant Medications, n: hypotensive drugs: 4 vitamins: 4 10 patients were on undisclosed prescribed medications</p> <p>Duration of ED, mean (range): 6.7 (2-16) y</p> <p>Underlying disease, n: Diabetes: 1 Multiple sclerosis: 1 Thyroidectomy: 1 Hx of musculoskeletal back injuries: 3</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 + digital compression by penile clamp IG2: PgE1 + hand compressin IG3: PgE1 with no compression</p> <p>IG1/IG3: Dose: mean (sd) 17.5 (16.5), range 2.5 to 50 µg (according to the dose used pre-trail) Duration: 3-5 s Frequency: total 3, once/d /tx Compliance: 100%</p> <p>IG2: Dose: NA (pressure = 100 mm Hg) Duration: 3.8-4.5 min Frequency: once Compliance: 100%</p> <p>Run In period: NR Wash out period: NR (min 3 d between any injections at home & clinic injection)</p> <p>F/u duration: NR</p>	<p>Primary outcome results:Erection (at least some degree of tumescence): 100% of pts; only 7/15 (47%) had response comparable to home injection result Presence of erection: no consistent evidence in favour of use of clamping or compression of any sort to obtain better erection Rating of erection in laboratory compared to erections at home: no consistent indication that clamp was more useful than being at home</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: n=1 (excluded from analysis due to withdrawal in IG1)</p> <p>WDAE NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Patient perception, clinical palpation, RigiScan, pulse, BP</p>

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<p>Floth A (1991) ¹⁶⁷</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 87 (two cross over design studies)</p> <p>IG1 n = 49 IG2, n = 38 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: NR</p> <p>Exclusion: NR</p> <p>Data reported for IG1 (a vs. b) vs. IG2 (a vs. b)</p>	<p>Age, mean (sd): 51(13) vs. 53 (12) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: Diabetes in 9 (18.9 %)</p> <p>Psychogenic ED, n (%): 6 (12.3) vs. 4 (10.5)</p> <p>Physiologic ED: Arterial restriction: 32 (65.3) vs. 26 (68.4); venous leak: 8 (16.3) vs. 5 (13.2); neurogenic: 3 (6.1) vs. 3 (7.9); DM: 8 (16.3) vs. 1 (2.5)</p> <p>Mixed ED: Acknowledged but NR</p>	<p>IG1 a: Papaverine + phentolamine b: Papaverine + PgE₁</p> <p>IG2: a: PgE₁ alone b: same as IG1b</p> <p>IG1 a: Dose: papaverine 7.5 mg + phentolamine 0.25 mg Duration: NA Frequency: once</p> <p>IG1 b/IG2 b: Dose: papaverine 7.5 mg + PgE₁ 5 µg Duration: NA Frequency: once</p> <p>IG2 a: Dose: PgE₁ 10 µg + papaverine 7.5 mg Duration: NA Frequency: once</p> <p>Run In period: NR Wash out period: 2 d F/u duration: NR</p>	<p>Primary outcome: a vs. b Time to erection, mean (sd): IG1: 8.6 (4) vs. 8.2 (5) min IG2: 7.3 (3) vs. 8.3 (5) min Duration of erection, mean (sd): IG1: 178.5 (133) vs. 146.6 (131) min IG2: 109.3 (61) vs. 124.3 (111) min Quality of erection (objective), n (%): IG1, between arms p< 0.01 score 1-2: 12 (25) vs. 6 (12) score 3: 9 (18) vs. 5 (10) score 4-5: 28 (57) vs. 38 (78) IG2, between arms, p= 0.03 score 1-2: 3 (8) vs. 2 (5) score 3: 12 (32) vs. 8 (21) score 4-5: 23 (61) vs. 28 (74) (b more effective than a)</p> <p>Other outcomes assessed: Duplex Ultrasound Peak velocity flow (no data)</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0 TAE: NR (AE Prolonged erection: > 5 hrs IG1: 4 vs. 4; IG2: 0 vs. 4 Pain: IG1: 0 vs. 8 (16.3%); IG2: 13 (34.2%) vs. 7 (18.4%) SAE: NR</p> <p>Ascertainment of outcomes assessed: Researcher observed erection scale 1-5:</p>

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<p>Fu (2004) ¹⁶⁸</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 42 cross over</p> <p>IG1/IG2, n=42 CG, n= NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: normal range of serum testosterone, PRL, estradiol, FSH, LH and glucose</p> <p>Exclusion: neurogenic or endocrinopathic ED</p>	<p>Age, mean (range): 43.5 (27-65) yr</p> <p>Race: 100% Chinese</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: sodium nitroprusside IC IG2: papaverine + phentolamine by IC</p> <p>IG1: Dose: sodium nitroprusside 300 micrograms Duration: NA Frequency: once Compliance: NR</p> <p>IG1: Dose: papaverine 30 mg + phentolamine 1mg Duration: NA Frequency: once Compliance: NR</p> <p>Run In period: NR Wash out period: 1 wk</p> <p>F/u duration: NR</p> <p>Other: <i>N of pts reported slightly different in the report</i></p>	<p>Primary outcome results:Erection characteristics: in IG1: Length: ▲ 4.75 (1.45) cm Circumference ▲ 2.59 (1.65) cm Rigidity: all patients scored >10, with 25 >100 Duration of erection (scores >100): 24.23(7.96), range 15-45 min IG2: Length ▲ 4.00 (1.80) cm Circumference ▲ 2.71 (2.05) cm Rigidity: all patients scored >10, with 28 >100 Duration of erection (scores >100): 37.68 (15.36), range 20-55 min</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to follow: NR</p> <p>WDAE: 0 TAE: IG1: 0; IG2: 3 had priapism, 15 had local pain SAE: 0</p> <p>Ascertainment of outcomes assessed: physician assessment of outcomes</p>

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<p>Garceau (1996) ¹⁶⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 54</p> <p>IG/CG, n = 54</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: men with ED, previous PgE1 treatment</p> <p>Exclusion: Hx priapism; Sickle Cell anemia or trait, Untreated endocrine disorders, Cavernal fibrosis; anatomical deformation of penis, Peyronie's disease, thyroid condition causing ED; onset of acute illness, hx of Sexually Transmitted dx ≤ 6 mo, using hormonal or investigational medications, Previous use of IC to tx ED</p> <p>Note: baseline pts data reported for pooled data (n=365) of this RCT (n=54) and a dose titration study of n=294</p>	<p>Age, mean (range): 48.9 (21-75) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 100% PgE₁ users</p> <p>Smoking status: NR</p> <p>Body weight: mean: 71 (range: 45 - 121) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 3.8 y (2 – 35 mo)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 101 (27.7%)</p> <p>Physiologic ED: Vascular: 150 (41.1%) Neurogenic: 10 (2.7%)</p> <p>Mixed ED: 74 (20.3%)</p> <p>Other: 30 (8.2%) other causes</p>	<p>IG1: PgE₁ (in three formulation: aqueous injection, sterile powder, or Prostin VR ^(R))</p> <p>CG: placebo</p> <p>IG: Dose: 2.5, 5, 10 or 20 µg (randomized based on past dose, <10 mg to 2.5 or 5 µg; >10 µg to either Duration: NR Frequency: 3 (one injection of each formulation at assigned dose if randomized to IG) Compliance: NR</p> <p>CG: Dose: NR Duration: NR Frequency: once (?) Compliance all: NR</p> <p>Run In period: 3 wks (no PgE1 injections)</p> <p>Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Optimal erectile response, n/N (%): 2.5 µg: 2/13 (15%) 5 µg: 10/16 (63%) 10 µg: 4/10 (40%) 20 µg: 10/15 (67%) CG: NR</p> <p>Other outcomes assessed: Optimal erectile response, latency of erection, duration of erection, time to complete de-tumescence, also reported for pooled population</p> <p>Withdrawals/drop-outs/loss to f/u: 1 in due to pain post IC injection</p> <p>WDAE: NR TAE: NR AE: NR [Pooled data (n=365): 45 (12%) of pts experience drug related (as reported by authors) events; pain: 53 episodes in 39 (11%) pts] SAE: 0</p> <p>Ascertainment of outcomes assessed: a five-point scale ranging from 0 ("not effective") to 4 ("very effective")</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gherchiu (1996) 170</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 11 (cross over)</p> <p>IG1/IG2, n = 11 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts with previous self injection of PGE1 at home</p> <p>Exclusion: NR</p>	<p>Age, range: 44-72 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: PGE1</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: fast injection of PgE1 at</p> <p>IG2: slow injection of PgE1</p> <p>IG1/2: Dose: NR (same dose as at home use); injected in 5 s in IG1, and in 60 s in IG2 Duration: NA Frequency: single injection Compliance (%): 100%</p> <p>Run In period: NR Wash out period: 7 d</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IG1 vs. IG2, mean (sd):</p> <p>Intensity of pain: 1.5 (1.8) vs. 0.6 (1.5), p = 0.04 Duration of pain: 29 (70.5) vs. 11 (27.5), p = 0.11</p> <p>Note: n=1 experienced pain for 250 min (IG1), and 65 min (IG2); n=10 experienced pain for 25 min or less)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR (AE pain, n (%): n=8: 26(55%) vs. 2 (18%) SAE: NR</p> <p>Ascertainment of outcomes assessed: Intensity of pain by 10 point Likert scale (0 =no pain; 10 =worse pain)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Godschalk (1994) 171</p> <p>Funding source: NR</p>	<p>N screened = 28 N randomized = 15</p> <p>IG/CG, n = 15 (crossover design; 3 phases: phase I double blind; phase II and III nonblind. Non responders from phase I moved to phase II, responders of phase I & II move to phase III)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED of all causes</p> <p>Exclusion: major illness within previous 6 mo; uncontrolled diabetes or hypertension; hypogonadism; laboratory value \geq 25% above or below normal range; previous IC injections for treatment of ED</p> <p>Phase II / III may not be randomized</p>	<p>Age, mean (sd): 55.8 (9.2)</p> <p>Race (%): white 7, black 7, Hispanic 1</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: mean number of pts (sd) 2.7 (1.3)</p> <p>Duration of ED (yr): 7.61 (SD 9.85)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 15</p> <p>Mixed ED: 0</p>	<p>IG1: PgE₁ CG: placebo</p> <p>IG/CG Dose: Phase I: 0 (placebo) 2.5, 5, 7.5 and 10 μg Phase II: 12.5 (15-50) μg Phase III: maintenance dose Duration: 8 wks [4 wks (I & II); 4 wks (III)] Frequency: 2/wk; total Phase I=II: 10 doses</p> <p>Run In period: NR</p> <p>Wash out period: 0.5 wk</p> <p>F/u duration: 120 min post dosing</p>	<p>Primary outcome results:All means approximate Penile rigidity (%), from scale of 0-100%, phase I: IG, 2.5 μg 30%; 5 μg 47%, 7.5 μg 38%; 10 μg 43%(Overall in 5-10 μg dose: 40%) vs. CG: 7%</p> <p>Full erection (60% rigidity) or experienced intolerance in phase I, n: 6/15 (moved to phase III) Phase II, (n=8): Adequate erection, n: 4/8 (entered phase III) Phase III, (n=10): Partial or full erection, in 85%</p> <p>Other outcomes assessed: Rigidity (absent, partial or full) as assessed by palpation</p> <p>Withdrawals/drop-outs/loss to f/u: n=1 in phase II</p> <p>WDAE: 0 TAE: NR SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Godschalk (1996) 172</p> <p>Funding source: NR</p>	<p>N screened = 13 N randomized = 10 (cross over)</p> <p>IG1/IG2, n = 10 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: 18-75 yr with ED who had experienced penile pain after at least 70% of IC PgE1 self injections at home</p> <p>Exclusion: recent major illness, uncontrolled hypertension, or diabetes, a hx of priapism, Peyronie's plaques or laboratory abnormalities greater than 25% above or below accepted normal ranges, use of analgesics</p>	<p>Age, range: 18-75 yr</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: Pg E1</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 + sodium bicarbonate (alkaline) IG2: PgE1 alone (acidic)</p> <p>IG1: Dose:PgE1 20 µg+ 42 mg/ml sodium bicarbonate, to reach PH of > 7 Duration: 2 d Frequency: single dose Compliance: 100%</p> <p>IG2: Dose: PgE1 20 µg Duration: as IG1 Frequency: single dose Compliance: 100%</p> <p>Run In period: NR Wash out period: at least 1 d</p> <p>F/u duration: NR</p>	<p>Primary outcome results: IG1 vs. IG2, mean (sd): Degree of pain: 3.4 (2.9) vs. 2.7 (1.9), (p = 0.27) Duration of penile pain: 50.9 (45.3) vs. 56.9 (59.5) min, NS (p=0.37) Frequency of pain: ▼ in IG1 (not sign.)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: n=0</p> <p>WDAE n=0 TAE: NR [AE, n (%): pain, IG1 vs. IG2, 70% vs. 80%; n=6 experienced pain with both injections] SAE: NR</p> <p>Ascertainment of outcomes assessed: Pain and its duration by pts filled questionnaire Severity of pain by 10 point Likert scale (0=no pain to 10=- worst pain)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gontero (2003) ¹⁷³</p> <p>Funding source: NR</p>	<p>N screened = 95 N randomized = 79 (parallel)</p> <p>IG1, n = 36 IG2, n = 37 CG, n = NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: Non-nerve sparing radical prostatectomy, diagnosis of localized prostate cancer, completion of IIEF</p> <p>Exclusion: NR</p>	<p>Age, mean: 65 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%) Adjuvant hormones; IG13 (8) vs. IG2 4 (11) Radiotherapy; IG1= IG2 4 (11)</p> <p>Duration of ED: NR</p> <p>Underlying disease: 100% Prostate cancer (palpable tumor)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 (early intervention) IG2: PgE1 (delayed intervention)</p> <p>IG1: Dose: 20 mg Duration: NA Frequency: once, 1-3 mo post operative Compliance: 100%</p> <p>IG2: Dose: 20 mg PgE1 Duration:NA Frequency: once, 4-12 mo post operative Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results:IG1 vs. IG2 Grade 3-4 erection post operatively, (%): IG1 80% vs. IG2 37% Mean visual analog scale (rating of discomfort with 0 = no pain and 10 maximal pain): 3.58 vs. 2.58</p> <p>Other outcomes assessed: Pathological stage, Gleason score, concomitant adjuvant treatment; Peak systolic velocity < 30 cm/s (n/grp): 8/36 (22.2%) vs. 19/37 (51.3%)</p> <p>Withdrawals/drop-outs/loss to f/u: n=6 (2 excluded for high scores on IIEF, 4 refused to undergo Doppler ultrasound)</p> <p>WDAE: 0 TAE: NR [AE prolonged erection, in n=3 (IG1)] SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, Dynamic colour Doppler ultrasound, Grading of erection (0-4: 3=suboptimal rigidity, sufficient for penetration; 4= full rigidity for at least 20 min), Visual Analog Scale Score</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kattan (1991) ¹⁷⁴</p> <p>Funding source: NR</p>	<p>N screened = 54 N randomized = 50 Crossover design</p> <p>IG1/IG2, n = 50 split in two grps (1 & 2) of 25 to receive 1st intervention and then switched to the 2nd intervention CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with vasculogenic impotence who failed Papaverine</p> <p>Exclusion: NR</p>	<p>Age, mean (sd): 57.08 (7.41) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE₁ IG2: Papaverine</p> <p>IG1: Dose: 20 µg in 2 ml volume Duration: NA Frequency: Single Compliance: 100%</p> <p>IG2: Dose: 60 mg in 2 ml volume Duration: NA Frequency: single Compliance: 100 %</p> <p>Run In period: NR Wash out period: 1 wk= half life of drug</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Researcher observed quality of erection, IG1 vs. IG2 Positive response: 34% vs. 2% (12% responded to both treatments) Satisfactory erection, (%): 46% vs. 14%</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 4 drop outs post first IC</p> <p>WDAE: 0 TAE: NR (Aepainat IC site < 10 min, (% of pts): 47% vs. 6%; Dizziness + headache: 2% vs. 4%) SAE: NR</p> <p>Ascertainment of outcomes assessed: Researcher observed quality of erection Partial or complete response vs. no response</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kattan (1995) ¹⁷⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 25 (crossover design)</p> <p>IG1/IG2, n = 25 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: NR</p> <p>Exclusion: Hx of MI; uncontrolled BP</p>	<p>Age, mean (sd): 53, range 40-60</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n: diabetes 17, heavy smoking (> 1 pack/day) 9, on antihypertensives 2, low serum testosterone levels 3, Peyronie's disease 1</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: PgE₁ IC IG2: PgE₁ plus lidocaine hydrochloride IC</p> <p>IG1: Dose: 20 µg (+ manual sexual stimulation for 10 min after injection) Duration: NR Frequency: 1 dose Compliance: NR</p> <p>IG2: Dose: 20 µg PgE₁ + 1 cc lidocaine 1% (+ manual sexual stimulation for 10 min after injection) Duration: NR Frequency: 1 dose Compliance: NR</p> <p>Run In period: NR Wash out period: 1 wk</p> <p>F/u duration: NR</p>	<p>Primary outcome results:Erection assessed by investigator on 4-point scale from 0 (none) to 3 (normal), (n) Grade 0: 2 vs. 2 Grade 1: 14 vs. 6 Grade 2 (adequate): 6 vs. 11 Grade 3: 0 vs. 3 Adequate erection, (% of pts): 27% vs. 64%</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: n=3 (2 due to AE)</p> <p>WDAE: 3 TAE: NR, (AE: pain in 22 (86% vs. 10 (45%); local edema at site of injection 1(5%) vs. 0) SAE: NR</p> <p>Ascertainment of outcomes assessed: NA</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kunelius (1998) ¹⁷⁶</p> <p>Funding source: NR</p>	<p>N screened = 30 N randomized = 30 (cross over)</p> <p>IG1-3/CG, n = 30</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: NR</p> <p>Exclusion: NR</p>	<p>Age, mean: 55 (21-71) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant Medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Physiologic ED: NR</p> <p>Psychogenic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: papaverine IG2: PgE1 IG 3: moxisylyte CG: placebo</p> <p>IG1: Dose: 40 mg (1 mL) Duration: NA Frequency: once /visit Compliance: 100%</p> <p>IG2: Dose: 20 µg Duration: NA Frequency: once /visit Compliance: 100%</p> <p>IG3: Dose: 20 mg Duration: NA Frequency: once /visit Compliance: 100%</p> <p>CG: Dose: 1 mL saline Duration: NA Frequency: once /visit Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 15 min post injection</p>	<p>Primary outcome results:IG1 vs. IG2 vs. IG3 vs. CG Tumescence: no difference between the agents Rigidity (maximal at tip (%▲): 120.7 vs. 33.9 vs. 14.2 vs. 0</p> <p>Rigidity (maximal at base (%▲): 16.8 vs. 34 vs. 14.2 vs. 0</p> <p>Clinician rating of erection, patients with grade 4/5, (%): 10 vs. 40 vs. 7 vs. NR</p> <p>Mean Duration of Erection (min) 13.4 vs. 40.2 vs. 6.5 vs. 0</p> <p>Other outcomes assessed: BP, pulse rate, patient satisfaction with erections</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WAED: 0 TAE: NR (AE: prolonged erection of > 2 hrs: 6 (20%); IG1 n=2, IG2 n=3; IG3 n=1 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan device; pts filled questionnaire; degree of erection 0-5 (4 & 5 sufficient for penetration)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Linnet (1996) ¹⁷⁷</p> <p>Funding source: Upjohn Company</p>	<p>N screened = NR N randomized = 296 (parallel design)</p> <p>IG1 n=57 IG2, n = 60 IG3, n= 62 IG4, n = 58 CG n = 59</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: ED ≥ 4 mo</p> <p>Exclusion: penile deformity (including fibrosis); hx of priapism; sickle-cell trait; recent major illness; uncontrolled DM or hypertension; major psychiatric disorder; human immunodeficiency virus infection or other transmittable disease; heavy smoking (> 40 cigarettes/day); endocrine causes of ED</p>	<p>Age, mean (range): 54, (21-74) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: IC treatment 7 (2%)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 39 (13%)</p> <p>Physiologic ED: Vasculogenic 130 (44%) Neurogenic 39 (13%)</p> <p>Mixed ED: 86 (29%)</p>	<p>IG1-4: PgE1 (alprostadil) CG: placebo</p> <p>IG1-4: Dose: 2.5 (IG1), 5 (IG2), 10 (IG3) or 20 (IG4) µg Duration: NA Frequency: 1 dose Compliance: 100%</p> <p>CG: Dose: placebo Duration: NA Frequency: 1 dose Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: % of pts with Radial rigidity clinician assessment) (RigiScan data: / ≥ 70% rigidity at tip or base of penis lasting ≥ 10 min) IG: 2.5 µg approx. 17% (21%) 5 µg approx. 27% (31%) 10 µg approx. 45% (27%) 20 µg approx. 50% (48%) CG: 0 (0) Note: above numbers extracted from bar graph Duration of erection (mean) 2.5 µg, 12 min; 20 µg, 44 min, p<0.025</p> <p>Other outcomes assessed: % of patients with satisfactory sexual activity (masturbation, and intercourse);</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE 0 TAE: NR (AE: IG only: Penile pain 54 (23%); priapism 6 () SAE: n=1 death (reported to be unrelated to study drug)</p> <p>Ascertainment of outcomes assessed: RigiScan™ Ambulatory Rigidity and Tumescence System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mahmoud (1992) 178</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 52 Cross over design (intervention a & b)</p> <p>IG1/IG2, n = 52 CG, n = NR</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts who consulted clinic for erectile failure</p> <p>Exclusion: NR</p> <p>Notes 1-on eligibility: to compare drug safety 8 patients with hx of priapism with Papaverine IC were included in PgE1 arm & excluded from Papaverine arm 2-This trial includes n=2 with SCI 3- pts were categorized by subgroups according to probable cause of ED dx at baseline</p>	<p>Age, mean (sd): mean 48.6 (10.4) y</p> <p>Race: 100% Egyptian</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: Papaverine hydrochloride in 8</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NA</p> <p>Duration of ED, mean (sd): 2.98 (1.19) y, range 0.7 - 6 y</p> <p>Underlying disease: (> 5 yr): Hypertension 8; Diabetes 7 ; diabetes + hypertension 3 ; Transverse Myelitis:2 SCI: 2 Radical cystectomy:1 Hyperprolactemia:5</p> <p>Psychogenic ED: 10 (19%) Physiologic ED: Vasculogenic 24 (46%) Neurogenic ED 5 (10%) Endocrinological 5 (10%) Mixed ED: NR; Undetermined cause 8 (15%)</p>	<p>IG1: PgE₁ IC with hand pressure around base and massage of shaft. IG2: Papaverine hydrochloride IC as above</p> <p>IG1: Dose: 20 µg/ml Duration: NA Frequency: Single</p> <p>IG2: Dose: 30 or 60 (if failed with low dose) mg/ml Duration: NA Frequency: Single</p> <p>Compliance all grps 100%</p> <p>Run In period: NR Wash out period: 3 d interval between injections</p> <p>F/u duration: 24-48 hrs post IC unless priapism then seen at 3hrs</p>	<p>Primary outcome results:IG1 vs. IG2, n (%) Positive response in: 42 (81%) vs. 33 (63%) Negative response: 10 (19%) vs. 19 (37%) Results also reported for subgroup based on dx (i.e. underlying dx) Erection duration, mean (sd): 2.5 (0.4) hrs vs. 2.52 (0.72) hrs Time to full erection, mean (sd): 15.4 (5.4) vs. 10 (3.7) min</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: NR (AE: Penile pain: Tolerable: 6 (11.5%) vs. 13 (25%) Intolerable: 0 vs. 4 (7.7%) SAE: Priapism: 0</p> <p>Ascertainment of outcomes assessed: Clinician measures of erection duration/angle; also rating of erections (positive/good ≥ 2hrs at nearly 90 degrees; negative/poor: < 2hrs at ≤ 90 degrees; negative/absent: no tumescence; Priapism:> 3 hrs)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mancini (2004) ¹⁷⁹</p> <p>Study a, and b</p> <p>Funding source: NR</p>	<p>N screened = 97 N randomized = 56 (36 vasculogenic (a) & 20 non-vasculogenic (b) pts randomized independently into 3 & 2 grps respectively)</p> <p>a: Vasculogenic IG1a n= 12 IG2a: n = 12 CG, n= 12</p> <p>b: Non-vasculogenic IG1b , n= 10 IG2b , n= 10</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts with atherosclerosis, and ED verified with IIEF Questionnaire; duration of ED no more than 3 mo in duration</p> <p>Exclusion: Organic cause of ED apart from vasculopathy</p>	<p>Age, mean range: 54.6-59.6 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: < 3 mo</p> <p>Underlying disease: IG1a & IG2a & CG: vasculogenic IG1b, IG2b: not vasculogenic</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 56</p> <p>Mixed ED: NR</p>	<p>IG1: PgE1 (alprostadil) IG2: oral Sildenafil; CG Placebo: (oral)</p> <p>IG1(a & b): Dose: 5-20 ug (dose assessment based on 1-3 injection to verify the dose inducing a full erection lasting 10 min) Duration: 1 mo Frequency: 1 /wk Compliance: 100%</p> <p>IG2 (a & b): Dose: 25 mg Duration: 1 mo Frequency: every night Compliance: 100%</p> <p>CG: Dose: placebo Duration: 1 mo Frequency: every night Compliance: 100%</p> <p>Run In period: 1 wk (dose assessment phase IG1 a & b) Wash out period: 1 wk</p> <p>F/u duration: 7d post last tx</p>	<p>Primary outcome results:Peak Systolic Velocity, mean (sd): IG1a: non sign. from baseline IG1b: pre 21(4) post 26(7).</p> <p>IG2a & b: non sign. from baseline CG: pre 20(5) post 28(9)</p> <p>Erectile rigidity (IIEF), mean (sd), pre vs. post treatment: IG1a: 15 (5) vs. 22 (3) IG1b: 13 (7) vs. 21 (9)</p> <p>IG2a: 13 (4) vs. 18 (3) IG2b: 11 (8) vs. 12 (11) CG: 15 (5) vs. 20 (6)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: n=1 in IG1a, excluded in dose assessment phase (no response to PgE1 injection)</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Duplex Sonography examination, IIEF-15 questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Martinez-Piñero (1995) ¹⁸⁰</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 105 (crossover design, intervention 1 and 2)</p> <p>IG1, n = 10 IG2, n = 60 IG3, n = 35 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED Exclusion: NR</p>	<p>Age, mean, (range): 53.6 (27-79) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1-3: PgE₁ IC [as first intervention (n=58); as second intervention, (n=57)] + one of 3 concentrations of sodium nitroprusside (SN)</p> <p>IG1: Dose: 20 µg cross over to 100 µg SN diluted in 5% dextrose Duration: NA Frequency: 1 dose of each Compliance: 100%</p> <p>IG2: Dose: 20 µg cross over to 300 µg SN diluted in 5% dextrose Duration: NA Frequency: as IG1 Compliance: 100%</p> <p>IG3: Dose: 20 µg cross over to 400 µg SN Duration: NA Frequency: as IG1 Compliance, all: 100%</p> <p>Run In period: NR Wash out period: 1-7 d</p> <p>F/u duration: NR</p>	<p>Primary outcome results:sodium nitroprusside 100 µg was not effective in producing erections Erectile response, % of pts, [no erection/ partial rigidity/ full rigidity]: IG2 (PgE1 vs. 300 µg): [25/ 55/ 20] vs. [33/ 52/ 15] IG3 (PgE1 vs. 400 µg): [29/ 51/ 20] vs. [40 / 46/ 14] Duration of erection: (PgE1 vs. 300 µg vs. 400 µg), mean (range): 88.5 (5-220) vs. 51(5-129) vs. 42 (5-129) min</p> <p>Other outcomes assessed: Time required to initiate tumescence; patient satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u: n=0 WDAE: 0 TAE: NR AE, n (%): IG1 vs. IG2 vs. IG3PgE1 vs. SN 100 µg vs. SN 300 µg vs. SN 400 µg: Pain during injection: 7 (7) vs. 0 vs. 0 vs. 0; Dizziness: 4 (4) vs. 1 (10) vs. 5 (8) vs. 1 (3); haematoma: 1 (0.9) vs. 0 vs. 1 (2) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: clinical & pts assessment</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Montorsi (1997) ¹⁸¹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 30</p> <p>IG, n = 15 CG, n = 15</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with clinically localized prostate cancer stage B1 or B2, Gleason sum 7 or greater, prostatic specific antigen cell less than 20 ng</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 62 (49-68) yr</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NA</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: clinical stage: B1 n=18, B2 n=12; Mean Gleason sum at biopsy = 4.2 (3-6); mean preoperative PSA = 9.2 (2.1-18.2) ng/ml</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NA</p> <p>Underlying disease: Prostate cancer</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: CG: no post-operative ED n=2 (13%)</p>	<p>IG: PgE1 (alprostadil), self injection CG: No treatment</p> <p>IG: Dose: 2.5-14 µg (mean dose used 8 µg) Duration: 12 wks Frequency: 3 times/wk, total 36 injections Compliance: 80%</p> <p>CG: Dose: NA Duration: as IG Frequency: NA Compliance: all</p> <p>Run In period: 1 mo Wash out period: NA</p> <p>F/u duration: 12 wks</p>	<p>Primary outcome results: IG1 vs. CG Recovery of spontaneous injections at 3 mo, n (%): Full: 8 (67) respond (needed injections once/4 time) vs. 3 (20) (p<0.01); Partial respond: 3 (33) (needed to inject more than 50% of times) vs. 10 failures (67) Color Doppler test (normal hemodynamics in n=10 (83%) (all responders, 2 partial responders) vs. n=2 (all responders); cavernous veno-occlusive dysfunction n=2 (all partial responders) vs. n=8 (failures) CG: cavernous artery insufficiency n=2 (17%)</p> <p>Other outcomes assessed: Nocturnal erections (during a 3-night period); hemodynamic results</p> <p>Withdrawals/drop-outs/loss to f/u, n: 3 vs. 0</p> <p>WDAE: IG: n=3 (20%), reduced sexual interest (n=2), penile nodule (n=1) TAE: IG1: n=3 with at least one AE: one event of cavernous haematoma in n=2 (13%); one event of prolonged erection in n=1 (6%); CG: no AE SAE: NR</p> <p>Ascertainment of outcomes assessed: Sexual hx, physical examination; hemodynamics post µg alprostadil + genital & audiovisual sexual stimulation; RigiScan</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Montorsi (1998) ¹⁸²</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 20 (crossover design to interventions a & b)</p> <p>IG n= 20 CG n= NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts who failed to produce an erection with 1 dose of PgE1 at initial session post randomization</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 54 (42-66) y</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 10 (50%)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 0.9, (0.6-3.2) y</p> <p>Underlying disease, n (%): diabetes 5 (25%), hypertension 4 (20%), coronary artery occlusive disease 4 (20%), hyperlipidemia 4 (20%)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>Intervention: a) PgE1 (alprostadil) b) PgE1& genital + audiovisual sexual stimulation</p> <p>IG a: Dose: 10 µg Duration: NA Frequency: 2 doses 10 min apart Compliance: 100%</p> <p>IG b: Dose: 10 µg Duration: NA Frequency: 1 dose followed by stimulation 10 min later Compliance: 100%</p> <p>Run In period: NR Wash out period: 1 wk between sessions</p> <p>F/u duration: NA</p>	<p>Primary outcome results:5-min period of max response (penile rigidity & tumescence–circumferential expansion), expressed as area under the curve, mean (sd) IGa vs. IGb Tumescence base 60 (3) vs. 70 (2) Tumescence tip 28.0 (2) vs. 35 (1) Rigidity base 53 (2) vs. 66 (2) Rigidity tip 33 (2) vs. 40 (1)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 5</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Moriel (1993) ¹⁸³</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 38 (cross over)</p> <p>IG1/IG2, n = 19 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED Exclusion: NR</p>	<p>Age, mean (range): 55 (23-77) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: NA</p>	<p>IG1: Trimix + sodium bicarbonate IG2: Trimix CG: NA</p> <p>IG1: Dose: 6 mg papaverine, 100 µg phentolamine + 10 µg PgE₁ (trimix), 7.5% sodium bicarbonate (0.03 mEq) Duration: NA Frequency: 1 dose Compliance: 100%</p> <p>IG2: Dose: trimix as IG1 Duration: NA Frequency: 1 dose Compliance: 100%</p> <p>Run In period: NR</p> <p>Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results:Erectile response, n (%) with positive response: IG1 15 (79%) vs. IG2 13 (68%)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: Patients' experience of discomfort or pain: IG1: 1 (5%); IG2: 11 (58%) SAE: 0</p> <p>Ascertainment of outcomes assessed: NR</p> <p>Other: Authors don't state how erectile response was evaluated.</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Ogrinc (1995) ¹⁸⁴</p> <p>Study a</p> <p>Funding source: Upjohn Company</p>	<p>N screened = NR N randomized = 153 (4-way cross over)</p> <p>IG, n= 153 (4 various doses) CG, n =NR</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED ≥ 4 mo</p> <p>Exclusion: anatomical deformation of penis; penile fibrosis; hx of priapism; recent onset of major disease; uncontrolled diabetes or hypertension; major psychiatric disorder; excessive cigarette use; use of other investigational agents. Previous use of IC vasoactive agents permitted.</p>	<p>Age, range: 23-69 y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: PgE1 (alprostadil) in four doses CG: placebo</p> <p>IG: Dose: 2.5, 5, 7.5 & 10 µg Duration: NR Frequency: single injection / dose in a randomized order Compliance: 100%</p> <p>CG: Dose: placebo IC Duration: NR Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results:Erection response (full, partial or none), IG vs. CG: NR Positive response (% of total injections): by clinical/ evaluation: 17% By RigiScan 15%</p> <p>Other outcomes assessed: Agreement vs. disagreement between clinical & RigiScan monitoring: --Using 70% axial rigidity as criteria: agreement: 418/521 injections (80%)/ Disagreements: 17% present by clinical evaluation only; 3% erection present by RigiScan only --Using 60% axial rigidity as criteria: 422/521 injections (80%)/ 11% Sensitivity, RigiScan = 47.6% (80/168 with clinical response) Specificity, RigiScan: 95.8% (338/353 injections)</p> <p>Withdrawals/drop-outs/loss to f/u: n=25</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan™ & clinical (palpation) evaluation</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Ogrinc (1995) ¹⁸⁴</p> <p>Study b</p> <p>Funding source: Upjohn Company</p>	<p>N screened = NR N randomized = 296 (parallel design)</p> <p>IG, n = 237 CG, n = 59</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED ≥ 4 mo</p> <p>Exclusion: anatomical deformation of penis; penile fibrosis; hx of priapism; recent onset of major disease; uncontrolled diabetes or hypertension; major psychiatric disorder; excessive cigarette use; use of other investigational agents. Previous use of IC vasoactive agents permitted.</p>	<p>Age, range: 21-74 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: IC PgE1 (alprostadil) in four various doses CG: IC placebo</p> <p>IG: Dose: 2.5, 5, 7.5 or 10 µg Duration: NR Frequency: single injection Compliance: NR</p> <p>CG: Dose: placebo Duration: NR Frequency: 1 dose Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 2 hr</p>	<p>Primary outcome results: Erection response (full, partial or none), 59 non response in CG (excluded from study) Positive response (% of total injections): by clinical/ evaluation: 11% By RigiScan: 23%</p> <p>Other outcomes assessed: Agreement vs. disagreement between clinical & RigiScan monitoring: --using 70% axial rigidity as criteria: agreement: 184/231injections (49.6%) disagreements: .11.3% erection present for clinical evaluation only; 9% erection noted by RigiScan criteria only --using 60% axial rigidity as criteria: agreement: 182/231 injections (79%) disagreements: 5.6% erection noted by clinical not RigiScan; 16% erection noted by RigiScan only Sensitivity, RigiScan = 67% (53/79 with clinical response) Specificity, RigiScan: 82% (131/152 injections)</p> <p>Withdrawals/drop-outs/loss to f/u: 6 (all IG)</p> <p>WDAE NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System, & clinical (palpation) evaluation</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Porst (1993) ¹⁸⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 40 crossover design, a & b</p> <p>IG1, n= 40 IG2, n= non-randomized grp, nonresponders of IGa+ IGb: 5</p> <p>ITT analysis used for primary outcome? No</p> <p>Inclusion: men with ED, age 23-78 y (eligibility criteria not described in detail)</p> <p>Exclusion: NR</p> <p>This study a diagnostic evaluation of corpus cavernosus function</p>	<p>Age, mean (range): 55.9 (23-78)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): Diabetes 6 (15) Coronary heart disease 5 (12.5); hypertension: 9 (22.5); occlusive artery disease of lower limbs: 3 (7.5); cerebral infarction: 2 (5); post transurethral prostatectomy: 5 (12.5); radical prostatectomy: 2 (5) Rectum amputation: 1 (2.5)</p> <p>Psychogenic ED: 60%</p> <p>Physiologic ED: 40%</p> <p>Mixed ED: NR</p>	<p>IG1: PgE₁ IG2: nitric oxide donor linsidomine</p> <p>IG1: Dose: 20 µg Duration: NA Frequency: once Compliance (%): 100</p> <p>IG2: Dose: 1 mg Duration: NA Frequency: once Compliance (%): 100</p> <p>Run In period: NR Wash out period: ≥ 48 hrs between dose</p> <p>F/u duration: NR</p>	<p>Primary outcome: ▲ peak flow: averaged 1/3 less in IG1 vs. IG2 <u>With < 30 cm/sec, in right / left arteries:</u> <u>Pathological values (%):</u> IG1= 17.9% / 17.9 % IG2 a= 64.1% / 56.4% IG2 b: no erection observed in 5 (100%)</p> <p><u>Patient reported effectiveness of intervention, n (%)</u> IG2 > effective IG1: 0 (0%) IG1= IG2: 4 (10%) IG1 slightly superior IG2: 6 (15%) IG1 Moderately superior IG2: 8 (20%) IG1 much superior IG2: 22 (55%)</p> <p><u>Researcher rated erection:</u> IG1 vs. IG2: No erection: 0 vs. 3 (7%) Tumescence: 7 (17.5%) vs. 23 (57.5%) Semirigid: 7 (17.5%) vs. 9 (22.5%) Full: 26 (65%) vs. 5 (12.5%)</p> <p>Other outcomes assessed: peak systolic velocity</p> <p>Withdrawals/drop-outs/loss to f/u: 1 (2.5%) not included in analysis WDAE: NR TAE: Unpleasant tenseness or pain in penis: 17.5% Vs. NR Moderate/severe headache: NR vs. 7.5% SAE: NR</p> <p>Ascertainment of outcomes assessed: clinician and pts reported erection outcomes</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Roy (1990) ¹⁸⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 24 (3 x 3 factorial design, crossover study with assigned order of tx)</p> <p>IG1 & 2, n = 24 CG, n = 24 (same grp as IG)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Non vasculogenic ED; Seeking treatment in urology clinic (nocturnal penile test was)</p> <p>Exclusion: Penile BP index < 0.85</p> <p>Outcomes reported for IG 1 vs. IG2 vs. CG</p>	<p>Age, range: 50-70 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 4 previously papaverine 30 to 60 mg</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: Some psychogenic (no data)</p> <p>Physiologic ED: Diabetes (no data) Neurogenic (no data)</p> <p>Mixed ED: NR</p>	<p>IG1: Vasoactive Intestinal peptide (VIP) IC, low dose + compressed penile base (CPB) for 1 min IG2: VIP, high dose + CPB CG: Placebo +CPB</p> <p>IG1: Dose: 200 pmol in 1 ml volume Duration: 1 wk Frequency: once/ wk</p> <p>IG2: Dose: 400 pmol in 1 ml volume Duration: 1 wk Frequency: once/ wk</p> <p>CG: Dose: 1 ml saline Duration: 1 wk Frequency: once/ wk Compliance all grps: 100%</p> <p>Run In period: NR Wash out period: 1 wk</p> <p>F/u duration: 3 wks</p>	<p>Primary outcome results:Penile length increase by tx, mean %: 14.5 vs. 20.8 vs. 11(CG < IG1< IG2, p= 0.01) Diameter increase, mean %: 8.5 v. 13.7 vs. 3.9 (CG < IG1< IG2 p= 0.001) Penile rigidity score, mean: 1.3 vs. 1.4 vs. 1.3 (CG vs. IG1vs. IG2 p=0.056) Above parameters also reported by time (i.e. wk1, wk2, wk3) Repeat exposure to CG, IG1, IG2 ▼ diameter over time p=0.001 Repeat exposure to CG, IG1, IG2 ▼ rigidity over time p=0.008 Rigidity obtained: 0 vs. 0</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Observer measurements; Rigidity: 15 min post treatment with scale 1-1 (no rigidity to full rigidity):</p>

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<p>Sandhu (1999) ¹⁸⁷ Companion: ¹⁶⁴</p> <p>Funding source: Senetek plc</p>	<p>N screened = 304 (dose assessment phase) * N randomized = 240 [cross over, intervention (a and b); and placebo]</p> <p>IG, n= 240 (133 phase II, maintenance phase)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: pts with ED \geq 1 y in duration, \geq 18y, currently in stable heterosexual relationship</p> <p>Exclusion: overt psychogenic aetiology, ability, any known systemic disease which produces overall weakness (other exclusion criteria is listed in the report)</p> <p>*Note: non responders to the non randomized dose assessment phase (details not reported in this table) entered into phase I, the result of which reported in this table</p>	<p>Age, mean (range): 58.5 (27-79) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: IC Alprostadil: 106 IC Papaverine/ phentolamine: 45 Other (Yohimbine, vacuum devices): 32</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: atherogenic (n=58), DM (n=53), neurogenic (n=3), mixed</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 135</p> <p>Mixed ED: 152</p>	<p>IG: vasoactive intestinal polypeptide (VIP) + Phentolamine CG: placebo</p> <p>IG a & b: Dose: 25 μg VIP + a=1 mg, or b=2 mg (35 ml volume) Duration: 6 mo Frequency: max 3 times/ wk Compliance: 88.2%; 68.2% (133/195) completed phase I; 94.7% (105/126)</p> <p>CG: Dose: placebo (35ml volume) Duration: as IG Frequency: as IG Compliance: as IG</p> <p>Run In period: NR Wash out period: 36 hrs between injections</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Duration of erection, median, IGa vs. IGb vs. CG: Phase I (n=132): 50 vs. 30 vs. 15 min Phase II (n=126): 60 vs. 40 vs. 27.5 min Grade III erection, IG (a or b) vs. CG (a or b) (%): Phase I, a=72.2 vs. 13.1; b= 65.3 vs. 15.9; overall IG vs. CG=73.7 vs. 12.9 Phase II, a=75 vs. 12.6; b= 75 vs. 10.6; overall IG vs. CG= 69.1 vs. 13.7</p> <p>Other outcomes assessed: OS: Satisfied or very satisfied: 80% of pts; quality of life improvement: 81% of pts and 76% or partners</p> <p>Withdrawals/drop-outs/loss to f/u: 107 (44.5%); n=45 (18.8%) no injection, n=62 post 1st injection (AE, non compliance, other)</p> <p>WDAE: n=2 (death & priapism) TAE (n): a vs. b vs. placebo: % of injections with one or more AE: 47.5 vs. 45.4 vs. 68; bruising+ bleeding, 8 vs. 6 vs. 7; priapism (n=1) 0.05 vs. 0 vs. 0 <u>Overall incidence of urethral bleeding 0.9% for both phases</u> SAE: death n=1 (also n=1 MI)</p> <p>Ascertainment of outcomes assessed: Home filled diaries, f/u questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Schramek (1994) 188</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 24 (2 crossover design studies)</p> <p>Study I IG1, n= 7 (cross over a and b)</p> <p>Study II IG2, n= 17 (interventions a & b in random order)</p> <p>CG randomized = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED with hx of PgE₁-induced penile pain</p> <p>Exclusion: NR</p> <p>Results reported for all pts (n=24) or by interventions (IG1 + IG2 (a), vs. IG1 + IG2 (b))</p>	<p>Age, median (range): 48, (28-62) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: PgE₁ in all cases</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 3</p> <p>Physiologic ED: 21 (arteriogenic, neurogenic, caverno-venogenic)</p> <p>Mixed ED: 0</p>	<p>IG1 & 2: a PgE₁ b PgE₁ + procaine IC</p> <p>IG1/IG2 (a) Dose: 20 µg Duration: NR Frequency: 1 dose</p> <p>IG1/IG2 (b): Dose: 20 µg PgE₁ + 10 mg (IG1b), or 20 mg (IG2b) procaine Duration: NR Frequency all grps: 1 dose of each a and b Compliance all grps: 100%</p> <p>Run In period: NR</p> <p>Wash out period: ≥ 2 days</p> <p>F/u duration: 2 in 2 d intervals</p> <p>Other: Authors combined results from 2 studies</p>	<p>Primary outcome results: Full erection (grade 5), proportion of pts: IGa: 16/24 vs. IG1b 5/7 vs. IG2b 11/17 ▼ by 1 grade in n=7 (all improved to grade 5 after cross over tx): IG1: 2/7; IG2: 5/17 ▲ in grade: IG1 0/7 vs. IG1/17 Duration of erection IGa vs. IG1b vs. IG2b, median (range): 142 (20-360) vs. 122 (20-180) vs. 111 (15-360) min</p> <p>Time from injection to erection: NR</p> <p>Other outcomes assessed: BP, pulse rate, penile sensitivity</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE 0 TAE, n (%) of pts/grp: 37; IG1a vs. IG1b vs. IG2b: no pain 4 vs. 2 vs. 7; moderate pain 9 vs. 5 vs. 6; severe 2 vs. 0 vs. 4 Priapism: 2 events in n=1 after a and b SAE: 0</p> <p>Ascertainment of outcomes assessed: Clinical evaluation of degree of erection on 5-point scale (1= no erection & 5 = full erection)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Seyam (2005) ¹⁸⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 180 (crossover)</p> <p>IG1-9 n= 20 (in each grp) CG, n= 180</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: ED \geq 6 mo in duration</p> <p>Exclusion: Hx of priapism, sickle cell anemia, previous surgical intervention for ED</p>	<p>Age, mean (sd): 50.5 (11.7) yrs</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: IIEF-5 for 158 pts (Mean degree of ED = 7.6, sd = 5.8) Complete ED in 36; weak erection in 137; difficulty to maintain erection 6; recreational drug users = 12 (6.7%)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean: 40.2 mo</p> <p>Underlying disease, n (%): Organic disease 137 (76.5) 20 (11.2) arterial disease 6 (3.4) pure venous leakage</p> <p>Psychogenic ED, n (%): 16 (8.9)</p> <p>Physiologic ED, n (%): 163</p> <p>Mixed ED: 67 (37.4)</p> <p>Other: NR</p>	<p>IG: PgE1, papaverine, phentolamine [trimix] CG: PgE1</p> <p>IG1-3: Dose: 2.5 μg PgE1 + 5, 10 (IG2), 20 (IG3), mg Papaverine + 1 mg Phentolamine</p> <p>IG4-6: Dose: 5 μgs PgE1 + 5, or 10 (IG5), or 20 (IG6) mg Papaverine + 1 mg Phentolamine</p> <p>IG7-9: Dose: 10 μg PgE1 + 5, or 10 (IG8), or 20 (IG9) mg Papaverine + 1 mg Phentolamine</p> <p>CG: Dose: 20 μgs PgE1 Duration, all grps: approx 6hrs Frequency all grps: once Compliance all grps: 100%</p> <p>Run In period: NR Wash out period: 1 wk F/u duration NR</p>	<p>Primary outcome results:(IG vs. CG) Grade 4 + 5 erections, n (%): 122 (68) vs. 120 (67) Grade 5 erections, n (%): 61 (34) vs. 66 (37): Overall Cavernous artery diameter mean (sd), mm: IG: Right: 0.9(.21); Left: 0.9 (.2) vs. CG Right: 0.9 (0.2); Left: 0.9 (0.2), NS Peak systolic velocity, cm/s: IG Right: 29 (12); Left: 29 (12) vs. CG- Right: 30 (12); Left: 27 (12), NS Duration of erection, min: 120 (91) vs. 93 (67), NS Satisfaction, %: 63 (28) vs. 64 (26), NS</p> <p>Other outcomes assessed: Cost assessment, patient preference</p> <p>Withdrawals/drop-outs/loss to f/u: n=0</p> <p>WDAE: n=1 (IG9) TAE: NR [AE: Priapism n=10 (none in IG2, IG4, and IG8); pain IG 32 (18%) vs. CG 26 (15%)] SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF-5, Ultrasound imaging</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Soderdahl (1997) 190</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 50 (cross over design)</p> <p>IG1, n= 27 (pts were cross over to other arm post wash-out) IG2 n= 23 (pts were cross over to other arm post wash-out) CG, n= NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with untreated organic impotence, & a stable sexual partnership</p> <p>Exclusion: pts with hormonal therapy (low testosterone treatment); psychogenic impotence; stated preference for either of the treatments, pts not achieving erection after either of the treatment regiments were excluded from analysis</p>	<p>Age, mean (range): 62.3 (38-84) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): 40 (6-120) mo</p> <p>Underlying disease: Vascular n=15; surgical n=13; diabetic n=9; unknown n=7</p> <p>Psychogenic ED: 0%</p> <p>Physiologic ED: All organic pts</p> <p>Mixed ED: NA</p>	<p>IG1: Trimix IG2: vacuum device CG: NA</p> <p>IG1: Dose: 0.25 –0.6 mL [30 mg/mL papaverine HCl, 5 mg/ mL phentolamine, 0.5 mg/ mL PGE) for at least 15 doses Duration: 18-20 mo Frequency: mean 5.8 uses /mo Compliance: 71%</p> <p>IG2: Dose: NA Duration: 18-20 mo Frequency: at least 15 times; mean 5.4 use / mo Compliance: 80%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 18-20 mo</p>	<p>Primary outcome results: Satisfaction scores rated 0-10, IG1 vs. IG2, mean: Erection quality 5 vs. 4 (mean pre-treatment/ pre-impotence score = 1.6/ 6.6 for all) Penile sensation: 5 vs. 5 (pre impotence mean score = 6.5)</p> <p>Other outcomes assessed: partner reported quality & satisfaction</p> <p>Withdrawals/drop outs/loss to f/u: n=6 (12%)</p> <p>WDAE: NR TAE: NR [AE: n=11 bruising, injury or skin changes causing to stop treatment or drop out, IG1 n=4 (9%), vs. IG2 n=7 (16%)] SAE: required an extra visit to doctor IG1 n=5 (11%), IG2 n=2 (4.5%)</p> <p>Ascertainment of outcomes assessed: Pt filled questionnaire at end of 1st period; clinician filled questionnaire at end of study</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sogari (1997) ¹⁹¹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 230</p> <p>IG1 n = 115 IG2 n = 115 CG n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED</p> <p>Exclusion: NR</p> <p>Data reported as IG1 vs. IG2</p>	<p>Age: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: 50 (43.9%) vs. 38 (33.3%)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): IG1: 32.2 (40.2) vs. 33.5 (54.8) mo</p> <p>Underlying disease (diagnosis): Hypertension; alcoholism; diabetes; Peyronie's disease; acute MI, or angina, all non sign. between grps</p>	<p>IG1: Trimix + atropine sulfate in combination (IC)</p> <p>IG2: Trimix alone</p> <p>IG1: Dose: 50 mg papaverine, 10 µg PgE₁, 0.2 mg phentolamine (trimix), 0.075 atropine Duration: NA Frequency: 1 dose Compliance: NR</p> <p>IG2: Dose: Trimix as IG1 Duration: NA Frequency: 1 dose Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results:erectile response assessed subjectively by examiner, IG1 vs. IG2: Tumescence 40 (35%) vs. 45 (40%) Poor erection 22 (19%) vs. 17 (15%) Full erection 52 (46%) vs. 52 (46%)</p> <p>Other outcomes assessed: intracorporeal pressure</p> <p>Withdrawals/drop-outs/loss to f/u: n=2; one from each grp</p> <p>WDAE: 0 TAE: (NR) AE: Painful sensation: 57 (50%), vs. 63 (53.8%)NR SEA: 0</p> <p>Ascertainment of outcomes assessed: NA</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Titta (2006) ¹⁹²</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 57</p> <p>IG1, n = 29 IG2, n = 28 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with non-nerve sparing (NNS) radical pelvic surgery screened one d prior to surgery; in a stable heterosexual relationship for at least 6 mo</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 63.5 (55-72) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment:</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NA</p> <p>Underlying disease, n (%): clinically localized prostate cancer 50 (87.7); invasive bladder cancer 7 (12.3)</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 57 (100)</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: PgE1-IC + sexual counseling IG2: PgE1 alone</p> <p>IG1: Dose: 10µg (lowest efficacious dose= 18.1µg, mean 9.1 µg) Duration: 18 mo Frequency: twice/wk Compliance: 72.4%</p> <p>IG2: Dose: as IG1(lowest efficacious dose= 19.5µg, mean 13.8 µg) Duration: as IG1 Frequency: as IG1 Compliance: 28.5%</p> <p>Run In period: NA Wash out period: NR</p> <p>F/u duration: 18 mo (3, 6, 9, 12, and 18 mo)</p> <p>Note: open label sildenafil 100 mg (1 hr prior to sexual intercourse, min 4 doses/3 mo); all responders switched to sildenafil twice/wk at the end of trial</p>	<p>Primary outcome results: IIEF, mean score at 18 mo (IG1 vs. IG2): 26.5 vs. 24.3, p<0.05 IIIEF, mean pre vs. post surgery: 26.3 vs. 8.4 18 mo, IG1 vs. IG2: 26.5 vs. 24.3 Sexual satisfaction: pre vs. post surgery: 10.2 vs. 3 18 mo, IG1 vs. IG2: 9.7 vs. 6.8 IIEF-OF[®]: Pre vs. post surgery: 9.8 vs. 3.3 18 mo, IG1 vs. IG2: 9.2 vs. 7.8 IIEF-SD: Pre vs. post surgery: 8.6 vs. 8.5 18 mo, IG1 vs. IG2: 9 vs. 6.2 IIEF-SD: Pre vs. post surgery: 9.1 vs. 6.8 18 mo, IG1 vs. IG2: 9.0 vs. 7.3</p> <p>Sildenafil responder rate, n (%): 8 (27.5) vs. 5 (17.8)</p> <p>Other outcomes assessed:</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0 vs. 8 (28.5), p<0.05</p> <p>WDAE, n (%): prolonged post injection pain 0 vs. 3 (10.7) TAE, n (%): NR SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF, and IC training test</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Van der Windt, F (2002) ¹⁹³</p> <p>Funding source: Byk BV</p>	<p>N screened = NR N randomized = 70 (parallel)</p> <p>IG1, n = 35 IG2, n = 35</p> <p>CG: NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: age range 20-70 yrs, medically & psychologically fit to use IC injection, in a stable & monogamous sexual relationship</p> <p>Exclusion: major organic cause for ED</p>	<p>Age, mean (range) 56 (23-75) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: premature ejaculation 20 patients (35%)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: mean= 3.4 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED (n): 12 vs. 13</p> <p>Physiologic ED: 5 vs. 3</p> <p>Mixed ED: 11 vs. 13</p>	<p>IG1: papaverine-phentolamine (Androskat) + sexula counseling</p> <p>IG2: papaverine + phentolamine</p> <p>IG1: Dose: mean 0.34 ml (titrated from 0.25 ml) Duration: NR Frequency: NR Compliance: 10 (29%)</p> <p>IG2: Dose: mean dose = .27ml Duration: NR Frequency: Compliance: 7 (20%)</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration, mean (range): 11.3 (2-19) mo</p> <p>Other: Screening determined dosage with use of hx, visual sexual stimulation and vibro-tactile stimulation</p>	<p>Primary outcome results: IG1 vs. IG2: Increase in penile circumference: mean (millimetres): 27 vs. 30</p> <p>Duration of erection: mean: 47 vs. 56 min</p> <p>% (self reported) erection score: mean %: 84% vs.79%</p> <p>Other outcomes assessed: Acceptance of IC injection (mo used before stopping): 4.7 vs. 1.7</p> <p>Withdrawals/drop-outs/loss to f/u: N= 13</p> <p>WDAE: 12% discontinued due to prolonged erection TAE: NR AE in 14% of patients; 3 (5%) priapism, 4 (7%) haematoma, and 1 (2%) curvature of the penis SAE: 0</p> <p>Ascertainment of outcomes assessed: Physical exam, telephone interview</p>

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<p>Vanderschueren (1995) ¹⁹⁴</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 210 (cross over)</p> <p>IG1-3 & CG, n = 210 (NR for dose allocations)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED, at least 4 mo in duration, with stable responders to PG-E1 (ED defined as inability to achieve rigidity sufficient for vaginal penetration)</p> <p>Exclusion: cavernous fibrosis, anatomical deformation of the penis, Peyronie's disease or a hx of priapism, major disease, drugs that could substantially affect the evaluation of EF</p>	<p>Age, mean (range): 53 (29-70) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 4.8 (0.5- 41) y</p> <p>Underlying disease: diabetes in 7%; other NR</p> <p>Psychogenic ED: 36%</p> <p>Physiologic ED: 28%; (vasculogenic 21%, diabetes 7%)</p> <p>Mixed ED: 15%</p>	<p>IG1: PgE1 new sterile solution IG2: PgE1 sterile powder IG3: PgE1 pediatric sterile solution Each administered in 4 doses) CG: placebo</p> <p>IG1-3: Dose: a= 2.5, or b=5, or c=10, or d=20 µg Duration: NR Frequency: one injection of each formulation at the randomized dose Compliance: NR</p> <p>CG: Dose: 0 µg PgE1 Duration: NR Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: at least 3 d</p> <p>F/u duration: NR</p>	<p>Primary outcome results:Duration of erection, mean (sd): [IG1 vs. IG2 vs. IG3], min: 2.5 µg: 30 (9) vs. 27 (8) vs. 33 (8) 5 µg: 52 (10) vs. 68 (12) vs. 64 (12) 10 µg c: 29 (8) vs. 35 (9) vs. 35 (9) 20 µg: 52 (11) vs. 50 (10) vs. 51 (11) CG: 0 (0) vs. 0.5 (0.5) vs. 1.6 (1.4) % of pts with positive response ,RigiScan (>=70% for >= 10 min), and clinical assessment, data extracted from bar graph and it is approximate: 2.5 µg: RigiScan: 33 s. 27 vs. 40; clinical assessment: 40 vs. 33 vs. 44 5 µg: RigiScan 50 vs. 48 vs. 52; clinical assessment: 65 vs. 75 vs. 70 10 µg: RigiScan 38 vs. 48 vs. 39, clinical assessment 50 vs. 52 vs. 63 20 µg: RigiScan 43 vs. 45 vs. 42; clinical assessment 55 vs. 58 vs. 55 CG: RigiScan 0 vs. 2 vs. 5; clinical assessment 0 vs. 0 vs. 5</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 3 (1.5%)</p> <p>WDAE: n=3; severe penile pain 1 (0.5%); systemic medical events 2 (1%) TAE: NR; AE: penile pain, IG1 9% vs. IG2 14% vs. IG3 17% vs. CG 11% SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan; clinical assessment</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Viswaroop (2005) 195</p> <p>Funding source: NR</p>	<p>N screened = N randomized = 50</p> <p>IG1, n = 25 IG2, n = 25 CG, n = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 21-65 y wit ED (irrespective of aetiology, marital status and duration of ED)</p> <p>Exclusion: contraindication to use of sildenafil or papaverine</p>	<p>Age, mean (sd): 30 (10.2)</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM 6 (12); hypertension 3 (6); abused alcoholic 2 (4); depressive illness 4 (8)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 30 (60)</p> <p>Physiologic ED, n (%): 20 (40)</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: papaverine IC then oral sildenafil</p> <p>IG2: oral sildenafil then papaverine IC injection</p> <p>IG1: Dose: papaverine 30 mg; sildenafil 50 mg Duration: NA Frequency: single dose Compliance: NR</p> <p>IG2: Dose: as IG1 Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>Run In period: Wash out period: 2 d between tx for each arm</p> <p>F/u duration: 5 min post injection of papaverine; 30 min post ingestion of sildenafil</p>	<p>Primary outcome results: Penile length (cm), mean (sd): baseline 7.71 (1.26) papaverine: 11.98 (2.4) sildenafil 11.66 (2.20) Penile circumference (cm), mean (sd): Baseline: 7.50 (1.07) Papaverine: 10.2 (1.5) Sildenafil: 9.67 (1.39)</p> <p>Other outcomes assessed: angle of erection; Pts tx preference</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE: NR; AE reported, priapism n=5 (10) with injection; headache 2(4), blurring vision 1 (2) and dyspepsia 1 (2) SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: Penile measurement; interview</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>von Heyden (1993)¹⁹⁶</p> <p>Funding source: Deutsche Forschungsge- meinschaft</p>	<p>N screened = NR N randomized = 16</p> <p>IG/ CG, n = 16 (crossover design)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: undergoing home auto-injection with PgE₁</p> <p>Exclusion: ED due to severe venous incompetence, sickle cell anemia, or endocrinological, neurological or psychiatric dx; Peyronie's dx; hx of priapism, coagulopathy, recent MI, unstable angina or stroke; use of medication known to interfere with EF within 1 mo of study entry</p>	<p>Age, mean (sd): 56, range 46-70 y</p> <p>Co-morbidities: DM 2, heart attack 2, coronary bypass 2, hypertension 1, transurethral prostatic resection 1</p> <p>Previous ED treatment: PgE₁ for mean of 1.3 yr (range 0.3-6); mean dosage 6.21 µg (95% confidence interval 4.33-8.10)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: arterial insufficiency 9, moderate venous insufficiency 1, mixed vascular disease 6</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 16</p> <p>Mixed ED: 0</p> <p>Other: 1 patient had borderline hypergonadotropic hypogonadism</p>	<p>IG: PgE₁ CG: placebo</p> <p>IG: Dose: mean effective dose 21.4 (2.5 –40) µg Duration: NR Frequency: varied (injections were repeated until erection lasted longer than 2 hr, or drug intolerance developed with minimum of 2 d between injections) Compliance:</p> <p>CG: Dose: placebo (saline) Duration: NR Frequency: Placebo was given at random during the escalating dose schedule Compliance:</p> <p>Run In period: NR</p> <p>Wash out period: 2 or more d</p> <p>F/u duration: 2 hrs post injection</p>	<p>Primary outcomes: Approximate % of patients with highest value at or below dosage IG [2.5-40 µg (range)] vs. CG Maximal rigidity base: 19-98% vs. 0% Maximal rigidity tip: 19-98% vs. 7% Maximal sustained rigidity base: 19-98% vs. 0% Maximal sustained rigidity tip: 12-98% vs. 0% Total duration of ≥ 60% rigidity base 22-100% vs. 0% Total duration of ≥ 60% rigidity tip 41- 100% vs. 8%</p> <p>Other outcomes assessed: Rigidity assessed with penis buckling test; cavernous artery peak flow velocity; systolic & diastolic BP</p> <p>Withdrawals/drop-outs/loss to f/u: 4</p> <p>WDAE: 4 (pain on last dose (15 µg in 2; 20 µg, and 25 µg in 2) TAE: 22/135 injections (16.3%); all: Burning sensation or mild to moderate penile pain 18/135 IG (13.3%) Haematoma 2/135 IG (1.5%) SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Wegner (1994) ¹⁹⁷</p> <p>Funding source:</p>	<p>N screened = 60 N randomized = 20 (crossover trial)</p> <p>IG1/ IG2 (a,b), n =20</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men with ED who presented to ED clinic for evaluation. Who undergo evaluation of the cause of their dysfunction, including sexual hx, physical exam.</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 54.2 (29-87) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status, n (%): (30)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: n (%); DM 4 (20)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: n (%); Alcohol abuse 2 (10) Primary neurologic causes 1 (5)</p>	<p>IG1: PgE1 IG2 (a,b): SIN-1</p> <p>IG1: Dose: 20 µg Duration: NR Frequency: once min 3 days inbetween Compliance (%): 100%</p> <p>IG2a: Dose: 1 mg Duration: NR Frequency: once Compliance: 100%</p> <p>IG2b: Dose: 2 mg Duration: Frequency: once Compliance: 100%</p> <p>Run In period: NR Wash out period: 3 d between injections</p> <p>F/u duration (on and off treatment): NR</p>	<p>Primary outcome results: IG1vs. IG2 a vs. IG2 b Erectile Response, n (%):</p> <p>Full rigidity (5): 2 (10) vs. 0, vs.0 Full medium rigidity (4): 4 (20) vs. 2 (10) vs. 2 (10) Minimal to Full without rigidity (1-3): 14(70) vs. 18 (90), vs. 18 (90)</p> <p>No response: 0 in all grps</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: No dropouts</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Clinician assessed quality of erection using a 6 point scale, (0-5, with 0 being no response, 4 Full medium rigidity. and 5 Full rigidity)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Wegner (1995) ¹⁹⁸</p> <p>Funding source: NR</p>	<p>N screened = 60 N randomized = 40 (cross over)</p> <p>IG1-3, n= 40</p> <p>ITT analysis used for primary outcome? NR</p> <p>Inclusion: Pts with ED => 6 mo duration</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 53 (34-71) yr</p> <p>Co-morbidities: NR (see 'Other')</p> <p>Previous ED treatment: NR</p> <p>Smoking status: n=12</p> <p>Body weight: NR</p> <p>Other: alcohol abuse (n=3), DM (n=8)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 3.2 y (6 mo – 7 y)</p> <p>Underlying disease: pelvic surgery (n=3), neurological causes (n=2)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: Diagnosis of ED included testing with PGE1, cause of ED, sexual hx, physical examination</p>	<p>IG1: Pg-E1 IG2: linsidomine chlorhydrate (SIN-1) IG3: SIN-1 + urapidil</p> <p>IG1: Pg-E1 Dose: 20 µg Duration: NR Frequency: once</p> <p>IG2: SIN-1 Dose: 1 mg Duration: NR Frequency: once</p> <p>IG3: SIN-1 + urapidil Dose: 1 mg (SIN-1), 10 mg (urapidil) Duration: NR Frequency: once Compliance all: NR</p> <p>Run In period: NR Wash out period: 3 d</p> <p>F/u duration: 3 d (assessed 5, 10, 20, 30 min after injection)</p>	<p>Primary outcome results: N pts with full response (grade 6) (rigidity)/ rigid erection (grade 5), n (%) IG1: 8 (20)/ 8 (20) IG2: 0 (0)/ 3 (8) IG3: 2 (5)/ 8 (20) IG1 vs. IG2, p = 0.0001 IG2 vs. IG3, p = 0.0004</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: NR AE, n of events: 5 severe hypotension in IG3; pain upon injection IG1=3; IG2=1; IG3=3 SAE: NR</p> <p>Ascertainment of outcomes assessed: inspection and palpation (0= no response; 5= full tumescence; 6= full tumescence with rigidity)</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C6-Subcutaneous Treatment Trials

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rosen, RC (2004) ¹⁹⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 25</p> <p>IG1/IG2/CG, n = 25 (3 way cross over)</p> <p>ITT analysis for primary outcomes: NR</p> <p>Inclusion: age 21-55 y; within 40% of ideal weight, ED diagnosis of 6 mo or longer; IIEF EF score 16 or less; inadequate response to 100 mg Viagra defined by ability to attain erection sufficient for intercourse equal or less than 50% of times within last 12 mo</p> <p>Exclusion: Current use of Viagra (last 4 wks prior to enrolment); ED due to untreated endocrine disease, penile anatomic deformities, prostate cancer or radical prostatectomy; clinically S hepatic, renal, cardiovascular, psychiatric or CNS disease, (i.e. stroke or SCI)</p>	<p>Age, mean (sd): 48 (5), range 37-54 y</p> <p>Race, n (%): White 19 (76), Black 5 (20), Hispanic 1 (4), other 0</p> <p>Co-morbidities, n (%): DM 2 (8); hypertension 7 (29); hyperlipidemia 3 (12)</p> <p>Previous ED treatment: Viagra (100 mg)</p> <p>Smoking status: 11 (42%)</p> <p>Body weight, mean (sd): 97 (18) kg, range 64-129 kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 8 (5) y, range 2-22 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: subcutaneous PT-141 low dose (+ visual sexual stimulation)</p> <p>IG2: subcutaneous PT-141 high dose (+ visual sexual stimulation)</p> <p>CG: placebo</p> <p>IG1/IG2: Dose: 0.4 mg (IG1), 0.6 mg (IG2) injected in the lower right quadrant of abdomen (3 way crossover design always starting with lower dose) Duration: NA Frequency: once/ dose, three visits Compliance: 100%</p> <p>CG: Dose: NA Duration: NA Frequency: as IG Compliance: 100</p> <p>Run In period: NA Wash out period: 3-14 d</p> <p>F/u duration: last outcome measure taken up to 145 min post injection (pts were monitored for 12 & 24 hr post injection)</p>	<p>Primary outcomes (EF): IG1 (n=24) vs. IG2 (n=21) vs. CG (n=23), mean (SE): Duration of rigidity, min: >= 60%, base: 28 (6), vs. 41 (8), vs. 6. (2)/; tip: 19 (5) vs. 24 (6), vs. 4 (2)</p> <p>>= 80% base: 14 (4), vs. 17 (5), vs. 2 (0.6)/; tip: 5 (2), vs. 8.(3), vs. 0.4 (0.2)</p> <p>RAU: Base: 29 (5), vs. 41 (6), vs. 9 (2) Tip: 23 (4), vs. 33 (5), vs. 7 (2)</p> <p>Other outcomes assessed: Tumescence activity untis (TAU)</p> <p>Withdrawals/drop-outs/loss to f/u: n=1 (this pts was replaced) WDAE: n=0 TAE: 24 vs. 24 vs. 0; including nausea, headache, vomiting, back pain, diaphoresis, flushing, fatigue, muscle cramps SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan TM; Rigidity Assessment System (Pharmacokinetic data, 3)</p> <p>Other: pts with severe ED (IIEF- EF score 6-10) (n=10): 6 mg PT-141 resulted in mean duration of >= 60 and >=80% base rigidity of 36 and 15 min (p<0.01) respectively compared to 8 and 2 min after placebo</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Segraves (1991) 200</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 12</p> <p>IG/ CG, n = 12</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: coital erectile failure for at least 6 mo, and any 1 or more of hx of adequate erections upon awakening at least 2/wk for preceding mo, hx of adequate erections lasting \geq 5 min during foreplay and/or hx of adequate EF during masturbation</p> <p>Exclusion: current use of hypotensive or psychoactive medication; prior use of neuroleptic medications; penile blood pressure index \leq 0.70; serum testosterone \leq 450 ng/mL; serum PRL \geq 30 ng/mL; erectile problem judged to be related to current marital discord; presence of dx known to be frequently associated with ED</p>	<p>Age: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 12</p> <p>Physiologic ED: 0</p> <p>Mixed ED: 0</p>	<p>IG: apomorphine hydrochloride subcutaneously (brachial) CG: placebo subcutaneously (brachial)</p> <p>IG1: Dose: (titrated wkly until full rigidity or AE) 0.25, and 0.50 0.75 and 1.0 mg n=12 received only first 2 doses; n=9 first 3 doses, and n=5 all doses Duration: NR Frequency: once/wk Compliance: NR</p> <p>CG: Dose: placebo Duration: NR Frequency: once /wk Compliance: NR</p> <p>Run In period: NR Wash out period: 50 min between injections in each session; 1 wk between sessions</p> <p>F/u duration: NR</p>	<p>Primary outcome results: penile tumescence (\blacktriangle in circumference): n=11 exceeded 1 cm after apomorphine injection</p> <p>Average max erection = 2 cm, range 0.3–3.0 cm</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: NR; AE, n (%): 8 (67); yawning, drowsiness, nausea, and extreme SAE: NR</p> <p>Ascertainment of outcomes assessed: Barlow strain gauges; Max erection, made by visual inspection without palpation, rated independently by subject and investigator on scale of 0–100%; Max level of SD rated on scale of 0–100% by subject</p> <p>Other: 3 pts (25%) did not proceed to the next dose level due to AE; sign. relationship between nicotine use and absence of AE (chi-square 6.9, p<0.01)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Wessells (2000) 201</p> <p>Companion study (part II) 202</p> <p>Study I (psychogenic study)</p> <p>Funding source:</p>	<p>N screened = NR N randomized = 10 (cross over)</p> <p>IG/ CG= 10</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: age 18-75 y, part I: psychogenic ED pts with normal organic etiology & normal nocturnal penile tumescence (> 10 in of tip rigidity > 70%); part II, men with organic ED (mean organic risk factor of 2.2) (ED defined as the persistent inability to obtain and maintain erection sufficient for sexual satisfaction)</p> <p>Exclusion: Concurrent use of erectogenic medications, radical prostatectomy, cancer-chemotherapy, Peyronie's disease, or other genital anomalies</p>	<p>Age, mean (range): Reported for study I + Study II: 51.6 (22-67) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n: IC injection; sildenafil 5; IU Pg E- IU 1</p> <p>Smoking status: smokers n=2</p> <p>Body weight: NR</p> <p>Other: mean serum testosterone level: 362 mg/ml; mean IIEF score (items 3 and 4) 0.77 (0-2)</p>	<p>Concomitant medications: testosterone replacement therapy (n=3)</p> <p>Duration of ED: NR</p> <p>Underlying disease, n: reported for total pts, hypogonadism 3; hypercholesterolemia 5; obesity 4; hypertension 3; peripheral neuropathic injury 2; DM 2; heart dx 2; venoocclusive dysfunction 1; pudendal arterial insufficiency 1</p> <p>Psychogenic ED: 100%</p> <p>Physiologic ED: 0</p> <p>Mixed ED: 0</p> <p>Other: NPT (mean baseline): 3 erectile events /night, 30 min of base rigidity > 60%, 9 min tip rigidity > 80%</p>	<p>IG: subcutaneous injection Melanotan II CG: placebo</p> <p>IG1: Dose: 0.025-0.157 mg/kg (total injections, part I & II = 39) Duration: NR Frequency: 2 injections Compliance: 100%</p> <p>CG: Dose: placebo (total injections study I & II) Duration: NR Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: 48 hrs</p> <p>F/u duration: 6 hrs post injection</p> <p>Other: one subject (no allocation to study grps) received three placebo and one active injections erroneously</p>	<p>Primary outcome results: Erectile activity/injection: NR (combined results of Study I & study II 27/39 (69%) vs. 1/41 (2.4%) RigiScan (mean), n=16 injections: Erections with response (%): 75 vs.0 Erectile events (n): 3.45 vs. 2.35 Total erectile duration (min): 163 vs. 55 Tip rigidity 80-100% (min): 38 vs. 3 Tip rigidity 60-79% (min): 40 vs. 5 Average tip rigidity (%): NR Erectile latency (min): 127 vs. ND Tip RAU: 78 vs. 10 Tip TAU: 50 vs. 14</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0 TAE: combined results for Study I & II; n of events/total injections, (%) Nausea: 15/39 (38) vs. 4/41 (10) Stretch/yawn: 22/39 (56) vs. 5/41 (12) SAE: 0</p> <p>Ascertainment of outcomes assessed: Penile rigidity by RigiScan and visual analog scale; SD and side effects by questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Wessells, (2000) 201</p> <p>Companion study (part II) 202</p> <p>Study II (organic study)</p> <p>Funding source:</p>	<p>N screened = NR N randomized = 10 (cross over)</p> <p>IG/ CG= 10</p> <p>Inclusion: age 18-75 y, men with organic ED (mean organic risk factor of 2.2) (ED defined as the persistent inability to obtain and maintain erection sufficient for sexual satisfaction)</p> <p>Exclusion: Concurrent use of erectogenic medications, radical prostatectomy, cancer-chemotherapy, Peyronie's disease, or other genital anomalies</p>	<p>Age, mean (range): Part II 56.2 (37-67) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n: intracavernous injection; sildenafil 5; IU Pg E- IU 1</p> <p>Smoking status: smokers n=2</p> <p>Body weight: NR</p> <p>Other: mean serum testosterone level: 362 mg/ml; mean IIEF score (items 3 and 4) 0.77 (0-2)</p>	<p>Concomitant medications: testosterone replacement therapy (n=3)</p> <p>Duration of ED: NR</p> <p>Underlying disease, n: as study I</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: 0</p> <p>Other: see study I</p>	<p>IG: subcutaneous injection Melanotan II CG: placebo</p> <p>IG1: Dose: 0.025-0.157 mg/kg Duration: NR Frequency: two injections; total injections = 19 Compliance: 100%</p> <p>CG: Dose: placebo Duration: NR Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: 48 hrs</p> <p>F/u duration: 6 hrs post injection</p> <p>Other: * n=1 received three placebo and only one Melanotan II injections erroneously</p>	<p>Primary outcome results: Erectile activity/injection: NR (combined results of Study I & study II 27/39 (69%) vs. 1/41 (2.4%)) RigiScan (mean): Erections with response (%): 63 vs. 5 Erectile events (n): 3 vs. 0.7 Total erectile duration (min): 98 vs. 25 Tip rigidity 80-100% (min): 45 vs. 2 Tip rigidity 60-79% (min): 10 vs. 1 Average tip rigidity (%): 47 vs. 6 Erectile latency (min): 8 vs. ND Tip RAU: 59 vs. 5 Tip TAU: 29 vs. 6 IIEF- Q12 (sd), [IG (19 injections) vs. CG (21 injections)] very low or none 6 vs. 1 Low 3 vs. 3, Moderate 5 vs. 1, High 5 vs. 0, Very high 0 vs. 0</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0</p> <p>TAE: combined results for Study I & II; n of events/total injections, (%) Nausea: 15/39 (38) vs. 4/41 (10) Stretch/yawn: 22/39 (56) vs. 5/41 (12)</p> <p>SAE: 0</p> <p>Ascertainment of outcomes assessed: Penile rigidity by RigiScan and visual analog scale; SD and side effects by questionnaire</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E, IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C7- Intra-urethral Suppositories

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Ekman, P (2000) 203</p> <p>Funding source: Astra Lakemedel AB</p>	<p>N screened = NR N randomized = 166</p> <p>IG1, n = 83 IG2, n = 83 CG, n = NA</p> <p>Intention to Treat (ITT) analysis: yes</p> <p>Inclusion: men 18 y or older, with ED</p> <p>Exclusion: hypersensitivity to alprostadil (MUSE), abnormal penile anatomy, acute or chronic urethritis or indwelling catheter, penile implant, untreated hypogonadism, testosterone substitution for < 3 mo, known risk of priapism, concomitant tx with appetite suppressants or anticoagulants, partner planning to become or already pregnant. Also concomitant dx (poorly controlled diabetes, hypertension, unstable angina, heart failure, severe vascular dx, severe neurological or psychiatric dx)</p>	<p>Age, mean (sd): 60 (10) y</p> <p>Race: 100% Caucasian</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 86 (12) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 41 (31) mo</p> <p>Underlying disease, (%): > 1 cause: Vascular 47 vs. 43 neurogenes 18 vs. 17 Diabetes 21 vs. 21 hormonal 0 vs. 4 Psychogenic 12 vs. 7 Unknown 27 vs. 27 Other 22 vs. 17</p> <p>Psychogenic ED: NA</p> <p>Physiologic ED: NA</p> <p>Mixed ED: NA</p> <p>Other: capable of partial erection mean (%)= 78 (76 vs. 81)</p>	<p>IG1: PgE1 alprostadil (MUSE) (optional pubic band)</p> <p>IG2: PgE1 alprostadil (MUSE), (optional pubic band)</p> <p>IG1: Dose: starting dose of 250 µg (clinic), titrated up to 250,500,1000 µg or down to 125 µg after 4 wks at 4 wk intervals (home application) Duration: 12 wks Frequency: at least 4 applications/ 4 wk Compliance: NR</p> <p>IG2: Dose: as IG1, starting dose of 500 µg (titration regiment as IG1) Duration: 12 wks Frequency: as IG1</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcomes (EF): Quality of erection reported for both IG1 & IG2 combined: Grade 4/5 at least once, n (%): 122 (73); these pts all reported coitus Grade below 4, n (%): 44 (27) IIEF (Q1-5 & 15), mean change in score (%): Q1= 1.8 (100); Q2= Q3=1.7 (100); Q4=1.9 (146); Q5=1.9 (136); Q15=1.2 (136) all sign. p <0.001 Final dose (% of total n=142): 125 µg - 1%; 250 µg - 6%; 500 µg - 18%; 1000 µg - 75% Sexual intercourse at least once: 113 (68%)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 24 (included 1 due to depression, and 3 unknown)</p> <p>WDAE: 9 (5%) penile pain, hypotension) TAE: NR AE, n (%): Pain 50 (30%) with 4 (2%) rated severe; Hypotension, dizziness: (no detail reported) SAE: 0</p> <p>Ascertainment of outcomes assessed: Pts filled personal diary; IIEF; Erection Assessment Scale (EAS)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Lazzeri (1994) 204</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 20 (parallel design)</p> <p>IG1, n = 5 IG2, n = 5 IG3, n = 5 CG, n = 5</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED</p> <p>Exclusion: NR</p>	<p>Age, mean (SE): 55.4 (5) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 20</p> <p>Physiologic ED: 0</p> <p>Mixed ED: 0</p>	<p>IG1: capsaicin IU IG2: papaverine IC IG3: papaverine IC + capsaicin IU CG: placebo IU</p> <p>IG1: Dose: capsaicin 10⁻⁵ M Duration: NR (injection length= 2 min) Frequency: 1 dose</p> <p>IG2: Dose: 8 mg Duration: as IG1 Frequency: 1 dose</p> <p>IG3: Dose: 8 mg + capsaicin 10⁻⁵ M Duration: as IG1 Frequency: 1 dose</p> <p>CG: Dose: saline Duration: as IG1 Frequency: 1 dose</p> <p>Compliance all grps: NR</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: NR</p>	<p>Primary outcome results: No response was reported for all variables with placebo, results for IG1 vs. IG2 vs. IG3:</p> <p>Penile diameter, Mean (sd) maximal ▲ : 2.9 (0.93) vs. 3.7 (1.1) vs. 3.8 (0.96)</p> <p>Rigidity, mean maximal (%): 43 (12) vs. 63 (10) vs. 74 (16)</p> <p>Mean latency (seconds) 219 (44) vs. 198 (10) vs. 107 (29)</p> <p>Mean duration (seconds) 322 (58) vs. 248 (39) vs. 390 (48)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Padma-Nathan (1997) ²⁰⁵ Companions ²⁰⁶⁻²⁰⁸</p> <p>Funding source: Vivus Inc.</p>	<p>N screened = NR N randomized, phase I-clinic test = 1511 (at clinic test with alprostadil) N randomized – Phase II-home tx= 996 (responders to alprostadil test)</p> <p>IG, n = 485 CG, n = 511</p> <p>ITT analysis used for primary outcome: no</p> <p>Inclusion: men with chronic ED without spontaneous erection sufficient for intercourse within past 3 mo; response = 4 or 5 to initial dose response test (125 – 1000 µg alprostadil)</p> <p>Exclusion: hx of urethral stricture or obstruction, indwelling urethral catheter, penile implant or prior penile surgery, sickle cell dx, paraplegia or quadriplegia, congestive heart failure, unstable angina, or recent acute MI; poorly controlled DM (complete list could be found in original study)</p>	<p>Age, mean (range): 62 (38-84) vs. 61 (30-83) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: 52% vs. 57%</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 51 (3-528) mo</p> <p>Underlying disease: Vascular disease: 29% v. 28% Diabetes: 19 vs. 19 Surgery or trauma: 32% vs. 31% Other: 21% vs. 21%</p> <p>Psychogenic ED: NA</p> <p>Physiologic ED: 100% primary organic ED</p> <p>Mixed ED: NA</p> <p>Other: capable of partial erection (% of men): 63.3% vs. 60.9%</p>	<p>IG: alprostadil home tx CG: placebo home tx</p> <p>IG1: Dose: 125 µg (n=116, 12%), 250 µg (n=171, 17%), 500 µg (n=302, 30%), 1000 µg (n=407, 41%) Duration: 3 mo Frequency: NR Compliance: NR</p> <p>CG: Dose: same as IG Duration: 3 mo Frequency: NR Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 3 mo Other: 88% of IG rated the transurethral application of alprostadil as neutral</p>	<p>Primary outcome results: IG (n=411) vs. CG (n=500), % of successful tx</p> <p>Intercourse: 50 vs. 10 Intercourse/orgasm: 56 vs. 15 Intercourse/orgasm/10-min erection sufficient for intercourse: 57 vs. 15</p> <p>Other outcomes assessed: 88% of IG rated the transurethral MUSE neutral, comfortable or very comfortable</p> <p>Withdrawals/drop-outs/loss to f/u: n=123 (12)</p> <p>WDAE, n (%): 15 (2) TAE, n (%): Penile pain: 159 (33) vs. 17 (3); also in 11% of administrations of alprostadil Minor urethral trauma: 25 (5) vs. 5 (1) Urinary tract infection: 1 (0.2) vs. 3 (0.6) Priapism-prolonged erection: 0 vs. 0 Penile fibrosis: 0 vs. 0 Dizziness: 9 (2) vs. 1 (0.2) Hypotension (dose response observed): 0 v. 1 (0.2) SAE: NR</p> <p>Ascertainment of outcomes assessed: EAS (1= no response to 5= full rigidity); comfort by self assessment</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Peterson (1998) 209</p> <p>Funding source: VIVUS Inc.</p>	<p>N screened = NR N randomized = 234 (CCT-crossover design)</p> <p>IG1/IG2/IG3/ CG, n = 234</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with ED 3 mo before enrolment, in stable relationship, who tolerated, and had a measurable response to 500 µg alprostadil in clinic</p> <p>Exclusion: Waking or early-morning erections sufficient for vaginal penetration within past 3 mo; hx of urethral stricture or obstruction; penile implant; indwelling urethral catheter or penile surgery; sickle cell dx; paraplegia or quadriplegia; uncontrolled congestive heart failure; unstable angina or acute MI within in 3 mo; poorly controlled DM; use of investigational tx other than IC injections within 2 mo of study entry; hx of epilepsy; active vasculitis; life expectancy < 6 mo; morbid obesity</p>	<p>Age, mean SD): 60 (10), range 26.8-81.5 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): None 94 (40), counselling 22 (10), hormonal tx 44 (18.8), IC 78 (33), band therapy 10 (4), vacuum pump 43 (18), other 6 (3)</p> <p>Smoking status NR</p> <p>Body weight: NR</p> <p>Other: Acute onset 67 (29), gradual onset 167 (71)</p>	<p>Concomitant medications: Testosterone replacement therapy and concomitant medications for unrelated conditions continued at stable dose throughout study</p> <p>Duration of ED: 4, range 0.25-30</p> <p>Underlying disease: Vascular 92 (39), diabetes 42 (18), surgery/trauma 58 (25), other 42 (18)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: MUSE IG2: prazosin hydrochloride IG3: MUSE+prazosin (ratios 1:1, 1:2 and 1:4) CG: placebo</p> <p>IG1: Dose: 125, 250, 500 or 1000 µg Duration: 2-4 wks Frequency: 2 doses IG2: Dose: 250, 500, 1000 or 2000 µg Duration: 2-4 wks Frequency: 2 doses</p> <p>IG3: Dose: 1 of 9 combinations Duration: 2-4 wks Frequency: 2 doses</p> <p>CG: Dose: placebo Duration: 2-4 wks Frequency: 1 dose Compliance all: NR</p> <p>Run In period: NA Wash out period: at least 2 wks F/u duration: 7, -60 min after dosing</p>	<p>Primary outcome (EF): Grade 3 or higher, (%): 52 vs. 13 vs. 59 vs. 3 Grade 4 or 5, (%): 31 vs. 3 vs. 36 vs. 0.4 Median visual analogue scale (1-100), range: 37-50 vs. 8-22 vs. 42-60 vs. 4</p> <p>Other outcomes assessed: pts comfort with</p> <p>Withdrawals/drop-outs/loss to f/u: 17</p> <p>WDAE: 2 TAE: NR AEs, % (range) of total doses: penile pain or discomfort: 17–24 vs. 1-6 vs. 17–32 vs. 2 testicular pain: 2-4 vs. 0-1 vs. 2-7 vs. 0.4 urethral pain: 1-9 vs. 0-2 vs. 2-14 vs. 2 dizziness 0–6 vs. 0-1 vs. 0–12 vs. 0; hypotension: 1–4 (dose response for MUSE) vs. 0-2 vs. 0–14% vs. 0 prolonged erections, 4-6 hr, n (%): 2 (1) minor urethral bleeding, n (%): 12 (5) SAE: 0</p> <p>Ascertainment of outcomes assessed: erection grading system (0-5)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Shabsigh (2000) 210</p> <p>Funding source: Schwarz Pharmaceuticals AL</p>	<p>N screened = NR N randomized = 111 (two phase cross over study, Phase I: office dose titration; phase II: at home treatment)</p> <p>IG1/IG2, n = 111 CG, n = NA</p> <p>ITT analysis used for primary outcome: yes (Phase I, n= 95; Phase II, n= 68)</p> <p>Inclusion: ED at least 6 mo, stable heterosexual relationship</p> <p>Exclusion: pts with past IC or IU tx, chemotherapy, other meds that might produce bleeding or bruising after drug administration, monoamine oxidase inhibitors up to 2 wk before enrolment, concomitant medication for ED or oral alpha-adrenergic receptor blocking agents, had ED due to urologic abnormality, penile fibrosis or untreated endocrine disorder (hypogonadism) or systolic BP < 100 mm Hg</p>	<p>Age, mean (sd): 59.2 (10.6) y, range 30-79 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: Blood pressure, mean (sd): Systolic: 139(15) mm Hg Diastolic: 83 (8) mm Hg Heart rate: 73 (10) beats per minute</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 5 (4) y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: IC injection of alprostadil (EDEX) IG2: IU injection of alprostadil (MUSE) with option of ACTIS</p> <p>IG1: Dose: mean optimal dose = 27.3 µg (up to 40 µg, also most frequently used dose) Duration: phase I=1-14 d; phase II=21 d Frequency: phase II=max of 9 IU/ 21 d administrations in 21 d Compliance: NR</p> <p>IG2: Dose: optimal dose = 921 µg (up to 1000 µg, 33% of all administrations) Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>Run In period: 1 to 14 d Wash out period: NR</p> <p>F/u duration: 3 wk off treatment</p>	<p>Primary outcome results: IG1 vs. IG2 Grade \geq 3, n (%): By physician: 59 (62) vs. 19 (20) Patient assessment: 63 (66) vs. 25 (26) Positive buckling tests (1 kg), n (%): 58 (61) vs. 20 (21) Erection sufficient for intercourse, (%): 82 vs. 47 Satisfaction rating mean: 6 vs. 3 IIEF score, baseline all vs. IG1 vs. IG2, mean (sd): EF Q1-5, 15: 9 (6) vs. 25 (7) vs. 17 (9) Intercourse satisfaction Q6-8: 5 (4) vs. 11 (3) vs. 8 (4)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n: 43 (phase I, 16; phase II, 27)</p> <p>WDAE: NR TAE: pts with at least 1 AE [phase I]; [phase II], (%): [31 vs. 56], [53 vs. 58] Application site reaction: [4 vs. 16], [2 vs. 10] Other penile pain: [20 vs. 30], [34 vs. 25] Prolonged erection: [2 vs. 0], [3 vs. 0] SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF (Q1-5, 15; and Q9, 10; and Q6-8; and Q13, 14), Buckling test; grading system 0-3</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Shokeir (1999) 211</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 60 (parallel design)</p> <p>IG1, n = 30 IG2, n = 30 CG = NA</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: <u>men</u> 18 y or older, with ED of primarily organic aetiology, inability to achieve erection sufficient for intercourse at least 1 time during 3 mo before study period</p> <p>Exclusion: previous use of IC injections</p> <p>Data reported as IG1 vs. IG</p>	<p>Age, mean (sd): 55 (18) vs. 56 (17) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n (%): 16 (53) vs. 17 (57); vacuum pumps, band therapy, hormones</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (sd): 36 (8) vs. 38 (10)</p> <p>Underlying disease, n (%): Vascular disease: 9 (30) vs. 6 (20); diabetes: 15 (50) vs. 18 (60); surgery/trauma: 3 (10) vs. 3 (10); other causes 3 (10) vs. 3 (10)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: IC PgE1 (injection) IG2: IU MUSE</p> <p>IG1: Dose: 20 µg Duration: 3 mo Frequency: at least 1/wk Compliance: 33%</p> <p>IG2: Dose: 1 mg Duration: 3 mo Frequency: at least 1/wk Compliance: 83%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 3 mo</p>	<p>Primary outcome results: IG1 vs. IG2 Erection score of 4 and 5 in clinic, n (%): 27 (90) vs. 18 (60)</p> <p>Sexual intercourse (at least once) at home: 26 (87) vs. 16 (53)</p> <p>Other outcomes assessed: Ease of treatment</p> <p>Withdrawals/drop-outs/loss to f/u: n = 25, IG1 n=20 vs. IG2 n=5</p> <p>WDAE, n: 9 (due to pain) vs. 0 IG1: IG2: 0 TAE, n (%): All AE, Urogenital pain 14 (47) vs. 2 (7); dizziness 0 vs. 2; urethral bleeding 0 vs. 1 SAE: 0</p> <p>Ascertainment of outcomes assessed: Personal diaries, Erection Assessment Scale 0-5</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Williams (1998) 212</p> <p>Funding source: Grant from VIVUS Inc. Manufacturer of MUSE (Alprostadil (PGE₁) in transurethral route)</p>	<p>N screened = 249 N randomized = 159 (64% of screened pts who achieved erection adequate for intercourse on test dose)</p> <p>IG, n = 78 CG, n = 81</p> <p>ITT analysis used for primary outcome: ITT efficacy 44%</p> <p>Inclusion: men 18 y or older with primary organic ED 3 mo or longer in duration, inability to achieve erection for intercourse on all attempts for 3 mo before study, stable, heterosexual, monogamous relationship, willing to have intercourse 4/mo + use contraception</p> <p>Exclusion: NR</p> <p>Data reported for IG vs. CG</p>	<p>Age, mean (range): 57.3 (25-78) y vs. 57.3 (26-77) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, (%): 51 vs. 54 (constrictive bands, IC, vacuum, counseling)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 59.6 (3-644) vs. 63.3 (4-417) mo</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: Vascular disease: 33% vs. 41% Diabetes 18% vs. 15% Surgery/trauma: 24% vs. 21% Other organic (includes; alcohol or tobacco use; neurological diseases; medication adverse reaction): 24% vs. 24%</p> <p>Mixed ED: NR</p>	<p>IG1: Alprostadil (PgE1) transurethral pellet as per protocol CG: Placebo</p> <p>IG1: Dose: Escalating dose of 125, 250, 500 or 1000 µg Duration: 3 mo Frequency: at least 1/mo Compliance: 53 (68%)</p> <p>CG: Dose: Placebo Duration: 3 mo Frequency: as IG 1/mo Compliance: 64 (79%)</p> <p>Run In period: 3 mo Wash out period: NA</p> <p>F/u duration: 3 mo</p> <p>Other: Final patient selected dose distribution (µg), n (%): 1000 µg =103 (65%) 500 µg= 27 (17%) 250 µg =21 (13%) 125 µg =5 (5%)</p>	<p>Primary outcome results: EAS, score ≥ 4: in all pts, 159 (64%) Intercourse ≥ once during 3 mo, n (%): 46(69) vs. 8/73 (11%), p<0.001 Intercourse/ total injections: 390/ 763 (51) vs. 46/611 (7.5) CG</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 42 (26%) [n=25 vs. n=17]</p> <p>WDAE: 4 TAE: self reported AEs, n (%): Urogenital pain/ burning: 5 (6) vs. 0 Penile pain: 4 (5) vs. 1 (1) Testicular pain: 2 (3) vs. 0 Urethral bleeding/spotting: 1 (1) vs. 1 (1) Urinary tract infection: 0 vs. 0 Prolonged erection < 5 hr: 1 (1) two events vs. 0 Priapism (≥ 6 hr)= fibrosis= hypotension: 0 vs. 0 Dizziness: 2 (3) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: Erectile Assessment Scale (1=no response to 5=rigid erection) Comfort with therapy, intercourse rate, and AE by diary/self report</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C8-Topical Treatments of ED

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Cavallini (1991) 213</p> <p>Funding source: NR</p>	<p>N screened = 51 N randomized = 33 (crossover design)</p> <p>IG1/IG2/CG = 33 (random order in each session)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: chief complaint of impotence</p> <p>Exclusion: psychogenic impotence; uncontrolled diabetes; thyroid, renal or hepatic disease; recent myocardial infarction; hypotension; use of organic nitrates or nitrites or of minoxidil within previous 4 mo</p>	<p>Age, mean (range): 58, 42–68) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: DM 12 (36.4); arteriosclerosis 9 (27.3); hypertension 4 (12.1; pelvic fracture or surgery 6 (18.2); SCI 1 (3), multiple sclerosis 1 (1)</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 33</p> <p>Mixed ED: 0</p> <p>Other: NA</p>	<p>IG1: 10% topical Nitroglycerin paste IG2: 2% minoxidil topically to glans penis CG: placebo (lubricating gel) topically to glans penis</p> <p>IG1: Dose: 2.5 g Duration: NR Frequency: once/wk; applied to shaft Compliance (%): 100%</p> <p>IG2: Dose: 1 mL Duration: NR Frequency: one/wk applied to glans Compliance (%): 100%</p> <p>CG: Dose: 2.5 g Duration: NR Frequency: as IG2 Compliance (%): 100%</p> <p>Run In period: NR</p> <p>Wash out period: 1 wk</p> <p>F/u duration: outcomes were measured one hr post dosing each; trail duration 3 wks</p>	<p>Primary outcome results: Change in circumference of base of penis and in rigidity over baseline values, assessed a few minutes after drug application</p> <p>Circumference (mm), mean (sd): IG1: 9.5 (5.3) IG2: 17.2 (7.5) CG: 4.3 (4.0)</p> <p>Rigidity, mean % (sd); range: IG1: 28.2 (11.1), range 0–80% IG2: 40.0 (13.3), range 0–85% CG: 13.6 (10.7), range 0–18%</p> <p>Other outcomes assessed: Examination of cavernous penile artery flow with Doppler sonography</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE, n: pts with AE 17 (51.5); nitroglycerine 15 (45.5) vs. minoxidil 2 (6.1) vs. 0 Burning pain at application site, headache, hypotension SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Cavallini (1994) 214</p> <p>Funding source:</p>	<p>N screened = NR N randomized = 132 cross over trial (data reported for n=116 completers)</p> <p>IG1, n = 39 IG2, n = 39 IG3, n = 38 CG, n = NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: pts with ED</p> <p>Exclusion: psychogenic, endocrine or pharmacological impotence, recent MI, hypotension, uncontrolled diabetes, liver or kidney disease, use of organic nitrates, nitrates or minoxidil in the previous 4 mo</p>	<p>Age, mean (range): 58 (42-71) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: at least 6 mo</p> <p>Underlying disease, n (%): diabetic neuropathy 11 (9.5); SCI 3 (2.6); pelvic fracture 6 (5.2), pelvic surgery 12 (10.3); diabetic angiopathy 18 (15.5); atherosclerosis 27 (23.3); hypertension 16 (13.8); DM 10 (8.6)</p> <p>Psychogenic ED: None</p> <p>Physiologic ED: Neurogenic (n=34), arterial (n=61)</p> <p>Mixed ED n=12</p>	<p>IG1: minoxidil – nitroglycerine - placebo IG2: nitroglycerine – placebo - minoxidil IG3: placebo – minoxidil - nitroglycerine</p> <p>IG1: minoxidil (2%) Dose: 1 ml Duration: 2 mo Frequency: twice/ d Compliance (%): NR</p> <p>IG2: nitroglycerine (10%) Dose: 2.5 g Duration: 2 mo Frequency: twice/ d Compliance (%): NR</p> <p>CG: placebo Dose: 2.5 g Duration: 2 mo Frequency: twice/ d Compliance (%): NR</p> <p>Run In period: Wash out period:</p> <p>F/u duration: 6 mo</p>	<p>Primary outcome results: N (%) pts with positive response (prompt erection, absence of penis flexure during intercourse, maintaining full erection until ejaculation): 51 (44) vs. 24 (20.7) vs. 2 (1.7%), p < 0.01 (IG1 vs. IG2 and IG2 vs. CG)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 16 (13.8)</p> <p>WDAE NR TAE, n (%): pts (IG1 vs. IG2 and IG2 vs. CG) = 7 (6.0) vs. 52 (44.8) vs. 0, p < 0.01 (IG1 vs. IG2 and IG2 vs. CG), p < 0.05 (IG1 vs. CG) SAE: NR</p> <p>Ascertainment of outcomes assessed: Questionnaire</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Claes (1992) ²¹⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 50 (cross over)</p> <p>IG/ CG, n = 50 (random order of active tx or placebo)</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: men with ED (defined as having erections insufficient in rigidity/ or duration for penetration during intercourse)</p> <p>Exclusion: hx of MI; hypotension, use of organic nitrates within previous 6 mo</p>	<p>Age, mean (range): 56 (</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant Medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Physiologic ED: NR</p> <p>Psychogenic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Nitroglycerine (Deponit (TM)) delivered by transdermal therapeutic system CG: placebo</p> <p>IG: Dose: 10 mg Duration: 24 hr/ dose: 3 night Frequency: 3/dose (active or placebo) Compliance (%):</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance (%):</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Excluded from analysis Rigidity >70% (normal): n=4 (9.8%) No erection, <70% rigidity: n=7 (17.1%);</p> <p>Change in rigidity from baseline, n (%); mean% (sd), range, IG:</p> <p>Base ▲ in n= 21 (51.2); 14 (3), 1-21% ▼ in n= 6 (14.6); 6 (2), 1-11 No change in n = 3 (7.3)</p> <p>Tip ▲: n=23 (56.1); 17 (4), 1-27% ▼: n=5 (12.2); 8 (3), 1-14% No change n = 2 (4.9)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 9 (51.2)</p> <p>WDAE: 4 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan ambulatory unit in laboratory (pts were evaluated at baseline with IC injection of papaverine 40-80 mg)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Diamond (2004) 216</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 24</p> <p>IG/ CG, n= 24 (3 way cross over, two active tx of high or low dose, and placebo)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18 or older, diagnosis of ED, treated successfully with Viagra within 6mo, current users of Viagra</p> <p>Exclusion: ED caused by untreated endocrine disease, penile anatomic deformations, prostatic disorders, evidence of clinically sign. hepatic, renal, cardiovascular, psychiatric or CNS disease (stroke or SCI)</p>	<p>Age, mean (se): 50.9 (8.1); range 38-64</p> <p>Race, n (%): White 16 (66.7) Black 6 (25.0) Hispanic 1 (4.2) Other 1 (4.2)</p> <p>Co-morbidities, n (%): DM 2 (8); hypertension 4 (17); hyperlipidemia 3 (13)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: N 14 (59)</p> <p>Body weight, mean (se): 89.1 (15.2) Range 61.3-120.8</p>	<p>Concomitant medications: viagra (all pts)</p> <p>Duration of ED, mean: 6.2 y</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1/2: cyclic heptapeptide melanocortin analog PT-141) delivered intranasally in 2 doses or placebo CG: placebo</p> <p>IG1/2: Dose: 7 (IG1) or 20 mg (IG2) Duration: 12 hrs Frequency: 3 times Compliance (%): 100</p> <p>CG: Dose: NA Duration: 12 hrs Frequency: 1x Compliance (%): 100</p> <p>Run In period: NA Wash out period: NA</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Duration of erection (min) with rigidity \geq 60%:</p> <p>Base, mean (se): 26.0 (5.52) vs. 53.8 (8.54) vs. 18.5 (3.72)</p> <p>Tip, mean: 6.3 vs. 23.8 vs. 7.2</p> <p>List (narrative) other outcomes assessed: plasma concentrations of study drug (ng/ml), mean: IG1=38.8; IG2 = 122.1</p> <p>Withdrawals/drop-outs/loss to f/u [N and or %]: 0</p> <p>WDAE (N and/or %): 0 TAE, n (%): AE in 5% or more of pts, 7 mg vs. 20 mg vs. placebo: 9 (37.5) vs. 8 (33.3) vs. 3 (12.5); including: Nausea = 1 (4.2) vs. 4 (16.7) vs. 0 Headache = 1 (4.2) vs. 0 vs. 0 Feeling hot = 2 (8.3) vs. 0 vs. 1 (4.2) Somnolence = 1 (4.2) vs. 0 vs. 1 (4.2) Flushing = 4 (16.7) vs. 4 (16.7) vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan, blood tests, physical exam</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Foldvari (1998) 217</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 5 in crossover design</p> <p>IG1/IG2/IG3/CG, n= 5</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED caused by vascular impairment; and previous response to 10 or 20 µg PgE₁ IC; with no venous leak</p> <p>Exclusion: NR</p> <p>Note: this study compared the in vitro transdermal absorption of PgE₁ to in vivo efficacy of the medication in ED pts</p>	<p>Age, range: 54-70 y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: all pts PgE₁ IC, 10-20 µg</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: Vascular 5 (100%)</p> <p>Mixed ED: NR</p>	<p>IG1: topical PgE₁ + placebo IG2: PgE₁ + calcium thioglycolate+ placebo IG3: PgE₁ + methyl-salicylate+ placebo CG: placebo</p> <p>IG1-3: Dose: PgE₁=1.5 g (all grps); Calcium thioglycolate= 1% (IG2); Methyl-salicylate=2% (IG3) Duration: NR Frequency: single dose/ intervention Compliance (%): 100%</p> <p>CG: Dose:1.5 g soy phosphatidylcholine 15% Duration: NA Frequency: as IG Compliance (%): 100%</p> <p>Run In period: NR Wash out period: at least 1 wk</p> <p>F/u duration: 45 min post dosing</p>	<p>Primary outcome results: Quality of erection: no dose reached threshold for erection.</p> <p>PSV (cm/s) at 0 min vs. 45 min, mean (sd): IG1 = 0 vs.12.3 (1.1) IG2 = 5.5 (2.6) vs. 1.3 (0.8) IG3 = 0 vs. 14.2 (4.4) CG = 2.0 (1.9) vs. 7.7 (6.8)</p> <p>Max peak flow Velocity: IG3 =32 cm/s</p> <p>Other outcomes assessed: Steady State Flux (mg/cm²/ hr) of PgE₁: IG3 (0.191) > b (0.083) > IG2 (0.010) > CG Permeability coefficient (cm/hr x 10⁻⁴) (i.e. rate + extent of penetration): IG3 (3.82) > IG1 (1.66) > CG (0.84) > IG2 (0.10); Total amount of PgE₁ absorbed: IG3 = 3.5 µg (microgram)/cm²</p> <p>Withdrawals/drop-outs/loss to f/u: IG1 1 vs. IG2 2 vs. IG3 0 vs. CG 2</p> <p>WDAE: NR TAE: 0 SAE: NR</p> <p>Ascertainment of outcomes assessed: Peak Systolic Flow Velocity (arterial) by Duplex color Doppler: every 15 min for1 hr at 60 degree angle Normal at > 25 cm/s</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Goldstein (2001) 218</p> <p>Funding source: MacroChem Co. sponsor for study drug. Some authors supported by MacroChem Co., Pfizer, Bayer, TAP, Zonagen and Schering Plough</p>	<p>N screened = 62 N randomized = 60</p> <p>IG, n = 30 CG, n = 32</p> <p>ITT analysis used for primary outcome: yes (n=60)</p> <p>Inclusion: male 21 or older; with ED of 6 mo or longer (decrease or absent of morning erection)</p> <p>Exclusion: Previously enrolled in a Topiglan study; untreated endocrine or Peyronie's disease; radical prostatectomy; CAD; hypertension</p> <p>(Screening exclusion criteria: Placebo+ Erotic movie at 30 min from onset + vibrator at 45 min and then discontinued at 60 min. If erectile response \geq 70 degree angle or grade 3 as rated by pts were withdrawn)</p>	<p>Age, range: 24-78 yr</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: all Oral (Sildenafil); PgE1 in IC or IU route or PgE1 + papaverine + phentolamine IC or papaverine + phentolamine IC tx</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED, %: Vascular: 97%</p> <p>Mixed ED: NR</p>	<p>IG1: Topiglan 1% (PgE1 formula)+ VS. + vibration CG: Placebo +VS + vibration</p> <p>IG: Dose: 0.25 ml Duration: Single Frequency: once Compliance: 100%</p> <p>CG: Dose: 0.25 ml (formulation similar to Topiglan without PgE1) Duration: Single Frequency: 2 Compliance: 100%</p> <p>Run In period: 7 d Wash out period: NA</p> <p>F/u duration: 2 wks (VS and vibration stopped at 60 min post dosing, outcome measured at 90 min post dosing)</p>	<p>Primary outcome results: Erection rigidity measured by angle of erection: IG1 vs. CG 44.5° (3.8)° vs. 33.5° (3.4)° (p= 0.033)</p> <p>Mean change of angle from baseline: 24.2° vs. 13.5° (p= 0.039)</p> <p>Rigidity as per Investigator assessment: Overall IG1 vs. CG: p= 0.003</p> <p>Erection sufficient for vaginal penetration, n (%): 12 (38) vs. 2 (6.9), p =0.005</p> <p>No tumescence, n (%): 3 (9.7) vs. 8 (27.6)</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 2 (3.2)</p> <p>WDAE: 0 TAE: 3 vs. 0 Conjunctivitis: 2 vs. 0 Hypotension: 1 vs. 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: Penile angle: measured by placing a protractor next to penis in standing position. Measure of angle at vertical axis; erection rigidity scale investigator assessed at 15-90 min (1-5)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gomaa (1996) 219</p> <p>Funding source: no additional funding; no conflict of interest</p>	<p>N screened = NR N randomized = 36</p> <p>ITT analysis used for primary outcome: NR</p> <p>IG, n= 36 CG, n= 36</p> <p>Inclusion: Pts whose chief complaint was ED aged 31-65 y</p> <p>Exclusion: Pts with hypotension or glaucoma</p>	<p>Age, median (range): 48 (31-65) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR Body weight: NR</p> <p>Other: mean arterial flow = IG1: 0.06 (0.02) vs. CG: 0.06 (0.02)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, median (range): 39 (5-72) mo</p> <p>Underlying disease: DM, hypertension, anxiety, depression, and surgery</p> <p>Psychogenic ED, n (%): 9 (25)</p> <p>Physiologic ED, n (%): 8 (22.2) (neurogenic), 7 (19.4) (arterial insufficiency)</p> <p>Mixed ED, n (%): 8 (22.2)</p>	<p>IG: Topical cream CG: Placebo cream</p> <p>IG: Topical cream (3% aminophylline, 0.25% isosorbide dinitrate, 0.05% co-dergocrine mesylate) Dose: 2 g/d Duration: 7 d Frequency: once Compliance (%): NR</p> <p>CG: Placebo (lubricating gel) Dose: 2 g/d Duration: 7 d Frequency: once Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (both on and off treatment): 7 d</p>	<p>Primary outcome results: IG vs. CG Mean arterial flow: 0.25 (0.1) vs. 0.08 (0.07), p (between-arm) = NR, p (within-arm for IG1) < 0.001 and p (within-arm for CG) > 0.05.</p> <p>Erection sufficient for successful intercourse, n: 21 vs. 3, p < 0.001 Partial erection, n: 2 vs. 0, p = NR No response, n: 11 vs. 33, p = NR</p> <p>(3/9 pts with Psychogenic impotence reported improvement with both creams)</p> <p>Other outcomes assessed: erection outcome reported for three etiology type</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR TAE: No prolonged erection, priapism, CVD, headache SAE: NR</p> <p>Ascertainment of outcomes assessed: penile tumescence and arterial flow in laboratory measures; other outcomes from pts diary</p> <p>Other: the active cream was most effective in pts with psychogenic and neurogenic ED</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gramkow (1999) 220</p> <p>Funding source: The Bryde Nielson Foundation</p>	<p>N screened = NR N randomized = 19 (cross-over design with 2 part study A, B)</p> <p>Laboratory study: IG/ ICG, n = 19</p> <p>Home study: IG/ ICG, n = 18</p> <p>ITT analysis used for primary outcome: no</p> <p>Inclusion: unable to complete intercourse, some erectile response to IC injection of 30 mg papaverine, with penile-brachial index > 60%</p> <p>Exclusion: Arterial hypotension, arterial insufficiency < 60 %, former coronary occlusion, hypersensitivity to nitroglycerine, used any kind of drug containing nitroglycerine within last 2 mo.</p>	<p>Age, median (range): 56 (39-5-65) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): cancer (rectum, bladder), peyroni plaque, slipped disc, multiple sclerosis, chronic prostatitis</p> <p>Previous ED treatment: IC injection of 30 mg papaverine</p> <p>Smoking status, n (%): smokers 7 (39)</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: various medication</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: no specific cause reported</p> <p>Psychogenic ED: 12</p> <p>Physiologic ED: 5</p> <p>Mixed ED: 1</p> <p>Other: N/A</p>	<p>IG: nitroglycerine plasters, topical absorption +VS CG: placebo of nitroglycerine plasters, topical absorption+ VS</p> <p>IG: Dose: 10 mg Duration: lab period 2 hr/session; home period varied in each pts Frequency: lab study: twice (1/d); home study 6 times Compliance (%): lab 100%; home study 94.4% used all plasters</p> <p>CG: Dose: 10 mg Duration: as IG Frequency: as IG Compliance (%): lab 100%; home study: 66.7% used all plasters</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: <i>Laboratory period</i> Penile rigidity: (only figure provided within text but N of patients in each % range category clear) No effect: 11 vs. 12 Poor effect: 1 vs. 1 Moderate effect: 3 vs. 3 Good effect: 2 vs. 0 Excellent effect: 1 vs. 2 No sign tx effect found in IG vs. CG p=0.7656</p> <p><i>Home period</i> Median score (scale 1-3), median range: 1-2 vs. 1-2.5</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u: 1 (5.3) RigiScan data could not be collected during lab test</p> <p>WDAE: 1 vs. 0 (severe pain with plaster) TAE: IG: headache 35 cases; 23 cases of smarting pain at the application site SAE: NR</p> <p>Ascertainment of outcomes assessed: Laboratory study: RigiScan monitoring; home study: questionnaire (3 item point Scale; 1= no effect; 3= good effect)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Le Roux (1999) 221</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 14</p> <p>IG, /CG, n = 14</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: pts with erectile failure who previously responded to IC injections</p> <p>Exclusion: NR</p>	<p>Age, mean (range): 44 (23-57) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: all had tx with IC injection 14 (100%)</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n: pelvic fracture (n=1), spinal paraplegia from tuberculosis (n=1), spinal myelopathy of unknown aetiology (n=1), vasculogenic impotence (n=1)</p> <p>Psychogenic ED, n (%): 10 (71.4)</p> <p>Physiologic ED, n (%): 4 (28.6)</p> <p>Mixed ED: NR</p>	<p>IG: vasoactive cream (aminophylline, co-dergocrine mesylate, isosorbide dinitrate) CG: placebo (gel)</p> <p>IG1: Dose: 2 mL syringes (aminophylline 3%, co-dergocrine mesylate 0.05%, isosorbide dinitrate 0.25%); total applications =77 Duration: NR Frequency: 8 application with each cream used alternatively Compliance (%): NR</p> <p>CG: Dose: NA Duration: NR Frequency: as IG; total applications =76 Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 wks</p>	<p>Primary outcome results: Penile response 77 vs. 76 applications in n=8: Erection adequate for intercourse: 3 (3.9) vs. 4 (5.3) [all in one pt] Partial response: 13 (16.9) vs. 13 (17.1) No response: 61 (79.2) vs. 59 (77.6)</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 6 (43%) did not complete the trial</p> <p>WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: Penile response by grading system (good, partial, no response) by pts diary</p>

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<p>Padma-Nathan (2002) ²²²</p> <p>Study a</p> <p>Funding source: NedMex Inc.</p>	<p>N screened = NR N randomized = 161</p> <p>IG1, n = 42 IG2, n = 39 IG3, n = 40 CG, n = 40</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: ED \geq 3mo, monogamous & stable relationship with consenting female partner, mild-moderate ED classified by IIEF-EF domain (score 14-21)</p> <p>Exclusion: ED caused by untreated endocrine disease, clinically sign. renal or hepatic disease, use of prescribed or over the counter medication, supplements, or devices for ED</p>	<p>Age, mean (sd): 56.5 (7.1), range 21-65 y</p> <p>Race, %: IG vs. CG White 86 vs. 75; African-American 7.3 vs. 10; Asian 0 vs. 2.5; Hispanic 5.8 vs. 12.5; Other 2.6 vs. 0</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 93.4 (37.3) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 95% of pts had ED for longer than 1 y; 5% under 1 y</p> <p>Underlying disease, %: CVD 54.3%; DM 15.7%</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NR</p>	<p>IG1-3: Topical alprostadil cream CG: Placebo cream</p> <p>IG1: Dose: IG1= 0.05 mg, IG2= 0.1mg, IG3= 0.2 mg Duration: 6 wks Frequency: 3 application in 3 wks Compliance (%): 100</p> <p>CG: Dose: NA Duration: 6 wks Frequency: as IG Compliance (%): 100</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 wks</p>	<p>Primary outcome results: IIEF- EF, change from baseline, mean (sd): IG: 1.8 (1.1) vs. 0.7 (1.2) vs. 3.7 (1.2) CG: -0.8 (1.1) Total IIEF score, change from baseline, mean (sd): IG: 4.7 (2.3) vs. 1.4 (2.4) vs. 7.2 (2.5) CG: -1.7 (2.2)</p> <p>SEP-Q3/Q1 (penetration success rate), mean (sd): IG: 69.4 (34.2) vs. 69.1 (39.3) vs. 82.9 (24.6) CG: 55.3 (40.0)</p> <p>GAQ, % improved: IG: 80% vs. 70% vs. 93% CG: 54%</p> <p>Other outcomes assessed: Other IIEF domains</p> <p>Withdrawals/drop-outs/loss to f/u: IG 22 (18.2) vs. CG 0</p> <p>WDAE, n (%): IG 6 (14.3) vs. 7 (17.9) vs. 9 (22.5), CG 0 (urogenital pain) TAE, n (%): IG 28 (66.7) vs. 26 (66.7) vs. 31 (77.5), CG 21 (52.5) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, GAQ, SEP</p>

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<p>Padma-Nathan (2002) ²²²</p> <p>Study b</p> <p>Funding source: NedMex Inc.</p>	<p>N screened = NR N randomized = 142</p> <p>IG1, n = 37 IG2, n = 35 IG3, n = 35 CG, n = 35</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: ED \geq 3mo, monogomous & stable relationship with consenting female partner, severe ED classified by IIEF EF Domain score (score < 14)</p> <p>Exclusion: ED caused by untreated endocrine disease, clinically sign. renal or hepatic disease, use of prescribed or over the counter medication, supplements, or devices for ED</p>	<p>Age, mean (sd): 55.6 (8.0), range: 21-70 y</p> <p>Race (% by respective grp): Caucasian 88.8%; African-American 4.3%; Asian 0.7% (only in IG2); Hispanic 4.8%; Other 2.1%</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 92.6 (36.8) kg</p> <p>Other: IIEF-EF, mean (sd): IG 6.7 (3.6); CG 7.8 (3.5)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (% by respective grp): .25 -1 yr 7.25%; > 1 y 92.75%</p> <p>Underlying disease, %: CVD 58.25% (slightly lower in IG1); DM 50.75 (slightly higher in IG1)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NR</p>	<p>IG1-3: Topical alprostadil cream CG: Placebo cream</p> <p>IG1: Dose: IG1= 0.1 mg, IG2= 0.2mg, IG3= 0.3 mg Duration: 6 wks Frequency: 3 application /3 wk Compliance (%): 100</p> <p>CG: Dose: NA Duration: 6 wks Frequency: as IG Compliance (%): 100</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 wks</p>	<p>Primary outcome results: Data reported for IG n=34, 29, 29; CG n=35 IIEF, change from baseline, mean (sd) EF domain IG: 6.29 (1.38) vs. 6.49 (1.48) CG: 2.67 (1.34) Total IIEF score: IG: 11.47 (2.74) vs. 12.96 (2.96) vs. 17.65 (2.92); CG: 6.24 (2.67)</p> <p>SEP-Q3/Q1 (penetration success rate), mean (sd): IG: 32.3 (18.0) vs. 36.2 (29.3) vs. 38.6 (22.8); CG: 15.6 (17.2)</p> <p>GAQ, % improved: IG: 59% vs. 76% vs. 83%; CG 26%</p> <p>Other outcomes assessed: Other IIEF domain scores</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): IG 15 (14) vs. CG 0</p> <p>WDAE, n (%): IG 1 (3) vs. 7 (20) vs. 8 (23); CG 0 TAE, n (%): IG 11 (30) vs. 21 (60) vs. 18 (51); CG 4 (11) SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF, SEP, GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Padma-Nathan (2006) ²²³</p> <p>Funding source: NexMed (study drug supply); co-author a paid consultant of NexMed</p>	<p>N screened = N randomized = 1732</p> <p>IG1, n = 434 IG2, n = 430 IG3, n = 434 CG, n = 434</p> <p>ITT analysis used for primary outcome: yes (pts with at least one study medication)</p> <p>Inclusion: men at least 21 y, in a stable relationship, and hx of ED of at least 3 mo in duration</p> <p>Exclusion: ED due to untreated endocrine disease or sing penile pathology (i.e. penile fibrosis, Peyronie disease)</p>	<p>Age, mean (se): 61 (0.47) y</p> <p>Race: White 86%; Black 8.3%; Hispanic 3.9%; other 1.8%</p> <p>Co-morbidities, n (%): DM 305 (17.6); cardiac 503 (29); prostatectomy 220 (12.7) slightly higher in IG1; hypertension 783 (45.2)</p> <p>Previous ED treatment: sildenafil [failures 352 (18.8)]</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1-3: Alprostadil topical cream CG: Placebo cream</p> <p>IG1-3: Dose: IG1=100 µg, IG2 = 200 µg, IG3=300 µg Duration: 12 wks Frequency: up to 24 applications (2/wk) Compliance: NR</p> <p>CG: Dose: Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks drug free Wash out period:</p> <p>F/u duration: 16 wks</p>	<p>Primary outcome results: IIEF-EF, LS mean change from baseline (se): IG: 1.6 (0.34) vs. 2.5 (0.34) vs. 2.4 (0.34), CG -0.7 (0.34) SEP, LS mean % change form baseline (se): SEP-2: IG 2.9 (1.63) vs. 5.1 (1.65) vs. 7.2 (1.65), CG -4.5 (1.65) SEP-3: IG 7.0 (1.61) vs. 13.8 (1.63) vs. 9.1 (1.63), CG 0.4 (1.64) GAQ, % improved: IG 40% vs. 47% vs. 52%, CG 20%</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%):</p> <p>WDAE, n (%): 46 (2.7) TAE, n (%): 198 (45.6) vs. 267 (62.1) vs. 292 (67.3) vs. CG 54 (12.4) Body as whole: IG 5 (1.2) vs. 1 (0.2) vs. 0 CG 1 (0.2); nervous system IG 5 (1.2) vs. 7 (1.6) vs. 11 (1.2), CG 1 (0.2) Skin rash: IG 2 (0.5) vs. 5 (1.2) vs. 2 (0.5) CG 1 (0.2); urogenital system: IG 186 (42.9) vs. 254 (59.1) vs. 279 (64.9) CG 51 (10.6) SAE, n (%): IG 0, CG 1 (0.2) died due to cardiac arrest</p> <p>Ascertainment of outcomes assessed: IIEF-EF; SEP; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Steidle (2002) 224</p> <p>Funding source: NexMed manufacturer of Alprostadil topical</p>	<p>N screened = 303 N randomized = 265 from 2 Phase II RCT, 12 settings</p> <p>IG1, n = 36 IG2, n = 66 IG3, n = 61 IG4, n = 29 CC, n = 73</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 21-75 y, with diagnosed ED of at least 3 mo in duration, and IIEF score of 21 or less</p> <p>Exclusion: NR</p>	<p>Age, mean (sd): 82.1 (7.4) y</p> <p>Race (%): White: 84.7; African American: 6.5; Asian 0.6; Native American 1.9; Hispanic 6.6; Other 1.2</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 92.5 (38) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): 0.25 -1 yr: 7 % >1yr: 93 %</p> <p>Underlying disease, %: CVA 56.8; DM 37%</p> <p>Psychogenic ED, n (%): IG 48 (25) vs. CG 18 (25)</p> <p>Physiologic ED, n (%): IG 72 (37.5) vs. CG 28 (38)</p> <p>Mixed ED, n (%): IG 72 (37.5) vs. CG 27 (37)</p> <p>Other: Mean IIEF-EF domain, mean (sd): 12 (4.8)</p>	<p>IG1-4: Alprostadil (PgE₁) topical CG: Placebo</p> <p>IG1-4: Dose: 0.1ml IG1=50 µg IG2=100 µg IG3=200 µg IG4=300 µg Duration: 6 wks Frequency: 10 doses Compliance (%): NR</p> <p>CG: Dose: 0.1 ml placebo Duration: 6 wks Frequency: as IG Compliance (%): NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (both on and off treatment): 6 wks</p>	<p>Primary outcome results: IIEF-EF change from baseline, mean (sd): 3.36 (1.3), 3.40 (0.88, 5.34 (0.92), 9.44 (1.43) vs. 0.98 (0.84)</p> <p>GAQ, % improved: IG1 p= 0.028, IG2 p= 0.007, IG3 p< 0.001 or IG4 p<0.001 vs. CG</p> <p>SEP-Q3, %: 59.4 (6.3), 53.4 (4.4), 62.6 (4.5), 66.8 (7.1) vs. 42.6 (4.2)</p> <p>Other outcomes assessed: self evaluation of erection; SEP Q3/Q4</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): IG 0, 2 (3), 2 (3), 6 (21) vs. CG 3 (4); all IG 10 (5.2) vs. CG 3 (4.1)</p> <p>WDAE, n (%): IG 6 (14), 8 (11), 16 (21), 7 (20) vs. CG 1 (1)</p> <p>TAE, n (%): reported only if ≥ 3% (n) 214</p> <p>SAE: Near Syncopal episode for approximately 10 minutes: 1(1.3%) in IG3</p> <p>Ascertainment of outcomes assessed: IIEF-EF; GAQ; SEP Patient self-evaluation of erection (PSAE), score 1-5</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Yonessi, M (2005) ²²⁵</p> <p>Funding source: research council of Mazandaran University of Medical Sciences, Sari, Iran</p>	<p>N screened = 94 N randomized = 80</p> <p>IG1, n = 40 CG, n = 40</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED</p> <p>Exclusion: anatomical defects of penis or other sexual disorders; spinal cord injury; major psychiatric disorder; poorly controlled diabetes; stroke; heart attack within 6 mo; treatment with organic nitrate; active peptic ulcer disease; migraine; vision disorders; allergic rhinitis</p>	<p>Age, mean (range): 47.2 (26-63) vs. 50.8 (37-65) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, mean (range): 1.4 (0.6-2.8) vs. 1.5 (0.6-3.0)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: 23 (57) vs. 24 (60)</p> <p>Physiologic ED: 17 (42) vs. 16 (40)</p> <p>Mixed ED: 0</p>	<p>IG: 1% sildenafil topically to glans penis + placebo tablet CG: placebo topically to glans penis + sildenafil tablet</p> <p>IG1: Dose: 0.5 g 1% sildenafil gel + placebo tablet Duration: NR Frequency: NR Compliance (%): 100%</p> <p>CG: Dose: 100 mg oral sildenafil and placebo gel Duration: NR Frequency: NR Compliance (%): 100%</p> <p>Run In period: NR</p> <p>Wash out period: NA</p> <p>F/u duration: up to 2 wk</p> <p>Other: tablets were taken 1 hr before sexual activity</p>	<p>Primary outcome (EF): Erection (complete, moderate, none) and onset of erection, n (%):</p> <p>Full erection: 5 (12.5) vs. 28 (70.0) Moderate erection: 5 (12.5) vs. 6 (15.0) None: 6 (15) vs. 30 (75.0)</p> <p>Onset of erection (full E), mean (sd): IG1: 7.4 (3.6) vs. 37.8 (14.9) min</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE, n (%): 0 TAE, n (%): pts with AE, 4 (10) vs. 4 (8) including headache in IG, headache, dyspepsia, visual disturbances in CG SAE: 0</p> <p>Ascertainment of outcomes assessed: NR</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C9-Testosterone Treatment of ED

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Adel (2006) ²²⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 89</p> <p>IG, n = 45 CG, n = 44</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with 5 or more consecutive mo of ▼ libido and quality of sexual erections; 2 or more morning total T <300 ng/dl (plasma free T was not entry criterion); normal rectal examination; PSA <4 ng/ml; urine flow rate of 12 ml/s or greater</p> <p>Exclusion: generalized skin disease that could affect T absorption; body weight < 7% or above 140% of ideal weight; hx of alcohol or drug abuse; hypotension; primary hypogonadism</p>	<p>Age, mean (sd): 54 (12), range 35-65 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM, hypertension, anxiety and depression (no numeric data provided)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): various aetiologies (no specific cause)</p> <p>Psychogenic ED, n (%): 30 (33.7)</p> <p>Physiologic ED, n (%): 34 (38.2); vascular 18 (20.2), neurogenic 16 (18),</p> <p>Mixed ED, n (%): 25 (28.1)</p>	<p>IG: Testosterone cream CG: Placebo cream</p> <p>IG: Dose: 2 g cream containing testosterone 0.8%, isosorbide dinitrate 0.5% and co-dergocrine mesylate 0.06% Duration: 2 mo Frequency: 2/d on right upper arm shuoulder Compliance: NR</p> <p>CG: Dose: 2 g lubricating gel Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: Wash out period: at least 4 wks in pts with oral or injectable T tx</p> <p>F/u duration: 2 mo (fu every 15 d), last measure of RigiScan at 60 min post dosing</p>	<p>Primary outcome results: Result in bracket correspond to psychogenic, vasculogenic, neurogenic and mixed etiology sub-grps)</p> <p>RigiScan results, IG vs. CG: - Full erection: 18% vs. 0 [11, 1, 3, 3% vs. 0] - Partial erection: 53% vs. 6% [3, 5, 5, 4% vs. 2, 1, 2, 1%] - Tumescence: 3% vs. 2% [1, 0, 0, 2% vs. 1, 0, 1, 2%] - No response: 7% vs. 36% [1, 0, 0, 2% vs. 11, 8, 5, 12%] Pts diary results: - Full erection with successful intercourse: 40% vs. 0 - Partial erection insufficient for intercourse: 37% vs. 0 - Spontaneous erection: 38% vs. 0</p> <p>Other outcomes assessed: serum T concentration, sign increase with active cream compare to baseline and vs. CG</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): NR; skin irritation 1 (1) vs. 0; headache 11% vs. 0; no priapism SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: RigiScan post dosing in laboratory (5, 10, 15, 30, 60 min); pts diary every 15 d</p>

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<p>Aversa (2003) 227</p> <p>Funding source: Ministro dell'Universita e della Ricerca Scientifica e Tecnologica</p>	<p>N screened = 105 (reference sample) N randomized = 20</p> <p>IG, n = 10 CG, n = 10</p> <p>ITT analysis used for primary outcome: N</p> <p>Inclusion: arteriogenic ED (reduced PSV, but normal end systolic velocity) ED lasting 6 mo or longer. stable relationship, normal ECG, no hx of haematological or prostate dx, no antiandrogen drugs ingestion and response to Sildenafil scored as < 24 on the EF score of the IIEF; serum testosterone values between 10-13 nmol/l and serum free testosterone values between 200-300 pmol/l; no response to past T tx (100 mg) on 6 consecutive attempts</p> <p>Exclusion: pts with T levels in hypogonadal range (< 10 nmol/l)</p>	<p>Age, mean (sd): 54 (2) vs. 56 (4)</p> <p>Race (%): NR</p> <p>Co-morbidities, n: Systemic hypertension 3 vs. 4; DM type 2: 3 vs. 2; Cardiovascular disease: 3 vs. 2; Dyslipidaemia: 5 vs. 3</p> <p>Previous ED treatment: NR</p> <p>BMI, mean (sd): 23 (2) vs. 24 (2) kg/m²</p> <p>Smoking status, n: 6 vs. 6</p> <p>Body weight: NR</p>	<p>Concomitant medications: Pts using less than 2 medications, n 3 vs. 6; using more than 2 medications: 4 vs. 7</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: 20</p> <p>Mixed ED: NR</p> <p>Other: Measurement of flow parameters on cavernous arteries (Measured in morning after standardized pharmacostimulation using 10 µg PgE1 with option of additional re-dosing of 10 µg PgE1 + 1 mg phentolamine),</p>	<p>IG1: Testosterone (patch) + Viagra CG: placebo (patch) + Viagra</p> <p>IG: Dose: 5 mg testosterone + 100 mg Viagra Duration: 1 mo Frequency: patch (daily), Viagra as needed (max of 20 tablets) Compliance: 100%</p> <p>CG: Dose: placebo + 100 mg Viagra Duration: 1mo Frequency: placebo (daily), Viagra as needed (max of 20 tablets) Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 1 mo</p>	<p>Primary outcome results:IG vs. CG, mean (sd) IIEF-EF (>24) baseline: 14 (1) vs. 13 (1); post tx: 22 (2) vs. 14 (0.7)</p> <p>IIEF-intercourse satisfaction: (0-15), baseline: 7 (1) vs. 8 (2); post tx: post tx: 12 (2) vs. 8 (1) GAQ, (% yes): 80 vs. 10</p> <p>PSA, baseline: 1 (0.7) vs. 1 (0.8); post tx: 2 (1) vs. 1 (0.8)</p> <p>Free T (200-700 pmol/l, baseline: 251 (17) vs. 236 (22) vs. 473 (40) vs. 256 (19)</p> <p>Other outcomes assessed: Hormonal and biochemical outcomes; IIEF domains of SD, OF, OS; LH, total T</p> <p>Withdrawals/drop-outs/loss to f/u: 0</p> <p>WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Boyanov (2003) 228</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 48 (Open-label trial)</p> <p>IG, n = 24 CG, n = 24</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men aged 45-65 y, type 2 DM, and symptoms of mild androgen deficiency or ED; in a stable relationship; waist-hip ratio of 0.9 or greater; low testosterone levels (total testosterone < 15.1 nmol/l)</p> <p>Exclusion: concurrent dx other than DM, or surgical intervention likely to impair sexual function, amputation or chronic renal failure, ACE inhibitors' use, hx of alcoholism, prostate enlargement or abnormalities</p>	<p>Age, mean (sd): 58 (5) y</p> <p>Race (%): NR</p> <p>Co-morbidities, (%): peripheral or autonomic neuropathy or retinopathy (50%), CHD (17%), nephropathy (33%)</p> <p>Blood glucose, mean (sd): 10 (2) HbA1C</p> <p>Previous ED treatment: NR</p> <p>BMI, mean (sd): 31 (5) kg/m²</p> <p>Smoking status: NR</p> <p>Body weight: 94 (19) vs. 95 (20) kg</p>	<p>Concomitant medications: oral hypoglycaemic agents in 62.5% (metformin in 25%, metformin + sulphonylurea in 37.5%), insulin mono therapy 12.5%, hypoglycaemic agents + insulin 25% (metformin in 12.5%, sulphonylurea in 12.5%); ACE inhibitors in 35%</p> <p>Duration of ED: NR</p> <p>Underlying disease: diabetes, andropause</p> <p>Psychogenic ED: NR Physiologic ED: NR Mixed ED: NR</p> <p>Other: Mean duration DM = 6 (1-18) y</p>	<p>IG: Testosterone- oral CG: No treatment</p> <p>IG: Dose: 120 mg/d Duration: 3 mo Frequency: twice (80 and 40 mg)/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: NA Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 3 mo</p>	<p>Primary outcome results: IG vs. CG, mean (sd) IIEF (abridged 5-item version) score at Baseline: 2 (0.7) vs. 2.5 (0.8) 3 mo: 1.1 (0.9) vs. 2 (0.9), p < 0.05</p> <p>SBP (mmHg), mean (sd): Baseline: 122 (8) vs. 120 (8); Post tx: 120 (10) vs. 122 (8) mmHg</p> <p>DBP (mmHg), mean (sd): Baseline: 80 (4) vs. 76 (6) Post tx: 82 (4) vs. 76 (6) mmHg</p> <p>Total serum T (nmol/l), mean (sd): Baseline: 9.6 (2.3) vs. 10.8 (3) Post tx (10 hr post last drug administration): 15.5 (3.4) vs. 11.2 (3.2)</p> <p>Other outcomes assessed: body weight, BMI reduction (evident in IG), fasting blood glucose level (sign drop in IG); serum triglyceride levels (drop in both grps); symptoms of androgen deficiency (nervousness, weakness, insomnia, libido)</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF-5; SD by 4 point scale (0-3) questionnaires</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Boyanov (2003) 228</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 48 (Open-label trial)</p> <p>IG, n = 24 CG, n = 24</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men aged 45-65 y with DM type 2 and symptoms of mild androgen deficiency or ED, married or living in a stable relationship with a female sexual partner for 6 mo or longer, waist-hip ratio of 0.9 or more, T levels below the normal range of adults or in the lower third of this range (total T < 15.1 nmol/l)</p> <p>Exclusion: concurrent dx other than DM or surgical intervention likely to impair sexual function, amputation or chronic renal failure, ACE inhibitors' use, hx of alcoholism, prostate enlargement or abnormalities</p>	<p>Age, mean (sd): 58 (5) y</p> <p>Race (%): NR</p> <p>Co-morbidities: peripheral or autonomic neuropathy or retinopathy (50%), CHD (16.7%), nephropathy (33%)</p> <p>Blood glucose, mean (sd): 10 (2) HbA1C</p> <p>Previous ED treatment: NR</p> <p>BMI, mean (sd): 31 (5) kg/m²</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 94 (19) vs. 95 (20) kg</p>	<p>Concomitant medications: insulin therapy (12.5%), hypoglycaemic agents (25%), or ACE inhibitors only</p> <p>Duration of ED: NR</p> <p>Underlying disease: DM (mean duration = 6, range 1-18 y), andropause</p> <p>Psychogenic ED: NR Physiologic ED: NR Mixed ED: NR</p>	<p>IG: Testosterone- oral CG: No treatment</p> <p>IG: Testosterone (oral) Dose: 120 mg/d Duration: 3 mo Frequency: twice (80 and 40 mg)/d Compliance: NR</p> <p>CG: No treatment Dose: NA Duration: as IG Frequency: NA Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 3 mo</p>	<p>Primary outcome results: IG vs. CG, mean (sd): IIEF (abridged 5-item version) score at baseline: 2 (0.7) vs. 2.5 (0.8) 3 mo: 1.1 (0.9) vs. 2 (0.9), p < 0.05</p> <p>SBP (mmHg): Baseline: 122 (8) vs. 120 (8) 3 mo: 120 (10) vs. 122 (8)</p> <p>DBP (mmHg): Baseline: 80 (4) vs. 76 (6) 3 mo: 82 (4) vs. 76 (6)</p> <p>Total T (nmol/L): Baseline: 9.6 (2.3) vs. 10.8 (3) 3 mo: 15.5 (3.4) vs. 11 (3.2)</p> <p>Other outcomes assessed: insomnia, nervousness, weakness, libido, fasting blood glucose, total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, triglyceride</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF questionnaires, anthropometrical measures, routine blood biochemistry</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Cavallini (2004) 229</p> <p>Funding source: NR</p>	<p>N screened = 224 N randomized = 150 (n/ grp is not reported)</p> <p>N (total) completed = 130 IG1, n = 40 IG2, n = 45 CG, n = 45</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: pts > 60 yrs with symptoms of androgen decline: ▼ libido and erectile quality, depressed mood, irritability, fatigue, and free testosterone < 6 pg/ml</p> <p>Exclusion: lower urinary tract obstructive symptoms, prostate volume > 20 cm³, ▲ PSA level and/or prostate cancer, alcohol or cigarette consumption, < 6 mo after major surgery or MI, diabetes, untreated hypertension, CVD, neoplasm, ongoing psychological/pharmacological or antineoplastic therapy, ▲ PRL serum levels</p>	<p>Age, mean (range): 66 (60-74) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Body weight: NR</p> <p>Other: testosterone (nmol/l) =10 (2) vs. 11 (2) vs. 11 (2)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Testosterone undecanoate -oral IG2: Propionyl-L carnitine + acetyl -L-carnitine(carnitine)- IM CG: Placebo (starch)-oral</p> <p>IG1: Dose: 160 mg/d Duration: 6 mo Frequency: daily Compliance: NR</p> <p>IG2: Dose: 2 g/d Duration: 6 mo Frequency: daily Compliance: NR</p> <p>CG: Dose: 500 mg starch tablet Duration: 6 mo Frequency: daily Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: at 6 mo (immediately post tx), and 6 mo post end tx (12 mo)</p>	<p>Primary outcome results: IIEF-15 EF, median (range): Baseline= 8 (5-22); 6 mo= 16 (6-29) vs. 24 (8-29) vs. 9 (6-22), p < 0.01; 12 mo= 8 (5-22) Sexual intercourse satisfaction, median (range): baseline= 4 (2-7); 6 mo= 5 (3-10) vs. 6 (3-10) vs. 4 (3-5) PSA, mean (sd): 2 (1) vs. 2 (1) vs. 2 (1) ng/mL (not different from baseline)</p> <p>NPT (3-night full erection duration): baseline= 83 (19) min; 6 mo =120 (26) vs. 158 (28) vs. 88 (23) min; 12 mo 87 (21) vs. 85 (23) vs. 87 (19)</p> <p>Free T (pg/mL) mean (sd): baseline= </=5 (0.9); 6 mo= 23 (4) vs. 5 (1) vs. 4 (0.7); 12 mo= 10 (2) vs. 11 (2) vs. 10 (2), (IG1 vs. IG2, p=> 0.05)</p> <p>Other outcomes assessed: PSA, prostate volume, PSV, Total T, LH, EDV, resistive index (RI), IIEF domains of orgasm, SD, sexual well-being</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 20 (13) WDAE: 0 TAE, n (%): 3 (2); 2 mild epigastralgia, 1 mild headache SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF (Q15); nocturnal penile tumescence (NPT) by RigiScan</p>

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<p>Clopper (1993) 230</p> <p>Funding source: USPHS grant, NIH General Clinical Research Centre Grant, and fund from the Children's Growth Foundation</p>	<p>N screened = 11 N randomized = 9 (Blind crossover design)</p> <p>IG1, n = 3 IG2, n = 3 CG, n = 3</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Hypogonadal male subjects at least 15 y, and being treated for hypopituitarism.</p> <p>Exclusion: Non-hypogonadal men and younger than 15 yrs.</p>	<p>Age, mean (range); 18 (16.2-20.9) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment; n (%): 7 (78), T enanthate tx (50 –400 mg/mo)</p> <p>Smoking status: NR</p> <p>Body weight mean (range): 66 (51-113) kg</p>	<p>Concomitant medications: None</p> <p>Duration of ED: NR</p> <p>Underlying disease: Previous pituitary tumours.</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Testosterone IM IG2: Gonadotropin IM CG: Placebo IM</p> <p>IG1: Dose: 2000 units human chorionic gonadotropin (1cc IM) Duration: 6mo Frequency: 1/2 wks (5 injections of saline to maintain 3 times/ wk) Compliance: 100 %</p> <p>IG2: Dose: 1cc IM injection Duration: 6 mo Frequency: 3 times/wk Compliance: 100%</p> <p>CG: Dose: 1cc IM injection Duration: 2 mo Frequency: 3 x per wk Compliance (%): (100)</p> <p>Run In period: 4 wks Wash out period: min 4 wks (mean 6.7wks)</p> <p>F/u duration (on and off treatment): NR</p> <p>Other: Min of 6mo on either treatment and then placebo for 2mo</p>	<p>Primary outcome results: Weekly frequency, mean (sd): Erection, wkly frequency: baseline =4 (3); Post tx: 8 (6) vs. 8 (7) vs. 5 (3)</p> <p>% of sleep with erection: Baseline = 0.3 (0.1); Post tx: 0.6 (0.2) vs. 0.6 (0.2) vs. 0.4 (0.2) % Time erection with max circumference: baseline= 0.6 (0.04); Post tx: 0.3 (0.1) vs. 0.2 (0.2) vs. 0.1 (0.05) # of erections per night: Baseline =7 (2); Post tx: 6 (2) vs. 6 (3) vs. 7 (3) Coitus, mean #/ wk (sd): Baseline =1.4 (1); Post tx: 0.9 (1) vs. 0.8 (1) Plasma T (ng/dl): baseline =23 (43); Post tx: 921 (383) vs. 1028 (773) vs. 34 (30) Urinary LH: 5265 (3294) vs. 8017 (10232) vs. 20047 (11864) vs. 8105 (6401)</p> <p>Other outcomes assessed: ejaculation, masturbation</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: None TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Self reports of sexual behaviour (7-point Likert scale)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Gomaa (2001) 231</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 42 (crossover-two phases)</p> <p>IG1/IG2 n = 42</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ▼ in libido, Serum total testosterone near lower end of normal [defined as > 250 ng/dl] 200 – 350 ng/dl selected</p> <p>Exclusion: hx prostate dx, including: prostate cancer, recurrent prostatitis, benign hyperplasia or prostatic hypertrophy. Cavernous fibrosis, anatomical deformation of penis, glaucoma, hypotension or cardiac arrhythmia</p>	<p>Age, mean (range): 54 (41- 67) y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: all non-smoker</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED, n (%): 19 (90)</p> <p>Physiologic ED, n: Vasculogenic: 18 Neurogenic; 5</p> <p>Mixed ED: 0</p>	<p>IG1: Co-dergocrine mesylate 0.06% + isosorbide dinitrate 0.5% + topical T 0.8% (polypharmacy cream) IG2: topical T 0.8%</p> <p>IG1: Dose: 2 g in 2 x15 divided doses Duration: 1 mo Frequency: once/d applied to shaft at bedtime or 15 min before sexual activity Compliance: 100%</p> <p>IG2: Dose: 2 g in 2 x 15 divided doses Duration: 1 mo Frequency: once/d Compliance: 100%</p> <p>Run In period: If on IC vasodilator or androgen preparation: 6 wks- 2 wks post Papaverine test Wash out period: 1 wk</p> <p>F/u duration: 2 mo</p>	<p>Primary outcome results: Full erection with intercourse, mean n (%): 6 (3) vs. 4 (2), (p<0.05)</p> <p>Erectile response (30 d), n of pts with at least 2 positive response/mo (%): Full: 28 (66) vs. 13 (31); Partial: 2 (5) vs. 2 (5); Tumescence: 3 (7) vs. 0 No response: 9 (21) vs. 27 (64)</p> <p>Other outcomes assessed: Serum T level ▲ in all compared to onset (p<0.05); penile arterial flow ▲ IG1 vs. IG2, p<0.001; SPV: IG1 vs. IG2, p <0.001; quality of life (QOL) in favour of T-gel</p> <p>Withdrawals/drop-outs/loss to f/u: 0 WDAE: 0 TAE, n (%): 5 (12), all in IG1 with mild transient headache SAE: 0</p> <p>Ascertainment of outcomes assessed: Questionnaire for SD (analogue), frequency of activity, erectile response (full, partial, tumescence, no response)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Haren (2005) ²³²</p> <p>Funding source: Organon Pty Ltd</p>	<p>N screened = NR N randomized = 76</p> <p>IG, n = 39 CG, n = 37</p> <p>ITT analysis used for primary outcome: Y</p> <p>Inclusion: healthy men, at least 2 symptoms on the St-Louis University ADAM questionnaire, a free testosterone index (FTI) between 0.3 and 0.5 total T>8 nmol/l.</p> <p>Exclusion: prostate cancer or a PSA > 5 ng/ml, International Prostate Symptoms Score (IPSS) > 20, abnormal prostate on digital rectal examination, hx of testicular, liver, or renal dx, DM, cardiac failure, a score of greater than 15 on the Geriatric Depression Scale, sign. joint pain, prior use of androgen, bisphosphonates, oral, IV or intraarticular glucocorticoid within the preceding 6 mos. or an haematocrit greater than 50%.</p>	<p>Age, mean (sd), range: 68.5 (6), 60-86 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Testosterone -oral CG: Placebo- oral</p> <p>IG: Dose: 80 mg TU (Andriol) Duration: 12 mo Frequency: twice/d Compliance: 69.7% took 90% or more of tablets; 27% took between 51-89% of the assigned tablets</p> <p>CG: Dose: placebo Duration: 12 mo. Frequency: twice/d Compliance: 80% took 90% or more of tablets; 20% took between 51-89% of the assigned tablets</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 12 mo</p>	<p>Primary outcome results: Androgen deficiency (ADAM) questionnaire (% 'yes' response): Report of less strong erections: baseline: 95 vs. 95 12 mo: 86 vs. 93 (p>0.05) ADAM questionnaire when calculated bioavailable T (cBT) < 3.1 nmol/l): Report of less strong erections: Baseline: 100 vs. 95 12 mo: 89 vs.94 (p>0.05).</p> <p>Other outcomes assessed: improvement in libido, energy, strength, enjoyment of life, mood, ability to play sports, and work performance</p> <p>Withdrawals/drop-outs/loss to f/u: 6 vs. 12</p> <p>WDAE: NR TAE: NR SAE: 0</p> <p>Ascertainment of outcomes assessed: Androgen deficiency (ADAM) questionnaire: (ED: are your erections less strong?); cBT: calculated from TT</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kunelius (2002) 233</p> <p>Funding source: Laboratories Besins Iscovesco supplied the study drug Funding: Sigrid Juselius Foundation and the Academy of Finland</p>	<p>N screened = 178 N randomized = 120</p> <p>IG, n = 60 CG, n = 60</p> <p>ITT analysis for primary outcome: NR</p> <p>Inclusion: Nocturnal penile tumescence ≤ 1 / wk; One of the following andropause symptoms: ∇ libido, ED, urinary dx, asthenia or a depressive mood; total serum T ≤ 15 nmol/L and/or serum SHBG > 30 nmol/l</p> <p>Exclusion: abnormal liver parameters; PSA > 10 $\mu\text{g/l}$; prostate weight > 100 g; acute prostatitis, abnormal prostate in clinical or ultrasonographic exam; prostactectomy/transurethral resection of the prostate; sign cardiovascular dx; abnormal lipid profile; alcohol abuse; uncured cancer, neurological impotence, psychiatric dx; taking hormones or drugs affecting sexual function (other criteria could be found in the full report)</p>	<p>Age, mean (sd): 58.4 (5.3, range 50-70 y) y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment, n: 5 vs. 9 (not specified)</p> <p>BMI, mean (sd): 26 (2) vs. 26 (3) kg/m^2. ($p > 0.05$)</p> <p>Smoking status: NR</p> <p>Body weight: 79.5 (9) vs. 81 (9.7) kg</p> <p>Other, n: Testosterone ≤ 15 nmol/L: 51 Testosterone < 9 nmol/L: 5 SHBG > 30 nmol/L: 111 SHBG > 62 nmol/L: 22 Free Androgen Index: 35.5 ± 10.8</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Dihydrotestosterone (DHT) gel Transdermal CG: Placebo Transdermal gel</p> <p>IG: Dose: 125 mg/ d for 30 d, titrated up to 250 mg/day according to DHT levels Duration: 6 mo Frequency: Once/d Compliance: 100%</p> <p>CG: Dose: placebo (NA) Duration: 6 mo Frequency: Once daily Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 6 mo</p>	<p>Primary outcome results: IG vs. CG, mean (sd): Ability to maintain erection during intercourse: 3.2 (1.4) vs. 3 (1.6), $p < 0.04$</p> <p>Serum T (nmol/l): 6 (4) vs. 15 (5) $p < 0.001$)</p> <p>Other outcomes assessed: SHBG: 39 (13) vs. 43 (17) nmol/l $p = 0.003$ FSH: 4 (4) vs. 16 (5) IU/l, $p < 0.001$ LH: 2 (2) vs. 5 (3) IU/l, $p < 0.001$; DHT: 8 (5) vs. 2 (0.7) nmol/l, $p < 0.001$</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 6 (5), All in IG1</p> <p>WDAE: 0 TAE: Mild headache: 3 vs. 2 Skin irritation: 0 vs. 0 Hair growth on shoulder/arm: 1 vs. 0 Mild depression: 2 vs. 2 SAE: 0</p> <p>Ascertainment of outcomes assessed: General well being questionnaire: A modified Psychological General Well-Being scale (13 items) and 12 items from IIEF</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>McNicholas (2002) ²³⁴</p> <p>Funding source: Auxilium UK Ltd.</p>	<p>N screened = NR N randomized = 208</p> <p>IG1, n= 68 IG2, n = 72 IG3, n= 68 CG, n= NA</p> <p>ITT analysis used for primary outcome: No</p> <p>Inclusion: ageing men with low serum T (≤ 10.4 nmol/l) and associated signs and symptoms of hypogonadism</p> <p>Exclusion: NR</p>	<p>Age, mean (sd): 58 (10) y; range: 31-80 y</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI, mean (sd): 28 (4) kg/m²</p> <p>Smoking status: NR</p> <p>Body weight mean (sd): 86 (12) vs. 88 (12) vs. 89 (12) kg</p> <p>Other: Testosterone, (mean, SD): all pts 8 (2.3) nmol/l PSA, mean (sd): all pts 1.3 (1.3) ng/mL</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n: Primary hypogonadism: 6 vs. 10 vs. 4; Secondary hypogonadism: 62 vs. 62 vs. 64 (aging (%): 60 vs. 56 vs. 59; Normogonadotrophic (%): 13 vs. 22 vs. 25) Psychogenic ED: 0</p> <p>Physiologic ED: 100%</p> <p>Mixed ED: NR</p>	<p>IG1: Testim, testosterone gel IG2: Testim, testosterone gel IG3: Andropatch, patch (open label)</p> <p>IG1: Dose: 50 mg Duration: 90 d Frequency: daily Compliance: 97%</p> <p>IG2: Dose: 100 mg Duration: 90 d Frequency: daily Compliance: 97%</p> <p>IG3: Dose: 2 x 2.5 mg Duration: 90 d Frequency: daily Compliance: 96%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NA</p>	<p>Primary outcome results: IG1 vs. IG2 vs. IG3, change from baseline, mean (sd): Sexual function: Spontaneous erections, mean /wk: 0.6 (1.4) vs. 0.5 (1.4) vs. 0.3 (1.2) Motivation, mean/wk: 0.4 (1.2) vs. 0.4 (1.3) vs. 0.5 (1.4) Desire mean/wk: 0.8 (1.0) vs. 0.7 (1.4) vs. 0.5 (1.2) Performance mean/wk: 0.3 (1) vs. 0.4 (0.9) vs. 0.3 (1)</p> <p>Other outcomes assessed: serum free T; C-average T; C-average dihydrotestosterone</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE, (%): 4 vs. 0 vs. 13 most related to skin irritation TAE: incidence of 1 or more AE= 35% vs. 29% vs. 63%, erythema, irritation, and reactions at application site SAE: 0</p> <p>Ascertainment of outcomes assessed: sexual function and mood questionnaires for hypogonadal men physical exam, scoring system for skin irritation</p>

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<p>Merza (2005) ²³⁵</p> <p>Funding source: Ferring Pharmaceuticals Ltd.</p>	<p>N screened = NR N randomized = 39(the trial was followed by a 6 mo open label phase)</p> <p>IG, n = 20 CG, n = 19</p> <p>ITT analysis used for primary outcome: NR (analysed for 20 vs.18)</p> <p>Inclusion: men 40 or older, with borderline hypogonadism defined as T level <10 nmol/L or a free androgen index <30%), presenting with sexual dysfunction</p> <p>Exclusion: prostate or breast cancer, prostatic hypertrophy, raised serum PSA (>2.5 µg); uncontrolled hypertension; DM; uncontrolled cardiac disease; renal failure; liver disease; polycythaemia; hx of aggressive behaviour, alcohol or drug abuse; anticoagulant tx or testosterone replacement tx</p>	<p>Age, mean (sd): 62 (9.7), range 40-77.4 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Testosterone patch CG: Placebo</p> <p>IG: Dose: 328 mg patch delivering 5 mg/d Duration: 6 mo Frequency: one/d (in the morning) Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: 6 mo</p>	<p>Primary outcome results: Not measured</p> <p>MED QoL score, mean (sd): Baseline: 61.4 (17.5) vs. 54.2 (15.9) 6 mo: 61.8 (22.1) vs. 43.6 (4.21), p=0.017</p> <p>GWBI score, mean (sd): Baseline: 75.8 (13.4) vs. 63.5(16) 6 mo: 75.8 (13) vs. 60.8 (11)</p> <p>Other outcomes assessed: Hormones; bone turnover markers, bone mineral density, fat mass, lean mass, laboratory safety measures</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0 vs. 1 (5.3)</p> <p>WDAE, n (%):0 vs. 1 (5.3) due to angina TAE, n (%): NR SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: laboratory testing for body composition, markers of bone turnover, hormone measurements; QoL measured by questionnaires (the Male Erectile Dysfunction Quality of Life questionnaire, MEDQoL; and General Well-Being Index, GWBI) scored 0-100</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Padma-Nathan (2006) ²²³</p> <p>Funding source: NexMed (study drug supply); co-author a paid consultant of NexMed</p>	<p>N screened = N randomized = 1732</p> <p>IG1, n = 434 IG2, n = 430 IG3, n = 434 CG, n = 434</p> <p>ITT analysis used for primary outcome: yes (pts with at least one study medication)</p> <p>Inclusion: men at least 21 y, in a stable relationship, and hx of ED of at least 3 mo in duration</p> <p>Exclusion: ED due to untreated endocrine disease or sing penile pathology (i.e. penile fibrosis, Peyronie disease)</p>	<p>Age, mean (se): 61 (0.47) y</p> <p>Race: White 86%; Black 8.3%; Hispanic 3.9%; other 1.8%</p> <p>Co-morbidities, n (%): DM 305 (17.6); cardiac 503 (29); prostatectomy 220 (12.7) slightly higher in IG1; hypertension 783 (45.2)</p> <p>Previous ED treatment: sildenafil [failures 352 (18.8)]</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1-3: Alprostadil topical cream CG: Placebo cream</p> <p>IG1-3: Dose: IG1=100 µg, IG2 = 200 µg, IG3=300 µg Duration: 12 wks Frequency: up to 24 applications (2/wk) Compliance: NR</p> <p>CG: Dose: Duration: 12 wks Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks drug free Wash out period:</p> <p>F/u duration: 16 wks</p>	<p>Primary outcome results: IIEF-EF, LS mean change from baseline (se): IG: 1.6 (0.34) vs. 2.5 (0.34) vs. 2.4 (0.34), CG -0.7 (0.34) SEP, LS mean % change form baseline (se): SEP-2: IG 2.9 (1.63) vs. 5.1 (1.65) vs. 7.2 (1.65), CG -4.5 (1.65) SEP-3: IG 7.0 (1.61) vs. 13.8 (1.63) vs. 9.1 (1.63), CG 0.4 (1.64) GAQ, % improved: IG 40% vs. 47% vs. 52%, CG 20%</p> <p>Other outcomes assessed: NA</p> <p>Withdrawals/drop-outs/loss to f/u, n (%):</p> <p>WDAE, n (%): 46 (2.7) TAE, n (%): 198 (45.6) vs. 267 (62.1) vs. 292 (67.3) vs. CG 54 (12.4) Body as whole: IG 5 (1.2) vs. 1 (0.2) vs. 0 CG 1 (0.2); nervous system IG 5 (1.2) vs. 7 (1.6) vs. 11 (1.2), CG 1 (0.2) Skin rash: IG 2 (0.5) vs. 5 (1.2) vs. 2 (0.5) CG 1 (0.2); urogenital system: IG 186 (42.9) vs. 254 (59.1) vs. 279 (64.9) CG 51 (10.6) SAE, n (%): IG 0, CG 1 (0.2) died due to cardiac arrest</p> <p>Ascertainment of outcomes assessed: IIEF-EF; SEP; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rabkin (2000) 236</p> <p>Funding source: NR</p>	<p>N screened = 104 N randomized = 74</p> <p>IG, n = 39 CG, n = 35</p> <p>ITT analysis used for primary outcome: N</p> <p>Inclusion: men 18 yrs, HIV seropositive (CD4 cell counts less than $0.4 \times 10^9/L$), clinically deficient or low-normal serum T < 17.4 nmol/L (except acquired immunodeficiency syndrome with severe fatigue, upper limit 22.6 nmol/L), sexual dysfunction, at least one associated hypogonadal mood symptom, receiving medical care for HIV illness</p> <p>Exclusion: substance use in past 6 mo, psychotic symptoms, sign suicidal risk, sign cognitive impairment, unstable medical condition including new onset of an opportunistic infection in the past mo, symptomatic benign prostate hyperplasia, current or anticipated use of a new antiretroviral medication within 4 wks, or use of anabolic steroids in past mo</p>	<p>Age, mean (sd): 38 (7.3) vs. 40 (9) y</p> <p>Race, n (%): non-white 18 (47) vs. 18 (56)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: T level (nmol/L), mean (sd): 13 (5) vs. 3 (4); n=14 (20) baseline T levels below 10.4 nmol/l (hypogonadal)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: HIV-positive with hypogonadal symptoms and sexual dysfunction 74 (100%)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: testosterone cypionate,- IM CG: placebo- IM</p> <p>IG: Dose: initial 200 mg, ▲ to 400 mg Duration: 6 wks Frequency: bi-weekly Compliance: NR</p> <p>CG: Dose: initial 200 mg, ▲ to 400 mg Duration: 6 wks Frequency: bi-weekly Compliance: NR</p> <p>Run In period: NA Wash out period: NR</p> <p>F/u duration: 6 wks + 12 wks (maintenance for responders) = 18 wks</p>	<p>Primary outcome results: CGI, sexual interest, EF& mood, mean (%): 28(74) vs. 6 (19) = P < 0.001 CGI, improved/much improved among completers, n (%): 20 (63) vs. 4 (20); not different between hypogonadal men and men with normal T levels Reynolds sexual function scale, mean (SE): morning erections 5.4 (0.4) vs. 4 (0.4), P=0.008 Total serum T (nmol/L), mean change from baseline: IG responders=non responders 35 (15) vs. CG responders = 11.4 (7.4), non responders= 2 (6.4), p=0.005</p> <p>Other outcomes assessed: mood, depression, anxiety, quality of life, laboratory measures</p> <p>Withdrawals/drop-outs/loss to f/u: 4 (vs.3)</p> <p>WDAE: NR TAE, n (%): Pts with 1 or more AE: 16 (41) vs. 7 (20), p=0.05; AE include ▼ ejaculation; testicular atrophy; irritability; acne (21% of pts vs. 0); tension; bossiness; hair loss SAE: 2 (IG) hospitalized due to HIV</p> <p>Ascertainment of outcomes assessed: Clinical global impressions scale ratings (CGI): 7-point scale Reynolds sexual function scale (self report 10-point); Structured assessment of tx emergent AEs</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Raul (1997) ²³⁷</p> <p>Funding source: National Institute on Aging</p>	<p>N screened = 40 N randomized = 18 (cross over design)</p> <p>IG/ CG, n = 18</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 45-74 yr, with primary diagnosis of ED or hypo active SD, (ED: inability to achieve and maintain vaginal penetration until orgasm on at least 50% of the attempts during the preceding 6 mo; Hypoactive SD: SD for any sexual activity of less than twice per mo during the preceding 6 mo)</p> <p>Exclusion: evidence of medical disorder, intake of drug especially neurological, vascular or endocrine action drugs; alcohol or other substances of abuse; presence of major psychopathology; obesity (> 20% above ideal body weight)</p>	<p>Age, median (range): Median 60 (46-67) y</p> <p>Race (%): Caucasian 97; NR 3</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, median (range): 4 y (6 mo- 12 yr)</p> <p>Underlying disease: NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG: Testosterone IM (enanthate) CG: placebo (sesame oil vehicle)</p> <p>IG1: Dose: 200 mg Duration: 6 wks Frequency: twice/ wk Compliance: NR</p> <p>CG: Dose: NR (0) Duration: 6 wks Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: 4 wks</p> <p>F/u duration: 16 wks</p>	<p>Primary outcome results: Frequency (times/ wk), median (range): SD 6 (0-7) vs. 4 (0-7) Masturbation 1 (0-2) vs. 0.16 (0-2); Sex with partner 1 (0-2) vs. 0.54 (0-2.7) Morning erections 1.25 (0-7) vs. 0.67 (0-7) Degree of erection (score 1-6): Masturbation: 6 (3-6) vs. 6 (1-6) Sex with partner: 6 (4-6) vs. 6 (1-6) T (ng/ml), mean (sd): Baseline: 412 (48) vs. 481 (205) Period 1: 318 (66) vs. 455 (143) Period 2: 420 (87) vs. 397 (73)</p> <p>Other outcomes assessed: Sexual behaviour and mood Plasma T, LH (sign. compare to baseline in IG), dihydrotestosterone</p> <p>Withdrawals/drop-outs/loss to f/u: n=6 (n=1 excluded from analysis due to diagnosis of primary hypoactive SD)</p> <p>WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Psychological assessment: 1) ED by brief sexual function questionnaire (19 items), 2) mood assessment by POMS (65 items), 3) distress by SCI-90-R (90 items each on a 5-point scale)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Rochira (2006) 238</p> <p>Funding source: Ministero dell'Università e della Ricerca Scientifica</p>	<p>N screened = NR N randomized = 24 (Italy)</p> <p>Grp 1 Hypogonadal not treated IG1/CG1, n = 12</p> <p>Grp 2 Hypogonadal treated IG2/CG2, n = 12</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: hypogonadal men (serum T level of 20 ng/dL used as cut-off); pts included 14 pts who had been withdrawn from T replacement tx for at least 3 mo and 10 hypogonadal pts at 1st diagnosis</p> <p>Exclusion: NR</p> <p>Note: n=24 healthy subjects were recruited as control grp; data not shown in this table</p>	<p>Age, mean (sd): 34.54 (11.5) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): hypogonadal 24(100) including Klinefelter syndrome 7 (29)</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): hypogonadism</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG1/2: Sildenafil CG: Placebo</p> <p>IG1/2: Dose: 50 mg Duration: 3 nights Frequency: 1 hr before bedtime; on 2nd (IG1) or 3rd (IG2) night post nocturnal monitoring Compliance: 100%</p> <p>CG1-2: Dose: NA Duration: as IG Frequency: as IG Compliance: 100%</p> <p>Run In period: 1 night (adaptation) Wash out period: NR F/u duration:</p> <p>Note: T tx started for grp1 no longer than 20 d post enrolment (250 IM/ 21d); T tx period was a non-randomized open label 6 mo study for all hypogonadal men; NR in this evidence table</p>	<p>Primary outcome results: IG vs. CG, mean (sd): N of valid erections: Grp 1: 2.71 (0.18) vs. 0.76 (0.22) Grp 2: 4.29 (0.24) vs. 2.79 (0.27)</p> <p>Duration of rigidity >70% (min): Grp 1: 43.59 (5.14) vs. 10.57 (3.83) Grp 2: 105 (13.02) vs. 52.02 (8.75)</p> <p>Max rigidity, %: Grp 1: 79.21 (3.44) vs. 60.83 (3.83) Grp 2: 91.75 (1.54) vs. 84 (2.10)</p> <p>Max ▲ of circumference (mm): Grp 1: 33.46 (0.89) vs. 25.79 (1.45) Grp 2: 43.58 (1.31) vs. 40 (1.70)</p> <p>Other outcomes assessed: duration of ▲ of circumference of at least 30 mm (sign more in IG vs. CG)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 0</p> <p>WDAE, n (%): 0 TAE, n (%): 0 SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: RigiScan monitoring for nocturnal penile tumescence measures</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Seftel (2004) ²³⁹ Companion study ²⁴⁰</p> <p>Funding source: Auxilium Pharmaceuticals Inc.</p>	<p>N screened = NR N randomized = 406</p> <p>IG1, n = 99 (double blind) IG2, n = 106 (double blind) IG3, n = 102 (open label) CG, n = 99</p> <p>ITT analysis used for primary outcome: Yes</p> <p>Inclusion: hypogonadal men 20-80 (secondary to aging and also normogonadotrophic) with morning T level up to 300 ng/dL (10.4 nmol/L), with one or more symptoms of low testosterone (fatigue, reduced libido, reduced sexual functioning, ▼ muscle mass)</p> <p>Exclusion: NR</p> <p>Note: pts with T levels of > 300 were also randomized as protocol deviations (n=15) *n of pts evaluated for frequency of intercourse differs from those evaluated for SD & night time erections because requirement for steady sexual partner was not a requirement for study entry*</p>	<p>Age, mean: 58 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI, mean: all pts 30 kg/m²</p> <p>Smoking status: NR</p> <p>Body weight, mean range: 95-99 kg</p> <p>Other: Testosterone (nmol/L) all pts: 10.4-34.7; Mean (sd): 234 (57) vs. 232 (62) vs. 239 (69) vs. 229 (80) ng/dL</p> <p>Sexual function (likert scale), mean (sd) Baseline: 2 (1) vs. 3 (1) vs. 2 (1) vs. 2 (1)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: primary 6%, or secondary 94% (58-71% due to aging 19-32% due to normogonadotrophic)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Testosterone gel IG2: Testosterone gel IG3: Testosterone patch CG: placebo gel</p> <p>IG1: Dose: 50 mg (n= 43 titrate ▲ at 60 d) Duration: 90 d Frequency: daily Compliance: 100%</p> <p>IG2: Dose: 100 mg (n=4 titrated ▼ at 60 d) Duration: 90 d Frequency: daily Compliance: 100%</p> <p>IG3: Dose: 2 x 12.2 mg patches Duration: 90 d Frequency: daily Compliance: 100%</p> <p>CG: Dose: NA Duration: 90 d Frequency: daily Compliance: 100%</p> <p>Run In period: 7 d Wash out period: NR</p> <p>F/u duration: 30 and 90 d</p>	<p>Primary outcome results: IG1 vs. IG2 vs. IG3 vs. CG (at 90 d) ▲ SD from baseline (likert scale, mean daily score): 0.5 vs. 1 vs. 0.6 vs. 0.5 Pts with ▲ # of night time erections/ wk (%): 30 vs. 51 vs. 40 vs. 26 (at 30 d; no sign. difference at 90 d)</p> <p>Pts with ▲ in intercourse from baseline (%): 6 vs. 36 vs. 13 vs. 28 % of full erection: no data (not sign)</p> <p>C-average Serum T, mean (sd): 218 (74) vs. 315 (112) vs. 373 (145) vs. 487 (213)</p> <p>Other outcomes assessed: change in # of d/wk with nighttime or d time erections, former correlated with serum T levels at 30, and 90 d; mood; PSA levels</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 21 (5) due to AE</p> <p>WDAE, n (%): all 21 (5%); 1 vs. 5 vs. 15 vs. 0 TAE: NR (AE included: in IG2 vertigo; CA; depression with suicidal intent; UTI/pneumonia; hypertension; 15 in IG3 due to local dermal site reactions) SAE: NR</p> <p>Ascertainment of outcomes assessed: Self report daily diary, SD by Likert scale (0-7)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Seidman (2006) 241</p> <p>Funding source: NIH (partnership for Gender-Specific Medicine)</p>	<p>N screened = NR N randomized = 30</p> <p>IG, n = NR CG, n = NR</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 35 or older with MDD, and low serum T (350 ng/dl or less)</p> <p>Exclusion: bipolar illness, schizophrenia, substance abuse or dependence (current or within last yr); active suicidal ideation; or acute severe or unstable medical illness; men age over 50 with PSA level of 4.0 or higher or an abnormal digital rectal exam were excluded</p>	<p>Age, mean (sd): 52 (8) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: T level, mean (sd) ng/dl HAMD score 21 (8)</p>	<p>Concomitant medications, n (%):</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): MDD in all</p> <p>Psychogenic ED, n (%): 100%</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p> <p>Other: duration of current MDD, median 26 mo, range 4-120 mo</p>	<p>IG: T enanthate IM injection CG: placebo injection (sesame oil)</p> <p>IG: Dose: 200 mg Duration: 6 wks Frequency: once/wk Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NA</p> <p>F/u duration: 6 wks</p>	<p>Primary outcome results: DSPS-M section II, mean (sd): -Full erection on awakening: Baseline: 1.15 (1.82) vs. 1.47 (1.66) Post tx: 2.08 (2.29) vs. 2.18 (2.0) -Full erection on fantasy/ daydream: baseline 1.15 (1.72) vs. 1.88 (1.86) Post tx 1.78 (2.16) vs. 1.71 (1.83) -Full erection on masturbation: Baseline 1.08 (1.66) vs. 1.59 (1.91) Post tx 1.69 (2.25) vs. 1.71 (1.90) -Full erection during sexual activity: Baseline 1.54 (1.94) vs. 1.18 (1.78) Post tx 1.77 (2.17) vs. 1.53 (1.62) -A satisfying orgasm: Baseline 1.92 (1.44) vs. 1.82 (1.81) Post tx 2.31 (2.06) vs. 2.06(1.44) -Serum T level, mean: Baseline 262.5 (8) Post tx 981.3 vs. 297.7 ng/dl</p> <p>Other outcomes assessed: no association for changes in T level and depressive symptoms</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 1 (3.3)</p> <p>WDAE, n (%): 1 (3.3) TAE, n (%): NR SAE: 1 MI in CG</p> <p>Ascertainment of outcomes assessed: self reported sexual function; HAMD; DSPS-M section II (scale 0-8, 0=none; 8=4 or more per d)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Shabsigh (2004) 242</p> <p>Funding source: Solvay Pharmaceuticals Inc.</p>	<p>N screened = 354 N randomized = 75</p> <p>IG, n = 39 (ITT, n=37) CG, n = 36 (ITT, n=33)</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 18-80 y, with ED of 3 mo or longer, in a stable sexual relationship with a female \geq 6mo, morning serum total T of 400ng/dl or less at screening visits, nonresponders to Sildenafil monotherapy (determined by IIEF)</p> <p>Exclusion: hx of prostate or breast cancer, clinically sign or uncontrolled medical or psychiatric conditions (including DM), neurological dx that cause ED, generalized skin dx that would affect gel absorption, hyperprolactinemia, drug or alcohol abuse, prostate dx with concomitant urine flow rate of less than 12 ml/s</p>	<p>Age, mean (sd): 57 (10), range = 26-73 vs. 59 (9), range = 40-79 y</p> <p>Race, n (%): White 53 (71); Black 7 (9); Asian 2 (3); Hispanic 8 (11)</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI, mean (sd): 32 (5) vs. 31 (6) kg/m²</p> <p>Smoking status, n (%): 4 (11) vs. 6 (18)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED, n (%): 6-12 mo: 2 (5) vs. 4 (12); > 12 mo: 35 (95), vs. 29 (88)</p> <p>Underlying disease, n (%): DM 7 (19) vs. 4 (12) Hypertension 12 (32) vs. 13 (39); Hypertension 10 (27) vs. 4 (12); Prostate dx 5 (14) vs. 1 (3)</p> <p>Psychogenic ED, n (%): 1 (3) vs. 2 (6)</p> <p>Physiologic ED n, (%): 20 (54) vs. 14 (42)</p> <p>Mixed ED, n (%): 16 (43) vs. 17 (52)</p>	<p>IG: Testosterone gel + Sildenafil- oral CG: Placebo gel + Sildenafil -oral</p> <p>IG: Dose: 1% T gel + 100 mg Sildenafil Duration: 12 wks Frequency: gel 1x/day + Sildenafil as indicated Compliance: 100%</p> <p>CG: Dose: 5 g placebo gel + 100 mg Sildenafil Duration: 12 wks Frequency: gel: 1/day + Sildenafil as indicated Compliance: 100 %</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: longer than 12 wks (end point not specified)</p>	<p>Primary outcome results: IIEF- EF domain, mean change from baseline: 4.4 vs. 2.1, p =0.029</p> <p>IIEF-Q5: IG better than CG, (12 wk, p=0.008, end point p=0.004)</p> <p>Pts who improved at least 1 category from baseline for IIEF-Q3 or 4, n (%): 26 (79) vs. 22 (71)</p> <p>IIEF-Q3-4, n (%) with positive response: 12 wks: 19 (58) vs. 13 (42) Endpoint: 19 (51) vs. 13 (39)</p> <p>Serum T levels \blacktriangle from baseline at 12 wks: IG, p\leq0.004; IG vs. CG, p\leq0.001</p> <p>Other outcomes assessed: no correlation between serum T levels and IIEF at endpoint; QoL</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 7 (19) vs. 5 (14)</p> <p>WEAE, n: 1(3) vs. 0 TAE: 1 vs. 0; detail not reported SAE: 0</p> <p>Ascertainment of outcomes assessed: IIEF; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Shamloul (2005) 243</p> <p>Funding source: NR</p>	<p>N screened = 40 N randomized = 40</p> <p>IG1 (non responders to sildenafil), n = 10 CG1, n = 10 (1) IG2 (partially responders to sildenafil), n = 10 CG2, n = 10 (2)</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Men with ED associated with PADAM (partial androgen deficiency in aging men) symptoms. Suffering from ED for at least 6 mo. All patients were married and engaged in regular sexual activity (2 x wk); pts recruited after a sildenafil trial.</p> <p>Exclusion: Patients with prostate hypertrophy, prostate carcinoma and mammary carcinoma. No patients were diabetic or hypertensive</p>	<p>Age, mean (sd): 56 (2.4) y</p> <p>Race: NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: Sildenafil for 2wks</p> <p>BMI, mean (sd): 29 (3.2) kg/m²</p> <p>Smoking status: NR</p> <p>Body weight, mean (sd): 81 (1.4) kg</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: at least 6 mo</p> <p>Underlying disease: None</p> <p>Psychogenic ED: None</p> <p>Physiologic ED: None</p> <p>Mixed ED: None</p>	<p>IG1: Sildenafil + TRT (Testosterone undecanoate- oral) CG1: TRT IG2: Sildenafil + TRT CG2: TRT</p> <p>IG1/IG2: Dose: 50 or 100 mg + 120 mg Duration: 2 mo Frequency: 3 capsules/d Compliance: all</p> <p>CG1/CG2: Dose: 120 mg Duration: 2 mo Frequency: as IG Compliance: all</p> <p>Run In period: 2 wks Wash out period: None F/u duration: 2 mo</p>	<p>Primary outcome results: IIEF-5, mean (sd): IG1 vs. CG1: Baseline: 10 (1.3) vs. 10 (1.4) Post-tx: 15 (1.4) vs. 11 (1.5)</p> <p>IG2 vs. CG2: Baseline: 15 (1.6) vs. 15 (1.2) Post-tx: 17.5 (2) vs. 16 (1)</p> <p>Serum total T (nmol/L) level, IG+CG, baseline vs. post tx, mean (sd): 7.3 (1.4) vs. 11 (1.3)</p> <p>Other outcomes assessed: PADAM score mean (sd): baseline 28.4 (2) vs. post tx 22.4 (1.3); serum FSH, LH, PRL levels</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: None TAE, n: 3, headache (sildenafil 100 mg) SAE: None</p> <p>Ascertainment of outcomes assessed: partial androgen deficiency in aging men (PADAM) rating score and IIEF-5 questionnaires</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Wang (2000) ²⁴⁴</p> <p>Funding source: Unimed Pharmaceuticals Inc Grant from NIH GrantM0-00543</p>	<p>N screened = NR N randomized = 227 (16 centres)</p> <p>IG1, n = 73 IG2, n = 78 IG3, n = 76 CG, n = NA</p> <p>ITT analysis used for primary outcome:</p> <p>Inclusion: men with morning T ≤ 10.4 nmol/L (300 ng/dL); clinically healthy, if on lipid lowering agents or tranquilizers: dose stabilized for at least 3 mo prior to screening.</p> <p>Exclusion: hx of chronic medical illness or alcohol and drug use; presence of a generalized skin dx, hx of skin irritability with T patches; Ideal body weight < 80% or > 140 %</p>	<p>Age, mean: 58 y</p> <p>Race (%): NR</p> <p>Co-morbidities: NR</p> <p>Previous ED treatment: NR</p> <p>BMI, mean: all pts 30 kg/m²</p> <p>Smoking status: NR</p> <p>Body weight, mean range: 95-99 kg</p> <p>Other: Testosterone (nmol/L) all pts: 10.4-34.7; Mean (sd): 234 (57) vs. 232 (62) vs. 239 (69) vs. 229 (80) ng/dL</p> <p>Sexual function (likert scale), mean (sd) Baseline: 2 (1) vs. 3 (1) vs. 2 (1) vs. 2 (1)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease: primary 6%, or secondary hypogonadal 94% (58-71% due to aging 19-32% due to normo-gonadotrophic)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: all 100%</p> <p>Mixed ED: NR</p>	<p>IG1/ IG2: Testosterone transdermal gel IG3: Testosterone patch</p> <p>IG1: Dose: 50 mg/d (↑ to 75 mg/d at 90 d in n=20 with T <10.4nmol/l at 60) Duration: 180 d Frequency: daily Compliance: 93%</p> <p>IG2: Dose: 100 mg/d (↓ to 75 mg/d at 90 d if T >34.7 nmol/l at 60 d) Duration: as IG Frequency: daily Compliance: 96%</p> <p>IG3: Dose: 2 patch, 5 mg/d Duration: 180 d Frequency: daily Compliance: 65% (1st 90 d); 74% (2nd 90 d)</p> <p>Run In period: 7 d Wash out period: NR</p> <p>F/u duration: 180 d (f/u at 0 and every 30 d)</p>	<p>Primary outcome results: Self assessment: Satisfaction of erection: ▲ from baseline in both grps, p=0.0001 % of full erection: ▲ from baseline in both grps, p=0.0001 (slightly better in 100 mg/d T gel)</p> <p>Other outcomes assessed: sexual function (desire, enjoyment, motivation, performance) and mood; lean mass, muscle strength, ▼ fat mass all improved with T gel and T patch with less skin irritation using T gel</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): 17 (22.4) vs. 8 (5.3)</p> <p>WDAE, n (%): 17 (22.4) vs. 8 (5.3) TAE, n (%): skin irritation 5.5% with T gel, vs. 66% in T patch; other PSA elevation; depression memory loss, high blood pressure, Hct and Hgb rise (in T patch); gynecomastia; transient abnormal laboratory tests, headache, asthma, hypertension, dizziness anxiety and nervousness SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: pts questionnaire, laboratory and clinical examination</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Yassin (2006) ²⁴⁵</p> <p>Funding source: NR</p>	<p>N screened = N randomized = 69 (open label randomized)</p> <p>IG1, n = 35 IG2, n = 34</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: hypogonadal (serum T 3.4 ngml⁻¹ or less) age 34-78 y, with at least 6 mo hx of ED of any severity; hx of no response to 6-8 attempts with 20 mg tadalafil (poor EF score, persistent dissatisfaction)</p> <p>Exclusion: clinically sign disease known to contradict with T or tadalafil; severe DM, IPSS > 18; prostatitis, hyperprolactinaemia (>20 ngml⁻¹); CV attacks in last 6 mo</p>	<p>Age, mean (sd): 58.3 (9.7) vs. 59.9 (9.1) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): DM type I 2 (5.9) vs. 0; DM type II 6 (17.6) vs. 5 (14.3); hypertension 11 (32.4) vs. 13 (37.1); dyslipidaemia 7 (20.6) vs. 6 (17.1); BPH/LUTS 16 (47.1) vs. 11 (31.4)</p> <p>Previous ED treatment: all pts had tadalafil monotherapy</p> <p>Smoking status: 13 (38.2) vs. 15 (42.9)</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): hypogonadism</p> <p>Psychogenic ED, n (%): 0</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): 0</p> <p>Other: ED severity, n (%): midland moderate 23 (67.7) vs. 26 (74.3); severe 12 (35.3) vs. 8 (22.9)</p> <p>Mean IPSS: 15 (both grps)</p>	<p>IG: sildenafil + T gel (Testogel®) CG: T gel alone</p> <p>IG1: Dose: 20 m sildenafil + 5 g containing 50 mg T Duration: 10 wks Frequency: sildenafil twice/wk; T gel NR Compliance: 100%</p> <p>IG2: Dose: 5 g containing 5 mg T Duration: 10 wks Frequency: NR Compliance:</p> <p>Run In period: 4 wks T gel tx Wash out period: 2 wks (post tadalafil Monotherapy)</p> <p>F/u duration: 10 wks</p> <p>Other: IG CG were assigned to add tadalafil to T tx at the end of 10 wk trial</p>	<p>Primary outcome results: Mean (sd), IG1 vs. IG2 IIEF-EF domain: Baseline 11.3 (3.0) vs. 11.3 (2.8) 10 wks: 18.3 (0.2) vs. 18.2 (0.4) (% improved in IIEF-EF with T-gel monotherapy in IG1 wk 4 = 43% vs. IG2 at wk 10 65%) IIEF-OF: Baseline 5.4 (2.6) 10 wks: 7.1 (1.4) vs. 7.1 (0.3) IIEF SD: Baseline 6.1 (2.8) 10 wks: 8.7 (0.8) vs. 7.8 (0.9) IIEF-IS: Baseline 8.9 (1.6) 10 wks: 13.1 (1.4) vs. 12.8 (1.2) IIEF-OS: Baseline 5.0 (1.5) 10 wks 8.2 (0.4) vs. 8.6 (0.3) Other outcomes assessed: partner satisfaction</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR WDAE: 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: Serum hormone analysis; IIEF; pts and partner questionnaire on efficacy of erectile quality/rigidity</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

C10-Off Label Treatments

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Aydin (1996) ²⁴⁶</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 79</p> <p>IG1, n = 20 IG2, n = 21 IG3, n = 20 CG, n = Placebo</p> <p>ITT analysis used for primary outcome:</p> <p>Inclusion: men of various ages with hx of ED confirmed with clinical examination</p> <p>Exclusion: NR</p>	<p>Age, mean (sd): 38 (11.3) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1: Testosterone IG2: Trazadone IG3: Hypnosis CG: Placebo</p> <p>IG1: Dose: 120 mg/d Duration: 16 wks Frequency: daily Compliance: NR</p> <p>IG2: Dose: 100-150 mg/d Duration: as IG1 Frequency: as IG1 Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 16 wks</p>	<p>Primary outcome results: Improved in sexual function (full erection or ability to have intercourse with occasional failure), n (%): IG1: 12 (60) IG2: 14 (66.7) IG3: 16 (80) CG: 7 (38.9) Overall improvement achieved by 60, 67, and 80% of IG1, IG2, and IG3 respectively</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): 0 vs. 5 (23.8) vs. 0 vs. 0; pts in trazadone grp experienced sedation SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: pts diary</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
Becker (1998) ²⁴⁷ Funding source: Zonagen USA	N screened = 40 N randomized = 40 IG1, n = 10 IG2, n = 10 IG3, n = 10 CG, n = 10 ITT analysis used for primary outcome: NR Inclusion: hx of ED for less than 3 y; ED likely to be organic who not responded positively to placebo test Exclusion: CVA; DM, neurological disease, tolerance to the study medication	Age, mean (range): 48 (26-70) y Race: NR Co-morbidities, n (%): NR Previous ED treatment: NR Smoking status: NR Body weight: NR	Concomitant medications, n (%): NR Duration of ED: NR Underlying disease, n (%): NR Psychogenic ED, n (%): NR Physiologic ED, n (%): likely 100% Mixed ED, n (%): NR	IG: Phentolamine CG: Placebo IG1-3: Dose: 20 mg (IG1), 40 mg (IG2), 60 mg (IG3) Duration: NR Frequency: NR Compliance: NR CG: Dose: NA Duration: as IG Frequency: NR Compliance: NR Run In period: NR Wash out period: NA F/u duration: NR	Primary outcome results: Full erection (sufficient for vaginal penetration), n (%): IG1: 3 (30) IG2: 5 (50) IG3: 4 (40) CG: 2 (20) Other outcomes assessed: NA Withdrawals/drop-outs/loss to f/u, n (%): NR WDAE, n (%): 0 TAE, n (%): 1 events (stuffy nose) only with 60 mg SAE, n (%): 0 Ascertainment of outcomes assessed: pts diary

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Costabile, R. (1999) ²⁴⁸</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 51 cross over</p> <p>IG screened = NR IG randomized = 51 cross over</p> <p>CG screened = NR CG randomized = 51 cross over</p> <p>Inclusion: At least 3 mos. of ED</p> <p>Exclusion: Pts with sign. cardiac disease</p>	<p>Age, mean (range): 65 yrs (range 31-80)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p> <p>Other: NA</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (mos./ yr)(mean [range]): 36 mos. (range 4 mos.- 30 yrs)</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED (N [%]): psychogenic 4(2)</p> <p>Physiologic ED (N [%]): arterial insufficiency 39(20), hypertension 18(9), diabetes 12(6), veno-occlusive dysfunction 10(5), surgical 6(3), neurogenic 4(2)</p> <p>Unknown ED (N [%]): unknown 7(4)</p> <p>Other: NA</p>	<p>IG: trazodone, oral CG: placebo, oral</p> <p>IG: Dose: 50 mg Duration: 3 mos. Frequency: 1/d, bedtime Compliance: 94% 1</p> <p>CG: Dose: 50 mg Duration: 3 mos. Frequency: 1/d, bedtime Compliance: 94% 1</p> <p>Run In period: 3 nights Wash out period: 3 wks</p> <p>F/u duration (both on and off treatment): NA</p> <p>Other: NA</p>	<p>Primary outcome results: Index of sexual satisfaction (mean): IG 27.5, CG 30.8 = no sign. difference Patient diary evaluations (%): first treatment interval, erection improvement IG 19, CG 24; sex drive improvement IG 35, CG 40 = no sign. difference when both treatment intervals combined List (narrative) other outcomes assessed: physical examination, laboratory evaluations, pre screening penile Doppler ultrasound ITT analysis used for primary outcome? N Withdrawals/drop-outs/loss to f/u [N and/or %]: N=3 WDAE (N and/or %): NR TAE (N [%]): dry mouth IG 12(25), CG 8(16.7); drowsiness IG 9(18.8), CG 6(12.5); fatigue IG 7(14.6), CG 4(8.3) SAE: NR</p> <p>Ascertainment of outcomes assessed: Index of sexual satisfaction: details not provided. Patient diary evaluations: self reported, administered monthly, documented sexual activity, libido and AE, extracted 2 questions-did this medicine improve your erection? did you notice a change in your sex drive while taking this medicine?</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Enzlin, P (2000) 249</p> <p>Funding source: Searle Continental Pharma Inc.</p>	<p>N screened = 39 N randomized = 34</p> <p>IG1 randomized = 16 IG2 randomized = NA CG randomized = 17</p> <p>Inclusion: age 18-65; in stable heterosexual relationship for ≥6 mo; ED ≥4 mo</p> <p>Exclusion: ED caused by sickle cell anemia and trait, thyroid or endocrine disorders (except diabetes), spinal cord lesion, or pelvic surgery or trauma; hx of myocardial infarction, coronary angioplasty or coronary bypass graft surgery in past 3 mo (except antihypertensive drugs since 2 mo before onset of ED); ejaculation disorder; medication known to possibly cause ED</p>	<p>Age, mean (sd): IG1 49 (11) CG 46 (8)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): Diabetes 1</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: Antihypertensives 1</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: trazodone orally IG2: NA CG: placebo orally</p> <p>IG1: Dose: 200 mg Duration: 4 wk Frequency: 1 dose/day Compliance (%): 1 wk: 71.4% good 4 wk: 57.1% good</p> <p>IG2: NA Dose: Duration: Frequency: Compliance (%):</p> <p>CG: Dose: placebo Duration: 4 wk Frequency: 1 dose/day Compliance (%): NR</p> <p>Run In period: 2 wk, including 2 or 3 nights of adaptation with RigiScan Plus®</p> <p>Wash out period: NA</p> <p>F/u duration (both on and off treatment): 4 wk and 2 or 3 days</p>	<p>Primary outcome results: Mean difference in total duration of nocturnal erection, minutes Base IG1 ▲ 8, CG ▲ 3 Tip IG1 ▲ 7, CG ▼ 4</p> <p>List (narrative) other outcomes assessed: Rigidity and tumescence; SD (Derogatis Sexual Functioning Inventory); quality of partner relationship (Dyadic Adjustment scale); depressive symptoms (Hamilton Depression Rating scale)</p> <p>ITT analysis used for primary outcome? N</p> <p>Withdrawals/drop-outs/loss to f/u [N and/or %]: 1 (CG)</p> <p>WDAE (N and/or %): NR</p> <p>TAE: NR</p> <p>SAE: NR</p> <p>Ascertainment of outcomes assessed: RigiScan Plus® Rigidity Assessment System</p> <p>Other: Not a very well reported study</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Georgitis, W. (1995) ²⁵⁰</p> <p>Funding source: U.S. Army Health Services Command</p>	<p>N screened = NR N randomized = NR</p> <p>IG1, n = 34 CG, n = 26</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Non insulin-dependent DM men. Patients with fasting serum glucose > 200mg/dl or HbA_{1c}>10% included only if impotence persisted after improved glycemic control</p> <p>Exclusion: Patients receiving anticoagulants, with past Hx of peptic ulcer disease or whose impotence was not cause by diabetes. Patients on beta-blockers, alomet or clonidine excluded</p>	<p>Age: Mean IG1: 59.1 ± 6.4 Mean CG: 64.6 ± 7.6</p> <p>Race: (n) Black: 20; Hispanic: 5; White: 35</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): Initial: IG1 vs. CG: 8.1 ± 1.8 vs. 7.4 ± 1.5. End: 8.0 ± 1.7 vs. 7.2 ± 1.3</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): Mean IG1 vs. CG: 28.0 ± 4.2 vs. 28.5 ± 3.0</p> <p>Smoking status: IG1 vs. C: Active 3 vs. 8; Quit: 15 vs. 19; Nonsmokers: 8 vs. 7</p> <p>Pack yrs: 39 ± 5 vs. 37 ± 9</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: IG1 vs CG: 5.2 ± 3.8 vs 6.0 ± 5.0</p> <p>Underlying disease (diagnosis): Diabetes Duration (yrs): IG1:13.6 ± 8.7 CG: 14.2 ± 10.9</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: Treatment for diabetes, IG1 vs CG: Diet:3 vs 0. Oral:18 vs 12. Insulin:13 vs 9. Combination: 0 vs 2</p> <p>Onset of ED, gradual/abrupt IG1 vs CG: 31/3 vs 24/2</p> <p>Duration of hypertension, IG1 vs CG:16.6 ± 12.6 vs 10.9 ± 8.6 yrs</p> <p>Ankle brachial SBP ratios abnormal in 6% of IG1 vs 0% CG</p> <p>Penile brachial blood pressure rations abnormal in 38% of IG1 vs 27% CG</p> <p>Autonomic dysfunction in IG1 vs CG: 82% vs 100%.</p>	<p>IG1: Oral Pentoxifylline (Trental™) CG: Placebo</p> <p>IG1: Pentoxifylline Dose: 400 mg Duration: 3 mo Frequency: 3/day Compliance (%): NR</p> <p>CG: Placebo Dose: N/A Duration: 3 mo Frequency: 3/day Compliance (%): NR</p> <p>Run In period: NR</p> <p>Wash out period: NR</p> <p>F/u duration (on and off treatment): 3 mo</p> <p>Other: NR</p>	<p>Primary outcome results: Self reported EF: IG1 vs CG: No difference Frequency of nocturnal penile tumescence IG1 vs CG: No difference Frequency of attempted intercourse or desired intercourse IG1 vs CG: No difference</p> <p>Other outcomes assessed: Rigidity, change in tumescence, erectile events /night, all abnormal in both IG1 and CG at baseline: No improvement observed in both IG1 and CG after 3 mo</p> <p>Withdrawals/drop-outs/loss to f/u: NR</p> <p>WDAE: NR</p> <p>TAE: NR</p> <p>SAE: NR</p> <p>Ascertainment of outcomes assessed: Self assessed EF using questionnaire and Likert scale at 3 time points Nocturnal penile tumescence: Monitored at 3 time points before and after intervention using RigiScan™ monitor. Peripheral vascular measurements done by Doppler ultrasound using Model 1059 Mini-lab III and a PVR IV Pulse Volume recorder</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Hatzichristou (2001) ²⁵¹</p> <p>Funding source: Schering-Plough Corporation</p>	<p>N screened = NR N randomized = NR</p> <p>IG1 randomized = 5 CG randomized = 5</p> <p>Inclusion: hx of ED ≥ 3mons, mild to moderate ED defined from IIEF</p> <p>Exclusion: impotence caused by untreated endocrine disease, penile curvature, clinical hx of sign. liver or renal disease, symptomatic uncontrolled heart disease, concomitant nitrate therapy for underlying condition; sitting or supine SBP > 160 mmHg or diastolic > 95mmHg, symptomatic postural hypotension < 6 mons, psychoses, uncontrolled bipolar disorder or depression, prior or current use of therapy for ED</p>	<p>Age, mean (SE): 34.8 (8.13)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): 1 person had pulmonary disease, 1 had prostatitis-like syndrome</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: None</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (mons) mean (SE): 31.8 (23.56)</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): Mild arteriogenic ED: n = 1 Mild veno-occlusive dysfunction: n= 2</p> <p>Psychogenic ED: 0</p> <p>Physiologic ED: 5</p> <p>Mixed ED: 0</p>	<p>IG1: oral phentolamine (Vasomax) tablets CG: oral placebo tablets</p> <p>IG1: Dose: 40 milligrams Duration: 3 nights Frequency: 1x/ night Compliance (%): 100%</p> <p>CG: Dose: NA Duration: 3 nights Frequency: 1x/night Compliance (%): 100%</p> <p>Run In period: NR Wash out period: ≥ 6 days, ≤ 30 days</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Penile tumescence (non sig.) Penile rigidity at tip: IG1: 5.24 ± 1.6, at base, 5.77 ± 1.62 IG1: ▲ mean erectile events/sleep hr: 0.24 ± .08 CG: 0.13 ± .05 IG1: ▲ mean duration of events: 5.53 ± 2.57 CG: 2.6 ± 1.04</p> <p>List (narrative) other outcomes assessed: None</p> <p>ITT analysis used for primary outcome? No</p> <p>Withdrawals/drop-outs/loss to f/u [N and or %]: 0</p> <p>WDAE (N and/or %): 0 TAE: 0 SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan device, medical an sexual hx, IIEF score</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Korenman (1993) ²⁵²</p> <p>Funding source:</p>	<p>N screened = 24 N randomized = 18</p> <p>IG1, n = 8 CG, n = 10</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: Borderline to definite penile arterial insufficiency as determined by PBPI, interest to re-establish EF by both partners and willingness to participate.</p> <p>Exclusion: Actively progressive illness, severe physical disability, major mental or emotional disease, hepatic or renal insufficient, hx of major cardiac arrhythmia, abuse of alcohol and other substances, and those lacking sexual partner.</p> <p>Other: Open label study was done after initial 12 wks finished. All 18 pts went on drug.</p>	<p>Age, mean (range): 65 ± 1.4 (54-76)</p> <p>Race: NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: 6.2 ± 1.1 y</p> <p>Underlying disease (diagnosis): n(%) Hypertension 13 (72.2); Diabetes 6 (33.3); ASCVD 10 (55.6); Hypogonadism 4 (22.2); Compensated hypergonadotropic hypogonadism 1 (5.6)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: Pentoxifylline CG: Placebo</p> <p>IG1: Dose: 400mg Duration: 12 wks Frequency: NR Compliance (%): 100%</p> <p>CG: Dose: NR Duration: 12 wks Frequency: NR Compliance (%): 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (on and off treatment): NR</p>	<p>Primary outcome results: IG1 vs. CG n/N (%) No improvement (one episode of coitus) 4/8 (50) vs. 10/10 (100) Pentoxifylline improved the PBPI in 18 males (0.76 ± 0.01, p = <0.0001)</p> <p>Other outcomes assessed: Patients initially receiving placebo placed on pentoxifylline: 5/10 (50) experienced successful intercourse. Pentoxifylline improved the PBPI in 18 males 0.76 (0.01), mean (sd) 9 (50) improved into normal range</p> <p>Withdrawals/drop-outs/loss to f/u: None</p> <p>WDAE: None TAE: None SAE: None</p> <p>Ascertainment of outcomes assessed: Report of patient verified by partner; penile-brachial pressure index determination (PBPI), daily log of improvement in EF.</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Kurt, U. (1994) 253</p> <p>Funding source: NR</p>	<p>N screened = N randomized = 100</p> <p>IG1, n = 25 IG2, n = 25 IG3, n = 25 CG, n = 25</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: ED ≥ 6 mo. < 1 coitus within several 30 day periods. Absence of normal sexual performance periods in last 6 mo. Sufficient libido, no ejaculation problems. Absence of specific diseases: Eg. DM, neurological disorders, atherosclerotic vascular disease. No Hx of chronic or recent psychological problem. No Hx of recent trauma interfering with neurovascular structures related to erections. Positive papaverine test (30 -60 mg IC) producing a rigid > 30 min erection.</p> <p>Exclusion: NR</p>	<p>Age: Mean 47.0 (range 23-68) yrs</p> <p>Race: NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease (diagnosis): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other NR</p>	<p>IG1: Oral Trazodone IG2: Oral Ketanserin IG3: Oral Mianserin CG: Placebo</p> <p>IG1: Trazodone Dose: 50 mg Duration: 30 days Frequency: 3/day Compliance (%): NR</p> <p>IG2: Ketanserin Dose: 20 mg Duration: 30 days Frequency: 2/ day Compliance (%): NR</p> <p>IG3: Mianserin Dose: 10 mg Duration: 30 days Frequency: 3/ day Compliance (%): NR</p> <p>CG: Dose: placebo Duration: 30 days Frequency: NR Compliance (%): NR</p> <p>Run In period: Wash out period: NR</p> <p>F/u duration (on and off treatment): 30 days</p> <p>Other: NR</p>	<p>Primary outcome results: Positive response rate: IG1> IG3> IG2> CG (p=0.0004 in IG1 vs. CG) (p= 0.002 in IG1 vs. IG2) (p= 0.03 in IG1 vs. IG3) IG2 and IG3 Not sign. vs. CG</p> <p>Other outcomes assessed: NR</p> <p>Withdrawals/drop-outs/loss to f/u: Total N = 15 5 = loss to f/u 3= preferred IC treatment 2= preferred vacuum device 2= Hx concomitant drug use 2= social reasons 1= penile implant inserted</p> <p>Final analysis value: IG1: 23, IG2: 21, IG3: 19, CG: 22</p> <p>WDAE: TAE: IG1: N=5: Sedation (n=2), Xerostomia (n=2), blurred vision (n=1) IG2: N=2: Vertigo (n=1), Fatigue (n=1) IG3: N=2: Severe sedation (n=2) CG: N= 2: Nausea (n=2)</p> <p>SAE: IG1: priapism in 1 patient 7 days after onset of intervention. IG1: severe sedation in 1 patient requiring cessation</p> <p>Ascertainment of outcomes assessed: Positive response= 3+ successful intercourse events without manipulation (in patient with previously inadequate rigidity without manipulation)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Mann, K (2001) 254</p> <p>Funding source: Hoffmann-La Roche, Grenzach-Wyhlen</p>	<p>N screened = NR N randomized = 13</p> <p>IG1 screened = NR IG1 randomized = 6</p> <p>IG2 screened = NA IG2 randomized =</p> <p>CG screened = NR CG randomized = 7</p> <p>Inclusion: ED</p> <p>Exclusion: lifetime diagnosis of any psychiatric disorder except for sexual dysfunction; hx of alcohol or other substance abuse; current or recent evidence of sign. medical disorder; sleep disturbances; taking any drugs</p>	<p>Age, mean (sd): IG1 49.3 (SD 8.9) CG 37.8 (SD 8.2)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p> <p>Other: Degree of severity of ED (Clinical Global Impression scale, mean [and standard error]) IG1 5.17 (0.31) CG 5.00 (0.37)</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): IG1 3.8, CG 2.8</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Psychogenic ED: 13</p> <p>Physiologic ED: 0</p> <p>Mixed ED: 0</p>	<p>IG1: moclobemide orally orally IG2: NA CG: placebo orally</p> <p>IG1: Dose: 450 mg during wk 1, 600 mg during wk 2-8 Duration: 8 wk Frequency: 1 dose/day Compliance (%): NR</p> <p>IG2: NA Dose: Duration: Frequency: Compliance (%):</p> <p>CG: Dose: placebo Duration: 8 wk Frequency: 1 dose/day Compliance (%): NR</p> <p>Run In period: NR</p> <p>Wash out period: NA</p> <p>F/u duration (both on and off treatment): 8 wk</p>	<p>Primary outcome results: Clinical Global Impression severity subscale at 8 wk (1=normal, 2=borderline ill, 3=mildly ill, 4=moderately ill, 5=markedly ill, 6=severely ill, 7=among most extremely ill) IG1 3.50, CG 4.50 Clinical Global Impression improvement subscale at 8 wk (-3=very much worse, -2=much worse, -1=minimally worse, 0=no change, 1=minimally improved, 2=much improved, 3=very much improved) IG1 1.50, CG 0.50 Change in mean nocturnal tumescence and rigidity of penis base and tip (averaged of the two) at 8 wk Tumescence, cm: IG1 -0.24, CG -0.13 Rigidity, %: IG1 2.58, CG 2.67</p> <p>List (narrative) other outcomes assessed: NA</p> <p>ITT analysis used for primary outcome? Y N/NR N</p> <p>Withdrawals/drop-outs/loss to f/u [N and/or %]: 1 (CG) WDAE (N and/or %): 1 (CG) TAE: IG1: 4 events in 3 patients CG: 7 events in 3 patients SAE: 0</p> <p>Ascertainment of outcomes assessed: RigiScan™ Rigidity Assessment System</p>

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<p>Meinhardt, W. (1997) ²⁵⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 69</p> <p>IG screened = NR IG randomized = 32</p> <p>CG screened = NR CG randomized = 37</p> <p>Inclusion: ED</p> <p>Exclusion: severe kidney or liver disorders, pts using anti-hypertensives or other drugs (especially alpha or beta blocking agents)</p>	<p>Age, mean (range): IG 54(26-80), CG 55(39-81)</p> <p>Race (%): Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment (N): self-injections IG 5, CG 16; psychotherapy IG 1, CG 0; vacuum device IG 1, CG 1</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p> <p>Other: NA</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): ED 69(100)</p> <p>Psychogenic ED (N): IG 16, CG 20</p> <p>Physiologic ED (N): vascular IG 5, CG 5; diabetes IG 5, CG 7; neurogenic IG 1, CG 0; peyronie's disease IG 1, CG 1;</p> <p>Mixed/unknown ED: IG 4, CG 4</p> <p>Other: NA</p>	<p>IG: trazodone, oral CG: placebo, oral</p> <p>IG: Dose: 50 mg Duration: 4 or 6 wks Frequency: X3/d = 150 mg Compliance (%): NR</p> <p>CG: Dose: 50 mg Duration: 4 or 6 wks Frequency: X3/d = 150 mg Compliance (%): NR</p> <p>Run In period: 2 wks Wash out period: NA</p> <p>F/u duration (both on and off treatment): NA</p> <p>Other: NA</p>	<p>Primary outcome results: Patients diary: NR in results Questionnaire (N [%]): medication did not work IG 15(58), CG 20(62); it works, but insufficiently IG 6(23), CG 6(19); it works, but too many side-effects IG 1(4), CG 1(3); medication works well IG 4(15), CG 5(16) = [p> 0.05] for all</p> <p>List (narrative) other outcomes assessed: RigiScan</p> <p>ITT analysis used for primary outcome? N</p> <p>Withdrawals/drop-outs/loss to f/u [N and or %]: N=2 lost to f/u</p> <p>WDAE (N and/or %): N= 6,7 or 9 side effects</p> <p>TAE: dizziness IG 5, CG 0; sleepiness IG5, CG 2; headache IG 3, CG 1; nausea IG 3, CG 0; rash IG 0, CG 1; conjunctivitis IG 0, CG 1</p> <p>SAE: NR</p> <p>Ascertainment of outcomes assessed: Patients diary: details on sexual function and complaints Questionnaire: opinion of treatment</p> <p>Other: NA</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Nickle (2007) ²⁵⁶</p> <p>Funding source: NR</p>	<p>N screened = N randomized = 50</p> <p>IG, n = 25 CG, n = 25</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men > 18 y, suffering from chronic stress and anxious or depressive mood with ED</p> <p>Exclusion: psychotic disorders, organic ED, current use of cabergoline, other dopamine agonists, any kind of current anti-ED, use of antidepressants, antianxiety drugs or psychotherapy</p>	<p>Age, mean (sd): 39.3 (15.3) vs. 38.8 (12.9) y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment:</p> <p>Smoking status:</p> <p>Body weight: NR</p> <p>Other: BMI: 26.1 (5.9) vs. 26.9 (5.4)</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: > 6 mo</p> <p>Underlying disease, n (%): as in inclusion</p> <p>Psychogenic ED, n (%): 100%</p> <p>Physiologic ED, n (%): 0</p> <p>Mixed ED, n (%): NR</p> <p>Other: moderate baseline hyperprolactinemia in 38 (18 vs. 20)</p>	<p>IG: Cabergoline CG: Placebo</p> <p>IG: Dose: 0.5 mg Duration: 4 mo Frequency: once/d Compliance: NR</p> <p>CG: Dose: NA Duration: 4 mo Frequency: as IG Compliance: NR</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: 4 mo</p>	<p>Primary outcome (EF): Improvement from baseline (in mean): IIEF-EF: 11.7 vs. 6.9 IIEF-OF: 3.6 vs. 1.8 IIEF-IS: 5.7 vs. 2.6 IIEF-OS: 3.6 vs. 0.9 IIEF-SD: 3.5 vs. 2.0</p> <p>ED-QoL change from baseline score: -16.9 vs. -9.6</p> <p>Other outcomes assessed: SFQ partner questionnaire</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): 10 (40) vs. 9 (36) SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF domains; ED quality of life questionnaire</p>

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<p>Peskircioglu (1996) ²⁵⁷</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 36</p> <p>IG1 randomized = 20 CG randomized = 16</p> <p>Inclusion: patients with borderline arterial insufficiency</p> <p>Exclusion: patients with correctable secondary causes (endocrine, metabolic, pharmacological & Peyronie's disease)</p>	<p>Age, mean (sd): 54 (\pm 7)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: oral pentoxifylline CG: placebo (vitamin B complex)</p> <p>IG1: Dose: 1.2 grams in 3 doses Duration: 2 mons Frequency: 3 doses/day Compliance (%): 100</p> <p>CG: Dose: NA Duration: 2 mons Frequency: 3 doses/day Compliance (%): 100</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Penile blood flow IG1: 12/20 \blacktriangle (mean change = 6.25 cm) CG: 4/20 \blacktriangle (mean change = 0.38 cm)</p> <p>List (narrative) other outcomes assessed: Potency</p> <p>ITT analysis used for primary outcome?</p> <p>Withdrawals/drop-outs/loss to f/u [N and or %]: 0</p> <p>WDAE (N and/or %): 0</p> <p>TAE: IG1: n =2 (nausea), n = 2 (headache)</p> <p>SAE: 0</p> <p>Ascertainment of outcomes assessed: Penile duplex ultrasonography</p>

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<p>Piha J. (2003) ²⁵⁸</p> <p>Funding source: Finnish Hypertension Society and Slovay Pharma/ Algol.</p>	<p>N screened = NR N randomized = 12 Crossover design</p> <p>IG1, n = 11 IG1 crossover, n = 11</p> <p>ITT analysis used for primary outcome:</p> <p>Inclusion: Hypertensive</p> <p>Exclusion: NR</p>	<p>Age: Mean 50.5 (range 41-58)</p> <p>Race: NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: Mean IIEF-5 score: 15.8± 8.5 4= score ≥ 21 7= score <21 Mean serum T 13.1 ± 3.3 nmol/L Weekly resting Blood Pressure</p>	<p>Concomitant medications: For Hypertension (n): 2 on ACE inhibitor 5 on ACE inhibitor + beta-blocker + thiazide diuretic 1 on beta-blocker 2 on calcium channel</p> <p>Duration of ED: NR</p> <p>Underlying disease (diagnosis): Hypertension</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p> <p>Other: NR</p>	<p>IG1: Moxonidine IG1 crossover: Metoprolol</p> <p>IG1: Moxonidine Dose: 0.4 mg ▲ 0.6mg if BP >160/100 mmHg Duration: 8 wks Frequency: daily Compliance (%): NR</p> <p>IG1 crossover: Metoprolol Dose: 100 mg ▲ 200 mg if needed Duration: 8wks Frequency: daily Compliance (%): NR</p> <p>Run In period: Wash out period: 1-3 days</p> <p>F/u duration (on and off treatment): 16 wks</p> <p>Other: NR</p>	<p>Primary outcome results: Resting vs. stimulated penile Peak artery velocity for IG1: Mean peak velocity ▲: 19.8 ± 5.8 vs. 64.0 ± 32.4 cm/sec (p=0.008) Resting vs. stimulated penile Peak artery velocity for IG1 crossover Mean peak velocity ▲: 15.6 ± 55.2 vs. 53.9 ± 26.4 cm/sec (p=0.038) Resting vs. stimulated penile diameter for IG1: ▲ diameter: 0.54 ± 0.13 vs. 0.89 ± 0.14 mm (p=0.004) Resting vs. stimulated penile diameter for IG1crossover: ▲ diameter: 0.43 ± 0.16 vs. 0.66 ± 0.14 mm (p= 0.0001)</p> <p>Other outcomes assessed: Patient reported Subjective Erectile capacity <u>improved</u>: IG1 vs. baseline: 9/11 (p<0.001). IG1 crossover vs. baseline: 9/11 reported <u>impaired</u> EF (p<0.0002)</p> <p>Withdrawals/drop-outs/loss to f/u: 1 withdrawal due to not hypertensive (BP below 170/110 mmHg) WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: Stimulated erection induced by Alprostadil 10 microgram + phentolamine 0.1 mg IC. Peak systolic velocity measured via Doppler at 2 sites, mean of 4 measurements after 10-15 min Other: Mean Blood pressure with IG1 vs. IG1 crossover: 163.8 (± 16.0) / 96.2 (± 6.3) mmHg vs. 157.8 (± 19.2) / 93.6 (± 11.1) mmHg. P= not sign.</p>

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<p>Reiter, WJ (1998) ²⁵⁹</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 40</p> <p>IG1, n = 20 CG, n = 20</p> <p>ITT analysis used for primary outcome: N</p> <p>Inclusion: hx of ED > 6 mos., serum levels of testosterone, PRL, and PSA within normal range, and serum DHEAS level < 1.5 µmol/L, International Prostate Symptom Score < 7, full erection after intracavernosal administration of 10 µg PGE1</p> <p>Exclusion: well known causes of ED (hypertension, DM, ischemic heart disease, hyperlipidemia, neurological disorders, veno-occlusive dysfunction, and hx of radical prostatectomy)</p>	<p>Age [mean yr (range)]: IG 56.6(43-68), CG 56.4(41-69)</p> <p>Race: NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status [N (%)]: non-smokers 40(100)</p> <p>Body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED: NR</p> <p>Underlying disease (diagnosis)[N (%)]: ED 40(100)</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: oral dehydroepiandrosterone (DHEA) CG: oral placebo DHEA</p> <p>IG1: Dose: 50 µg Duration: 24 wks Frequency: 1X/d Compliance: NR</p> <p>CG: Dose: 50 µg Duration: 24 wks Frequency: 1X/d Compliance: NR</p> <p>Run In period: NA Wash out period: NA</p> <p>F/u duration (on and off treatment): 24 wks (0, 8, 16, and 24 wks)</p>	<p>Primary outcome results: IIEF (~mean score /30): EF IG scored higher ~29 vs. CG ~8; OF IG scored higher ~10 vs. CG ~2; SD IG scored higher ~8 vs. CG ~2; intercourse satisfaction IG scored higher ~14 vs. CG ~4; OS IG scored higher ~9 vs. CG ~4 (no indication of sign.)(data provided in Figure 2) Testosterone serum levels (~ mean ng/ml): IG ~4.6 vs. CG ~3.6 no sign. difference (p >0.05)(data provided in Figure 1) DHEA serum levels (~ mean µg/ml): IG levels ▲~2.4 vs. CG ~1.0 (no indication of sign.)(data provided in Figure 1)</p> <p>Other outcomes assessed: PRL and PSA serum levels</p> <p>Withdrawals/drop-outs/loss to f/u (N): insufficient response IG 0, CG 6; inadequate PSA IG 0, CG 1 WDAE: NR TAE: NR SAE: NR</p> <p>Ascertainment of outcomes assessed: IIEF: 15-item questionnaire, questions rated 0-5. Testosterone serum levels: via blood sample. DHEA serum levels: via blood sample.</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Safarinejad (2001) ²⁶⁰</p> <p>Funding source: NR</p>	<p>N screened = 44 N randomized = 44</p> <p>IG1 screened = 44 IG1 randomized = 44</p> <p>CG screened: 44 CG randomized: 44</p> <p>Inclusion: No organic diseases, laboratory findings were normal, peak flow values on Duplex ultrasonography were > 30cm/s in both cavernous arteries, the end diastolic flow on duplex Doppler ultrasonography was < 2cm/s, intra cavernous injection test produced good rigidity, neurologic findings were normal.</p> <p>Exclusion: clinically obvious psychogenic impotence, verified or suspected malignancy, diabetes, neurological problems such as parkinsonism and paraplegia, impotence of clearly arterial or venous origin, genital anomaly or disease, cardiovascular disorders</p>	<p>Age , mean (range): 42 (28-55) y</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant Medications (n/grp): NR</p> <p>Duration of ED (yr): NR</p> <p>Underlying disease (diagnosis) (N or % of diseased/grp): NR</p> <p>Physiologic ED: NR</p> <p>Psychogenic ED: NR</p> <p>Mixed ED: 44</p>	<p>IG1: isoxsuprine hydrochloride, oral medication (pill form) CG: oral medication (pill form)</p> <p>IG1: Dose: 60 milligrams Duration: 30 days Frequency: 1x/day Compliance (%): NR</p> <p>CG: Dose: NA Duration: 30 days Frequency: 1x/day Compliance (%): 82</p> <p>Run In period: NR Wash out period: 2 wks</p> <p>F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Erectile response for IG1: n (%) - Complete: 3 (8.3); Partial: 3 (8.3); None: 27 (75); Worse: 3 (8.3) Erectile response for CG: n (%) - Complete: 3 (8.3); Partial: 4 (11); None: 29 (80.5); Worse: 0</p> <p>List (narrative) other outcomes assessed: Pulse rate, blood pressure, Libido, orgasm, duration of erection, rigidity of penis</p> <p>ITT analysis used for primary outcome? Y N/NR: No</p> <p>Withdrawals/drop-outs/loss to f/u [N and/or %]: 6</p> <p>WDAE (N and/or %): 2 (IG1, hypotension) TAE: 47 IG1: n (%) - ▼ arterial pressure: 8 (22.2); Headache: 7 (19.4) Trembling: 3 (8.3); Nervousness: 4 (11.1); Gastrointestinal problems: 9 (25) Skin rash: 4 (11.1); Facial redness: 4 (11.1); Tachycardia: 2 (5.55) CG: n (%) - Headache: 2 (5.55); Skin rash: 2 (5.55); Tachycardia: 3 (8.3) SAE: 0</p> <p>Ascertainment of outcomes assessed: Doppler ultrasonography, patient perception questionnaire, laboratory tests</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sommer (2006) 261</p> <p>Funding source: NR (medication by LO.LI Pharma Co. Italy)</p>	<p>N screened = NR N randomized = 176</p> <p>IG, n = NR CG, n = NR</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men with diagnosed DM type II and ED of longer than 6 mo who were in stable relationships</p> <p>Exclusion: current or recent ED treatment (including vacuum devices, IC or IU injections)</p>	<p>Age, range: 50-70 y</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: BMI, mean (sem) 26.2 (3.5) vs. 27.4 (3.0) kg/m²</p>	<p>Concomitant medications, n (%):NR</p> <p>Duration of ED: > 6 mo</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 0</p> <p>Physiologic ED, n (%): 100%</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Myoinositol/folic acid combination (oral) CG: Placebo</p> <p>IG: Dose: 4 g/400 µg Duration: 12 wks Frequency: once/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 2 wks Wash out period: NA</p> <p>F/u duration: 90 d</p>	<p>Primary outcome results: IIEF-5 score, mean (sem): Baseline: 12 (5) vs. 14 (4) Post tx: 20 (3) vs. 13 (4)</p> <p>Sexual function, mean (sem) Baseline: 8 (3) vs. 9 (2) Post tx: 11 (1) vs. 9 (1)</p> <p>Sexual diary, mean (sem) Baseline: 1 (1) vs. 1 (1) Post tx: 6 (1) vs. 3 (1)</p> <p>Other outcomes assessed: PSV, EDV and RI (resistance index); results indicated sign. improvement in PSV and EDV after tx in IG only (p<0.05)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): NR SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: IIEF-5, pts diary</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sommer (2006) 262</p> <p>Funding source: NR</p>	<p>N screened = 237 N randomized = 68 (cross over design)</p> <p>IG/CG, n = 68</p> <p>ITT analysis used for primary outcome: NR</p> <p>Inclusion: men 18 or older, with diagnosed depressive disorder and ED of longer than 6 mo who were in stable relationships</p> <p>Exclusion: other axis I psychiatric disorder (i.e. substance abuse or dependence), use of any antidepressant medication, abnormal serum hormone levels, hx of major organ disease or poorly controlled DM</p>	<p>Age, mean (sd): 36.1 (6.7) vs. 35 (8.3)</p> <p>Race: NR</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p> <p>Other: BMI, mean (sem) 26.2 (3.5) vs. 27.4 (3.0) kg/m²</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: 6.5 (1.4) VS. 7.2 (1.5) y</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): 100%</p> <p>Physiologic ED, n (%): 0</p> <p>Mixed ED, n (%): NR</p>	<p>IG: Tianeptine (oral) CG: Placebo</p> <p>IG: Dose: NR Duration: 8 wks Frequency: once/d Compliance: NR</p> <p>CG: Dose: NA Duration: as IG Frequency: as IG Compliance: NR</p> <p>Run In period: 4 wks Wash out period: NR</p> <p>F/u duration: 8 and 16 wks (end of each cross over tx phase)</p>	<p>Primary outcome results: Brief Sexual Inventory score for erection, mean (sd): Baseline: 5.4 (1.9) vs. 4.1 (2.3) Post tx: 8.5 (2.4) vs. 5.7 (1.1), p<0.05</p> <p>GAQ, % yes (successful sexual intercourse): 89.4% vs. 50%</p> <p>Responders: 48 (72.2%) vs. 19 (27.9%)</p> <p>Other outcomes assessed: depressive scores (ED improvement highly correlated with changes in depressive symptoms)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): 5 (3.4) vs. 1 (1.5) including headache, GI or CNS symptoms SAE, n (%): NR</p> <p>Ascertainment of outcomes assessed: Anxiety Depression Scale, Brief Sexual Inventory, and QoL and erection questionnaire; GAQ</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Sommer (2006) 263</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 18 (likely parallel)</p> <p>IG1, n = NR IG2, n = NR CG, n = NR</p> <p>ITT analysis used for primary outcome: yes</p> <p>Inclusion: men 21-62 y; diagnosed with ED (by IIEF-EF)</p> <p>Exclusion: ED due to any neurological or endocrine causes, an anatomical deformity such as severe penile fibrosis, SCI or radical prostatectomy, DM, other relevant comorbidities, major psychiatric illness or concomitant tx</p>	<p>Age, mean (sd): 41.6 (11.9) y</p> <p>Race: 100% White</p> <p>Co-morbidities, n (%): NR</p> <p>Previous ED treatment: NR</p> <p>Smoking status: NR</p> <p>Body weight: 78.8 (7.9) kg</p> <p>Other: IIEF-EF baseline: range 14-19</p>	<p>Concomitant medications, n (%): NR</p> <p>Duration of ED: NR</p> <p>Underlying disease, n (%): NR</p> <p>Psychogenic ED, n (%): NR</p> <p>Physiologic ED, n (%): NR</p> <p>Mixed ED, n (%): NR</p>	<p>IG1-2: Tetrahydrobiopterine (BH₄) + VSS CG: Placebo</p> <p>IG1/2: Dose: 200 mg or 500 mg Duration: NA Frequency: single dose Compliance: 100%</p> <p>CG: Dose: NA Duration: NA Frequency: as IG Compliance: 100%</p> <p>Run In period: NR Wash out period: NR</p> <p>F/u duration: NR</p>	<p>Primary outcome results: Time, base rigidity 60-100%, mean (sd): 71.6 (40.5) vs. 74.2 (44.1) vs. 38.1 (26.4) min Duration of event at base, mean (sd): 74.1 (36.1) vs. 77.9 (41.1) vs. 51.2 (26.9)</p> <p>Time, tip rigidity 60-100%, mean (sd): 54.6 (33.4) vs. 58.9 (46.1) vs. 25.2 (22.3) min Duration of event at tip, mean (sd): 67.2 (37.2) vs. 78.9 (42.2) vs. 37.7 (29.8) min</p> <p>Other outcomes assessed: Other RigiScan measures (base and tip RAU, time rigidity of 80-100%, TAU, average event rigidity, average event tumescence)</p> <p>Withdrawals/drop-outs/loss to f/u, n (%): NR</p> <p>WDAE, n (%): NR TAE, n (%): 2 () vs. 1 () vs. 1 () SAE, n (%): 0</p> <p>Ascertainment of outcomes assessed: RigiScan</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Speel (2005) ²⁶⁴</p> <p>Funding source:</p>	<p>N screened = 59 N randomized = 59</p> <p>IG1, n = 30 CG, n = 29</p> <p>ITT analysis used for primary outcome: None</p> <p>Inclusion: Patients with complaints of ED and impaired cavernosal perfusion as demonstrated with PPDU. Patients between 35 to 75yrs.</p> <p>Exclusion: Men with penile implants; heart failure or low ejection fraction; uncontrolled hypertension; hypotension; nephropathy or renal artery stenosis; abnormal kidney function; dehydration; taking diuretic; myocardial infraction or stroke within 4 wks; hypersensitivity for ACE, participating in any other trial; has medical, psychiatric or substance abuse disorders, hx of malignancy.</p>	<p>Age, mean (sd); 60 (6.8) yrs</p> <p>Race: NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C): NR</p> <p>Previous ED treatment: None</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Body weight: NR</p>	<p>Concomitant medications: Sildenafil, self – injection with papaverine/ phentolamine prior to sexual intercourse. (70% used)</p> <p>Duration of ED, mean (95% CI) mo IG1: 40 (25-55) CG: 48 (29-67)</p> <p>Underlying disease (diagnosis): n (%) IG1: 9 (30) CG: 3 (10.3) suffered from diabetes</p> <p>Psychogenic ED: None</p> <p>Physiologic ED: None</p> <p>Mixed ED: None</p>	<p>IG1: Quinapril CG: Placebo</p> <p>IG1: Dose: 20mg Duration: 26 – 46 wks Frequency: once a day Compliance (%): (87)</p> <p>CG: Dose: Duration: 26 – 46 wks Frequency: once a day Compliance (%): (93)</p> <p>Run In period: None Wash out period: None</p> <p>F/u duration (on and off treatment): day 14, wk 4, and 2 mo</p>	<p>Primary outcome (EF): Change AT: -13 vs.-18 Change IMT: 0.03 vs. 0.01 Sexual Activity (% change): 8 vs. 20 Severe ED (% change): -32 vs. -35</p> <p>Other outcomes assessed: IIEF score erection domain (who were sexually active) n (%) >19 (mild): 4 (25) vs. 4 (24) 13-18 (moderate): 7 (44) vs. 6 (35) 5-12 (severe): 5 (31) vs.7 (41)</p> <p>Withdrawals/drop-outs/loss to f/u: n (%). IG1: 2 (6.7) were exclude for lack of compliance. CG: 2 (6.9) Lack of compliance</p> <p>WDAE: n (%). IG1: 2 (6.7) dropped out because of discomfort in the epigastria region. CG: 1 (3.4) had a stroke during study 1 (3.4) died during study because of cerebral hemorrhage.</p> <p>TAE: n (%). IG1: 3 (10) dry cough, 4 (13.3) nausea, 3 (10) joint and muscle pain, and 1 (3.3) twinkle feeling in feet. CG: 2 (6.9) epigastric pain, 1 (3.4) dry cough, 1 (3.4) nausea, 1 (3.4) headache.</p> <p>SAE: n (%). CG: 1 (3.4) had a stroke during study. 1 (3.4) died during study because of cerebral hemorrhage.</p> <p>Ascertainment of outcomes assessed: Cavernosal acceleration time measures during PPDU, IMT, and EF determined by the erection domain of the IIEF questionnaire. (Physician and vascular technologist)</p>

Author Funding	N; study design; eligibility	Participants characteristics	Diagnosis details	Intervention	Outcomes
<p>Van Ahlen (1995) ²⁶⁵</p> <p>Funding source: NR</p>	<p>N screened = NR N randomized = 20</p> <p>IG1 randomized = 20 IG2 randomized = 20 CG randomized = 20</p> <p>Inclusion: normal results for evaluation of pharmacotesting, evaluation of relevant hormones, pharmaco-Doppler studies and nocturnal penile tumescence</p> <p>Exclusion: severe organic causes of ED, severe cardiac disease, hypertension, DM, elevated liver enzyme concentrations.</p>	<p>Age, mean (sd): 46.3 (\pm2.7)</p> <p>Race (%): NR</p> <p>Co-morbidities (unrelated to disease): NR</p> <p>Blood glucose (or HbA1C)(%): NR</p> <p>Previous ED treatment: NR</p> <p>BMI (kg/m²): NR</p> <p>Smoking status: NR</p> <p>Initial body weight: NR</p>	<p>Concomitant medications: NR</p> <p>Duration of ED (yr) SD: 3.6 (\pm 0.5)</p> <p>Underlying disease (diagnosis) (N or % of diseased/ grp): NR</p> <p>Psychogenic ED: NR</p> <p>Physiologic ED: NR</p> <p>Mixed ED: NR</p>	<p>IG1: oral naltrexone IG2: oral naltrexone CG: oral placebo</p> <p>IG1: Dose: 25 milligrams (phase 1) Duration: 4wks Frequency: 1x/day Compliance (%): 90</p> <p>IG2: Dose: 25 milligrams (50 total) Duration: 4wks (phase 2) Frequency: 2x/day Compliance (%): 90</p> <p>CG: Dose: matching to treatment Duration: 8 wks Frequency: matching IG1 & IG2 Compliance (%): 90</p> <p>Run In period: 4 wks Wash out period: NR F/u duration (both on and off treatment): NR</p>	<p>Primary outcome results: Intercourse (non-sig), libido (non-sig) Spontaneous early morning erections Baseline: 2.83 \pm 0.28 IG1: 4.22 \pm 0.31 IG2: 3.78 \pm 0.31</p> <p>List (narrative) other outcomes assessed: None</p> <p>ITT analysis used for primary outcome? NR</p> <p>Withdrawals/drop-outs/loss to f/u [N and or %]: IG1: 1 = psychological reasons IG2: 1= psychological reasons</p> <p>WDAE (N and/or %): 0</p> <p>TAE: 0</p> <p>SAE: 0</p> <p>Ascertainment of outcomes assessed: Daily patient questionnaire, hormonal measurements – no objective evaluations</p>

List of abbreviations: %=percent, ▲=increased, ▼=decreased, AE=adverse event, SAE=serious adverse event, BMI=body mass index, CC=controlled clinical trials, CG=comparator/control group, ctrls=controls, DM=diabetes mellitus, E₁IC=intracavernosal injection, ECG=electrocardiograms, ED=erectile dysfunction, EDV=end-diastolic velocity, f/u=follow-up, FMD=flow mediated dilation, GAQ=global assessment question, GEQ=global efficacy question, grp=group/s, HbA1C=haemoglobin, hr=hour(s), hx=history, IG=intervention group, IIEF= international index of erectile function (EF=erectile function, OF=orgasmic function, OS=overall satisfaction, SD=sexual desire), ITT=intent-to-treat (Y = yes, N = no, NR = not reported), IU=intraurethral, kg=kilograms, lbs=pounds, LUTS=lower urinary tract symptoms, M=male, max=maximum, mo=month(s), NA=not applicable, PADAM=partial androgen deficiency of the aging male, PgE₁=Prostaglandin, PRL=prolactin, PSA=prostate-specific antigen, RAU=rigidity activity unit, RCT=randomized control trial, SBP=systolic blood pressure, sign.=significant; TAE=total adverse events, TAU=tumescence activity unit, vs.=versus, WDAE=withdrawals resulting from adverse events, wk=week(s), yr=year(s).

References

- (1) Abdel-Naser MB, Imam A, Wollina U. Sildenafil citrate significantly improves nocturnal penile erections in sildenafil non-responding patients with psychogenic erectile dysfunction. *Int J Impot Res* 2004; 16(6):552-556.
- (2) Albuquerque DC, Miziara LJ, Saraiva JFK et al. Efficacy, safety and tolerability of sildenafil in Brazilian hypertensive patients on multiple antihypertensive drugs. *Int Braz J Urol* 2005; 31(4):342-355.
- (3) Althof SE, O' Leary MP, Cappelleri JC et al. Self-esteem, confidence, and relationships in men treated with sildenafil citrate for erectile dysfunction: results of two double-blind, placebo-controlled trials. *J Gen Intern Med* 2006; 21(10):1069-1074.
- (4) Bank AJ, Kelly AS, Kaiser DR et al. The effects of quinapril and atorvastatin on the responsiveness to sildenafil in men with erectile dysfunction. *Vasc Med* 2006; 11(4):251-257.
- (5) Bawa AS, Sharma DR, Singh R et al. Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo-controlled, crossover study. *Indian J Pharmacol* 2004; 36(5):317.
- (6) Becher E, Tejada NA, Gomez R et al. Sildenafil citrate (Viagra) in the treatment of men with erectile dysfunction in southern Latin America: a double-blind, randomized, placebo-controlled, parallel-group, multicenter, flexible-dose escalation study. *Int J Impot Res* 2002; 14(Suppl 2):33-41.
- (7) Boolell M, Gepi-Attee S, Gingell JC et al. Sildenafil, a novel effective oral therapy for male erectile dysfunction. *Br J Urol* 1996; 78(2):257-261.
- (8) Boulton AJ, Selam JL, Sweeney M et al. Sildenafil citrate for the treatment of erectile dysfunction in men with Type II diabetes mellitus. *Diabetologia* 2001; 44(10):1296-1301.
- (9) Cappelleri JC, Siegel RL, Osterloh IH et al. Relationship between patient self-assessment of erectile function and the erectile function domain of the international index of erectile function. *Urology* 2000; 56(3):477-481.
- (10) Lewis R, Bennett CJ, Borkon WD et al. Patient and partner satisfaction with Viagra (sildenafil citrate) treatment as determined by the Erectile Dysfunction Inventory of Treatment Satisfaction Questionnaire. *Urology* 2001; 57(5):960-965.
- (11) Cavallini G, Modenini F, Vitali G et al. Acetyl-L-carnitine plus propionyl-L-carnitine improve efficacy of sildenafil in treatment of erectile dysfunction after bilateral nerve-sparing radical retropubic prostatectomy. *Urology* 2005; 66(5):1080-1085.
- (12) Chen KK, Hsieh JT, Huang ST et al. ASSESS-3: a randomised, double-blind, flexible-dose clinical trial of the efficacy and safety of oral sildenafil in the treatment of men with erectile dysfunction in Taiwan. *Int J Impot Res* 2001; 13(4):221-229.
- (13) Choi HK, Ahn TY, Kim JJ et al. A double-blind, randomised- placebo, controlled, parallel group, multicentre, flexible-dose escalation study to assess the efficacy and safety of sildenafil administered as required to male outpatients with erectile dysfunction in Korea. *Int J Impot Res* 2003; 15(2):80-86.
- (14) Choppin A, Blue DR, Hegde SS et al. Evaluation of oral ro70-0004/003, an alpha1A-adrenoceptor antagonist, in the treatment of male erectile dysfunction. *Int J Impot Res* 2001; 13(3):157-161.
- (15) Christiansen E, Guirguis WR, Cox D et al. Long-term efficacy and safety of oral Viagra (sildenafil citrate) in men with erectile dysfunction and the effect of randomised treatment withdrawal. *Int J Impot Res* 2000; 12(3):177-182.
- (16) DeBusk RF, Pepine CJ, Glasser DB et al. Efficacy and safety of sildenafil citrate in

- men with erectile dysfunction and stable coronary artery disease. *Am J Cardiol* 2004; 93(2):147-153.
- (17) Deveci S, Peskircioglu L, Aygun C et al. Sublingual sildenafil in the treatment of erectile dysfunction: faster onset of action with less dose. *Int J Urol* 2004; 11(11):989-992.
- (18) Diamond LE, Earle DC, Garcia WD et al. Co-administration of low doses of intranasal PT-141, a melanocortin receptor agonist, and sildenafil to men with erectile dysfunction results in an enhanced erectile response. *Urology* 2005; 65(4):755-759.
- (19) Dinsmore WW, Hodges M, Hargreaves C et al. Sildenafil citrate (Viagra) in erectile dysfunction: near normalization in men with broad-spectrum erectile dysfunction compared with age-matched healthy control subjects.[erratum appears in *Urology* 1999 May;53(5):1072]. *Urology* 1999; 53(4):800-805.
- (20) Dunzendorfer U, Behm A, Dunzendorfer E et al. Drug combinations in the therapy of low response to phosphodiesterase 5 inhibitors in patients with erectile dysfunction. *In Vivo* 2002; 16(5):345-348.
- (21) Eardley I, Brooks J, Yates PK et al. Sildenafil citrate (VIAGRA): an oral treatment for erectile function with activity for up to four hours' duration. *Int J Clin Pract* 1999; 102(Suppl Jun.):102-104.
- (22) Eardley I, Morgan R, Dinsmore W et al. Efficacy and safety of sildenafil citrate in the treatment of men with mild to moderate erectile dysfunction. *Br J Psychiatry* 2001; 178(Apr.):325-330.
- (23) Eardley I, Ellis P, Boolell M et al. Onset and duration of action of sildenafil for the treatment of erectile dysfunction. *Br J Clin Pharmacol* 2002; 53(Suppl 1):61-65.
- (24) Eardley I, Mirone V, Montorsi F et al. An open-label, multicentre, randomized, crossover study comparing sildenafil citrate and tadalafil for treating erectile dysfunction in men naive to phosphodiesterase 5 inhibitor therapy. *BJU Int* 2005; 96(9):1323-1332.
- (25) Fava M, Nurnberg HG, Seidman SN et al. Efficacy and safety of sildenafil in men with serotonergic antidepressant-associated erectile dysfunction: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2006; 67(2):240-246.
- (26) Fowler CJ, Miller JR, Sharief MK et al. A double blind, randomised study of sildenafil citrate for erectile dysfunction in men with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2005; 76(5):700-705.
- (27) Gentile V, Vicini P, Prigiotti G et al. Preliminary observations on the use of propionyl-L-carnitine in combination with sildenafil in patients with erectile dysfunction and diabetes. *Curr Med Res Opin* 2004; 20(9):1377-1384.
- (28) Gingell C, Sultana SR, Wulff MB et al. Duration of action of sildenafil citrate in men with erectile dysfunction. *J Sex Med* 2004; 1(2):179-184.
- (29) Glina S, Bertero E, Claro J et al. Efficacy and safety of sildenafil citrate for the treatment of erectile dysfunction in Latin America. *Braz J Urol* 2001; 27(2):148-154.
- (30) Glina S, Bertero E, Claro J et al. Efficacy and safety of flexible-dose oral sildenafil citrate (Viagra) in the treatment of erectile dysfunction in Brazilian and Mexican men. *Int J Impot Res* 2002; 14(Suppl 2):27-32.
- (31) Goldstein I, Lue TF, Padma-Nathan H et al. Oral sildenafil in the treatment of erectile dysfunction. Sildenafil Study Group. *N Engl J Med* 1998; 338(20):1397-1404.
- (32) Padma-Nathan H. Oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: assessment of erections hard enough for sexual intercourse. *Int J Clin Pract* 1999; 102(Jun.):13-15.
- (33) Barry MJ. Sildenafil improved sexual function in erectile dysfunction. *Int J Impot Res* 1998; 3(6):184.
- (34) Gomez F, Davila H, Costa A et al. Efficacy and safety of oral sildenafil citrate (Viagra) in the treatment of male erectile dysfunction

- in Colombia, Ecuador, and Venezuela: a double-blind, multicenter, placebo-controlled study. *Int J Impot Res* 2002; 14(Suppl 2):42-47.
- (35) Gopalakrishnan R, Jacob KS, Kuruvilla A et al. Sildenafil in the treatment of antipsychotic-induced erectile dysfunction: a randomized, double-blind, placebo-controlled, flexible-dose, two-way crossover trial. *Am J Psychiatry* 2006; 163(3):494-499.
- (36) Hartmann U, Meuleman EJ, Cuzin B et al. Sildenafil citrate (VIAGRA): analysis of preferred doses in a European, six-month, double-blind, placebo-controlled, flexible dose-escalation study in patients with erectile dysfunction. Multicentre Study Group. *Int J Clin Pract* 1999; 102(Suppl Jun.):102-109.
- (37) Heiman JR, Talley DR, Bailen JL et al. Sexual function and satisfaction in heterosexual couples when men are administered sildenafil citrate (Viagra) for erectile dysfunction: a multicentre, randomised, double-blind, placebo-controlled trial. *BJOG* 2007; 114(4):437-447.
- (38) Herrmann HC, Levine LA, Macaluso J, Jr. et al. Can atorvastatin improve the response to sildenafil in men with erectile dysfunction not initially responsive to sildenafil? Hypothesis and pilot trial results. *J Sex Med* 2006; 3(2):303-308.
- (39) Hussain IF, Brady CM, Swinn MJ et al. Treatment of erectile dysfunction with sildenafil citrate (Viagra) in parkinsonism due to Parkinson's disease or multiple system atrophy with observations on orthostatic hypotension. *J Neurol Neurosurg Psychiatry* 2001; 71(3):371-374.
- (40) Incrocci L, Koper PC, Hop WC et al. Sildenafil citrate (Viagra) and erectile dysfunction following external beam radiotherapy for prostate cancer: a randomized, double-blind, placebo-controlled, cross-over study. *Int J Radiat Oncol Biol Phys* 2001; 51(5):1190-1195.
- (41) Incrocci L, Hop WC, Slob AK. Efficacy of sildenafil in an open-label study as a continuation of a double-blind study in the treatment of erectile dysfunction after radiotherapy for prostate cancer. *Urology* 2003; 62(1):116-120.
- (42) Kaplan SA, Gonzalez RR, Te AE. Combination of alfuzosin and sildenafil is superior to monotherapy in treating lower urinary tract symptoms and erectile dysfunction. *Eur Urol* 2007; 51(6):1717-1723.
- (43) Katz SD, Parker JD, Glasser DB et al. Efficacy and safety of sildenafil citrate in men with erectile dysfunction and chronic heart failure. *Am J Cardiol* 2005; 95(1):36-42.
- (44) Kongkanand A, Ratana-Olarn K, Ruangdilokrat S et al. The efficacy and safety of oral sildenafil in Thai men with erectile dysfunction: a randomized, double-blind, placebo controlled, flexible-dose study. *J Med Assoc Thai* 2003; 86(3):195-205.
- (45) Koulikov D, Fridmans A, Chertin B et al. Is sildenafil citrate associated with an amelioration of the symptomatology of androgen decline in the aging male? *J Urol* 2007; 177(6):2267-2271.
- (46) Levinson IP, Khalaf IM, Shaeer KZ et al. Efficacy and safety of sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men in Egypt and South Africa. *Int J Impot Res* 2003; 15(Suppl 1):25-29.
- (47) Lindsey I, George B, Kettlewell M et al. Randomized, double-blind, placebo-controlled trial of sildenafil (Viagra) for erectile dysfunction after rectal excision for cancer and inflammatory bowel disease. *Dis Colon Rectum* 2002; 45(6):727-732.
- (48) Mahon A, Sidhu PS, Muir G et al. The efficacy of sildenafil for the treatment of erectile dysfunction in male peritoneal dialysis patients. *Am J Kidney Dis* 2005; 45(2):381-387.
- (49) McVary KT, Monnig W, Camps JL, Jr. et al. Sildenafil citrate improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract

- symptoms associated with benign prostatic hyperplasia: a randomized, double-blind trial. *J Urol* 2007; 177(3):1071-1077.
- (50) Melnik T, Abdo CH. Psychogenic erectile dysfunction: comparative study of three therapeutic approaches. *J Sex Med* 2005; 31(3):243-255.
- (51) Meuleman E, Cuzin B, Opsomer RJ et al. A dose-escalation study to assess the efficacy and safety of sildenafil citrate in men with erectile dysfunction. *BJU Int* 2001; 87(1):75-81.
- (52) Montorsi F, McDermott TE, Morgan R et al. Efficacy and safety of fixed-dose oral sildenafil in the treatment of erectile dysfunction of various etiologies. *Urology* 1999; 53(5):1011-1018.
- (53) Montorsi F, Maga T, Strambi LF et al. Sildenafil taken at bedtime significantly increases nocturnal erections: results of a placebo-controlled study. *Urology* 2000; 56(6):906-911.
- (54) Nurnberg HG, Hensley PL, Gelenberg AJ et al. Treatment of antidepressant-associated sexual dysfunction with sildenafil: a randomized controlled trial. *JAMA* 2003; 289(1):56-64.
- (55) O'Leary MP, Althof SE, Cappelleri JC et al. Self-esteem, confidence and relationship satisfaction of men with erectile dysfunction treated with sildenafil citrate: a multicenter, randomized, parallel group, double-blind, placebo controlled study in the United States. *J Urol* 2006; 175(3 Pt 1):1058-1062.
- (56) Olsson AM, Speakman MJ, Dinsmore WW et al. Sildenafil citrate (Viagra) is effective and well tolerated for treating erectile dysfunction of psychogenic or mixed aetiology. *Int J Clin Pract* 2000; 54(9):561-566.
- (57) Olsson AM, Persson CA, Swedish Sildenafil Investigators Group. Efficacy and safety of sildenafil citrate for the treatment of erectile dysfunction in men with cardiovascular disease. *Int J Clin Pract* 2001; 55(3):171-176.
- (58) Orr G, Weiser M, Polliack M et al. Effectiveness of sildenafil in treating erectile dysfunction in PTSD patients: a double-blind, placebo-controlled crossover study. *J Clin Psychopharmacol* 2006; 26(4):426-430.
- (59) Padma-Nathan H, Steers WD, Wicker PA. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction: a double-blind, placebo-controlled study of 329 patients. Sildenafil Study Group. *Int J Clin Pract* 1998; 52(6):375-379.
- (60) Padma-Nathan H, Stecher VJ, Sweeney M et al. Minimal time to successful intercourse after sildenafil citrate: results of a randomized, double-blind, placebo-controlled trial. *Urology* 2003; 62(3):400-403.
- (61) Palmer JS, Kaplan WE, Firlit CF. Erectile dysfunction in spina bifida is treatable. *Lancet* 1999; 354(9173):125-126.
- (62) Palmer JS, Kaplan WE, Firlit CF. Erectile dysfunction in patients with spina bifida is a treatable condition. *J Urol* 2000; 164(3 Pt 2):958-961.
- (63) Perimenis P, Karkoulias K, Markou S et al. Erectile dysfunction in men with obstructive sleep apnea syndrome: a randomized study of the efficacy of sildenafil and continuous positive airway pressure. *Int J Impot Res* 2004; 16(3):256-260.
- (64) Perimenis P, Karkoulias K, Konstantinopoulos A et al. Sildenafil versus continuous positive airway pressure for erectile dysfunction in men with obstructive sleep apnea: a comparative study of their efficacy and safety and the patient's satisfaction with treatment. *Asian J Androl* 2007; 9(2):259-264.
- (65) Pickering TG, Shepherd AMM, Puddey I et al. Sildenafil citrate for erectile dysfunction in men receiving multiple antihypertensive agents: A randomized controlled trial. *Am J Hypertens* 2004; 17(12):1135-1142.
- (66) Price DE, Gingell JC, Gepi-Attee S et al. Sildenafil: study of a novel oral treatment for erectile dysfunction in diabetic men. *Diabet Med* 1998; 15(10):821-825.

- (67) Rendell MS, Rajfer J, Wicker PA et al. Sildenafil for treatment of erectile dysfunction in men with diabetes: a randomized controlled trial. Sildenafil Diabetes Study Group. *JAMA* 1999; 281(5):421-426.
- (68) Safarinejad MR. Oral sildenafil in the treatment of erectile dysfunction in diabetic men: a randomized double-blind and placebo-controlled study. *J Diabetes Complications* 2004; 18(4):205-210.
- (69) Safarinejad MR. Salvage of sildenafil failures with cabergoline: a randomized, double-blind, placebo-controlled study. *Int J Impot Res* 2006; 18(6):550-558.
- (70) Seibel I, Poli de Figueiredo CE, Teloken C et al. Efficacy of oral sildenafil in hemodialysis patients with erectile dysfunction. *J Am Soc Nephrol* 2002; 13(11):2770-2775.
- (71) Seidman SN, Roose SP, Menza MA et al. Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. *Am J Psychiatry* 2001; 158(10):1623-1630.
- (72) Rosen RC, Seidman SN, Menza MA et al. Quality of life, mood, and sexual function: a path analytic model of treatment effects in men with erectile dysfunction and depressive symptoms. *Int J Impot Res* 2004; 16(4):334-340.
- (73) Shabsigh R. Efficacy of sildenafil citrate (VIAGRA) is not affected by aetiology of erectile dysfunction. *Int J Clin Pract* 1999; 102(Jun.):19-20.
- (74) Sharma RK, Prasad N, Gupta A et al. Treatment of erectile dysfunction with sildenafil citrate in renal allograft recipients: a randomized, double-blind, placebo-controlled, crossover trial. *Am J Kidney Dis* 2006; 48(1):128-133.
- (75) Salonia A. Sildenafil citrate: A safe and effective treatment for erectile dysfunction after renal transplantation? Commentary. *Nature Clinical Practice Nephrology* 2007; 3(2):80-81.
- (76) Sommer F, Klotz T, Engelmann U. Improved spontaneous erectile function in men with mild-to-moderate arteriogenic erectile dysfunction treated with a nightly dose of sildenafil for one year: a randomized trial. *Asian J Androl* 2007; 9(1):134-141.
- (77) Stuckey BG, Jadzinsky MN, Murphy LJ et al. Sildenafil citrate for treatment of erectile dysfunction in men with type 1 diabetes: results of a randomized controlled trial. *Diabetes Care* 2003; 26(2):279-284.
- (78) Tan HM, Moh CL, Mendoza JB et al. Asian sildenafil efficacy and safety study (ASSESS-1): a double-blind, placebo-controlled, flexible-dose study of oral sildenafil in Malaysian, Singaporean, and Filipino men with erectile dysfunction. The Assess-1 Study Group. *Urology* 2000; 56(4):635-640.
- (79) Lim PH, Ng FC, Cheng CW et al. Clinical safety profile of sildenafil in Singaporean men with erectile dysfunction: pre-marketing experience (ASSESS-I evaluation). *J Int Med Res* 2002; 30(2):137-143.
- (80) Tignol J, Furlan PM, Gomez-Beneyto M et al. Efficacy of sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men in remission from depression. *Int Clin Psychopharmacol* 2004; 19(4):191-199.
- (81) Ugarte F, Hurtado-Coll A. Comparison of the efficacy and safety of sildenafil citrate (Viagra) and oral phentolamine for the treatment of erectile dysfunction. *Int J Impot Res* 2002; 14(Suppl 2):48-53.
- (82) Webster LJ, Michelakis ED, Davis T et al. Use of sildenafil for safe improvement of erectile function and quality of life in men with New York Heart Association classes II and III congestive heart failure: a prospective, placebo-controlled, double-blind crossover trial. *Arch Intern Med* 2004; 164(5):514-520.
- (83) Young JM, Bennett C, Gilhooly P et al. Efficacy and safety of sildenafil citrate (Viagra) in black and Hispanic American men. *Urology* 2002; 60(2 Suppl 2):39-48.

- (84) Zinner N. Do food and dose timing affect the efficacy of sildenafil? A randomized placebo-controlled study. *J Sex Med* 2007; 4(1):137-144.
- (85) Carson CC, Hatzichristou DG, Carrier S et al. Erectile response with vardenafil in sildenafil nonresponders: a multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial.[erratum appears in *BJU Int*. 2005 Aug;96(3):466]. *BJU Int* 2004; 94(9):1301-1309.
- (86) Hatzichristou DG, Aliotta P, Auerbach S et al. Erectile response to vardenafil in men with a history of nonresponse to sildenafil: A time-from-dosing descriptive analysis. *Eur Urol* 2005; 27(9):1452-1461.
- (87) Demir E, Balal M, Paydas S et al. Efficacy and safety of vardenafil in renal transplant recipients with erectile dysfunction. *Transplant Proc* 2006; 38(5):1379-1381.
- (88) Edwards D, Hackett G, Collins O et al. Vardenafil improves sexual function and treatment satisfaction in couples affected by erectile dysfunction (ED): a randomized, double-blind, placebo-controlled trial in PDE5 inhibitor-naive men with ED and their partners. *J Sex Med* 2006; 3(6):1028-1036.
- (89) Goldstein I, Young JM, Fischer J et al. Vardenafil, a new phosphodiesterase type 5 inhibitor, in the treatment of erectile dysfunction in men with diabetes: a multicenter double-blind placebo-controlled fixed-dose study. *Diabetes Care* 2003; 26(3):777-783.
- (90) Goldstein I, Fisher WA, Sand M et al. Women's sexual function improves when partners are administered vardenafil for erectile dysfunction: A prospective, randomized, double-blind, placebo-controlled trial. *J Sex Med* 2005; 2(6):819-832.
- (91) Fisher WA, Rosen RC, Mollen M et al. Improving the sexual quality of life of couples affected by erectile dysfunction: A double-blind, randomized, placebo-controlled trial of vardenafil. *J Sex Med* 2005; 2(5):699-708.
- (92) Hatzichristou D, Montorsi F, Buvat J et al. The efficacy and safety of flexible-dose vardenafil (levitra) in a broad population of European men. *Eur Urol* 2004; 45(5):634-641.
- (93) Hatzichristou DG, Cuzin B, Martin-Morales A et al. Vardenafil improves satisfaction rates, depressive symptomatology, and self-confidence in a broad population of men with erectile dysfunction. *J Sex Med* 2005; 2(1):109-116.
- (94) Hellstrom WJ, Gittelman M, Karlin G et al. Vardenafil for treatment of men with erectile dysfunction: efficacy and safety in a randomized, double-blind, placebo-controlled trial. *J Androl* 2002; 23(6):763-771.
- (95) Hellstrom WJ, Elhilali M, Homering M et al. Vardenafil in patients with erectile dysfunction: achieving treatment optimization. *J Androl* 2005; 26(5):604-609.
- (96) Donatucci C, Taylor T, Thibonnier M et al. Vardenafil improves patient satisfaction with erection hardness, orgasmic function and overall sexual experience, while improving quality of life in men with erectile dysfunction. *J Sex Med* 2004; 1(2):185-192.
- (97) Hellstrom WJ, Gittelman M, Karlin G et al. Sustained efficacy and tolerability of vardenafil, a highly potent selective phosphodiesterase type 5 inhibitor, in men with erectile dysfunction: results of a randomized, double-blind, 26-week placebo-controlled pivotal trial. *Urology* 2003; 61(4 Suppl 1):8-14.
- (98) Ishii N, Nagao K, Fujikawa K et al. Vardenafil 20-mg demonstrated superior efficacy to 10-mg in Japanese men with diabetes mellitus suffering from erectile dysfunction. *Int J Urol* 2006; 13(8):1066-1072.
- (99) Klotz T, Sachse R, Heidrich A et al. Vardenafil increases penile rigidity and tumescence in erectile dysfunction patients: a RigiScan and pharmacokinetic study. *World J Urol* 2001; 19(1):32-39.

- (100) Martin-Morales A, Meijide F, Garcia N et al. Efficacy of vardenafil and influence on self-esteem and self-confidence in patients with severe erectile dysfunction. *J Sex Med* 2007; 4(2):440-447.
- (101) Mazo E, Gamidov S, Iremashvili V. The effect of vardenafil on endothelial function of brachial and cavernous arteries. *Int J Impot Res* 2006; 18(5):464-469.
- (102) Montorsi F, Padma-Nathan H, Buvat J et al. Earliest time to onset of action leading to successful intercourse with vardenafil determined in an at-home setting: A randomized, double-blind, placebo-controlled trial. *J Sex Med* 2004; 1(2):168-178.
- (103) Nagao K, Ishii N, Kamidono S et al. Safety and efficacy of vardenafil in patients with erectile dysfunction: result of a bridging study in Japan. *Int J Urol* 2004; 11(7):515-524.
- (104) Nehra A, Grantmyre J, Nadel A et al. Vardenafil improved patient satisfaction with erectile hardness, orgasmic function and sexual experience in men with erectile dysfunction following nerve sparing radical prostatectomy. *J Urol* 2005; 173(6):2067-2071.
- (105) Brock G, Nehra A, Lipshultz LI et al. Safety and efficacy of vardenafil for the treatment of men with erectile dysfunction after radical retropubic prostatectomy. *J Urol* 2003; 170(4 Pt 1):1278-1283.
- (106) Porst H, Rosen R, Padma-Nathan H et al. The efficacy and tolerability of vardenafil, a new, oral, selective phosphodiesterase type 5 inhibitor, in patients with erectile dysfunction: the first at-home clinical trial. *Int J Impot Res* 2001; 13(4):192-199.
- (107) Porst H, Young JM, Schmidt AC et al. Efficacy and tolerability of vardenafil for treatment of erectile dysfunction in patient subgroups. *Urology* 2003; 62(3):519-523.
- (108) Porst H, Sharlip ID, Hatzichristou D et al. Extended duration of efficacy of vardenafil when taken 8 hours before intercourse: a randomized, double-blind, placebo-controlled study. *Eur Urol* 2006; 50(5):1086-1094.
- (109) Rosen R, Shabsigh R, Berber M et al. Efficacy and tolerability of vardenafil in men with mild depression and erectile dysfunction: The depression-related improvement with vardenafil for erectile response study. *Am J Psychiatry* 2006; 163(1):79-87.
- (110) Stark S, Sachse R, Liedl T et al. Vardenafil increases penile rigidity and tumescence in men with erectile dysfunction after a single oral dose. *Eur Urol* 2001; 40(2):181-188.
- (111) Stief C, Porst H, Saenz dT, I et al. Sustained efficacy and tolerability with vardenafil over 2 years of treatment in men with erectile dysfunction. *Int J Clin Pract* 2004; 58(3):230-239.
- (112) Valiquette L, Young JM, Moncada I et al. Sustained efficacy and safety of vardenafil for treatment of erectile dysfunction: a randomized, double-blind, placebo-controlled study. *Mayo Clin Proc* 2005; 80(10):1291-1297.
- (113) Valiquette L, Montorsi F, Auerbach S et al. First-dose success with vardenafil in men with erectile dysfunction and associated comorbidities: RELY-I. *Int J Clin Pract* 2006; 60(11):1378-1385.
- (114) van Ahlen H, Wahle K, Kupper W et al. Safety and efficacy of vardenafil, a selective phosphodiesterase 5 inhibitor, in patients with erectile dysfunction and arterial hypertension treated with multiple antihypertensives. *J Sex Med* 2005; 2(6):856-864.
- (115) Ziegler D, Merfort F, Van AH et al. Efficacy and safety of flexible-dose vardenafil in men with type 1 diabetes and erectile dysfunction. *J Sex Med* 2006; 3(5):883-891.
- (116) Aversa A, Greco E, Bruzziches R et al. Relationship between chronic tadalafil administration and improvement of endothelial function in men with erectile dysfunction: a pilot study. *Int J Impot Res* 2007; 19(2):200-207.

- (117) Carrier S, Brock GB, Pommerville PJ et al. Efficacy and safety of oral tadalafil in the treatment of men in Canada with erectile dysfunction: A randomized, double-blind, parallel, placebo-controlled clinical trial. *J Sex Med* 2005; 2(5):685-698.
- (118) Carson C, Shabsigh R, Segal S et al. Efficacy, safety, and treatment satisfaction of tadalafil versus placebo in patients with erectile dysfunction evaluated at tertiary-care academic centers. *Urology* 2005; 65(2):353-359.
- (119) Chen KK, Jiann B-P, Lin JSN et al. Efficacy and safety of on-demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study. *J Sex Med* 2004; 1(2):201-208.
- (120) Choi H-K, Kim JJ, Kim S-C et al. A randomized, double-blind, parallel, placebo-controlled study of the efficacy and safety of Tadalafil administered on-demand to men with erectile dysfunction in Korea. *Taehan Pinyogikwa Hakhoe Chapchi* 2006; 47(8):852-858.
- (121) De Rose AF, Gallo F, Carmignani G. Evaluation of sexual activity in patients treated with tadalafil: a randomized prospective placebo-controlled trial. *Int J Impot Res* 2005; 17(1):76-79.
- (122) Eardley I, Gentile V, Austoni E et al. Efficacy and safety of tadalafil in a Western European population of men with erectile dysfunction. *BJU Int* 2004; 94(6):871-877.
- (123) Govier F, Potempa AJ, Kaufman J et al. A multicenter, randomized, double-blind, crossover study of patient preference for tadalafil 20 mg or sildenafil citrate 50 mg during initiation of treatment for erectile dysfunction. *Eur Urol* 2003; 25(11):2709-2723.
- (124) Guo YL, Zhu JC, Pan TM et al. Efficacy and safety of on-demand tadalafil for the treatment of erectile dysfunction in South-East Asian men. *Int J Urol* 2006; 13(6):721-727.
- (125) Incrocci L, Slagter C, Slob AK et al. A randomized, double-blind, placebo-controlled, cross-over study to assess the efficacy of tadalafil (Cialis) in the treatment of erectile dysfunction following three-dimensional conformal external-beam radiotherapy for prostatic carcinoma. *Int J Radiat Oncol Biol Phys* 2006; 66(2):439-444.
- (126) McMahon CG, Stuckey BG, Lording DW et al. A 6-month study of the efficacy and safety of tadalafil in the treatment of erectile dysfunction: a randomised, double-blind, parallel-group, placebo-controlled study in Australian men. *Int J Clin Pract* 2005; 59(2):143-149.
- (127) McMahon C, Kloner RA, Hutter Jr AM et al. Comparison of efficacy, safety, and tolerability of on-demand tadalafil and daily dosed tadalafil for the treatment of erectile dysfunction. *J Sex Med* 2005; 2(3):415-427.
- (128) McVary KT, Roehrborn CG, Kaminetsky JC et al. Tadalafil relieves lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Urol* 2007; 177(4):1401-1407.
- (129) Mirone V, Costa P, Damber JE et al. An evaluation of an alternative dosing regimen with tadalafil, 3 times/week, for men with erectile dysfunction: SURE study in 14 European countries. *Eur Urol* 2005; 47(6):846-854.
- (130) Moncada I, Damber J-E, Mirone V et al. Sexual intercourse attempt patterns with two dosing regimens of tadalafil in men with erectile dysfunction: Results from the SURE study in 14 European countries. *J Sex Med* 2005; 2(5):668-674.
- (131) Montorsi F, Nathan HP, McCullough A et al. Tadalafil in the treatment of erectile dysfunction following bilateral nerve sparing radical retropubic prostatectomy: a randomized, double-blind, placebo controlled trial.[erratum appears in *J Urol*. 2005 Feb;173(2):664]. *J Urol* 2004; 172(3):1036-1041.
- (132) Nagao K, Kimoto Y, Marumo K et al. Efficacy and safety of tadalafil 5, 10, and 20 mg in Japanese men with erectile dysfunction: results of a multicenter, randomized, double-blind, placebo-

- controlled study. *Urology* 2006; 68(4):845-851.
- (133) Porst H, Padma-Nathan H, Giuliano F et al. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: a randomized controlled trial. *Urology* 2003; 62(1):121-125.
- (134) Rajfer J, Aliotta PJ, Steidle CP et al. Tadalafil dosed once a day in men with erectile dysfunction: a randomized, double-blind, placebo-controlled study in the US. *Int J Impot Res* 2007; 19(1):95-103.
- (135) Tolra JR, Campana JM, Ciutat LF et al. Prospective, randomized, open-label, fixed-dose, crossover study to establish preference of patients with erectile dysfunction after taking the three PDE-5 inhibitors. *J Sex Med* 2006; 3(5):901-909.
- (136) Rosano GM, Aversa A, Vitale C et al. Chronic treatment with tadalafil improves endothelial function in men with increased cardiovascular risk. *Eur Urol* 2005; 47(2):214-220.
- (137) Rosen RC, Padma-Nathan H, Shabsigh R et al. Determining the earliest time within 30 minutes to erectogenic effect after tadalafil 10 and 20 mg: A multicenter, randomized, double-blind, placebo-controlled, at-home study. *J Sex Med* 2004; 1(2):193-200.
- (138) Saenz dT, I, Anglin G, Knight JR et al. Effects of tadalafil on erectile dysfunction in men with diabetes. *Diabetes Care* 2002; 25(12):2159-2164.
- (139) Saylan M, Khalaf I, Kadioglu A et al. Efficacy of tadalafil in Egyptian and Turkish men with erectile dysfunction. *Int J Clin Pract* 2006; 60(7):812-819.
- (140) Seftel AD, Wilson SK, Knapp PM et al. The efficacy and safety of tadalafil in United States and Puerto Rican men with erectile dysfunction.[erratum appears in *J Urol*. 2005 Feb;173(2):664]. *J Urol* 2004; 172(2):652-657.
- (141) Skoumal R, Chen J, Kula K et al. Efficacy and treatment satisfaction with on-demand tadalafil (Cialis) in men with erectile dysfunction. *Eur Urol* 2004; 46(3):362-369.
- (142) Staab A, Tillmann C, Forgue ST et al. Population dose-response model for tadalafil in the treatment of male erectile dysfunction. *Pharm Res* 2004; 21(8):1463-1470.
- (143) von Keitz A, Rajfer J, Segal S et al. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil. *Eur Urol* 2004; 45(4):499-507.
- (144) Yip WC, Chiang HS, Mendoza JB et al. Efficacy and safety of on demand tadalafil in the treatment of East and Southeast Asian men with erectile dysfunction: a randomized double-blind, parallel, placebo-controlled clinical study. *Asian J Androl* 2006; 8(6):685-692.
- (145) Young JM, Feldman RA, Auerbach SM et al. Tadalafil improved erectile function at twenty-four and thirty-six hours after dosing in men with erectile dysfunction: US trial. *J Androl* 2005; 26(3):310-318.
- (146) Dula E, Keating W, Siami PF et al. Efficacy and safety of fixed-dose and dose-optimization regimens of sublingual apomorphine versus placebo in men with erectile dysfunction. The Apomorphine Study Group. *Urology* 2000; 56(1):130-135.
- (147) Dula E, Bukofzer S, Perdok R et al. Double-blind, crossover comparison of 3 mg apomorphine SL with placebo and with 4 mg apomorphine SL in male erectile dysfunction. *Eur Urol* 2001; 39(5):558-3.
- (148) Eardley I, Wright P, MacDonagh R et al. An open-label, randomized, flexible-dose, crossover study to assess the comparative efficacy and safety of sildenafil citrate and apomorphine hydrochloride in men with erectile dysfunction. *BJU Int* 2004; 93(9):1271-1275.
- (149) Gontero P, D'Antonio R, Pretti G et al. Clinical efficacy of Apomorphine SL in erectile dysfunction of diabetic men. *Int J Impot Res* 2005; 17(1):80-85.

- (150) Hagemann JH, Berding G, Bergh S et al. Effects of visual sexual stimuli and apomorphine SL on cerebral activity in men with erectile dysfunction. *Eur Urol* 2003; 43(4):412-420.
- (151) Lammers PI, Rubio-Aurioles E, Castell R et al. Combination therapy for erectile dysfunction: a randomized, double blind, unblinded active-controlled, cross-over study of the pharmacodynamics and safety of combined oral formulations of apomorphine hydrochloride, phentolamine mesylate and papaverine hydrochloride in men with moderate to severe erectile dysfunction. *Int J Impot Res* 2002; 14(1):54-59.
- (152) Perimenis P, Markou S, Gyftopoulos K et al. Efficacy of apomorphine and sildenafil in men with nonarteriogenic erectile dysfunction. A comparative crossover study. *Andrologia* 2004; 36(3):106-110.
- (153) Perimenis P, Gyftopoulos K, Giannitsas K et al. A comparative, crossover study of the efficacy and safety of sildenafil and apomorphine in men with evidence of arteriogenic erectile dysfunction. *Int J Impot Res* 2004; 16(1):2-7.
- (154) Porst H, Behre HM, Jungwirth A et al. Comparative trial of treatment satisfaction, efficacy and tolerability of sildenafil versus apomorphine in erectile dysfunction--an open, randomized cross-over study with flexible dosing. *Eur J Med Res* 2007; 12(2):61-67.
- (155) von Keitz A, Stroberg P, Bukofzer S et al. A European multicentre study to evaluate the tolerability of apomorphine sublingual administered in a forced dose-escalation regimen in patients with erectile dysfunction. *BJU Int* 2002; 89(4):409-415.
- (156) Allen RP, Engel RM, Smolev JK et al. Objective double-blind evaluation of erectile function with intracorporeal papaverine in combination with phentolamine and/or prostaglandin E1. *J Urol* 1992; 148(4):1181-1183.
- (157) Aversa A, Rocchietti-March M, Caprio M et al. Anxiety-induced failure in erectile response to intracorporeal prostaglandin-E1 in non-organic male impotence: a new diagnostic approach. *Int J Androl* 1996; 19(5):307-313.
- (158) Baum N, Randrup E, Junot D et al. Prostaglandin E1 versus sex therapy in the management of psychogenic erectile dysfunction. *Int J Impot Res* 2000; 12(3):191-194.
- (159) Bechara A, Casabe A, Cheliz G et al. Prostaglandin E1 versus mixture of prostaglandin E1, papaverine and phentolamine in nonresponders to high papaverine plus phentolamine doses. *J Urol* 1996; 155(3):913-914.
- (160) Bechara A, Casabe A, Cheliz G et al. Comparative study of papaverine plus phentolamine versus prostaglandin E1 in erectile dysfunction. *J Urol* 1997; 157(6):2132-2134.
- (161) Buvat J, Costa P, Morlier D et al. Double-blind multicenter study comparing alprostadil alpha-cyclodextrin with moxisylyte chlorhydrate in patients with chronic erectile dysfunction. *J Urol* 1998; 159(1):116-119.
- (162) Colli E, Calabro A, Gentile V et al. Alprostadil sterile powder formulation for intracavernous treatment of erectile dysfunction. *Eur Urol* 1996; 29(1):59-62.
- (163) Costa P, Sarrazin B, Bressolle F et al. Efficiency and side effects of intracavernous injections of moxisylyte in impotent patients: a dose-finding study versus placebo. *J Urol* 1993; 149(2):301-305.
- (164) Dinsmore WW, Gingell C, Hackett G et al. Treating men with predominantly nonpsychogenic erectile dysfunction with intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector system: a multicentre double-blind placebo-controlled study. *BJU Int* 1999; 83(3):274-279.
- (165) Earle CM, Keogh EJ, Wisniewski ZS et al. Prostaglandin E1 therapy for impotence, comparison with papaverine. *J Urol* 1990; 143(1):57-59.

- (166) el-Saleh JC, Keogh EJ, Chew KK et al. Does compression of the base of the penis improve the efficacy of intracavernosal injection of prostaglandin E1 for impotence? A randomized controlled study. *Int J Impot Res* 1995; 7(1):23-31.
- (167) Floth A, Schramek P. Intracavernous injection of prostaglandin E1 in combination with papaverine: enhanced effectiveness in comparison with papaverine plus phentolamine and prostaglandin E1 alone. *J Urol* 1991; 145(1):56-59.
- (168) Fu Q, Yao DH, Jiang YQ. A clinical comparative study on effects of intracavernous injection of sodium nitroprusside and papaverine/phentolamine in erectile dysfunction patients. *Asian J Androl* 2000; 2(4):301-303.
- (169) Garceau RJ, Zhang IX, Jen L. Dose-response studies of intracavernous injection therapy with alprostadil in Asian and Australian men with erectile dysfunction. *Curr Ther Res Clin Exp* 1996; 57(1):50-61.
- (170) Gheorghiu D, Godschalk M, Gheorghiu S et al. Slow injection of prostaglandin E1 decreases associated penile pain. *Urology* 1996; 47(6):903-904.
- (171) Godschalk MF, Chen J, Katz PG et al. Treatment of erectile failure with prostaglandin E1: a double-blind, placebo-controlled, dose-response study. *J Urol* 1994; 151(6):1530-1532.
- (172) Godschalk M, Gheorghiu D, Katz PG et al. Alkalinization does not alleviate penile pain induced by intracavernous injection of prostaglandin E1. *J Urol* 1996; 156(3):999-1000.
- (173) Gontero P, Fontana F, Bagnasacco A et al. Is there an optimal time for intracavernous prostaglandin E1 rehabilitation following nonnerve sparing radical prostatectomy? Results from a hemodynamic prospective study. *J Urol* 2003; 169(6):2166-2169.
- (174) Kattan S, Collins JP, Mohr D. Double-blind, cross-over study comparing prostaglandin E1 and papaverine in patients with vasculogenic impotence. *Urology* 1991; 37(6):516-518.
- (175) Kattan S. Double-blind randomized crossover study comparing intracorporeal prostaglandin E1 with combination of prostaglandin E1 and lidocaine in the treatment of organic impotence. *Urology* 1995; 45(6):1032-1036.
- (176) Kunelius P, Lukkarinen O. Intracavernous injection test in the evaluation of patients with erectile dysfunction: a blind, cross-over placebo-controlled study between three different vasoactive agents in 30 impotent inpatients. *Sexual Dysfunct* 1998; 1(1):35-38.
- (177) Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. *N Engl J Med* 1996; 334(14):873-877.
- (178) Mahmoud KZ, el Dakhli MR, Fahmi IM et al. Comparative value of prostaglandin E1 and papaverine in treatment of erectile failure: double-blind crossover study among Egyptian patients. *J Urol* 1992; 147(3):623-626.
- (179) Mancini M, Raina R, Agarwal A et al. Sildenafil citrate vs intracavernous alprostadil for patients with arteriogenic erectile dysfunction: a randomised placebo controlled study. *Int J Impot Res* 2004; 16(1):8-12.
- (180) Martinez-Pineiro L, Lopez-Tello J, onso Dorrego JM et al. Preliminary results of a comparative study with intracavernous sodium nitroprusside and prostaglandin E1 in patients with erectile dysfunction. *J Urol* 1995; 153(5):1487-1490.
- (181) Montorsi F, Guazzoni G, Strambi LF et al. Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: results of a prospective, randomized trial. *J Urol* 1997; 158(4):1408-1410.
- (182) Montorsi F, Guazzoni G, Barbieri L et al. Genital plus audiovisual sexual stimulation following intracavernous vasoactive injection versus re-dosing for erectile dysfunction--results of a prospective study. *J Urol* 1998; 159(1):113-115.

- (183) Moriel EZ, Rajfer J. Sodium bicarbonate alleviates penile pain induced by intracavernous injections for erectile dysfunction. *J Urol* 1993; 149(5 Pt 2):1299-1300.
- (184) Ogrinc FG, Linet OI. Evaluation of real-time RigiScan monitoring in pharmacological erection. *J Urol* 1995; 154(4):1356-1359.
- (185) Porst H. Prostaglandin E1 and the nitric oxide donor linsidomine for erectile failure: a diagnostic comparative study of 40 patients. *J Urol* 1993; 149(5 Pt 2):1280-1283.
- (186) Roy JB, Petrone RL, Said SI. A clinical trial of intracavernous vasoactive intestinal peptide to induce penile erection. *J Urol* 1990; 143(2):302-304.
- (187) Sandhu D, Curless E, Dean J et al. A double blind, placebo controlled study of intracavernous vasoactive intestinal polypeptide and phenotolamine mesylate in a novel auto-injector for the treatment of non-psychogenic erectile dysfunction. *Int J Impot Res* 1999; 11(2):91-97.
- (188) Schramek P, Plas EG, Hubner WA et al. Intracavernous injection of prostaglandin E1 plus procaine in the treatment of erectile dysfunction. *J Urol* 1994; 152(4):1108-1110.
- (189) Seyam R, Mohamed K, Akhras AA et al. A prospective randomized study to optimize the dosage of trimix ingredients and compare its efficacy and safety with prostaglandin E1. *Int J Impot Res* 2005; 17(4):346-353.
- (190) Soderdahl DW, Thrasher JB, Hansberry KL. Intracavernous drug-induced erection therapy versus external vacuum devices in the treatment of erectile dysfunction. *Br J Urol* 1997; 79(6):952-957.
- (191) Sogari PR, Teloken C, Souto CA. Atropine role in the pharmacological erection test: study of 228 patients. *J Urol* 1997; 158(5):1760-1763.
- (192) Titta M, Tavolini IM, Moro FD et al. Sexual counseling improved erectile rehabilitation after non-nerve-sparing radical retropubic prostatectomy or cystectomy--results of a randomized prospective study. *J Sex Med* 2006; 3(2):267-273.
- (193) Van der WF, Dohle GR, Van Der TJ et al. Intracavernous injection therapy with and without sexological counselling in men with erectile dysfunction. *BJU Int* 2002; 89(9):901-904.
- (194) Vanderschueren D, Heyrman RM, Keogh EJ et al. A study in patients with erectile dysfunction comparing different formulations of prostaglandin E1. Alprostadil Study Group. *J Urol* 1995; 154(5):1744-1747.
- (195) Viswaroop B, B A, Gopalakrishnan G. Evaluating erectile dysfunction: oral sildenafil versus intracavernous injection of papaverine. *Natl Med J India* 2005; 18(6):299-301.
- (196) von Heyden B, Donatucci CF, Marshall GA et al. A prostaglandin E1 dose-response study in man. *J Urol* 1993; 150(6):1825-1828.
- (197) Wegner HE, Knispel HH, Klan R et al. Prostaglandin E1 versus linsidomine chlorhydrate in erectile dysfunction. *Urol Int* 1994; 53(4):214-216.
- (198) Wegner HE, Knispel HH, Klan R et al. Efficacy of linsidomine chlorhydrate, a direct nitric oxide donor, in the treatment of human erectile dysfunction: results of a double-blind cross over trial. *Int J Impot Res* 1995; 7(4):233-237.
- (199) Rosen RC, Diamond LE, Earle DC et al. Evaluation of the safety, pharmacokinetics and pharmacodynamic effects of subcutaneously administered PT-141, a melanocortin receptor agonist, in healthy male subjects and in patients with an inadequate response to Viagra. *Int J Impot Res* 2004; 16(2):135-142.
- (200) Segraves RT, Bari M, Segraves K et al. Effect of apomorphine on penile tumescence in men with psychogenic impotence. *J Urol* 1991; 145(6):1174-1175.

- (201) Wessells H, Levine N, Hadley ME et al. Melanocortin receptor agonists, penile erection, and sexual motivation: human studies with Melanotan II. *Int J Impot Res* 2000; 12(Suppl 4):74-79.
- (202) Wessells H, Gralnek D, Dorr R et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000; 56(4):641-646.
- (203) Ekman P, Sjogren L, Englund G et al. Optimizing the therapeutic approach of transurethral alprostadil. *BJU Int* 2000; 86(1):68-74.
- (204) Lazzeri M, Barbanti G, Beneforti P et al. Intraurethraly infused capsaicin induces penile erection in humans. *Scand J Urol Nephrol* 1994; 28(4):409-412.
- (205) Padma-Nathan H, Hellstrom WJ, Kaiser FE et al. Treatment of men with erectile dysfunction with transurethral alprostadil. Medicated Urethral System for Erection (MUSE) Study Group. *N Engl J Med* 1997; 336(1):1-7.
- (206) Costabile RA, Spevak M, Fishman IJ et al. Efficacy and safety of transurethral alprostadil in patients with erectile dysfunction following radical prostatectomy. *J Urol* 1998; 160(4):1325-1328.
- (207) Engel JD, McVary KT. Transurethral alprostadil as therapy for patients who withdrew from or failed prior intracavernous injection therapy. *Urology* 1998; 51(5):687-692.
- (208) Hellstrom WJ, Bennett AH, Gesundheit N et al. A double-blind, placebo-controlled evaluation of the erectile response to transurethral alprostadil. *Urology* 1996; 48(6):851-856.
- (209) Peterson CA, Bennett AH, Hellstrom WJ et al. Erectile response to transurethral alprostadil, prazosin and alprostadil-prazosin combinations. *J Urol* 1998; 159(5):1523-1527.
- (210) Shabsigh R, Padma-Nathan H, Gittleman M et al. Intracavernous alprostadil alfadex is more efficacious, better tolerated, and preferred over intraurethral alprostadil plus optional actis: a comparative, randomized, crossover, multicenter study. *Urology* 2000; 55(1):109-113.
- (211) Shokeir AA, Alserafi MA, Mutabagani H. Intracavernosal versus intraurethral alprostadil: a prospective randomized study. *BJU Int* 1999; 83(7):812-815.
- (212) Williams G, Abbou CC, Amar ET et al. Efficacy and safety of transurethral alprostadil therapy in men with erectile dysfunction. MUSE Study Group. *Br J Urol* 1998; 81(6):889-894.
- (213) Cavallini G. Minoxidil versus nitroglycerin: a prospective double-blind controlled trial in transcutaneous erection facilitation for organic impotence. *J Urol* 1991; 146(1):50-53.
- (214) Cavallini G. Minoxidil versus nitroglycerine: a prospective, double-blind, controlled trial in transcutaneous therapy for organic impotence. *Int J Impot Res* 1994; 6(4):205-212.
- (215) Claes H, Smet G, Baert L. The influence of transcutaneous nitroglycerine on nocturnal erections. *J Drug Dev* 1992; 4(4):229-233.
- (216) Diamond LE, Earle DC, Rosen RC et al. Double-blind, placebo-controlled evaluation of the safety, pharmacokinetic properties and pharmacodynamic effects of intranasal PT-141, a melanocortin receptor agonist, in healthy males and patients with mild-to-moderate erectile dysfunction. *Int J Impot Res* 2004; 16(1):51-59.
- (217) Foldvari M, Oguejiofor C, Afridi S et al. Liposome encapsulated prostaglandin E1 in erectile dysfunction: correlation between in vitro delivery through foreskin and efficacy in patients. *Urology* 1998; 52(5):838-843.
- (218) Goldstein I, Payton TR, Schechter PJ. A double-blind, placebo-controlled, efficacy and safety study of topical gel formulation of 1% alprostadil (Topiglan) for the in-office treatment of erectile dysfunction. *Urology* 2001; 57(2):301-305.

- (219) Gomaa A, Shalaby M, Osman M et al. Topical treatment of erectile dysfunction: randomised double blind placebo controlled trial of cream containing aminophylline, isosorbide dinitrate, and co-dergocrine mesylate. *BMJ* 1996; 312(7045):1512-1515.
- (220) Gramkow J, Lendorf A, Zhu J et al. Transcutaneous nitroglycerine in the treatment of erectile dysfunction: a placebo controlled clinical trial. *Int J Impot Res* 1999; 11(1):35-39.
- (221) Le Roux PJ, Naude JH. Topical vasoactive cream in the treatment of erectile failure: a prospective, randomized placebo-controlled trial. *BJU Int* 1999; 83(7):810-811.
- (222) Padma-Nathan H, Steidle C, Salem S et al. The efficacy and safety of a topical alprostadil cream, Alprox-TD, for the treatment of erectile dysfunction: two phase 2 studies in mild-to-moderate and severe ED. *Int J Impot Res* 2003; 15(1):10-17.
- (223) Padma-Nathan H, Yeager JL. An integrated analysis of alprostadil topical cream for the treatment of erectile dysfunction in 1732 patients. *Urology* 2006; 68(2):386-391.
- (224) Steidle C, Padma-Nathan H, Salem S et al. Topical alprostadil cream for the treatment of erectile dysfunction: a combined analysis of the phase II program. *Urology* 2002; 60(6):1077-1082.
- (225) Yonessi M, Saedi M. A double-blind placebo-controlled evaluation of the effect of topical sildenafil on erectile dysfunction. *J App Res* 2005; 5(2):289-294.
- (226) Gomaa AA, Hamed HA. Improvement of sexual function in partial testosterone-deficient ageing men treated with cream containing testosterone and vasoactive agents. *J Mens Health Gend* 2006; 3(1):47-55.
- (227) Aversa A, Isidori AM, Spera G et al. Androgens improve cavernous vasodilation and response to sildenafil in patients with erectile dysfunction. *Clin Endocrinol (Oxf)* 2003; 58(5):632-638.
- (228) Boyanov MA, Boneva Z, Christov VG. Testosterone supplementation in men with type 2 diabetes, visceral obesity and partial androgen deficiency. *Aging Male* 2003; 6(1):1-7.
- (229) Cavallini G, Caracciolo S, Vitali G et al. Carnitine versus androgen administration in the treatment of sexual dysfunction, depressed mood, and fatigue associated with male aging. *Urology* 2004; 63(4):641-646.
- (230) Clopper RR, Voorhess ML, MacGillivray MH et al. Psychosexual behavior in hypopituitary men: A controlled comparison of gonadotropin and testosterone replacement. *Psychoneuroendocrinology* 1993; 18(2):149-161.
- (231) Gomaa A, Eissa M, El-Gebaley A. The effect of topically applied vasoactive agents and testosterone versus testosterone in the treatment of erectile dysfunction in aged men with low sexual interest. *Int J Impot Res* 2001; 13(2):93-99.
- (232) Haren M, Chapman I, Coates P et al. Effect of 12 month oral testosterone on testosterone deficiency symptoms in symptomatic elderly males with low-normal gonadal status. *Age Ageing* 2005; 34(2):125-130.
- (233) Kunelius P, Lukkarinen O, Hannuksela ML et al. The effects of transdermal dihydrotestosterone in the aging male: a prospective, randomized, double blind study. *J Clin Endocrinol Metab* 2002; 87(4):1467-1472.
- (234) McNicholas TA, Dean JD, Mulder H et al. A novel testosterone gel formulation normalizes androgen levels in hypogonadal men, with improvements in body composition and sexual function. *BJU Int* 2003; 91(1):69-74.
- (235) Merza Z, Blumsohn A, Mah PM et al. Double-blind placebo-controlled study of testosterone patch therapy on bone turnover in men with borderline hypogonadism. *Int J Androl* 2006; 29(3):381-391.
- (236) Rabkin JG, Wagner GJ, Rabkin R. A double-blind, placebo-controlled trial of testosterone therapy for HIV-positive men

- with hypogonadal symptoms. *Arch Gen Psychiatry* 2000; 57(2):141-147.
- (237) Schiavi RC, White D, Mandeli J et al. Effect of testosterone administration on sexual behavior and mood in men with erectile dysfunction. *Arch Sex Behav* 1997; 26(3):231-241.
- (238) Rochira V, Balestrieri A, Madeo B et al. Sildenafil improves sleep-related erections in hypogonadal men: evidence from a randomized, placebo-controlled, crossover study of a synergic role for both testosterone and sildenafil on penile erections.[erratum appears in *J Androl*. 2006 May-Jun;27(3):480]. *J Androl* 2006; 27(2):165-175.
- (239) Seftel AD, Mack RJ, Secrest AR et al. Restorative increases in serum testosterone levels are significantly correlated to improvements in sexual functioning. *J Androl* 2004; 25(6):963-972.
- (240) Steidle C, Schwartz S, Jacoby K et al. AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function. *J Clin Endocrinol Metab* 2003; 88(6):2673-2681.
- (241) Seidman SN, Roose SP. The sexual effects of testosterone replacement in depressed men: randomized, placebo-controlled clinical trial. *J Sex Marital Ther* 2006; 32(3):267-273.
- (242) Shabsigh R, Kaufman JM, Steidle C et al. Randomized study of testosterone gel as adjunctive therapy to sildenafil in hypogonadal men with erectile dysfunction who do not respond to sildenafil alone. *J Urol* 2004; 172(2):658-663.
- (243) Shamloul R, Ghanem H, Fahmy I et al. Testosterone therapy can enhance erectile function response to sildenafil in patients with PADAM: A pilot study. *J Sex Med* 2005; 2(4):559-564.
- (244) Wang C, Swerdloff RS, Iranmanesh A et al. Transdermal testosterone gel improves sexual function, mood, muscle strength, and body composition parameters in hypogonadal men. *J Clin Endocrinol Metab* 2000; 85(8):2839-2853.
- (245) Yassin AA, Saad F, Diede HE. Testosterone and erectile function in hypogonadal men unresponsive to tadalafil: results from an open-label uncontrolled study. *Andrologia* 2006; 38(2):61-68.
- (246) Aydin S, Odabas O, Ercan M et al. Efficacy of testosterone, trazodone and hypnotic suggestion in the treatment of non-organic male sexual dysfunction. *Br J Urol* 1996; 77(2):256-260.
- (247) Becker AJ, Stief CG, Machtens S et al. Oral phentolamine as treatment for erectile dysfunction. *J Urol* 1998; 159(4):1214-1216.
- (248) Costabile RA, Spevak M. Oral trazodone is not effective therapy for erectile dysfunction: a double-blind, placebo controlled trial. *J Urol* 1999; 161(6):1819-1822.
- (249) Enzlin P, Vanderschueren D, Bonte L et al. Trazodone: a double-blind, placebo-controlled, randomized study of its effects in patients with erectile dysfunction without major organic findings. *Int J Impot Res* 2000; 12(4):223-228.
- (250) Georgitis WJ, Merenich JA. Trial of pentoxifylline for diabetic impotence. *Diabetes Care* 1995; 18(3):345-352.
- (251) Hatzichristou DG, Apostolidis A, Tzortzis V et al. Effects of oral phentolamine, taken before sleep, on nocturnal erectile activity: a double-blind, placebo-controlled, crossover study. *Int J Impot Res* 2001; 13(5):303-308.
- (252) Korenman SG, Viosca SP. Treatment of vasculogenic sexual dysfunction with pentoxifylline. *J Am Geriatr Soc* 1993; 41(4):363-366.
- (253) Kurt U, Ozkardes H, Altug U et al. The efficacy of anti-serotonergic agents in the treatment of erectile dysfunction. *J Urol* 1994; 152(2 Pt 1):t-9.
- (254) Mann K, Pankok J, Leissner J et al. Effects of moclobemide on sexual performance and nocturnal erections in psychogenic erectile

- dysfunction. *Psychopharmacology* 2001; 156(1):86-91.
- (255) Meinhardt W, Schmitz PI, Kropman RF et al. Trazodone, a double blind trial for treatment of erectile dysfunction. *Int J Impot Res* 1997; 9(3):163-165.
- (256) Nickel M, Moleda D, Loew T et al. Cabergoline treatment in men with psychogenic erectile dysfunction: a randomized, double-blind, placebo-controlled study. *Int J Impot Res* 2007; 19(1):104-107.
- (257) Paskircioglu L, Karabulut A, Deniz E et al. The role of pentoxifylline in the treatment of erectile dysfunction due to borderline arterial insufficiency. *Br J Urol* 1996; 77(4):563-565.
- (258) Piha J, Kaaja R. Effects of moxonidine and metoprolol in penile circulation in hypertensive men with erectile dysfunction: Results of a pilot study. *Int J Impot Res* 2003; 15(4):287-289.
- (259) Reiter WJ, Pycha A, Schatzl G et al. Dehydroepiandrosterone in the treatment of erectile dysfunction: a prospective, double-blind, randomized, placebo-controlled study. *Urology* 1999; 53(3):590-594.
- (260) Safarinejad MR. Therapeutic effects of high-dose isoxsuprine in the management of mixed-type impotence. *Urology* 2001; 58(1):95-97.
- (261) Agostini R, Rossi F, Pajalich R. Myoinositol/folic acid combination for the treatment of erectile dysfunction in type 2 diabetes men: a double-blind, randomized, placebo-controlled study. *Eur Rev Med Pharmacol Sci* 2006; 10(5):247-250.
- (262) El-Shafey H, Atteya A, el-Magd SA et al. Tianeptine can be effective in men with depression and erectile dysfunction. *J Sex Med* 2006; 3(5):910-917.
- (263) Sommer F, Klotz T, Steinritz D et al. Evaluation of tetrahydrobiopterin (BH4) as a potential therapeutic agent to treat erectile dysfunction. *Asian J Androl* 2006; 8(2):159-167.
- (264) Speel TGW, Kiemeny LA, Thien T et al. Long-term effect of inhibition of the angiotensin-converting enzyme (ACE) on cavernosal perfusion in men with atherosclerotic erectile dysfunction: A pilot study. *J Sex Med* 2005; 2(2):207-212.
- (265) van Ahlen H, Piechota HJ, Kias HJ et al. Opiate antagonists in erectile dysfunction: a possible new treatment option? Results of a pilot study with naltrexone. *Eur Urol* 1995; 28(3):246-250.

Appendix D. Reference List of Excluded Studies

Not relevant.

The link between erectile dysfunction and cardiovascular disease. *Cardiovasc J S Afr* 2006;17(5):277

Drugs for rare diseases: Mixed assessment in Europe. *Prescrire Int* 2007;16(87):36-42.

The 'effectiveness' scale therapeutic outcome of pharmacologic therapies for ED: An international consensus panel report. *Zhongguo Nankexue Zazhi* 2006;20(1):70-72.

Finasteride and minoxidil for alopecia revisited. *Medical Letter on Drugs & Therapeutics* 2005;47(1222):95-96.

Duloxetine (Cymbalta) for diabetic neuropathic pain. *Medical Letter on Drugs & Therapeutics* 2005;47(1215-1216):67-68.

Sildenafil (Revatio) for pulmonary arterial hypertension. *Medical Letter on Drugs & Therapeutics* 2005;47(1215-1216):65-67.

Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2004). *Hypertens Res* 2006;29(SUPPL.):S1-S102.

Reply by Authors. *Br J Urol* 2006;175(6):2367-2368.

Voices and choices: Physician, patient, and partner, and partner perspectives on the management of erectile dysfunction. *Br J Sex Med* 2006;3(SUPPL. 1):4-9.

Managing the side effects of androgen deprivation therapy. *The Journal of Supportive Oncology* 2006;4(2):97-98.

Aanestad O, Flink R, Norlen B J. Interference pattern in perineal muscles: A quantitative electromyographic study in patients before and after transurethral surgery of the prostate. *Neurourology & Urodynamics* 1997;16(2):101-109.

Aasebo U, Gyltnes A, Bremnes R M et al. Reversal of sexual impotence in male patients with chronic obstructive pulmonary disease and hypoxaemia with long term oxygen therapy [abstract]. *Eur Respir J Suppl* 1993;Supplement. .6 Suppl 17, pp.422S, 1993.

Abascal K, Yarnell E. Increasing vitality with adaptogens: Multifaceted herbs for treating physical and mental stress. *Alternative & Complementary Therapies* 2003;9(2):54-60.

Abbou C C, Salomon L, Hoznek A et al. Laparoscopic radical prostatectomy: preliminary results. *Urology* 2000;55(5):630-634.

Abdo C H. The male sexual quotient: a brief, self-administered questionnaire to assess male sexual satisfaction. *Br J Sex Med* 2007;4(2):382-389.

Abdo C H, Oliveira Junior W M, Moreira Junior E et al. The impact of psychosocial factors on the risk of erectile dysfunction and inhibition of sexual desire in a sample of the Brazilian population. *Sao Paulo Med J* 2005;123(1):11-14.

Aboseif S, Riemer R K, Stackl W et al. Quantification of prostaglandin E1 receptors in cavernous tissue of men, monkeys and dogs. *Urol Int* 1993;50(3):148-152.

Aboseif S, Shinohara K, Borirakchanyavat S et al. The effect of cryosurgical ablation of the prostate on erectile function. *Br J Urol* 1997;80(6):918-922.

Aboseif S, Shinohara K, Breza J et al. Role of penile vascular injury in erectile dysfunction after radical prostatectomy. *Br J Urol* 1994;73(1):75-82.

Abraham N G, Asija A, Drummond G et al. Heme oxygenase -1 gene therapy: Recent advances and therapeutic applications. *Curr Gene Ther* 2007;7(2):89-108.

Abrahamsson P-A, Anderson J, Boccon-Gibod L et al. Risks and benefits of hormonal manipulation as monotherapy or adjuvant treatment in localised prostate cancer. *Eur Urol* 2005;48(6):900-905.

Abts M, Claus V, Lataster M. Blood pressure control with valsartan and hydrochlorothiazide in clinical practice: The MACHT observational study. *Blood Press* 2006;15(SUPPL. 1):27-32.

Ackerman D L, Greenland S, Bystritsky A et al. Relationship between early side effects and therapeutic effects of clomipramine therapy in obsessive-compulsive disorder. *J Clin Psychopharmacol* 1996;16(4):324-328.

Adaikan P G, Gauthaman K, Prasad R N V et al. Proerectile pharmacological effects of Tribulus terrestris extract on the rabbit corpus cavernosum. *Ann Acad Med Singapore* 2000;29(1):22-26.

Adami H O, Baron J A, Rothman K J. Ethics of a prostate cancer screening trial.[see comment]. [Review] [31 refs]. *Lancet* 1994;343(8903):958-960.

Adamopoulos D A, Nicopoulou S C, Pangalos G et al. Attitudes of aging Athenians to andropenia and its consequences, and to potential hormone substitution therapy. *Aging Male* 1999;2(1):44-52.

Adamopoulos D, Venaki E, Koukkou E et al. Association of carotene rich diet with hypogonadism in a male athlete. *Asian J Androl* 2006;8(4):488-492.

- Adams Henry E, Motsinger Patrice, McAnulty Richard D et al. Voluntary control of penile tumescence among homosexual and heterosexual subjects. *Arch Sex Behav* 1992;21(1):17-31.
- Adams M C, Chalian V S, Rink R C. Congenital dorsal penile curvature: a potential problem of the long phallus.[see comment]. *Br J Urol* 1999;161(4):1304-1307.
- Ades T, Gansler T, Miller M et al. PC-SPES: Current evidence and remaining questions. *CA: a Cancer Journal for Clinicians* 2001;51(3):199-204.
- Adeyoju A B, Olujohungbe A B K, Morris J et al. Priapism in sickle-cell disease; incidence, risk factors and complications - An international multicentre study. *BJU Int* 2002;90(9):898-902.
- Adimoelja A. Phytochemicals and the breakthrough of traditional herbs in the management of sexual dysfunctions. *Int J Androl* 2000;23Suppl-4.
- Adler L A, Spencer T J, Milton D R et al. Long-term, open-label study of the safety and efficacy of atomoxetine in adults with attention-deficit/hyperactivity disorder: an interim analysis. *Hillside J Clin Psychiatry* 2005;66(3):294-299.
- Adler L, Dietrich A, Reimherr F W et al. Safety and tolerability of once versus twice daily atomoxetine in adults with ADHD. *Ann Clin Psychiatry* 2006;18(2):107-113.
- Adolfsson J. Health-related quality-of-life assessments in patients with advanced cancer of the prostate. *Pharmacoeconomics* 2003;21(4):241-247.
- Adolphe A B, Vlachakis N D, Rofman A B et al. Long term evaluation of amlodipine vs hydrochlorothiazide in patients with essential hypertension. *INT 1993;J. CLIN. PHARMACOL. RES.* 13(4):203-210.
- Adrees M, Boran G. Subclinical hypothyroidism. *Cpd Bulletin Clinical Biochemistry* 2002;4(3):67-70.
- Adsan O, Ozturk B, Cetinkaya M et al. The value of cavernous body biopsy in evaluating of impotent men. *Arch Ital Urol Androl* 1997;69(3):151-153.
- Adshead J M, Stricker P D. Localised prostate cancer questions patients ask. *Med Today* 2004;5(9):18-31.
- Aggour A, Mostafa H, el-Shawaf H. Evaluation of the role of corpus cavernosum electromyography as a noninvasive diagnostic tool in male erectile dysfunction. *International Urology & Nephrology* 1998;30(1):75-79.
- Agmo A, Turi A L, Ellingsen E et al. Preclinical models of sexual desire: Conceptual and behavioral analyses. *Pharmacology, Biochemistry & Behavior* 2004;78(3):379-404.
- Agrawal V, Minhas S, Ralph D J. Venogenic erectile dysfunction in Klippel-Trenaunay syndrome. *BJU Int* 2006;97(2):327-328.
- Ahlering T E, Eichel L, Skarecky D. Rapid communication: early potency outcomes with cauterly-free neurovascular bundle preservation with robotic laparoscopic radical prostatectomy. *J Endourol* 2005;19(6):715-718.
- Ahlering T E, Skarecky D, Borin J. Impact of cauterly versus cauterly-free preservation of neurovascular bundles on early return of potency. *J Endourol* 2006;20(8):586-589.
- Ahmed H U, Shergill I S, Arya M et al. Management of detrusor-external sphincter dyssynergia. *Nature Clinical Practice Urology* 2006;3(7):368-380.
- Ahn B O, Kang K K, Ahn G J et al. Efficacy of DA-8159, a new PDE5 inhibitor, for inducing penile erection in rabbits with acute spinal cord injury. *Int J Impot Res* 2003;15(6):405-411.
- Ahn H S, Lee S W, Yoon S J et al. A comparison of colour duplex ultrasonography after transurethral alprostadil and intracavernous alprostadil in the assessment of erectile dysfunction. *J Int Med Res* 2004;32(3):317-323.
- Ahuja S, Bivalacqua T J, Case J et al. A pilot study demonstrating clinical benefit from intralesional interferon alpha 2B in the treatment of Peyronie's disease. *J Androl* 1999;20(4):444-448.
- Aichhorn W, Whitworth A B, Weiss E M et al. Second-generation antipsychotics: Is there evidence for sex differences in pharmacokinetic and adverse effect profiles?. *Drug Saf* 2006;29(7):587-598.
- Aitchison M, Aitchison J, Carter R. Is the penile brachial index a reproducible and useful measurement?. *Br J Urol* 1990;66(2):202-204.
- Aizawa K, Hanaoka T, Kasai H et al. Long-term vardenafil therapy improves hemodynamics in patients with pulmonary hypertension. *Hypertens Res* 2006;29(2):123-128.
- Aizenberg D, Sigler M, Zemishlany Z et al. Lithium and male sexual function in affective patients. *Clin Neuropharmacol* 1996;19(6):515-519.
- Aizenberg D, Zemishlany Z, Dorfman-Etrog P et al. Sexual dysfunction in male schizophrenic patients. *Hillside J Clin Psychiatry* 1995;56(4):137-141.
- Akakura K, Suzuki H, Ichikawa T et al. A randomized trial comparing radical prostatectomy plus endocrine therapy versus external beam radiotherapy plus endocrine therapy for locally advanced prostate cancer: results at median follow-up of 102 months. *Jpn J Clin Oncol* 2006;36(12):789-793.

- Akduman B, Crawford E D. The PCPT: New Findings, New Insights, and Clinical Implications for the Prevention of Prostate Cancer. *European Urology Supplements* 2006;5(9):634-639.
- Akkus E, Carrier S, Rehman J et al. Is colchicine effective in Peyronie's disease? A pilot study. *Urology* 1994;44(2):291-295.
- Akkus E, Iscimen A, Tasli L et al. Paraffinoma and ulcer of the external genitalia after self-injection of vaseline. *Br J Sex Med* 2006;3(1):170-172.
- Akkus E, Ozkara H, Alici B et al. Incision and venous patch graft in the surgical treatment of penile curvature in Peyronie's disease. *Eur Urol* 2001;40(5):531-536.
- Al Sa'doni H H, Ferro A. S-Nitrosothiols as nitric oxide-donors: Chemistry, biology and possible future therapeutic applications. *Curr Med Chem* 2004;11(20):2679-2690.
- al-Abany M, Steineck G, gren Cronqvist A K et al. Improving the preservation of erectile function after external beam radiation therapy for prostate cancer. *Radiotherapy & Oncology* 2000;57(2):201-206.
- Al-Hesayan A, Floras J S, Parker J D. The effects of intravenous sildenafil on hemodynamics and cardiac sympathetic activity in chronic human heart failure. *Eur J Heart Fail* 2006;8(8):864-868.
- Al-Rifaei M A, Zaghoul S, Al-Rifaei A M. Bulboprostatic anastomotic urethroplasty with preservation of potency: anatomical study, operative approach and clinical results. *Scandinavian Journal of Urology & Nephrology* 2005;39(2):163-168.
- Albaugh J A. Intracavernosal injection algorithm. *Urol Nurs* 2006;26(6):449-453.
- Albert M, Tempany C M, Schultz D et al. Late genitourinary and gastrointestinal toxicity after magnetic resonance image-guided prostate brachytherapy with or without neoadjuvant external beam radiation therapy. *Cancer* 2003;98(5):949-954.
- Alderman C P. Developments in psychiatry - 2002. *Journal of Pharmacy Practice & Research* 2002;32(1):47-50.
- Alexander N J, Baker E, Kaptein M et al. Why consider vaginal drug administration?. *Fertility & Sterility* 2004;82(1):1-12.
- Alexander W D. The diabetes physician and an assessment and treatment programme for male erectile impotence. *Diabet Med* 1990;7(6):540-543.
- Alexianu M, Weiss G H. Radical prostatectomy versus brachytherapy for early-stage prostate cancer. *J Endourol* 2000;14(4):325-328.
- Ali R A. Management of diabetic neuropathy. *The Malaysian Journal of Medical Science* 2003;10(2):27-30.
- Ali S T, Shaikh R N, Siddiqi A. HIV-1 associated neuropathies in males; impotence and penile electrodiagnosis. *Acta Neurol Belg* 1994;94(3):194-199.
- Aliaev IuG, Vinarov A Z, Chalyi M E et al. [Causes of erectile dysfunction after transurethral resection of hyperplastic prostate and its prophylaxis]. *Urologii*[COMBINING LIGATURE LEFT HALF]a[COMBINING LIGATURE RIGHT HALF] (Moscow, Russia : 2005;1999) Issue 3, pp.28-32, 2005 May-Jun.
- Alibhai S M H, Gogov S, Allibhai Z. Long-term side effects of androgen deprivation therapy in men with non-metastatic prostate cancer: A systematic literature review. *Critical Reviews in Oncology-Hematology* 2006;60(3):201-215.
- Alkhayal S, Lehmann V, Thomas P. A simple noninvasive test to detect vascular disease in patients with erectile dysfunction: a novel method. *Br J Sex Med* 2006;3(2):331-336.
- Allal A S, Bieri S, Brundler M-A et al. Preoperative hyperfractionated radiotherapy for locally advanced rectal cancers: A phase I-II trial. *Int J Radiat Oncol Biol Phys* 2002;54(4):1076-1081.
- Allen A, Hollander E. Diagnosis and treatment of obsessive-compulsive disorder. *Primary Psychiatry* 2005;12(12):34-42.
- Allen R P, Engel R M, Smolev J K et al. Comparison of duplex ultrasonography and nocturnal penile tumescence in evaluation of impotence. [see comment]. *Br J Urol* 1994;151(6):1525-1529.
- Althof S E, Dean J, Derogatis L R et al. Current perspectives on the clinical assessment and diagnosis of female sexual dysfunction and clinical studies of potential therapies: A statement of concern. *Br J Sex Med* 2005;2(SUPPL. 3):146-153.
- Althof S E, Eid J F, Talley D R et al. Through the eyes of women: the partners' perspective on tadalafil. *Urology* 2006;68(3):631-635.
- Althof S E, Levine S B, Corty E W et al. A double-blind crossover trial of clomipramine for rapid ejaculation in 15 couples. *Hillside J Clin Psychiatry* 1995;56(9):402-407.
- Althof S E, O'Leary M P, Cappelleri J C et al. Impact of erectile dysfunction on confidence, self-esteem and relationship satisfaction after 9 months of sildenafil citrate treatment. *Br J Urol* 2006;176(5):2132-2137.
- Althof S E, Rosen R C, DeRogatis L et al. Outcome measurement in female sexual dysfunction clinical trials: review and recommendations. [Review] [25 refs]. *J Sex Marital Ther* 2005;31(2):153-166.

- Althof S E, Turner L A, Levine S B et al. Through the eyes of women: the sexual and psychological responses of women to their partner's treatment with self-injection or external vacuum therapy. *Br J Urol* 1992;147(4):1024-1027.
- Althof S, Dean J, Fitzpatrick J et al. Could urological questionnaires completely replace physiological testing?. *BJU Int* 2005;96(9):1210-1212.
- Althof Stanley E. Erectile dysfunction: Psychotherapy with men and couples. Leiblum, Sandra R (Ed); Rosen, Raymond C (Ed) 2000;(2000):514
- Althof Stanley E. New roles for mental health clinicians in the treatment of erectile dysfunction. *Journal of Sex Education & Therapy* 1998;23(3):229-231.
- Althof Stanley E. The Psychology of Premature Ejaculation: Therapies and Consequences. [References]. *Br J Sex Med* 2006;3(Suppl 4):324-331.
- Althof Stanley E, O'Leary, Michael P et al. Self-Esteem, Confidence, and Relationships in Men Treated with Sildenafil Citrate for Erectile Dysfunction. [References]. *J Gen Intern Med* 2006;21(10):1069-1074.
- Altinkilic B, Hauck E W, Weidner W. Evaluation of penile perfusion by color-coded duplex sonography in the management of erectile dysfunction. [Review] [23 refs]. *World J Urol* 2004;22(5):361-364.
- Alvarenga Tathiana A F, Andersen Monica L, Papale Ligia A et al. Effects of long-term food restriction on genital reflexes in paradoxically sleep-deprived male rats. [References]. *Brain Res* 2006;1115(1):148-154.
- Ameda K, Kakizaki H, Koyanagi T et al. The long-term voiding function and sexual function after pelvic nerve-sparing radical surgery for rectal cancer. *Int J Urol* 2005;12(3):256-263.
- Amr M M, Abbas E Z, El-Samra M et al. Neuropsychiatric syndromes and occupational exposure to zinc phosphide in Egypt. *Environ Res* 1997;73(1-2):200-206.
- Anafarta K, Aydos K, Yaman O. Is deep dorsal vein arterialization an alternative surgical approach to treat venogenic impotence?. *Urol Int* 1997;59(2):109-112.
- Anafarta K, Yaman O, Aydos K. Clinical experience with Dynaflex penile prostheses in 120 patients. *Urology* 1998;52(6):1098-1100.
- Anantharaman P, Schmidt R J. Sexual function in chronic kidney disease. *Adv Chronic Kidney Dis* 2007;14(2):119-125.
- Anastasiadis A G, Benson M C, Rosenwasser M P et al. Cavernous nerve graft reconstruction during radical prostatectomy or radical cystectomy: safe and technically feasible. *Prostate Cancer & Prostatic Diseases* 2003;6(1):56-60.
- Anastasiadis A G, Ghafar M A, Burchardt M et al. Economic aspects of medical erectile dysfunction therapies. *Expert Opin Pharmacother* 2002;3(3):257-263.
- Anastasiadis A G, Salomon L, Katz R et al. Radical retropubic versus laparoscopic prostatectomy: a prospective comparison of functional outcome. *Urology* 2003;62(2):292-297.
- Andersen M L, Tufik S E M. Inhibitory effect of GABAergic drugs in cocaine-induced genital reflexes in paradoxical sleep-deprived male rats. [References]. *Pharmacology, Biochemistry and Behavior* 2004;78(2):301-307.
- Andersen M L, D'Almeida V, Martins P J F et al. Effects of paradoxical sleep deprivation and cocaine on genital reflexes in hyperlipidic-fed rats. *Pharmacology, Biochemistry & Behavior* 2005;81(4):758-763.
- Andersen M L, Perry J C, Battisti M C et al. Association of paradoxical sleep deprivation and ecstasy (MDMA) enhances genital reflexes in male rats. [References]. *Behav Brain Res* 2006;170(2):287-292.
- Andersen Monica L, Tufik Sergio, E-Mail Address et al. The effects of dopaminergic agonists on genital reflexes in paradoxical sleep deprived male rats. [References]. *Physiol Behav* 2005;84(2):205-210.
- Andersen Monica L, Antunes Isabela B, Tufik Sergio et al. Effects of paradoxical sleep deprivation on genital reflexes in five rat strains. [References]. *Horm Behav* 2006;49(2):173-180.
- Andersen Monica L, Bignotto Magda, Tufik Sergio et al. The effect of apomorphine on genital reflexes in male rats deprived of paradoxical sleep. [References]. *Physiol Behav* 2003;80(2-3):211-215.
- Andersen Monica, Levy Bignotto, Magda Sergio et al. Influence of paradoxical sleep deprivation and cocaine on development of spontaneous penile reflexes in rats of different ages. [References]. *Brain Res* 2003;968(1):130-138.
- Anderson Monica L, Bignotto Magda, Tufik Sergio et al. Cocaine-induced genital reflexes during paradoxical sleep deprivation and recovery. [References]. *Physiol Behav* 2003;78(2):255-259.
- Anderson R B, Testa M A. Symptom distress checklists as a component of quality of life measurement: Comparing prompted reports by patient and physician with concurrent adverse event reports via the physician. *Drug Inf J* 1994;J. 28(1):89-114.

- Anderson R U, Wise D, Sawyer T et al. Sexual Dysfunction in Men With Chronic Prostatitis/Chronic Pelvic Pain Syndrome: Improvement After Trigger Point Release and Paradoxical Relaxation Training. *Br J Urol* 2006;176(4):1534-1539.
- Anderson T R, Goldberg J F, Harrow M. A review of medication side effects and treatment adherence in bipolar disorder. *Primary Psychiatry* 2004;11(9):48-54.
- Andersson K E, Stief C G. Neurotransmission and the contraction and relaxation of penile erectile tissues. *World J Urol* 1997;15(1):14-20.
- Andersson K-E, Schroder A. Therapeutic strategies for drug treatment of stress urinary incontinence. *Drug Discovery Today: Therapeutic Strategies* 2004;1(2):259-265.
- Andersson K-E, Hedlund P, Nehra Porst et al. New directions for erectile dysfunction therapies. *Int J Impot Res* 2002;14(SUPPL. 1):S82-S92.
- Andersson K-E, Mulhall J P, Wyllie M G. Pharmacokinetic and pharmacodynamic features of dapoxetine, a novel drug for 'on-demand' treatment of premature ejaculation. *BJU Int* 2006;97(2):311-315.
- Andolfi Maurizio, Haber Russell. Please help me with this family: Using consultants as resources in family therapy. (1994) 1994;xvii, 294 pp. Philadelphia, PA, US294
- Andresen R, Wegner H E H, Miller K et al. An intrapersonal comparison of ultrasound sonography, X-ray in mammography technique, computerized tomography, and nuclear magnetic resonance in 20 patients. *Eur Urol* 1998;34(2):128-135.
- Anegon M, Esteban J, Jimenez-Garcia R et al. A postmarketing, open-label study to evaluate the tolerability and effectiveness of replacing standard-formulation doxazosin with doxazosin in the gastrointestinal therapeutic system formulation in adult patients with hypertension. *Clin Ther* 2002;24(5):786-797.
- Anghelescu Ion, Urbanek Carsten, E-Mail Address et al. Tadalafil in a Patient With Treatment-Resistant Depression and Antidepressant Polypharmacy. [References]. *J Clin Psychopharmacol* 2005;25(2):191-192.
- Angulo J, Bischoff E, Gabancho S et al. Vardenafil reverses erectile dysfunction induced by paroxetine in rats. *Int J Impot Res* 2003;15(2):90-93.
- Angulo J, Cuevas P, Moncada I et al. Rationale for the combination of PGE(1) and S-nitroso-glutathione to induce relaxation of human penile smooth muscle. *Journal of Pharmacology & Experimental Therapeutics* 2000;295(2):586-593.
- Anis Tarek, Shamloul Rany, Ghanem Hussein. Pharmacological treatment of male erectile dysfunction. [References]. Owens, Annette Fuglsang (Ed); Tepper, Mitchell S (Ed) 2007;(2007):419
- Annie Potts. The Rise of Viagra: How the Little Blue Pill Changed Sex in America. *Men and Masculinities* 2006;9(1):110-112.
- Anon Anonymous. Sildenafil: an oral drug for impotence. *Med Lett Drugs Ther* 1998;40(1026):51-52.
- Anonymous. Bashing beta blockers' bad rap. *Harv Heart Lett* 2002;13(2):7
- Anonymous. Love, lust and libido. *Diabetes Obes Metab* 2001;3(5):381-382.
- Anonymous. Goserelin and locally advanced prostate cancer: new indication. Pros and cons. *Prescrire Int* 2000;9(47):75-76.
- Anonymous. PharmaCE Test Questions. *Ann Pharmacother* 2005;39(7-8):1383-1388.
- Anonymous. Weight-loss and regular exercise improves erectile dysfunction in obese men. *Evidence-based Healthcare & Public Health* 2004;8(6):406-407.
- Anonymous. Weight loss may improve erectile function in obese men. *Med Today* 2004;5(8):10
- Anonymous. Vincristine liposomal - INEX: Lipid-encapsulated vincristine, Onco TCS, transmembrane carrier system - Vincristine, vincacine, Vincristine sulfate liposomes for injection, VSLI. *Drugs in R & D* 2004;5(2):119-123.
- Anonymous. New study suggests benefits for insulin detemir. *British Journal of Diabetes & Vascular Disease* 2003;3(5):381
- Anonymous. Phosphodiesterase type 5 (PDE5) inhibitors: Looking beyond erectile dysfunction. *British Journal of Cardiology* 2003;10(SUPPL. 4):S1-S8.
- Anonymous. Custom-made evaluation. *Prescrire Int* 2003;12(67):195
- Anonymous. Treatment for male pattern baldness delays prostate cancer. *Hosp Formul* 2003;38(9):527
- Anonymous. Finasteride and prostate cancer. *Med Today* 2003;4(9):
- Anonymous. Early release of prostate cancer prevention results met with cautionary optimism. *Geriatrics and Aging* 2003;6(7):11
- Anonymous. EGb 761: Ginkgo biloba extract, Ginkor. *Drugs in R & D* 2003;4(3):188-193.
- Anonymous. Early prostate cancer: Surgery versus watchful waiting. *Med Today* 2002;3(11):10

- Anonymous. Surgery & watchful waiting for early prostate cancer provide similar outcomes. *Expert Review of Pharmacoeconomics & Outcomes Research* 2002;2(5):403-410.
- Anonymous. Editor's comment. *BJU Int* 2002;89(9):i-ii.
- Anonymous. News focus. *Current Drug Discovery* 2002;(pp 15-18):-18.
- Anonymous. Cardiovascular effects of sildenafil similar to placebo during exercise. *Can Pharm J* 2002;268(7185):201
- Anonymous. Individual wood construction. Numbered construction kits from Finland. *Holz - Kurier* 2000;55(33):6
- Ansong K S, Lewis C, Jenkins P et al. Help-seeking decisions among men with impotence. *Urology* 1998;52(5):834-837.
- Apfelbaum Bernard. Retarded ejaculation: A much misunderstood syndrome. Leiblum, Sandra R (Ed); Rosen, Raymond C (Ed) 2000;(2000):514
- Api M, G-rgen H, etin A et al. New diagnostic instrument for sexual function assessment in menopausal women: Libido scoring system. *Journal of the Turkish German Gynecology Association Artemis* 2005;6(1):24-29.
- Appelhof B C, Brouwer J P, Van Dyck R et al. Triiodothyronine addition to paroxetine in the treatment of major depressive disorder. *Journal of Clinical Endocrinology & Metabolism* 2004;89(12):6271-6276.
- Appelmans Claire, Gill Harcharan, Clerk Alex et al. Medical evaluation of sexual function. Charlton, Randolph S (Ed); Yalom, Irvin D (Ed) 1997;(1997):348-Bass.
- Arafa M, Shamloul R. Efficacy of sertraline hydrochloride in treatment of premature ejaculation: A placebo-controlled study using a validated questionnaire. *Int J Impot Res* 2006;18(6):534-538.
- Arai Y, Okubo K, Aoki Y et al. Patient-reported quality of life after radical prostatectomy for prostate cancer. *Int J Urol* 1999;6(2):78-86.
- Argiolas Antonio, Melis Maria, Rosaria E-Mail et al. The role of oxytocin and the paraventricular nucleus in the sexual behaviour of male mammals. [References]. *Physiol Behav* 2004;83(2):309-317.
- Argoff C E, Backonja M-M, Belgrade M J et al. Consensus guidelines: Treatment planning and options. *Mayo Clin Proc* 2006;81(4 SUPPL.):S12-S25.
- Ari G, Vardi Y, Finberg J P. Nitric oxide and penile erection in streptozotocin-diabetic rats. *Clin Sci* 1999;96(4):365-371.
- Arlt W, Hove U, Muller B et al. Frequent and frequently overlooked: Treatment-induced endocrine dysfunction in adult long-term survivors of primary brain tumors. *Neurology* 1997;49(2):498-506.
- Armagan A, Kim N N, Goldstein I et al. Dose-response relationship between testosterone and erectile function: evidence for the existence of a critical threshold. *J Androl* 2006;27(4):517-526.
- Armenakas N A, McAninch J W, Lue T F et al. Posttraumatic impotence: magnetic resonance imaging and duplex ultrasound in diagnosis and management. *Br J Urol* 1993;149(5 Pt 2):1272-1275.
- Armstrong E P, Skrepnek G H, Haim Erder M. Cost-utility comparison of escitalopram and sertraline in the treatment of major depressive disorder. *Current Medical Research & Opinion* 2007;23(2):251-258.
- Arrison D P, Cabelin M, Seidmon E J. Corporoscopic-assisted removal of ruptured inflatable penile prosthesis. *Tech Urol* 2001;7(3):249-250.
- Arvanitis L A, Goldstein J M. The Atypical Profile of Quetiapine Is Supported by Its Lack of Sustained Elevation of Plasma Prolactin Concentrations CONFERENCE ABSTRACT. 150th Annual Meeting of the American Psychiatric Association 1997;San Diego, California, USA. 17-22 May., 1997. 1997.
- Ascoli P, Cavagnini F. Hypopituitarism. *Pituitary* 2006;9(4):335-342.
- Ashburn T T, Thor K B. Drug repositioning: Identifying and developing new uses for existing drugs. *Nat Rev Genet* 2004;3(8):673-683.
- Ashraf V V, Taly A B, Nair K P et al. Role of clinical neurophysiological tests in evaluation of erectile dysfunction in people with spinal cord disorders. *Neurol India* 2005;53(1):32-35.
- Ashton A K, D'Mello D A, Dantz B et al. Treatment regimens for managing depression in family practice. *J Fam Pract* 2003;52(SUPPL.):S48-S60.
- Ashworth D M, Batt A R, Baxter A J et al. Nonpeptide oxytocin agonists. *Drugs of the Future* 2006;31(4):345-353.
- Asser Jonathan, E-Mail Address, Asser Jonathan et al. Working with prisoners in a transitional space. [References]. *Psychodynamic Practice: Individuals, Groups and Organisations* 2002;8(1):7-19.
- Astorga R, Cantero O, Contreras D et al. Intralesional recombinant interferon alpha-2b in Peyronie's disease. *Arch Esp Urol* 2000;53(7):665-671.
- Atahan O, Kayigil O, Metin A. Electrical activity of corpus cavernosum in vasculogenic and non-vasculogenic erectile dysfunction. *Scandinavian Journal of Urology & Nephrology* 1997;31(6):549-554.

- Atala A, Amin M. Current concepts in the treatment of genitourinary tract disorders in the older individual. [Review] [87 refs]. *Drugs Aging* 1991;1(3):176-193.
- Atan A, Basar M M, Aydoganli L. Comparison of the efficacy of fluoxetine alone vs. fluoxetine plus local lidocaine ointment in the treatment of premature ejaculation. *Arch Esp Urol* 2000;53(9):856-858.
- Atan A, Delibasi T, Tuncel A. Re: Edoardo Austoni, Vincenzo Mirone, Fabio Parazzini, Ciro Basile Fasolo, Paolo Turchi, Edoardo S. Pescatori, Elena Ricci and Vincenzo Gentile. Smoking as a risk factor for erectile dysfunction: data from the andrology prevention weeks 2001-2002, a study of the Italian society of andrology (S.I.A.). *Eur Urol* 2005;48:810-8. *Eur Urol* 2006;50(3):625-626.
- Ateyah A, El-Nashar A R, Zohdy W et al. Intracavernosal irrigation by cold saline as a simple method of treating latrogenic prolonged erection. *Br J Sex Med* 2005;2(2):248-253.
- Aung H H, Dey L, Rand V et al. Alternative therapies for male and female sexual dysfunction. *Am J Chin Med* 2004;32(2):161-173.
- Austoni E, Colombo F, Mantovani F et al. Venous surgery in erectile dysfunction: Therapeutic strategy and results. *Urol Int* 1992;49(1):63-68.
- Authors Kayigil, Ergen A. Caverno-occlusive and autonomic dysfunction: a new concept in young patients. *Eur Urol* 1998;34(2):124-127.
- Aversa A, Fabbri A. New oral agents for erectile dysfunction: What is changing in our practice?. *Asian J Androl* 2001;3(3):175-179.
- Aversa A, Basciani S, Visca P et al. Platelet-derived growth factor (PDGF) and PDGF receptors in rat corpus cavernosum: Changes in expression after transient in vivo hypoxia. *Rom J Endocrinol* 2001;170(2):395-402.
- Aversa A, Bruzziches R, Spera G. Diagnosing erectile dysfunction: the penile dynamic colour duplex ultrasound revisited. [Review] [16 refs]. *Int J Androl* 2005;28 Suppl 261-63.
- Aversa A, Bruzziches R, Pili M et al. Phosphodiesterase 5 inhibitors in the treatment of erectile dysfunction. *Curr Pharm Des* 2006;12(27):3467-3484.
- Aversano T, Marino P N. Effect of ischemic zone size on nonischemic zone function. *American Journal of Physiology - Heart & Circulatory Physiology* 1990;258(6 27-6):H1786-H1795.
- Avram M R, Cole J P, Gandelman M et al. The potential role of minoxidil in the hair transplantation setting. *J Dermatol Surg* 2002;28(10):894-900.
- Awwad Z, bu-Hijleh M, Basri S et al. Penile measurements in normal adult Jordanians and in patients with erectile dysfunction. *Int J Impot Res* 2005;17(2):191-195.
- Aydin S, Ercan M, Caskurlu T et al. Acupuncture and hypnotic suggestions in the treatment of non-organic male sexual dysfunction. *Scandinavian Journal of Urology & Nephrology* 1997;31(3):271-274.
- Aydogan S, Bircan M K, Sahin H et al. The importance of visual erotic stimulation in the differential diagnosis of erectile impotence. *International Urology & Nephrology* 1997;29(2):233-235.
- Azad N, Emanuele N V, Abraira C et al. The effects of intensive glycemic control on neuropathy in the VA cooperative study on type II diabetes mellitus (VA CSDM). *Journal of Diabetes & its Complications* 1999;13(5-6):307-313.
- Azadzoi K M, Schulman R N, Aviram M et al. Oxidative stress in arteriogenic erectile dysfunction: Prophylactic role of antioxidants. *Br J Urol* 2005;174(1):386-393.
- Azam U. Late-stage clinical development in lower urogenital targets: sexual dysfunction. [Review] [71 refs]. *Br J Pharmacol* 2006;147 Suppl 2S153-S159.
- Baba K, Yajima M, Carrier S et al. Delayed testosterone replacement restores nitric oxide synthase-containing nerve fibres and the erectile response in rat penis. *BJU Int* 2000;85(7):953-958.
- Babinski M A, Costa W S, Sampaio F J B et al. Immunohistochemical analysis of smooth muscle cells and volumetric density of the elastic system fibers of wild boar (*Sus scrofa*) penis. *Anim Reprod Sci* 2005;86(3-4):317-328.
- Bach S P, Mortensen N J M. Revolution and evolution: 30 Years of ileoanal pouch surgery. *Inflamm Bowel Dis* 2006;12(2):131-145.
- Badros A Z, Goloubeva O, Rapoport A P et al. Phase II study of G3139, a Bcl-2 antisense oligonucleotide, in combination with dexamethasone and thalidomide in relapsed multiple myeloma patients. *Am J Clin Oncol* 2005;23(18):4089-4099.
- Baggott Jonathan, Singh Ashok N E. Sildenafil-induced relapse in bipolar disorder: Is nitric oxide the mechanism? [References]. *Int J Neuropsychopharmacol* 2004;7(4):525
- Bailey Teresa. There is no such thing as an adolescent. [References]. Lanyado, Monica (Ed); Horne, Ann (Ed) 2006;(2006):252

- Baker Christine D. A cognitive-behavioural model for the formulation and treatment of sexual dysfunction. Ussher, Jane M (Ed); Baker, Christine D (Ed) 1993;(1993):272
- Bakircioglu M E, Lin C-S, Fan P et al. The effect of adeno-associated virus mediated brain derived neurotrophic factor in an animal model of neurogenic impotence. *Br J Urol* 2001;165(6 I):2103-2109.
- Bakircioglu M E, Sievert K-D, Nunes L et al. Decreased trabecular smooth muscle and caveolin-1 expression in the penile tissue of aged rats. *Br J Urol* 2001;166(2):734-738.
- Bakris G L, Bell D S, Fonseca V et al. The rationale and design of the Glycemic Effects in Diabetes Mellitus Carvedilol-Metoprolol Comparison in Hypertensives (GEMINI) trial. *J Diabetes Complications* 2005;19(2):74-79.
- Bakris G L, Ferdinand K C, Douglas J G et al. Optimal treatment of hypertension in African Americans: Reaching and maintaining target blood pressure goals. *Postgrad Med* 2002;112(4):73-84.
- Bakshi S, Miller D K. Assessment of the aging man. *Med Clin North Am* 1999;83(5):1131-1149.
- Balaraman R. Drugs for urological disorders. *Indian J Pharmacol* 2002;34(2):137-138.
- Baldinger S L, Yogman M W. Atomoxetine. *Hosp Formul* 2003;38(2):85-100.
- Baldo Omer, Eardley Ian, E-Mail Address et al. Diagnosis and investigation of men with erectile dysfunction. [References]. *Journal of Men's Health & Gender* 2005;2(1):79-86.
- Baldwin D S. Sexual dysfunction associated with antidepressant drugs. [Review] [96 refs]. *Expert Opin Drug Saf* 2004;3(5):457-470.
- Balercia G, Boscaro M, Lombardo F et al. Sexual symptoms in endocrine diseases: psychosomatic perspectives. *Psychother Psychosom* 2007;76(3):134-140.
- Ball R A, Lipton S A, Dreyer E B et al. Entubulization repair of severed cavernous nerves in the rat resulting in return of erectile function. *Br J Urol* 1992;148(1):211-215.
- Ball R A, Richie J P, Vickers M A. Microsurgical nerve graft repair of the ablated cavernous nerves in the rat. *J Surg Res* 1992;53(3):280-286.
- Ball T P. Editorial comment. *Urology* 2001;57(6):1162
- Balon Richard, E-Mail Address, Balon Richard et al. Sexual difficulties after traumatic brain injury and ways to deal with it. *Depress Anxiety* 2005;22(2):100-101.
- Baltaci S, Aydos K, Kosar A et al. Treating erectile dysfunction with a vacuum tumescence device: a retrospective analysis of acceptance and satisfaction. *Br J Urol* 1995;76(6):757-760.
- Bancroft J. The endocrinology of sexual arousal. *Rom J Endocrinol* 2005;186(3):411-427.
- Bancroft J. A history of sexual medicine in the United Kingdom. *Br J Sex Med* 2005;2(4):569-574.
- Bancroft J. Effects of alpha-2 blockade on sexual response: Experimental studies with delequamine (RS15385). *Int J Impot Res* 2000;12(SUPPL. 1):S64-S69.
- Bancroft J. Hormones and human sexual behavior. *J Sex Marital Ther* 1984;10(1):3-21.
- Bancroft J. Are the effects of androgens on male sexuality noradrenergically mediated? Some consideration of the human. *Neuroscience & Biobehavioral Reviews* 1995;19(2):325-330.
- Bancroft J, Malone N. The clinical assessment of erectile dysfunction: a comparison of nocturnal penile tumescence monitoring and intracavernosal injections. *Int J Impot Res* 1995;7(2):123-130.
- Bancroft John. Sexual problems. Clark, David Millar (Ed); Fairburn, Christopher G (Ed) 1997;(1997):437
- Bancroft John, Carnes Lori, Janssen Erick et al. Erectile and Ejaculatory Problems in Gay and Heterosexual Men. [References]. *Arch Sex Behav* 2005;34(3):285-297.
- Bancroft John, Herbenick Debra, Barnes Tricia et al. The relevance of the dual control model to male sexual dysfunction: The Kinsey Institute/BASRT collaborative project. [References]. *Sexual and Relationship Therapy* 2005;20(1):13-30.
- Bandi G, Rajpurkar A, MacDonald M F et al. Multiple retained needles: An unusual complication of intracavernous self-injection. *Urology* 2005;65(4):
- Bangalore S, Parkar S, Messerli F H. How useful are beta-blockers in cardiovascular disease?. *Anadolu Kardiyol Derg* 2006;6(4):358-363.
- Baniel J, Israilov S, Shmueli J et al. Sexual function in 131 patients with benign prostatic hyperplasia before prostatectomy. *Eur Urol* 2000;38(1):53-58.
- Banks Ian, E-Mail Address, Banks Ian et al. Back to Great Sex. *International Journal of Men's Health* 2003;2(3):230-231.
- Bannowsky A, Schulze H, van der et al. Nocturnal Tumescence: A Parameter for Postoperative Erectile Integrity After Nerve Sparing Radical Prostatectomy. *Br J Urol* 2006;175(6):2214-2217.
- Bar-Chama N, Schiff J, Yavorsky R et al. Erectile dysfunction and infertility. *Current Sexual Health Reports* 2007;4(1):20-23.

- Barbaree H E, Mewhort D J. The effects of the z-score transformation on measures of relative erectile response strength: a re-appraisal. *Behaviour Research & Therapy* 1994;32(5):547-558.
- Bari V, Ahmed M N, Rafique M Z et al. Evaluation of erectile dysfunction with color Doppler sonography. 2006;56(6):258-261.
- Barkin J, Guimaraes M, Jacobi G et al. Alpha-blocker therapy can be withdrawn in the majority of men following initial combination therapy with the dual 5 α -reductase inhibitor dutasteride. *Eur Urol* 2003;44(4):461-466.
- Barkin R L, Barkin S. The role of venlafaxine and duloxetine in the treatment of depression with decremental changes in somatic symptoms of pain, chronic pain, and the pharmacokinetics and clinical considerations of duloxetine pharmacotherapy. *Am J Ther* 2005;12(5):431-438.
- Barlow David H. *Clinical handbook of psychological disorders: A step-by-step treatment manual* (2nd ed.). Refuat Hapeh Vehashinayim 1993;x, 534 pp. New York, NY, US534
- Barnes D. How prescription drugs are developed. *Australian Prescriber* 2006;29(6):159-161.
- Barnes T, Eardley I. Premature ejaculation: The scope of the problem. *J Sex Marital Ther* 2007;33(2):151-170.
- Barnett C F, Machado R F. Sildenafil in the treatment of pulmonary hypertension. *Vascular Health & Risk Management* 2006;2(4):411-422.
- Barra S, Iacono F. Echo-Doppler-flowmetric assessment of penile dorsal arteries and their role in the erectile mechanism. *Eur J Radiol* 1997;25(1):67-73.
- Barreiro P, Soriano V, Gonzalez-Lahoz J et al. Prevention of nevirapine-associated rash [6]. *Lancet* 2001;357(9253):392-393.
- Bartlik B, Goldstein M Z. Maintaining sexual health after menopause. *Psychiatr Serv* 2000;51(6):751-753.
- Bartlik Barbara, Goldstein Marion, Zucker. Men's sexual health after midlife. [References]. *Psychiatr Serv* 2001;52(3):291-293.
- Bartolome S D, Channik R N. Sildenafil for pulmonary arterial hypertension. *Future Cardiology* 2006;2(2):137-143.
- Basar M M, Atan A, Tekdogan U Y. New concept parameters of RigiScan in differentiation of vascular erectile dysfunction: is it a useful test?. *Int J Urol* 2001;8(12):686-691.
- Basar M M, Yildiz M, Basar H et al. Electrical activity of the corpus cavernosum in denervated rats. *Int J Urol* 1999;6(5):251-256.
- Basar M, Basar H, Aydoganli L et al. Colour penile Doppler ultrasonography with intraurethral prostaglandin-E2: preliminary results. *International Urology & Nephrology* 1997;29(6):667-671.
- Bass Barry A. Behavior therapy and the medicalization of male sexuality. [References]. *Behavior Therapist* 2002;25(9):167-168.
- Bass Barry A. Two positions for sexual intercourse useful in the treatment of male sexual dysfunction. *Family Journal: Counseling and Therapy for Couples and Families* 2000;8(4):416-418.
- Bass Barry A. In further pursuit of the perfect penis: The comprehensive urology center and the medicalization of male sexual dysfunction. *J Sex Marital Ther* 1994;20(4):318-320.
- Bassas L, Ribe N, Rajmil O. Measurement of penile intracavernous pressure with a skin fold caliper. *Urol Int* 2004;72(3):225-228.
- Bassiouny H S, Levine L A. Penile duplex sonography in the diagnosis of venogenic impotence. *Eur J Vasc Surg* 1991;13(1):75-82.
- Basson R, McInnes R, Smith M D et al. Efficacy and safety of sildenafil citrate in women with sexual dysfunction associated with female sexual arousal disorder. *Sexuologie* 2002;9(3):116-124.
- Basson R, McInnes R, Smith M D et al. Efficacy and safety of sildenafil citrate in women with sexual dysfunction associated with female sexual arousal disorder. *Journal of Women's Health and Gender-Based Medicine* 2002;11(4):367-377.
- Basson Rosemary. Integrating new biomedical treatments into the assessment and management of erectile dysfunction. *Can J Hum Sex* 1998;7(3):213-229.
- Bates M G D, Thompson A A R, Baillie J K. Phosphodiesterase type 5 inhibitors in the treatment and prevention of high altitude pulmonary edema. *Curr Opin Investig Drugs* 2007;8(3):226-231.
- Batista J E, Palacio A, Torrubia R et al. Tamsulosin: effect on quality of life in 2740 patients with lower urinary tract symptoms managed in real-life practice in Spain. *Arch Esp Urol* 2002;55(1):97-105.
- Batra A K, Lue T F. The physiology of penile erection. *Problems in Urology* 1991;5(4):489-495.
- Bauersachs J, Schafer A. Endothelial dysfunction in heart failure: Mechanisms and therapeutic approaches. *Current Vascular Pharmacology* 2004;2(2):115-124.
- Bax G, Marin N, Piarulli F et al. RigiScan evaluation of specific nervous impairment in patients with diabetes and erectile disorders. *Diabetes Care* 1998;21(7):1159-1161.

- Bayes M, Rabasseda X, Prous J R. Gateways to clinical trials. *Methods & Findings in Experimental & Clinical Pharmacology* 2006;28(4):233-277.
- bdel-Hamid I A. Phosphodiesterase 5 Inhibitors in Rapid Ejaculation: Potential Use and Possible Mechanisms of Action. *Drugs* 2004;64(1):13-26.
- bdel-Hamid I A, Eraky I, Fouda M A et al. Role of penile vascular insufficiency in erectile dysfunction in renal transplant recipients. *Int J Impot Res* 2002;14(1):32-37.
- bdel-Salam Y, Budair Z, Renner C et al. Treatment of Peyronie's disease by extracorporeal shockwave therapy: evaluation of our preliminary results. *J Endourol* 1999;13(8):549-552.
- Beck J G, Bozman A W. Gender differences in sexual desire: the effects of anger and anxiety. *Arch Sex Behav* 1995;24(6):595-612.
- Beck-Peccoz P, Persani L. TSH-induced hyperthyroidism caused by a pituitary tumor. *Nat Clin Pract Endocrinol Metab* 2006;2(9):524-528.
- Becker A J, Uckert S, Stief C G et al. Growth hormone, somatomedins and men's health. *Aging Male* 2002;5(4):258-262.
- Becker A J, Uckert S, Stief C G et al. Plasma levels of angiotensin II during different penile conditions in the cavernous and systemic blood of healthy men and patients with erectile dysfunction. *Urology* 2001;58(5):805-810.
- Becker M E, Hertzberg M A, Moore S D et al. A placebo-controlled trial of bupropion sr in the treatment of chronic posttraumatic stress disorder. *J Clin Psychopharmacol* 2007;27(2):193-197.
- Beckman T J, Mynderse L A. Evaluation and medical management of benign prostatic hyperplasia. *Mayo Clin Proc* 2005;80(10):1356-1362.
- Beckwith Lesli, Jill. Men who seek treatment for erectile disorder at a veteran's administration sexuality clinic: Personality, health locus of control, and sexual functioning. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 1997;58(5-B):Nov
- Bedford S J, McDonnell S M. Measurements of reproductive function in stallions treated with trimethoprim-sulfamethoxazole and pyrimethamine. *J Am Vet Med Assoc* 1999;215(9):1317-1319.
- Befort Christie A. Aspects of health-related quality of life among clinically localized prostate cancer patients. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2005;65(8-B):2005, pp
- Belardinelli R, Lacalaprice F, Faccenda E et al. Effects of short-term moderate exercise training on sexual function in male patients with chronic stable heart failure. *Int J Cardiol* 2005;101(1):83-90.
- Belcaro G, Khan M A, Ledda A et al. Consensus statement. *Current Medical Research & Opinion, Supplement* 1999;16(1):s76-s78.
- Beleslin B D, Ostojic M, Djordjevic-Dikic A et al. Coronary vasodilation without myocardial erection. Simultaneous haemodynamic, echocardiographic and arteriographic findings during adenosine end dipyridamole infusion. *Eur Heart J* 1997;18(7):1166-1174.
- Bell A, Davis M, Close F et al. Sildenafil citrate (revatio) for the treatment of pulmonary arterial hypertension. *P & T* 2006;31(3):135-138.
- Bella A J, Brant W O, Brock G B. Contemporary intracavernous pharmacotherapy for erectile dysfunction in the aging male. *Aging Health* 2006;2(4):559-570.
- Bella A J, Hayashi N, Carrion R E et al. FK1706 enhances the recovery of erectile function following bilateral cavernous nerve crush injury in the rat. *Br J Sex Med* 2007;4(2):341-346.
- Bella A J, Sener A, Foell K et al. Nonpalpable scarring of the penile septum as a cause of erectile dysfunction: an atypical form of Peyronie's disease. *Br J Sex Med* 2007;4(1):226-230.
- Bender A T, Beavo J A. Cyclic nucleotide phosphodiesterases: Molecular regulation to clinical use. *Pharmacol Rev* 2006;58(3):488-520.
- Benet A E, Rehman J, Holcomb R G et al. The correlation between the new RigiScan plus software and the final diagnosis in the evaluation of erectile dysfunction. *Br J Urol* 1996;156(6):1947-1950.
- Benet A E, Sharaby J S, Melman A. Male erectile dysfunction assessment and treatment options. [Review] [15 refs]. *Compr Ther* 1994;20(12):669-673.
- Benson C B, Aruny J E, Vickers M A. Correlation of duplex sonography with arteriography in patients with erectile dysfunction. *AJR Am J Roentgenol* 1993;160(1):71-73.
- Bentas W, Wolfram M, Jones J et al. Robotic technology and the translation of open radical prostatectomy to laparoscopy: the early Frankfurt experience with robotic radical prostatectomy and one year follow-up. *Eur Urol* 2003;44(2):175-181.
- Benvenuti F, Boncinelli L, Vignoli G C. Male sexual impotence in diabetes mellitus: vasculogenic versus neurogenic factors. *Neurourology & Urodynamics* 1993;12(2):145-151.

- Bereczky Z, Bolus M, Chetty P et al. Management of benign prostatic hyperplasia - South African urological association guideline. *S Afr Med J* 2006;96(12 III):1275-1279.
- Berendsen H H G, Broekkamp C L E. Attenuation of 5-HT(1A) and 5-HT2 but not 5-HT(1C) receptor mediated behaviour in rats following chronic treatment with 5-HT receptor agonists, antagonists or anti-depressants. *Psychopharmacology (Berl)* 1991;105(2):219-224.
- Berendsen H H G, Jenck F, Broekkamp C L E. Involvement of 5-HT(1C)-receptors in drug-induced penile erections in rats. *Psychopharmacology (Berl)* 1990;101(1):57-61.
- Berendsen H H G, Kester R C H, Peeters B W M M et al. Modulation of 5-HT receptor subtype-mediated behaviours by corticosterone. *Eur J Pharmacol* 1996;308(2):103-111.
- Berges R. The impact of treatment on lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) progression. *European Urology Supplements* 2004;3(4):12-17.
- Berigan Timothy R, Harazin Jeffrey S. Sexual dysfunction associated with mirtazapine: A case report. *Hillside J Clin Psychiatry* 1998;59(6):319-320.
- Berkels R, Klotz T, Sticht G et al. Modulation of human platelet aggregation by the phosphodiesterase type 5 inhibitor sildenafil. *J Cardiovasc Pharmacol* 2001;37(4):413-421.
- Berkovitch M, Keresteci A G, Koren G. Efficacy of prilocaine-lidocaine cream in the treatment of premature ejaculation.[see comment]. *Br J Urol* 1995;154(4):1360-1361.
- Berlant J L. Antiepileptic Treatment of Posttraumatic Stress Disorder. *Primary Psychiatry* 2003;10(10):41-49.
- Berner M M, Hagen M, Kriston L. Management of sexual dysfunction due to antipsychotic drug therapy. [Review] [66 refs]. *Cochrane Database Syst Rev* 2007;(1):CD003546
- Berner M M, Hagen M, Kriston L. A systematic review of research on strategies for the management of antipsychotic-induced sexual dysfunction: high-level evidence is needed. [Review] [21 refs]. *Hillside J Clin Psychiatry* 2006;67(10):1649-1650.
- Bernstein A J, Peters K M. Expanding indications for neuromodulation. *Urol Clin North Am* 2005;32(1):59-63.
- Berrada S, Kadri N, Mechakra-Tahiri S et al. Prevalence of erectile dysfunction and its correlates: a population-based study in Morocco. *Int J Impot Res* 2003;15Suppl-7.
- Bertaccini A, Marchiori D, Giovannini C et al. Fibrous hamartoma of corpus cavernosum: A rare cause of congenital penile curvature associated with erectile dysfunction. *Br J Urol* 2004;172(2):642-643.
- Bertero E, Hallak J, Gromatzky C et al. Assessment of sexual function in patients undergoing vasectomy using the international index of erectile function. *International Braz J Urol* 2005;31(5):452-458.
- Bertol E, Fineschi V, Karch S B et al. Nymphaea cults in ancient Egypt and the New World: A lesson in empirical pharmacology. *J R Soc Med* 2004;97(2):84-85.
- Besharat Mohammad, Ali E-Mail, Address Besharat et al. Management strategies of sexual dysfunctions. *Journal of Contemporary Psychotherapy* 2001;31(3):161-180.
- Bestmann B, Loetters C, Diemer T et al. Prostate-specific symptoms of prostate cancer in a German general population. *Prostate Cancer & Prostatic Diseases* 2007;10(1):52-59.
- Bethke T D, Bohmer G M, Hermann R et al. Dose-proportional intraindividual single- and repeated-dose pharmacokinetics of roflumilast, an oral, once-daily phosphodiesterase 4 inhibitor. *J Clin Pharmacol* 2007;47(1):26-36.
- Beutel M. Psychosomatic aspects in the diagnosis and treatment of erectile dysfunction. [Review] [40 refs]. *Andrologia* 1999;31 Suppl 137-44.
- Beyer Carlos, Gonzalez-Mariscal Gabriela. Effects of sex steroids on sensory and motor spinal mechanisms. *Psychoneuroendocrinology* 1994;19(5-7):517-527.
- Bhalerao S S, Solanki N H. Therapeutic approaches to the management of common baldness. *Indian Drugs* 2002;39(11):567-573.
- Bhargava R, Srivastava D N, Thulkar S et al. Colour duplex doppler ultrasonography evaluation of non-vasculogenic male erectile dysfunction: An Indian perspective. *Australas Radiol* 2002;46(2):170-173.
- Bhasin S, Cunningham G R, Hayes F J et al. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. *Journal of Clinical Endocrinology & Metabolism* 2006;91(6):1995-2010.
- Bhasin S, Enzlin P, Coviello A et al. Sexual dysfunction in men and women with endocrine disorders. *Lancet* 2007;369(9561):597-611.
- Bhasin S, Woodhouse L, Casaburi R et al. Testosterone dose-response relationships in healthy young men. *American Journal of Physiology - Endocrinology & Metabolism* 2001;281(6 44-6):E1172-E1181.

- Bhatnagar V, Stewart S T, Huynh V et al. Estimating the risk of long-term erectile, urinary and bowel symptoms resulting from prostate cancer treatment. [Review] [131 refs]. *Prostate Cancer & Prostatic Diseases* 2006;9(2):136-146.
- Bhattacharyya A, Tymms D J, Naqvi N. Asymptomatic pituitary apoplexy after aortocoronary bypass surgery. *Int J Clin Pract* 1999;53(5):394-395.
- Bhugra D. Literature update: A critical review. *Sexual & Relationship Therapy* 2001;16(1):83-87.
- Bhugra D, Crowe M. Physical treatments of erectile disorders. *Int Rev Psychiatry* 1995;7(2):217-223.
- Bhugra Dinesh, Crowe Michael. Physical treatments of erectile disorders. *Int Rev Psychiatry* 1995;7(2):217-223.
- Biagiotti G, Cavallini G. Acetyl-L-carnitine vs tamoxifen in the oral therapy of Peyronie's disease: a preliminary report. *BJU Int* 2001;88(1):63-67.
- Bialy M, Sachs B D. Androgen implants in medial amygdala briefly maintain noncontact erection in castrated male rats. *Hormones & Behavior* 2002;42(3):345-355.
- Bialy Michal, Sachs Benjamin D E. Androgen implants in medial amygdala briefly maintain noncontact erection in castrated male rats. [References]. *Horm Behav* 2002;42(3):345-355.
- Bickerton A, Higgins B, Cummings M H. Observational study of ACE inhibitor prescribing habits of diabetes physicians in the UK. *Practical Diabetes International* 2003;20(1):21-24.
- Biederman J, Spencer T J. Psychopharmacology of adults with attention-deficit/hyperactivity disorder. *Primary Psychiatry* 2004;11(7):57-62.
- Biederman J, Wilens T E, Spencer T J et al. Diagnosis and treatment of adults with attention-deficit/hyperactivity disorder. *CNS Spectr* 2007;12(4 SUPPL. 6):1-14.
- Biering-Sorensen F, Sonksen J. Sexual function in spinal cord lesioned men. *Proc Annu Clin Spinal Cord Inj Conf* 2001;39(9):455-470.
- Bird S J, Hanno P M. Bulbocavernosus reflex studies and autonomic testing in the diagnosis of erectile dysfunction. *J Neurol Sci* 1998;154(1):8-13.
- Birk L. Pharmacotherapy for performance anxiety disorders: Occasionally useful but typically contraindicated. *J Clin Psychol* 2004;60(8):867-879.
- Bischoff E. Rabbits as models for impotence research. [Review] [17 refs]. *Int J Impot Res* 2001;13(3):146-148.
- Bischoff E, Schneider K. A conscious-rabbit model to study vardenafil hydrochloride and other agents that influence penile erection. *Int J Impot Res* 2001;13(4):230-235.
- Bishop J R, Moul J W, Sihelnik S A et al. Use of glycosylated hemoglobin to identify diabetics at high risk for penile periprosthetic infections. *Br J Urol* 1992;147(2):386-388.
- Bitner Robert S, Nikkel Arthur L, Otte Stephani et al. Dopamine D-sub-4 receptor signaling in the rat paraventricular hypothalamic nucleus: Evidence of natural coupling involving immediate early gene induction and mitogen activated protein kinase phosphorylation. [References]. *Neuropharmacology* 2006;50(5):521-531.
- Bivalacqua T J, Burnett A L, Hellstrom W J G et al. Overexpression of arginase in the aged mouse penis impairs erectile function and decreases eNOS activity: Influence of in vivo gene therapy of anti-arginase. *American Journal of Physiology - Heart & Circulatory Physiology* 2007;292(3):H1340-H1351.
- Bivalacqua T J, Champion H C, Rajasekaran M et al. Potentiation of erectile response and cAMP accumulation by combination of prostaglandin E1 and rolipram, a selective inhibitor of the type 4 phosphodiesterase (PDE 4). *Br J Urol* 1999;162(5):1848-1855.
- Bivalacqua T J, Deng W, Kendirci M et al. Mesenchymal stem cells alone or ex vivo gene modified with endothelial nitric oxide synthase reverse age-associated erectile dysfunction. *American Journal of Physiology - Heart & Circulatory Physiology* 2007;292(3):H1278-H1290.
- Bivalacqua T J, Usta M F, Kendirci M et al. Superoxide anion production in the rat penis impairs erectile function in diabetes: influence of in vivo extracellular superoxide dismutase gene therapy. *Br J Sex Med* 2005;2(2):187-197.
- Bjorklund M. Patterns of morphological variation among cardueline finches (Fringillidae: Carduelinae). *Biological Journal - Linnean Society* 1991;43(3):239-248.
- Black P C, Friedrich J B, Engrav L H et al. Meshed unexpanded split-thickness skin grafting for reconstruction of penile skin loss. *Br J Urol* 2004;172(3):976-979.
- Blake-James B, Attar K H, Emberton M. Treating coexistent benign prostatic hyperplasia/lower urinary tract symptoms and erectile dysfunction in the aging male. *Aging Health* 2007;3(2):191-200.
- Bland J. Breaking the thought barrier: Musings about placebos and a safer healthcare system. --- *2006;5(2):12-13.*
- Blanker Marco H, Verhagen Arianne P. Lipid-lowering drugs and erectile dysfunction. [References]. *Fam Pract* 2002;19(5):567

- Blaya C, Seganfredo A C, Dornelles M et al. The efficacy of milnacipran in panic disorder: An open trial. *Int Clin Psychopharmacol* 2007;22(3):153-158.
- Bloomgarden Z T. The European Association for the Study of Diabetes Annual Meeting, 1998: The U.K. Prospective Diabetes Study and other topics in type 2 diabetes. *Diabetes Care* 1999;22(6):989-995.
- Boccardo F, Rubagotti A, Barichello M et al. Bicalutamide monotherapy versus flutamide plus goserelin in prostate cancer patients: results of an Italian Prostate Cancer Project study.[see comment]. *Am J Clin Oncol* 1999;17(7):2027-2038.
- Bocchio M, Desideri G, Scarpelli P et al. Endothelial cell activation in men with erectile dysfunction without cardiovascular risk factors and overt vascular damage.[see comment]. *Br J Urol* 2004;171(4):1601-1604.
- Bocchio M, Scarpelli P, Necozone S et al. Penile duplex pharmaco-ultrasonography of cavernous arteries in men with erectile dysfunction and generalized atherosclerosis. *Int J Androl* 2006;29(4):496-501.
- Bochinski D, Lin G T, Nunes L et al. The effect of neural embryonic stem cell therapy in a rat model of cavernosal nerve injury. *BJU Int* 2004;94(6):904-909.
- Bodansky H J. Treatment of male erectile dysfunction using the active vacuum assist device. *Diabet Med* 1994;11(4):410-412.
- Bodenheimer Carol, Kerrigan Anthony J, Garber Susan L et al. Sexuality in persons with lower extremity amputations. *Disability and Rehabilitation: An International Multidisciplinary Journal* 2000;22(9):409-415.
- Bodner D R, Haas C A, Krueger B et al. Intraurethral alprostadil for treatment of erectile dysfunction in patients with spinal cord injury. *Urology* 1999;53(1):199-202.
- Boero R, Rollino C, Massara C et al. The verapamil versus amlodipine in nondiabetic nephropathies treated with trandolapril (VVANNTT) study. *Am J Kidney Dis* 2003;42(1 SUPPL. 2):67-75.
- Boger R H. Asymmetric dimethylarginine (ADMA): A novel risk marker in cardiovascular medicine and beyond. *Ann Med* 2006;38(2):126-136.
- Boger R H, Ron E S. L-arginine improves vascular function by overcoming the deleterious effects of ADMA, a novel cardiovascular risk factor. *Altern Med Rev* 2005;10(1):14-23.
- Bohart Arthur C. Mr. Lake. *Journal of Psychotherapy Integration* 1995;5(2):95-106.
- Bokarica P, Parazajder J, Mazuran B et al. Surgical treatment of Peyronie's disease based on penile length and degree of curvature. *Int J Impot Res* 2005;17(2):170-174.
- Bokarica P, Parazajder J, Mazuran B et al. Selecting the appropriate procedure for Peyronie's disease. *The American Journal of Urology Review* 2005;3(2):82-85.
- Bolukbasi Okan, Akyol Ali. Spontaneous erections and libido increase associated with venlafaxine. *Eur J Neurol* 1999;6(4):527-528.
- Bongale Rajshree N, Tekell Janet L, Haraguchi Gayle E et al. Continuation of clozapine after priapism. [References]. *Am J Psychiatry* 2001;158(12):2087
- Bongers V, Sabin G V. Comparison of the effect of two metoprolol formulations on total ischaemic burden. *Clinical Drug Investigation* 1999;17(2):103-110.
- Bookstein J J, Vandeberg J, Machado T. The cavernosal acetylcholine/papaverine response. A practical in vivo method for quantification of endothelium-dependent relaxation: Rationale and experimental validation. *Invest Radiol* 1990;25(11):1168-1174.
- Borer J S. Drug insight: If inhibitors as specific heart-rate-reducing agents. *Nature Clinical Practice Cardiovascular Medicine* 2004;1(2):103-109.
- Borgquist R, Gudmundsson P, Winter R et al. Erectile dysfunction in healthy subjects predicts reduced coronary flow velocity reserve. *Int J Cardiol* 2006;112(2):166-170.
- Borlaug B A, Melenovsky V, Marhin T et al. Sildenafil inhibits beta-adrenergic-stimulated cardiac contractility in humans. *Circulation* 2005;112(17):2642-2649.
- Borrelli-Kerner Sandra, Bernell Bonnie. Couple therapy of sexual disorders. Charlton, Randolph S (Ed); Yalom, Irvin D (Ed) 1997;(1997):348-Bass.
- Bortolotti A, Fedele D, Chatenoud L et al. Cigarette smoking: a risk factor for erectile dysfunction in diabetics. *Eur Urol* 2001;40(4):392-396.
- Bortolotti M, Mari C, Lopilato C et al. Effects of sildenafil on esophageal motility of patients with idiopathic achalasia. *Gastroenterology* 2000;118(2):253-257.
- Bosch X. Radiotherapy versus surgery for prostate cancer. *Lancet Oncol* 2005;6(5):263
- Bosshardt R J, Farwerk R, Sikora R et al. Objective measurement of the effectiveness, therapeutic success and dynamic mechanisms of the vacuum device. *Br J Urol* 1995;75(6):786-791.

- Brioni J D, Moreland R B, Cowart M et al. Activation of dopamine D4 receptors by ABT-724 induces penile erection in rats. *Proc Natl Acad Sci U S A* 2004;101(17):6758-6763.
- Brock G, Moreira E D, Glasser D B et al. Sexual disorders and associated help-seeking behaviors in Canada. *Can J Urol* 2006;13(1):2953-2961.
- Broderick G A. Changing practice patterns in erectile dysfunction: a diagnostic algorithm for the new millennium. [Review] [42 refs]. *Adv Ren Replace Ther* 1999;6(4):314-326.
- Broderick G A, Donatucci C F, Hatzichristou D et al. Efficacy of tadalafil in men with erectile dysfunction naive to phosphodiesterase 5 inhibitor therapy compared with prior responders to sildenafil citrate. *Br J Sex Med* 2006;3(4):668-675.
- Broekman C P, Haensel S M, van de V et al. Bisoprolol and hypertension: effects on sexual functioning in men. *J Sex Marital Ther* 1992;18(4):325-331.
- Brookes S T, Donovan J L, Peters T J et al. Sexual dysfunction in men after treatment for lower urinary tract symptoms: evidence from randomised controlled trial.[see comment]. *BMJ* 2002;324(7345):1059-1061.
- Brooks Gary R, Levant Ronald F E. Is Viagra Enough? Broadening the Conceptual Lens in Sex Therapy with (Heterosexual) Men: A Case Report. [References]. *International Journal of Men's Health* 2006;5(2):207-215.
- Brophy D F, Ripley E B D, Holdford D A. Pharmacoeconomic considerations in the health system management of anaemia in patients with chronic kidney disease and end stage renal disease. *Expert Opin Pharmacother* 2003;4(9):1461-1469.
- Brotons F B, Campos J C, Gonzalez-Correales R et al. Core document on erectile dysfunction: Key aspects in the care of a patient with erectile dysfunction. *Int J Impot Res* 2004;16(SUPPL. 2):S26-S39.
- Brown J A, Rodin D, Lee B et al. Transperitoneal versus extraperitoneal approach to laparoscopic radical prostatectomy: an assessment of 156 cases. [Review] [13 refs]. *Urology* 2005;65(2):320-324.
- Brown Judith, Lichtenberg Philip, Lukensmeyer Carolyn et al. The implications of Gestalt therapy for social and political change. *Gestalt Journal* 1993;16(1):7-54.
- Brownell J. Quinagolide (Norprolac(TM)). A novel non-ergot prolactin inhibitor. *Med Actual* 1996;32(SUPPL. B):1-31.
- Brufsky A, Fontaine-Rothe P, Berlane K et al. Finasteride and flutamide as potency-sparing androgen-ablative therapy for advanced adenocarcinoma of the prostate. *Urology* 1997;49(6):913-920.
- Bruner Deborah, Watkins. Determination of preferences and utilities for the treatment of prostate cancer. (quality of life, treatment utility). *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2000;60(7-B):Feb
- Bryan J. Inhaled products of the modern era: Drugs for non-respiratory conditions. *Can Pharm J* 2004;273(7310):161-162.
- Bryant J E, Bueschen A J, Cohn J H et al. Transurethral prostatectomy: analysis and comparison of four clinical series. *South Med J* 1990;83(4):386-389.
- Bschleipfer T, Cimniak H U, Beckert R et al. Possible hemodynamic pathways of intraurethral prostaglandin-E1 (MUSE). *Int J Impot Res* 2004;16(4):365-368.
- Buch J P, Zorn B H, Taylor R J. Cost-benefit analysis of pharmacologic erection program (PEP) versus penile prosthesis.[comment]. *Urology* 1991;37(2):116-118.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. [German]. *Urologe (Ausg 1048;A)*.(9):1045-1046.
- Budia A, Luis Palmero J, Broseta E et al. Value of semen culture in the diagnosis of chronic bacterial prostatitis: a simplified method. *Scandinavian Journal of Urology & Nephrology* 2006;40(4):326-331.
- Buhle Mari, Jo. Review of Freud's Free Clinics: Psychoanalysis and Social Justice, 1918-1938. [References]. *J Hist Behav Sci* 2006;42(4):401-402.
- Bui C, Glassburn J. IMRT for prostate cancer: Improving the therapeutic ratio. *Community Oncology* 2006;3(10):659-661.
- Bull E. Drug review - Pregabalin. *Drugs in Context* 2006;2(2):65-77.
- Buller K M, Crane J W, Spencer S J et al. Systemic apomorphine alters HPA axis responses to interleukin-1 beta administration but not sound stress. [References]. *Psychoneuroendocrinology* 2003;28(6):715-732.
- Bunnell B A, Deng W, Robinson C M et al. Potential application for mesenchymal stem cells in the treatment of cardiovascular diseases. *Canadian Journal of Physiology & Pharmacology* 2005;83(7):529-539.
- Burchardt M, Burchardt T, Anastasiadis A G et al. Application of angiogenic factors for therapy of erectile dysfunction: protein and DNA transfer of VEGF 165 into the rat penis. *Urology* 2005;66(3):665-670.

- Burke J P, Jacobson D J, McGree M E et al. Diabetes and sexual dysfunction: results from the Olmsted County study of urinary symptoms and health status among men. *Br J Urol* 2007;177(4):1438-1442.
- Burke M A, McEvoy J P, Ritchie J C. A pilot study of a structured interview addressing sexual function in men with schizophrenia. *Biol Psychiatry* 1994;35(1):32-35.
- Burnett A L. Nitric oxide-based therapy for erectile disorders. *Drug Discovery Today: Therapeutic Strategies* 2005;2(1):25-30.
- Burnett A L. Pathophysiology of priapism: Dysregulatory erection physiology thesis. *Br J Urol* 2003;170(1):26-34.
- Burnett A L. Rationale for cavernous nerve restorative therapy to preserve erectile function after radical prostatectomy. *Urology* 2003;61(3):491-497.
- Burnett A L. Role of nitric oxide in the physiology of erection. *Biol Reprod* 1995;52(3):485-489.
- Burnett A L. Salvage Techniques for Phosphodiesterase 5 Inhibitor Therapy: Purposeful but How Much?. *Eur Urol* 2006;50(1):29-30.
- Burnett A L, Lue T F. Neuromodulatory therapy to improve erectile function recovery outcomes after pelvic surgery. [Review] [50 refs]. *Br J Urol* 2006;176(3):882-887.
- Burnett A L, Allen R P, Davis Wright D C et al. Near infrared spectrophotometry for the diagnosis of vasculogenic erectile dysfunction. *Int J Impot Res* 2000;12(5):247-254.
- Burnett A L, Bivalacqua T J, Champion H C et al. Feasibility of the use of phosphodiesterase type 5 inhibitors in a pharmacologic prevention program for recurrent priapism. *Br J Sex Med* 2006;3(6):1077-1084.
- Burnett A L, Bivalacqua T J, Champion H C et al. Long-term oral phosphodiesterase 5 inhibitor therapy alleviates recurrent priapism. *Urology* 2006;67(5):1043-1048.
- Burnett A L, Musicki B, Bivalacqua T J. Molecular science of priapism. *Current Sexual Health Reports* 2007;4(1):9-14.
- Burnett A L, Musicki B, Jin L et al. Nitric oxide/redox-based signalling as a therapeutic target for penile disorders. *Expert Opin Ther Targets* 2006;10(3):445-457.
- Burnstock G. Purinergic signalling: Therapeutic potential. *Anales de la Real Academia Nacional de Farmacia* 2005;71(2):283-319.
- Burnstock G. Potential therapeutic targets in the rapidly expanding field of purinergic signalling. *Clin Med (Northfield Il)* 2002;2(1):45-53.
- Burnstock G. Pathophysiology and therapeutic potential of purinergic signaling. *Pharmacol Rev* 2006;58(1):58-86.
- Butler R N, Lewis M I, Hoffman E et al. Love and sex after 60: how to evaluate and treat the impotent older man. A roundtable discussion: Part 2.[see comment]. *Geriatrics* 1994;49(10):27-32.
- Buvat J, Bou Jaoude G. Significance of hypogonadism in erectile dysfunction. *World J Urol* 2006;24(6):657-667.
- Buyyounouski M K, Horwitz E M, Price R A et al. Intensity-modulated radiotherapy with MRI simulation to reduce doses received by erectile tissue during prostate cancer treatment. *Int J Radiat Oncol Biol Phys* 2004;58(3):743-749.
- Buzelin J M, Fonteyne E, Kontturi M et al. Comparison of tamsulosin with alfuzosin in the treatment of patients with lower urinary tract symptoms suggestive of bladder outlet obstruction (symptomatic benign prostatic hyperplasia). *Br J Urol* 1997;80(4):597-605.
- Byrne R R, Henry G D, Rao D S et al. Vascular endothelial growth factor restores corporeal smooth muscle function in vitro. *Br J Urol* 2001;165(4):1310-1315.
- Caballero J, Nahata M C. Atomoxetine Hydrochloride for the Treatment of Attention-Deficit/ Hyperactivity Disorder. *Clin Ther* 2003;25(12):3065-3083.
- Cade Brian W. Unpredictability and change: A holographic metaphor. *Weeks, Gerald R (Ed)* 1991;(1991):325
- Cakan M, Yalcinkaya F, Demirel F et al. Is dorsale penile vein ligation (dpvl) still a treatment option in veno-occlusive dysfunction?. *International Urology & Nephrology* 2004;36(3):381-387.
- Calil I, Tinel R A, Vicente W V D A et al. The concept of crosstalk and its implications for cardiovascular function and disease. *Arq Bras Cardiol* 2007;88(1):e25-e30.
- Cambio A J, Evans C P. Outcomes and quality of life issues in the pharmacological management of benign prostatic hyperplasia (BPH). *Therapeutics & Clinical Risk Management* 2007;3(1):181-196.
- Campbell B C, Prossinger H, Mbzivo M. Timing of pubertal maturation and the onset of sexual behavior among Zimbabwe school boys. *Arch Sex Behav* 2005;34(5):505-516.
- Campbell H E. Clinical monograph for drug formulary review: erectile dysfunction agents. [Review] [64 refs]. *Journal of Managed Care Pharmacy* 2005;11(2):151-171.

- Campbell S F. Science, art and drug discovery: a personal perspective. *Clin Sci* 2000;99(4):255-260.
- Campling Penelope, E-Mail Address, Campling Penelope et al. Connection and catastrophe, hope and despair in our borderline world. [References]. *British Journal of Psychotherapy* 2002;19(2):235-245.
- Campo B, Bergamaschi F, Ordesi G et al. Transurethral needle ablation (TUNA): 1 year of follow-up. *Acta Urologica Italica* 1996;10(3):205-207.
- Campo C, Segura J, Fernandez M L et al. A prospective comparison of four antihypertensive agents in daily clinical practice. *J Clin Hypertens* 2001;3(3):139-144.
- Campos A R, Lima R C P, Uchoa D E A et al. Pro-erectile effects of an alkaloidal rich fraction from *Aspidosperma ulei* root bark in mice. *J Ethnopharmacol* 2006;104(1-2):240-244.
- Canada A L, Neese L E, Sui D et al. Pilot intervention to enhance sexual rehabilitation for couples after treatment for localized prostate carcinoma. *Cancer* 2005;104(12):2689-2700.
- Canby-Hagino E D, Brandt T C, Hernandez J et al. Chemoprevention of prostate cancer with finasteride. *Expert Opin Pharmacother* 2006;7(7):899-905.
- Canby-Hagino E, Hernandez J, Brand T C et al. Looking Back at PCPT: Looking Forward to New Paradigms in Prostate Cancer Screening and Prevention{A figure is presented}. *Eur Urol* 2007;51(1):27-33.
- Candela J V, Hellstrom W J. Three-piece inflatable penile prosthesis implantation: a comparison of the penoscrotal and infrapubic surgical approaches. *J La State Med Soc* 1996;148(7):296-301.
- Cantor S B, Spann S J, Volk R J et al. Prostate cancer screening: a decision analysis.[see comment]. *J Fam Pract* 1995;41(1):33-41.
- Capaci K, Hegguler S. Comparison of the effects of amitriptyline and paroxetine in the treatment of fibromyalgia syndrome. *The Pain Clinic* 2002;14(3):223-228.
- Cappelleri J C, Rosen R C. The Sexual Health Inventory for Men (SHIM): A 5-year review of research and clinical experience. *Int J Impot Res* 2005;17(4):307-319.
- Cappelleri J C, Rosen R C, Smith M D et al. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology* 1999;54(2):346-351.
- Carbone D J, Hodges S. Medical therapy for benign prostatic hyperplasia: Sexual dysfunction and impact on quality of life. *Int J Impot Res* 2003;15(4):299-306.
- Carbone D J, Seftel A D. Erectile dysfunction. Diagnosis and treatment in older men. [Review] [33 refs]. *Geriatrics* 2002;57(9):18-24.
- Cardinale Vic. The use of a daily diary as a treatment for SSRI-induced sexual dysfunction. Dissertation Abstracts International: Section B: The Sciences and Engineering 2005;65(9-B):2005, pp
- Caretta N, Ferlin A, Palego P F et al. Erectile dysfunction in aging men: testosterone role in therapeutic protocols. *J Endocrinol Invest* 2005;28(11 Suppl Proceedings):108-111.
- Carey J C. Pharmacological Effects On Sexual Function. *Obstetrics & Gynecology Clinics of North America* 2006;33(4):599-620.
- Carey Michael P. Cognitive-behavioral treatment of sexual dysfunctions. Caballo, Vicente E (Ed) 1998;(1998):698
- Carey Michael P, Lantinga Larry J, Krauss Dennis J. Male erectile disorder. Hersen, Michel (Ed); Ammerman, Robert T (Ed) 1994;(1994):512
- Carlsen J E, Kober L, Torp-Pedersen C T et al. The optimal dosage of bendrofluazide in hypertension. A randomized double-blind dosage-response investigation. OPTIMAL DOSIS AF BENDROFLUMETIAZID VED HYPERTENSION. EN RANDOMISERET DOBBELTBLIND DOSIS-RESPONSUNDERSOGELSE. *UGESKR LAEG* 1990;152(42):3072-3075.
- Carmignani G, Oneto F. Medical therapy of prostate carcinoma. *Minerva Urol Nefrol* 2004;56(2):147-163.
- Carraro J C, Raynaud J P, Koch G et al. Comparison of phytotherapy (Permixon) with finasteride in the treatment of benign prostate hyperplasia: a randomized international study of 1,098 patients. *Prostate* 1996;29(4):231-240.
- Carrier S. Pharmacology of phosphodiesterase 5 inhibitors. [Review] [21 refs]. *Can J Urol* 2003;10Suppl-6.
- Carrier S. Office-based assessment of the suspected hypogonadal male. *Current Sexual Health Reports* 2006;3(1):45-50.
- Carrier S, Hricak H, Lee S S et al. Radiation-induced decrease in nitric oxide synthase--containing nerves in the rat penis. *Radiology* 1995;195(1):95-99.
- Carrier S, Zvara P, Lue T F. Erectile dysfunction. *Endocrinology & Metabolism Clinics of North America* 1994;23(4):773-782.
- Carson C, Gunn K. Premature ejaculation: Definition and prevalence. *Int J Impot Res* 2006;18(SUPPL. 1):S5-S13.
- Carson C C. PDE5 inhibitors: are there differences?. [Review] [27 refs]. *Can J Urol* 2006;13 Suppl 134-39.

- Carson C C. Combination of phosphodiesterase-5 inhibitors and alpha-blockers in patients with benign prostatic hyperplasia: treatments of lower urinary tract symptoms, erectile dysfunction, or both?. [Review] [21 refs]. *BJU Int* 2006;97 Suppl 239-43.
- Carson C C. Penile prosthesis implantation: surgical implants in the era of oral medication. [Review] [36 refs]. *Urol Clin North Am* 2005;32(4):503-509.
- Carson C C. Cardiac safety in clinical trials of phosphodiesterase 5 inhibitors. [Review] [25 refs]. *Am J Cardiol* 2005;96(12B):37M-41M.
- Carson C C, Mulcahy J J, Govier F E. Efficacy, safety and patient satisfaction outcomes of the AMS 700CX inflatable penile prosthesis: results of a long-term multicenter study. AMS 700CX Study Group. *Br J Urol* 2000;164(2):376-380.
- Carson C C, Porst Nehra, Althof Meuleman. Erectile dysfunction in the 21st century: Whom we can treat, whom we cannot treat and patient education. *Int J Impot Res* 2002;14(SUPPL. 1):S29-S34.
- Carson C, Giuliano F, Goldstein I et al. The 'effectiveness' scale-therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report. [Review] [7 refs]. *Int J Impot Res* 2004;16(3):207-213.
- Cartledge J J, Eardley I, Morrison J F. Advanced glycation end-products are responsible for the impairment of corpus cavernosal smooth muscle relaxation seen in diabetes. *BJU Int* 2001;87(4):402-407.
- Cartledge J, Minhas S, Eardley I. The role of nitric oxide in penile erection. *Expert Opin Pharmacother* 2001;2(1):95-107.
- Carvalho B, Smith M. Viagra(TM): Are anaesthetists rising to the challenge?. *Anaesthesia* 2001;56(1):91-93.
- Carver Christi. Premature ejaculation: A common and treatable concern. *J Am Psychiatr Nurses Assoc* 1998;4(6):199-204.
- Case Trevor I, Williams Kipling D. Ostracism: A Metaphor for Death. [References]. Greenberg, Jeff (Ed); Koole, Sander L (Ed); Pyszczyński, Tom (Ed) 2004;(2004):528
- Casey R, Tarride J E, Keresteci M A et al. The Erectile Function Visual Analog Scale (EF-VAS): a disease-specific utility instrument for the assessment of erectile function. *Can J Urol* 2006;13(2):3016-3025.
- Caspari D, Huebgen E M, Derouet H. Interdisciplinary assessment and follow-up of patients with erectile dysfunction - Psychiatric aspects. *Int J Impot Res* 1999;11(4):213-217.
- Cassels A, Wright J M, Mintzes B et al. Direct-to-consumer advertising. Finasteride for male pattern hair loss. *Can Fam Physician* 2001;47(SEPT.):1751-1752.
- Catalona W J. Patient selection for, results of, and impact on tumor resection of potency-sparing radical prostatectomy. *Urol Clin North Am* 1990;17(4):819-826.
- Catalona W J, Carvalhal G F, Mager D E et al. Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies. *Br J Urol* 1999;162(2):433-438.
- Catton C, Milosevic M, Warde P et al. Recurrent prostate cancer following external beam radiotherapy: Follow-up strategies and management. *Urol Clin North Am* 2003;30(4):751-763.
- Cavaletti G, Marmiroli P. Chemotherapy-induced peripheral neurotoxicity. *Expert Opin Drug Saf* 2004;3(6):535-546.
- Cavalla D. Therapeutic switching: A new strategic approach to enhance R&D productivity. *IDrugs* 2005;8(11):914-918.
- Cavalla D. Getting more mileage out of a tankful of new molecular entities?. *Drug Discov Today* 2004;9(7):304-305.
- Cavallini G, Biagiotti G, Koverech A et al. Oral propionyl-L-carnitine and intraplaque verapamil in the therapy of advanced and resistant Peyronie's disease. *BJU Int* 2002;89(9):895-900.
- Cavassini M L, D'Acromont V, Furrer H et al. Pharmacotherapy, vaccines and malaria advice for HIV-infected travellers. *Expert Opin Pharmacother* 2005;6(6):891-913.
- Cayan Selahi, tti Bozlu, Murat Canpolat et al. The assessment of sexual functions in women with male partners complaining of erectile dysfunction: Does treatment of male sexual dysfunction improve female partner's sexual functions? [References]. *J Sex Marital Ther* 2004;30(5):333-341.
- Century Gillian, Leavey Gerard, Payne Helen et al. The experience of working with refugees: Counsellors in primary care. [References]. *Br J Guid Coun* 2007;35(1):23-40.
- Cetinkaya M, Erdogan E, Adsan O et al. Evaluation of impotent men with intracorporeal injection of papaverine and colour Doppler ultrasound. *International Urology & Nephrology* 1995;27(6):779-782.
- Chahal H S, Drake W M. The endocrine system and ageing. *Am J Pathol* 2007;211(2):173-180.
- Chahal R, Sundaram S K. Laser ablation of the prostate versus transurethral resection of the prostate in men with benign prostatic hyperplasia [3]. *Urology* 2000;56(3):546-547.
- Challem J. Medical journal watch: Context and applications. *Alternative & Complementary Therapies* 2006;12(2):102-106.

- Champion H C. Erectile dysfunction and cardiovascular disease: Carrots, sticks, and better men's health. *Advanced Studies in Medicine* 2006;6(4):163-170.
- Champion H C, Bivalacqua T J, Wang R et al. [Tyr1]-nociceptin and nociceptin have similar naloxone-insensitive erectile activity in the cat. *J Androl* 1998;19(6):747-753.
- Champion H C, Bivalacqua T J, Wang R et al. Induction of penile erection by intracavernosal and transurethral administration of novel nitric oxide donors in the cat. *Br J Urol* 1999;161(6):2013-2019.
- Champion H C, Wang R, Hellstrom W J et al. Nociceptin, a novel endogenous ligand for the ORL1 receptor, has potent erectile activity in the cat. *Am J Physiol* 1997;273(1 Pt 1):E214-E219.
- Chan D C, Watts G F. Dyslipidemia in the metabolic syndrome. *Journal of Drug Evaluation* 2004;2(1):3-34.
- Chan N N, Tong P C Y, Chan J C N. Management of systemic hypertension: An update for primary care physicians. *Hong Kong Practitioner* 2005;27(1):4-14.
- Chan S W H, Yung M Y P, Que M B W et al. Adoption of laparoscopic technique for radical prostatectomy in a district hospital in Hong Kong. *Annals of the College of Surgeons of Hong Kong* 2004;8(3):83-89.
- Chancellor M B, Erhard M J, Hirsch I H et al. Prospective evaluation of terazosin for the treatment of autonomic dysreflexia. *Br J Urol* 1994;151(1):111-113.
- Chancellor M B, Rivas D A, Linsenmeyer T et al. Multicenter trial in North America of UroLume urinary sphincter prosthesis. *Br J Urol* 1994;152(3):924-930.
- Chancellor M B, Rivas D A, Panzer D E et al. Prospective comparison of topical minoxidil to vacuum constriction device and intracorporeal papaverine injection in treatment of erectile dysfunction due to spinal cord injury. *Urology* 1994;43(3):365-369.
- Chancellor M B, Tirney S, Mattes C E et al. Nitric oxide synthase gene transfer for erectile dysfunction in a rat model. *BJU Int* 2003;91(7):691-696.
- Chang S W, Fine R, Siegel D et al. The impact of diuretic therapy on reported sexual function.[see comment]. *Arch Intern Med* 1991;151(12):2402-2408.
- Chang S, Hypolite J A, Changolkar A et al. Increased contractility of diabetic rabbit corpora smooth muscle in response to endothelin is mediated via Rho-kinase beta.[see comment]. *Int J Impot Res* 2003;15(1):53-62.
- Chang S, Hypolite J A, Zderic S A et al. Enhanced force generation by corpus cavernosum smooth muscle in rabbits with partial bladder outlet obstruction. *Br J Urol* 2002;167(6):2636-2644.
- Chanson P, Brochier S. Non-functioning pituitary adenomas. *J Endocrinol Invest* 2005;28(11 Suppl):93-99.
- Chapman A H, Chapman-Santana Mirian. The use of humor in psychotherapy. *Arq Neuropsiquiatr* 1995;53(1):153-156.
- Chapple C R. Pharmacological therapy of benign prostatic hyperplasia/lower urinary tract symptoms: An overview for the practising clinician. *BJU Int* 2004;94(5):738-744.
- Charlton Randolph S, Brigel Faith W. Treatment of arousal and orgasmic disorders. Charlton, Randolph S (Ed); Yalom, Irvin D (Ed) 1997;(1997):348-Bass.
- Chavez M L. PC-SPES for the treatment of prostate cancer?. *Journal of Herbal Pharmacotherapy* 2002;2(3):73-89.
- Cheitlin M D. PDE5 inhibitors: Two new drugs and cardiovascular uses beyond erectile dysfunction. *Cardiology Review* 2005;22(9):18-22.
- Chen H H, Huntley B K, Schirger J A et al. Maximizing the renal cyclic 3'-5'-guanosine monophosphate system with type V phosphodiesterase inhibition and exogenous natriuretic peptide: A novel strategy to improve renal function in experimental overt heart failure. *J Am Soc Nephrol* 2006;17(10):2742-2747.
- Chen J, Chopp M. Neurorestorative Treatment of Stroke: Cell and Pharmacological Approaches. *NeuroRx* 2006;3(4):466-473.
- Chen J C, Tao P L, Li J Y et al. Endomorphin-1 and -2 induce naloxone-precipitated withdrawal syndromes in rats. [References]. *Peptides* 2003;24(3):477-481.
- Chen J, Greenstein A, Matzkin H. Is a second injection of vasoactive medication necessary during color duplex Doppler evaluation of young patients with veno-occlusive erectile dysfunction?. *Urology* 2000;55(6):927-930.
- Chen J, Greenstein A, Sofer M et al. Rigiscan versus snap gauge band measurements: is the extra cost justifiable?. *Int J Impot Res* 1999;11(6):315-318.
- Chen Jack J, Swope David M. A Case of Complex Movement Disorder Induced by Fluoxetine With Management of Dystonia by Botulinum Toxin Type A. [References]. *Hillside J Clin Psychiatry* 2005;66(2):267-268.
- Chen K K, Chou Y H, Chang L S et al. Sonographic measurement of penile erectile volume. *J Clin Ultrasound* 1992;20(4):247-253.

- Chen Y. Acupuncture treatment of functional non-ejaculation: a report of 70 cases. *J Trad Chin Med* 1993 Mar 1993;13(1):10-12.
- Chen Y, Yang R, Yao L et al. Differential expression of neurotrophins in penises of streptozotocin-induced diabetic rats. *J Androl* 2007;28(2):306-312.
- Cheng J L, Hu L Q. Effects of antihypertensive drugs on erectile function and number of nNOS-containing nerve fibers in spontaneously hypertensive rats. *Zhonghua Nan Ke Xue* 2003;9(2):115-117.
- Cheng J Y W, Ng E M L, Ko J S N et al. Physical activity and erectile dysfunction: Meta-analysis of population-based studies. *Int J Impot Res* 2007;19(3):245-252.
- Cherdshevasart W, Nimsakul N. Clinical trial of *Butea superba*, an alternative herbal treatment for erectile dysfunction. *Asian J Androl* 2003;5(3):243-246.
- Chevallier D, Benizri E, Volpp P et al. Peyronie's disease: Review of historical, epidemiologic, and physiopathologic data. Diagnosis and therapeutic approach. *Rev Med Interne* 1997;18(SUPPL. 1):
- Cheven E. Opioids: A review. *Current Pain & Headache Reports* 2003;7(1):15-23.
- Chi K N, Eisenhauer E, Fazli L et al. A phase I pharmacokinetic and pharmacodynamic study of OGX-011, a 2'-methoxyethyl antisense oligonucleotide to clusterin, in patients with localized prostate cancer. *J Natl Cancer Inst* 2005;97(17):1287-1296.
- Chiang H S, Wu C C, Wen T C. 10 years of experience with penile prosthesis implantation in Taiwanese patients. *Br J Urol* 2000;163(2):476-480.
- Chiang P H, Chiang C P, Wu C C et al. Colour duplex sonography in the assessment of impotence. *Br J Urol* 1991;68(2):181-186.
- Chiariello M. A double-blind comparison of the efficacy and safety of lacidipine and hydrochlorothiazide in essential hypertension. *J 1991;CARDIOVASC. PHARMACOL.* 17(SUPPL. 4):S35-S37.
- Chien G W, Aboseif S R. Corporeal plication for the treatment of congenital penile curvature. *Br J Urol* 2003;169(2):599-602.
- Chiou R K, Pomeroy B D, Chen W S et al. Hemodynamic patterns of pharmacologically induced erection: evaluation by color Doppler sonography.[see comment]. *Br J Urol* 1998;159(1):109-112.
- Chitale K, Webb R C, Dorrance A M et al. Decreased penile erection in DOCA-salt and stroke prone-spontaneously hypertensive rats. *Int J Impot Res* 2001;13 Suppl 5S16-S20.
- Choi H K, Choi Y J, Choi Y D et al. SS-Penogram: A new diagnostic test for erectile dysfunction. *Yonsei Med J* 2002;43(1):1-6.
- Choi H K, Seong D H, Rha K H. Clinical efficacy of Korean red ginseng for erectile dysfunction. *Int J Impot Res* 1995;7(3):181-186.
- Choi S, O'Connell L, Min K et al. Efficacy of vardenafil and sildenafil in facilitating penile erection in an animal model. *J Androl* 2002;23(3):332-337.
- Chong S T, Beasley H S, Daffner R H. POEMS syndrome: Radiographic appearance with MRI correlation. *Skeletal Radiol* 2006;35(9):690-695.
- Chow S C, Shao J, Ho H T. On statistical analysis for placebo-challenging designs in clinical trials. *Stat Med* 2000;19(8):1029-1037.
- Chowdhury A N, Mukherjee A, Ghosh K et al. Horizon of a new hope: Recovery of schizophrenia in India. *Med Sci Monit* 1999;6(3):181-185.
- Choy D S J. Percutaneous laser disc decompression: An update. *Photomedicine and Laser Surgery* 2004;22(5):393-406.
- Chrisofos M, Papatsoris A G, Dellis A et al. Can prostate biopsies affect erectile function?. *Andrologia* 2006;38(3):79-83.
- Christ G J, Rehman J, Day N et al. Intracorporal injection of hSlo cDNA in rats produces physiologically relevant alterations in penile function. *Am J Physiol* 1998;275(2 Pt 2):H600-H608.
- Christian K A, Griffiths A D, Bedford G et al. Androgen concentrations and behavior of frillneck lizards (*Chlamydosaurus kingii*). *Journal of Herpetology* 1999;33(1):12-17.
- Christman A K, Fermo J D, Markowitz J S. Atomoxetine, a novel treatment for attention-deficit-hyperactivity disorder. *Pharmacotherapy* 2004;24(8):1020-1036.
- Chrubasik S, Model A, Black A et al. A randomized double-blind pilot study comparing Doloteffin and Vioxx in the treatment of low back pain. *Rheumatology* 2003;42(1):141-148.
- Chu N V, Edelman S V. Erectile dysfunction and diabetes. [Review] [32 refs]. *Curr Diab Rep* 2002;2(1):60-66.
- Chueh S C, Yu H J, Chiu T Y et al. Treating benign prostatic hyperplasia with finasteride in Chinese men: one-year experience. *J Formos Med Assoc* 1996;95(8):650-652.
- Chung B H, Hong S J. Long-term follow-up study to evaluate the efficacy and safety of the doxazosin gastrointestinal therapeutic system in patients with benign prostatic hyperplasia with or without concomitant hypertension. *BJU Int* 2006;97(1):90-95.

- Chung W S, Choi H K. Erotic erection versus nocturnal erection.[see comment]. *Br J Urol* 1990;143(2):294-297.
- Chung W S, Nehra A, Jacobson D J et al. Lower urinary tract symptoms and sexual dysfunction in community-dwelling men. *Mayo Clin Proc* 2004;79(6):745-749.
- Chung W S, Park Y Y, Kwon S W. The impact of aging on penile hemodynamics in normal responders to pharmacological injection: a Doppler sonographic study.[see comment]. *Br J Urol* 1997;157(6):2129-2131.
- Chung W S, Shim B S, Park Y Y. Hemodynamic insult by vascular risk factors and pharmacologic erection in men with erectile dysfunction: Doppler sonography study. *World J Urol* 2000;18(6):427-430.
- Chung W S, Sohn J H, Park Y Y. Is obesity an underlying factor in erectile dysfunction?. *Eur Urol* 1999;36(1):68-70.
- Churchill B M, van Savage J G, Khoury A E et al. The dartos flap as an adjunct in preventing urethrocutaneous fistulas in repeat hypospadias surgery. *Br J Urol* 1996;156(6):2047-2049.
- Chye P L. Alternatives for non-PDE5-I responders in erectile dysfunction patients. *Int Surg* 2006;91(5 Suppl):S95-102.
- Ciancio S J, Kim E D. Penile fibrotic changes after radical retropubic prostatectomy. *BJU Int* 2000;85(1):101-106.
- Cilotti A, Forti G, Maggi M. Modulation of penile smooth muscle cells contractility. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):44-49.
- Cioanta I, Muschter R. Water-induced thermotherapy for benign prostatic hyperplasia. *Tech Urol* 2000;6(4):294-299.
- Cirino G, Fusco F, Imbimbo C et al. Pharmacology of erectile dysfunction in man. *Pharmacol Ther* 2006;111(2):400-423.
- Cisternino M. Omeprazole 20mg uid and ranitidine 150mg bid in the treatment of benign gastric ulcer. *Hepatogastroenterology* 1991;38(5):400-403.
- Claes H, Baert L. Pelvic floor exercise versus surgery in the treatment of impotence. *Br J Urol* 1993;71(1):52-57.
- Clark J A, Wray N P, Ashton C M. Living with treatment decisions: regrets and quality of life among men treated for metastatic prostate cancer. *Am J Clin Oncol* 2001;19(1):72-80.
- Clark P E, Torti F M. Prostate Cancer and Bone Metastases: Medical Treatment. *Clinical Orthopaedics & Related Research* 2003;(pp S148-S157):-S157.
- Clayton A H. Female sexual dysfunctions: What controversy?. *Hillside J Clin Psychiatry* 2006;67(6):991-992.
- Cohan P, Korenman S G. Commentary: Erectile dysfunction. *Journal of Clinical Endocrinology & Metabolism* 2001;86(6):2391-2394.
- Cohen A J, Bartlik B. Ginkgo biloba for antidepressant-induced sexual dysfunction.[see comment]. *J Sex Marital Ther* 1998;24(2):139-143.
- Cohen J L, Keoleian C M, Krull E A. Penile paraffinoma: Self-injection with mineral oil. *J Am Acad Dermatol* 2002;47(5 SUPPL.):S251-S253.
- Cohen J L, Keoleian C M, Krull E A. Penile paraffinoma: Self-injection with mineral oil. *J Am Acad Dermatol* 2001;45(6 SUPPL.):s222-s224.
- Cohn P F. Dementia/Alzheimer's disease, diabetes, erectile dysfunction, and other diseases of the elderly. *Cardiology Review* 2005;22(9):5+24
- Cole B E. Neuroendocrine implications of opioid therapy. *Current Pain & Headache Reports* 2007;11(2):89-92.
- Collett B S, Saliba J E. Post-tensioning and splicing of precast/prestressed bridge beams to extend spans. *Proceedings of SPIE - The International Society for Optical Engineering* 2002;4696363-375.
- Colombel M, Gelet A. Principles and results of high-intensity focused ultrasound for localized prostate cancer. *Prostate Cancer & Prostatic Diseases* 2004;7(4):289-294.
- Compton Michael T, Miller Andrew H. Priapism associated with conventional and atypical antipsychotic medications: A review. [References]. *Hillside J Clin Psychiatry* 2001;62(5):362-366.
- Compton Michael T, Saldivia Aida, Berry Sally A. Recurrent priapism during treatment with clozapine and olanzapine. *Am J Psychiatry* 2000;157(4):659
- Conaglen H M, Suttie J M, Conaglen J V. Effect of Deer Velvet on Sexual Function in Men and Their Partners: A Double-Blind, Placebo-Controlled Study. *Arch Sex Behav* 2003;32(3):271-278.
- Concannon P, Roberts P, Parks J et al. Collection of seasonally spermatozoa-rich semen by electroejaculation of laboratory woodchucks (*Marmota monax*), with and without removal of bulbourethral glands. *Lab Anim Sci* 1996;46(6):667-675.
- Constantinou J, Feneley M R. PSA testing: An evolving relationship with prostate cancer screening. *Prostate Cancer & Prostatic Diseases* 2006;9(1):6-13.
- Contrafouris Y. Medicinal Chemistry - XVIIth International Symposium: Pulmonary disease: 1-5 September 2002, Barcelona, Spain. *IDrugs* 2002;5(10):964-965.

- Cooke B M, Breedlove S M, Jordan C L. Both estrogen receptors and androgen receptors contribute to testosterone-induced changes in the morphology of the medial amygdala and sexual arousal in male rats. *Hormones & Behavior* 2003;43(2):336-346.
- Cooke Bradley M, Chowanadisai Winyoo, Breedlove S et al. Post-weaning social isolation of male rats reduces the volume of the medial amygdala and leads to deficits in adult sexual behavior. *Behav Brain Res* 2000;117(1-2):107-113.
- Cookson M S, Phillips D L, Huff M E et al. Analysis of microsurgical penile revascularization results by etiology of impotence. *Br J Urol* 1993;149(5:Pt 2):t-12.
- Cooper A J, Cernovovsky Z. The effects of cyproterone acetate on sleeping and waking penile erections in pedophiles: Possible implications for treatment. *Can J Psychiatry* 1992;37(1):33-39.
- Cooper A J, Sandhu S, Losztyn S et al. A double-blind placebo controlled trial of medroxyprogesterone acetate and cyproterone acetate with seven pedophiles. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1992;37(10):687-693.
- Cooper Alan J, Cernovsky Zack Z. Comparison of cyproterone acetate (CPA) and leuprolide acetate (LHRH agonist) in a chronic pedophile: A clinical case study. *Biol Psychiatry* 1994;36(4):269-271.
- Coopersmith Seymour E. The search for the authentic self. *Psychoanal Rev* 1997;84(3):397-416.
- Corbin J D, Francis S H, Webb D J. Phosphodiesterase type 5 as a pharmacologic target in erectile dysfunction. *Urology* 2002;60(2 SUPPL. 2):4-11.
- Cormio L, Bettocchi C, Ricapito V et al. Resistance index as a prognostic factor for prolonged erection after penile dynamic colour Doppler ultrasonography. *Eur Urol* 1998;33(1):94-97.
- Cormio L, Nisen H, Selvaggi F P et al. A positive pharmacological erection test does not rule out arteriogenic erectile dysfunction.[see comment]. *Br J Urol* 1996;156(5):1628-1630.
- Corona G, Petrone L, Mannucci E et al. Psycho-biological correlates of rapid ejaculation in patients attending an andrologic unit for sexual dysfunctions. *Eur Urol* 2004;46(5):615-622.
- Corona G, Petrone L, Mannucci E et al. The impotent couple: low desire. [Review] [46 refs]. *Int J Androl* 2005;28 Suppl 246-52.
- Cosgrove D J, Gordon Z, Bernie J E et al. Sexual dysfunction in combat veterans with post-traumatic stress disorder. *Urology* 2002;60(5):881-884.
- Costa P, Sarrazin B, Bressolle F et al. Is the volume injected a parameter likely to influence the erectile response observed after intracavernous administration of an alpha-blocking agent?. *Eur Urol* 1993;24(1):43-47.
- Costabile R A. Transurethral therapy for the treatment of erectile dysfunction: Infant or dinosaur?. *Mol Urol* 1999;3(2):135-139.
- Costabile R A. Topical alprostadil for the treatment of female sexual arousal disorder. *Women's Health* 2006;2(3):331-340.
- Costabile R A, Steers W D. How can we best characterize the relationship between erectile dysfunction and benign prostatic hyperplasia?. *Br J Sex Med* 2006;3(4):676-681.
- Couper J, Bloch S, Love A et al. Psychosocial adjustment of female partners of men with prostate cancer: a review of the literature. [Review] [47 refs]. *Psychooncology* 2006;15(11):937-953.
- Cournoyer Barry. Male erectile difficulty: Crisis intervention and short-term treatment. Roberts, Albert R (Ed) 1990;(1990):treatment-278.
- Courtois F J, Charvier K F, Leriche A et al. Clinical approach to erectile dysfunction in spinal cord injured men. A review of clinical and experimental data. [Review] [60 refs]. *Paraplegia* 1995;33(11):628-635.
- Courtois F J, Gonnaud P M, Charvier K F et al. Sympathetic skin responses and psychogenic erections in spinal cord injured men. *Proc Annu Clin Spinal Cord Inj Conf* 1998;36(2):125-131.
- Courtois Frederique J. Residual erectile capacity of paraplegic rats. *Dissertation Abstracts International* 1991;51(9-B):Mar
- Courtois Frederique J, MacDougall Jamie C, Sachs Benjamin D. Erectile mechanism in paraplegia. *Physiol Behav* 1993;53(4):721-726.
- Courtois Frederique, Mathieu Catherine, Charvier Kathleen F et al. Sexual rehabilitation for men with spinal cord injury: Preliminary report on a behavioral strategy. [References]. *Sex Disabil* 2001;19(2):149-157.
- Cox R. Medicinal Chemistry - 28th National Symposium: 8-12 June 2002, San Diego, CA, USA. *IDrugs* 2002;5(7):626-632.
- Cranston-Cuebas M A, Barlow D H, Mitchell W et al. Differential effects of a misattribution manipulation on sexually functional and dysfunctional men. *J Abnorm Psychol* 1993;102(4):525-533.
- Cranston-Cuebas Margaret, Anne. Attentional focus and the misattribution of male sexual arousal. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 1995;55(11-B):May

- Crasilneck Harold B. Hypnotic techniques for smoking control and psychogenic impotence. *Am J Clin Hypn* 1990;32(3):147-153.
- Crespo-Facorro B, Perez-Iglesias R, Ramirez-Bonilla M et al. A practical clinical trial comparing haloperidol, risperidone, and olanzapine for the acute treatment of first-episode nonaffective psychosis. *Hillside J Clin Psychiatry* 2006;67(10):1511-1521.
- Crimmel A S, Conner C S, Monga M. Withered Yang: A review of traditional Chinese medical treatment of male infertility and erectile dysfunction. *J Androl* 2001;22(2):173-182.
- Critchfield A, Barry. Improving training approaches. *Journal of the American Deafness & Rehabilitation Association* 1992;25(4):15-20.
- Croasdell G. JP Morgan Hambrecht & Quist - 21st Annual Healthcare Conference: The future of big pharma: 6-9 January 2003, San Francisco, CA, USA. *IDrugs* 2003;6(2):97-101.
- Crook J M. Sparing erectile structures during radiation therapy of the prostate using MRI. *Nature Clinical Practice Urology* 2005;2(4):164-165.
- Crook J M, Potters L, Stock R G et al. Critical organ dosimetry in permanent seed prostate brachytherapy: defining the organs at risk. *Brachytherapy* 2005;4(3):186-194.
- Csoka Antonei B, Shipko Stuart, E-Mail Address et al. Letters to the Editor: Persistent Sexual Side Effects after SSRI Discontinuation. [References]. *Psychother Psychosom* 2006;75(3):187-188.
- Cui D, Hu L, Li S et al. Restoration of erectile function by reconstructing cavernous nerves with sural nerve grafts. *Zhonghua Nan Ke Xue* 2004;10(5):330-333.
- Cunningham G R, Hirshkowitz M. Inhibition of steroid 5 alpha-reductase with finasteride: sleep-related erections, potency, and libido in healthy men. *Journal of Clinical Endocrinology & Metabolism* 1995;80(6):1934-1940.
- Cunningham G R, Hirshkowitz M, Korenman S G et al. Testosterone replacement therapy and sleep-related erections in hypogonadal man. *Journal of Clinical Endocrinology & Metabolism* 1990;70(3):792-797.
- Curri S B. Topic drugs for treatment of dysfunctional disorders of penile spraying. FARMACI TOPICI PER LE TURBE DISFUNZIONALI DELLA IRRORAZIONE PENIENA: GLI EFFETTI DI UN DERIVATO FOSFOLIPIDICO DEL 3-O-BETA- IDROSSIETIL-RUTOSIDE SUI PARAMETRI MICROVASCULOGENETICI DEL DANNO CIRCOLATORIO. *Policlinico - Sezione Medica* 1997;104(1):7-32.
- Cushman W C, Cohen J D, Jones R P et al. Comparison of the fixed combination of enalapril/diltiazem ER and their monotherapies in stage 1 to 3 essential hypertension. *American journal of hypertension : journal of the American Society of Hypertension* 1998;11(1 Pt 1):23-30.
- Cutler A J. Sexual dysfunction and antipsychotic treatment. *Psychoneuroendocrinology* 2003;28(SUPPL. 1):69-82.
- d'Ancona F C H, Debruyne F M J. Endocrine approaches in the therapy of prostate carcinoma. *Hum Reprod Update* 2005;11(3):309-317.
- D'haese S, Bottomley A. Short- and long-term HRQOL issues following brachytherapy for prostate cancer. *Expert Review of Pharmacoeconomics & Outcomes Research* 2004;4(3):277-286.
- D'haese S, Bottomley A, Efficace F. External beam radiotherapy in prostate cancer patients: Short- and long-term health-related quality of life issues. *Expert Review of Pharmacoeconomics & Outcomes Research* 2003;3(4):487-495.
- da Silva F C, Bono A, Whelan P et al. Intermittent androgen deprivation for locally advanced prostate cancer: preliminary experience from an ongoing randomized controlled study of the South European urooncological group. *Oncology* 2003;65(Suppl 1):24-28.
- da Silva F C, Fossa S D, Aaronson N K et al. The quality of life of patients with newly diagnosed M1 prostate cancer: experience with EORTC clinical trial 30853. *Eur J Cancer* 1996;32A(1):72-77.
- Da Silva J P, Santiago L, Goncalves J C. The corpus cavernous electromyography in the erectile dysfunction diagnosis. *Acta Chir Hung* 1994;34(3-4):243-252.
- Dachille G, Cardo G, Erinnio M et al. Penile Doppler ultrasound assessment of the cavernous arteries. *Arch Ital Urol Androl* 2005;77(4):189-190.
- Dahlof B, Sever P S, Poulter N R et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): A multicentre randomised controlled trial. *Lancet* 2005;366(9489):895-906.
- Dai Q, Silverstein A D, Davies M G et al. Systemic basic fibroblast growth factor induces favorable histological changes in the corpus cavernosum of hypercholesterolemic rabbits. *Br J Urol* 2003;170(2 I):664-668.
- Dai Y, Chitaley K, Webb R C et al. Topical application of a Rho-kinase inhibitor in rats causes penile erection. *Int J Impot Res* 2004;16(3):294-298.

- Daitch J A, Angermeier K W, Lakin M M et al. Long-term mechanical reliability of AMS 700 series inflatable penile prostheses: comparison of CX/CXM and Ultrex cylinders. *Br J Urol* 1997;158(4):1400-1402.
- Dal Piaz V, Castellana M C, Vergelli C et al. Synthesis and evaluation of some pyrazolo[3,4-d]pyridazinones and analogues as PDE 5 inhibitors potentially useful as peripheral vasodilator agents. *Journal of Enzyme Inhibition & Medicinal Chemistry* 2002;17(4):227-233.
- Daly K J, Torella F, Ashleigh R et al. Screening, diagnosis and advances in aortic aneurysm surgery. *Gerontology* 2004;50(6):349-359.
- Daniell H W. Opioid-induced androgen deficiency. *Current Opinion in Endocrinology & Diabetes* 2006;13(3):262-266.
- Darouiche R O, Mansouri M D, Raad I I. Efficacy of antimicrobial-impregnated silicone sections from penile implants in preventing device colonization in an animal model. *Urology* 2002;59(2):303-307.
- Das C J, Seith A, Gamanagatti S et al. On the AJR viewbox. Ectopic pituitary adenoma with an empty sella. *AJR Am J Roentgenol* 2006;186(5):1468-1469.
- Das U N. Is erectile dysfunction a low-grade systemic inflammatory condition?. *Eur Heart J* 2007;28(5):642-643.
- DasGupta R, Fowler C J. Sexual and urological dysfunction in multiple sclerosis: better understanding and improved therapies. [Review] [58 refs]. *Curr Opin Neurol* 2002;15(3):271-278.
- Daskalopoulou S S, Mikhailidis D P, Elisaf M. Prevention and treatment of the metabolic syndrome. *Angiology* 2004;55(6):589-612.
- David A K, Khwaja R, Hudes G R. Treatments for improving survival of patients with prostate cancer. *Drugs Aging* 2003;20(9):683-699.
- Davidson Julian M, Rosen Raymond C. Hormonal determinants of erectile function. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Davies Miranda. Heroic deeds, manic defense, and intrusive identification: Some reflections on psychotherapy with a sixteen-year-old boy. Sidoli, Mara (Ed); Bovensiepen, Gustav (Ed) 1995;(1995):328
- Davila H H, Rajfer J, Gonzalez-Cadavid N F. Corporal veno-occlusive dysfunction in aging rats: evaluation by cavernosometry and cavernosography. *Urology* 2004;64(6):1261-1266.
- Davis S R, Guay A T, Shifren J L et al. Endocrine aspects of female sexual dysfunction. *Br J Sex Med* 2004;1(1):82-86.
- Dawson Samuel O. Buying decisions for a finishing line. 1993;1-24.
- De Almeida, Claro J, Passerotti C C et al. Extracorporeal shock wave therapy as an alternative treatment for Peyronie's disease. *The American Journal of Urology Review* 2005;3(8):390+393
- De Berardis G, Pellegrini F, Franciosi M et al. Clinical and psychological predictors of incidence of self-reported erectile dysfunction in patients with type 2 diabetes. *Br J Urol* 2007;177(1):252-257.
- De Cuyper, Griet T'Sjoen, Guy Beerten et al. Sexual and Physical Health After Sex Reassignment Surgery. [References]. *Arch Sex Behav* 2005;34(6):679-690.
- de la, Rosette J. Optimising Assessment and Treatment Decisions for Men with BPH. *European Urology Supplements* 2006;5(12):710-715.
- De la, Taille A, Hayek O R et al. Effects of a phytotherapeutic agent, PC-SPEs, on prostate cancer: A preliminary investigation on human cell lines and patients. *BJU Int* 1999;84(7):845-850.
- De Luis D A, Becerra A, Lahera M et al. A randomized cross-over study comparing cabergoline and quinagolide in the treatment of hyperprolactinemic patients. *J Endocrinol Invest* 2000;23(7):428-434.
- De Meyer J M, Thibo P. The correlation among cavernous pressure, penile rigidity and resistance index. *Br J Urol* 1998;160(1):63-66.
- De Meyer J M, Thibo P, Oosterlinck W. The evaluation of arterial inflow by gravity cavernosometry. *Br J Urol* 1997;158(2):440-443.
- de Nesnera, Alexander. Successful treatment with clozapine at higher doses after clozapine-induced priapism. [References]. *Hillside J Clin Psychiatry* 2003;64(11):1394-1395.
- De Rose A F, Carmignani G, Corbu C et al. Observational multicentric trial performed with doxazosin: Evaluation of sexual effects on patients with diagnosed benign prostatic hyperplasia. *Urol Int* 2002;68(2):95-98.
- De Silva, Padmal. Psychological treatment of sexual problems. *Int Rev Psychiatry* 1994;6(2-3):163-173.
- de Andrade E, de Mesquita A A, Claro J de A et al. Study of the efficacy of Korean Red Ginseng in the treatment of erectile dysfunction. *Asian J Androl* 2007;9(2):241-244.
- De Bruin D, Dormehl I C, Du Plessis D J et al. Prostaglandin E1 and papaverine: a comparative study on the ability to increase the penile bloodpool as measured by the ^{99m}Tc-penogram in the baboon model. *Am J Physiol Imaging* 1991;6(3):129-132.

- De Leval J, Boca P, Youssef E et al. Intermittent versus continuous total androgen blockade in the treatment of patients with advanced hormone-naïve prostate cancer: Results of a prospective randomized multicenter trial. *Clinical Prostate Cancer* 2002;1(3):163-171.
- De Meyer J M, Oosterlinck W. Pharmacodynamics of intracavernously injected drugs and cavernous wall resistance. *Eur Urol* 1997;32(2):184-189.
- De Rosa M, Colao A, Di Sarno A et al. Cabergoline treatment rapidly improves gonadal function in hyperprolactinemic males: a comparison with bromocriptine. *Eur J Endocrinol* 1998;138(3):286-293.
- Dean J, de Boer B J, Graziottin A et al. Partner Satisfaction and Successful Treatment Outcomes for Men with Erectile Dysfunction (ED). *European Urology Supplements* 2006;5(13):779-785.
- Dean J, de Boer B J, Graziottin A et al. Psychological, Social, and Behavioural Benefits for Men Following Effective Erectile Dysfunction (ED) Treatment: Men Who Enjoy Better Sex Experience Improved Psychological Well-Being. *European Urology Supplements* 2006;5(13):773-778.
- Dean J, de Boer B J, Graziottin A et al. The Role of Erection Hardness in Determining Erectile Dysfunction (ED) Treatment Outcome. *European Urology Supplements* 2006;5(13):767-772.
- Dean J, de Boer B J, Graziottin A et al. Effective Erectile Dysfunction (ED) Treatment Enables Men to Enjoy Better Sex: The Importance of Erection Hardness, Psychological Well-Being, and Partner Satisfaction. *European Urology Supplements* 2006;5(13):761-766.
- Debruyne F, Barkin J, van Erps P et al. Efficacy and safety of long-term treatment with the dual 5 alpha-reductase inhibitor dutasteride in men with symptomatic benign prostatic hyperplasia. *Eur Urol* 2004;46(4):488-494.
- DeBusk R F. Erectile dysfunction therapy in special populations and applications: Coronary artery disease. *Am J Cardiol* 2005;96(12 SUPPL. 2):62M-66M.
- Deedwania P, Volkova N. Dyslipidemia and lipid-lowering therapy in the elderly. *Expert Review of Cardiovascular Therapy* 2005;3(3):453-463.
- Deedwania P C, Volkova N. Current treatment options for the metabolic syndrome. *Curr Treat Options Cardiovasc Med* 2005;7(1):61-74.
- Deforge D, Blackmer J, Garrity C et al. Male erectile dysfunction following spinal cord injury: a systematic review. [Review] [60 refs]. *Proc Annu Clin Spinal Cord Inj Conf* 2006;44(8):465-473.
- Deisenhammer Eberhard A, Trawoger Rudolf. Penile anesthesia associated with sertraline use. [References]. *Hillside J Clin Psychiatry* 1999;60(12):869-870.
- Del Monte P, Foppiani L, Ruelle A et al. Clinically non-functioning pituitary macroadenomas in the elderly. *Aging-Clinical & Experimental Research* 2007;19(1):34-40.
- Delate T, Simmons V A, Motheral B R. Patterns of use of sildenafil among commercially insured adults in the United States: 1998-2002. *Int J Impot Res* 2004;16(4):313-318.
- Deleu D, Hanssens Y, Northway M G. Subcutaneous apomorphine: An evidence-based review of its use in Parkinson's disease. *Drugs Aging* 2004;21(11):687-709.
- Deliveliotis C, Delis A, Papatsoris A et al. Local steroid application during nerve-sparing radical retropubic prostatectomy. *BJU Int* 2005;96(4):533-535.
- Delk I I J, Knoll L D, McMurray J et al. Early experience with the American Medical Systems new Tactile Pump: Results of a multicenter study. *Br J Sex Med* 2005;2(2):266-271.
- Della Chiesa A, Pfiffner D, Meier B et al. Sexual activity in hypertensive men. *J Hum Hypertens* 2003;17(8):515-521.
- Della M M, Renzi G, Renzi C et al. Low molecular weight heparins in chronic venous insufficiency: Controlled trial of parnaparin efficacy and tolerability. *Br J Clin Res* 1993;429-36.
- Demakis George J. Sex and the Brain. [References]. McAnulty, Richard D (Ed); Burnette, M 2006;Michele(Ed):2-36.
- Denil J, Ohl D A, Smythe C. Vacuum erection device in spinal cord injured men: Patient and partner satisfaction. *Archives of Physical Medicine & Rehabilitation* 1996;77(8):750-753.
- Denys P, Mane M, Azouvi P et al. Side effects of chronic intrathecal baclofen on erection and ejaculation in patients with spinal cord lesions. *Archives of Physical Medicine & Rehabilitation* 1998;79(5):494-496.
- DePalma R G, Olding M, Yu G W et al. Vascular interventions for impotence: Lessons learned. *Eur J Vasc Surg* 1995;21(4):576-585.
- DePalma R G, Schwab F J, Emsellem H A et al. Noninvasive assessment of impotence. *Surg Clin North Am* 1990;70(1):119-132.
- Derby C A, Mohr B A, Goldstein I et al. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk?. *Urology* 2000;56(2):302-306.

- Derouet H, Jost W H, Osterhage J et al. Penile sympathetic skin response in erectile dysfunction. *Eur Urol* 1995;28(4):314-319.
- Derry F A, Dinsmore W W, Fraser M et al. Efficacy and safety of oral sildenafil (Viagra) in men with erectile dysfunction caused by spinal cord injury. *Neurology* 1998;51(6):1629-1633.
- Desai Vinod, Srinivasan Nagan. Development, analysis and design of a 292 ft tall self-erecting flare tower for offshore application. Proceedings of the International Conference on Offshore Mechanics and Arctic Engineering - OMAE 1995;1(Part B):77-88.
- Desgrandchamps F. Who will benefit from combination therapy? The role of 5 alpha reductase inhibitors and alpha blockade: A reflection from MTOPS. *Curr Opin Urol* 2004;14(1):17-20.
- Devan B D, Duffy K B, Bowker J L et al. Phosphodiesterase type 5 (PDE5) inhibition and cognitive enhancement. *Drugs of the Future* 2005;30(7):725-736.
- DeVries C R, Anderson R U. Endoscopic urethroplasty: An improved technique. *Br J Urol* 1990;143(6):1225-1226.
- DeWire D M, Todd E, Meyers P. Patient satisfaction with current impotence therapy. *Wis Med J* 1995;94(10):542-544.
- Dey J, Shepherd M D. Evaluation and treatment of erectile dysfunction in men with diabetes mellitus. *Mayo Clin Proc* 2002;77(3):276-282.
- Di Matteo, Vincenzo Di, Giovanni Guiseppe et al. SB 242084: A selective 5-HT-sub(2C) receptor antagonist. *CNS Drug Rev* 2000;6(3):195-205.
- Di Stasi S M, Giannantoni A, Stephen R L et al. A prospective, randomized study using transdermal electromotive administration of verapamil and dexamethasone for Peyronie's disease.[see comment]. *Br J Urol* 2004;171(4):1605-1608.
- Di Lorenzo G, Autorino R, Perdoni S et al. Management of gynaecomastia in patients with prostate cancer: A systematic review. *Lancet Oncol* 2005;6(12):972-979.
- Di Rocco A, Tagliati M, Danisi F et al. A pilot study of L-methionine for the treatment of AIDS-associated myelopathy. *Neurology* 1998;51(1):266-268.
- Di Silverio F, Serio M, D'Eramo G et al. Zoladex vs. Zoladex plus cyproterone acetate in the treatment of advanced prostatic cancer: a multicenter Italian study. *Eur Urol* 1990;18(Suppl):61
- DiBenedetti D B, Gondek K, Sagnier P P et al. The treatment satisfaction scale: a multidimensional instrument for the assessment of treatment satisfaction for erectile dysfunction patients and their partners. *Eur Urol* 2005;48(3):503-511.
- DiBiase S J, Wallner K, Tralins K et al. Brachytherapy radiation doses to the neurovascular bundles. *Int J Radiat Oncol Biol Phys* 2000;46(5):1301-1307.
- Dickson Ruth A, Edwards Alun. Clozapine and fertility. *Am J Psychiatry* 1997;154(4):582-583.
- Dingli D, Tefferi A. A critical review of anagrelide therapy in essential thrombocythemia and related disorders. *Leuk Lymphoma* 2005;46(5):641-650.
- Dingli D, Tefferi A. Anagrelide: An update on its mechanisms of action and therapeutic potential. *Expert Rev Anticancer Ther* 2004;4(4):533-541.
- Dinsmore W W. Clinical aspects of erectile dysfunction. *Int J STD AIDS* 1996;7(Suppl 3):2-4.
- Dinsmore W W, Hackett G, Goldmeier D et al. Topical eutectic mixture for premature ejaculation (TEMPE): A novel aerosol-delivery form of lidocaine-prilocaine for treating premature ejaculation. *BJU Int* 2007;99(2):369-375.
- Dinsmore W W, Ralph D J, Kell P et al. Evaluation of the Sexual Assessment Monitor, a diagnostic device used to electronically quantify ejaculatory latency time: findings from three studies. *BJU Int* 2006;98(3):613-618.
- Diomedes M, Sallustio F, Rizzato B et al. Sildenafil increases cerebrovascular reactivity: A transcranial Doppler study. *Neurology* 2005;65(6):919-921.
- Dishy V, Sofowora G, Harris P A et al. The effect of sildenafil on nitric oxide-mediated vasodilation in healthy men. *Clinical Pharmacology & Therapeutics* 2001;70(3):270-279.
- Dittrich A, Vandendris M. Preoperative assessment of penile curvature by artificial erection. *Br J Urol* 1990;143(6):1238
- Dixon C M. Right-angle free beam lasers for the treatment of benign prostatic hyperplasia. *Semin Urol* 1994;12(3):165-169.
- Djamilian M, Stief C G, Hartmann U et al. Predictive value of real-time RigiScan monitoring for the etiology of organogenic impotence. *Br J Urol* 1993;149(5 Pt 2):1269-1271.
- Djavan B, Seitz C, Marberger M. Transurethral microwave thermotherapy. *Atlas of the Urologic Clinics of North America* 2002;10(1):63-73.
- Doggrell S. Do vardenafil and tadalafil have advantages over sildenafil in the treatment of erectile dysfunction?. *Int J Impot Res* 2007;19(3):281-295.
- Doggrell S A. After ALLHAT: doxazosin for the treatment of benign prostatic hyperplasia. [Review] [38 refs]. *Expert Opin Pharmacother* 2004;5(9):1957-1964.

- Doggrell S A. Combination of finasteride and doxazosin for the treatment of benign prostatic hyperplasia. *Expert Opin Pharmacother* 2004;5(5):1209-1211.
- Doggrell S A. Is amlodipine the best initial monotherapy for hypertension?. *Expert Opin Pharmacother* 2006;7(6):829-832.
- Dogra P N, Aron M, Rajeev T P. Core through urethrotomy with the neodymium:YAG laser for posttraumatic obliterative strictures of the bulbomembranous urethra. *Br J Urol* 1999;161(1):81-84.
- Dogra P N, Rajeev T P, Aron M. Medicolegal aspects in the management of erectile dysfunction. *Journal of Forensic Medicine & Toxicology* 1997;14(2):52-56.
- Doherty P C, Bivalacqua T J, Champion H C et al. Direct effects of selective type 5 phosphodiesterase inhibitors alone or with other vasodilators on the erectile response in cats. *Br J Urol* 2001;165(3):1004-1009.
- Donatucci C F, Greenfield J M. Recovery of sexual function after prostate cancer treatment. [Review] [30 refs]. *Curr Opin Urol* 2006;16(6):444-448.
- Donatucci Craig F, Lue Tom F. Pathophysiology of sexual dysfunction in males with physical disabilities. Haseltine, Florence P (Ed); Cole, Sandra S (Ed); Gray, David B (Ed) 1993;(1993):368
- Donnelly B J, Saliken J C, Ernst D S et al. Role of transrectal ultrasound guided salvage cryosurgery for recurrent prostate carcinoma after radiotherapy. *Prostate Cancer & Prostatic Diseases* 2005;8(3):235-242.
- Donovan Denis M. Therapeutic play. *Journal of the American Academy of Child & Adolescent Psychiatry* 1997;36(1):3-5.
- Dorey G. Pelvic floor exercises as a treatment for men with erectile dysfunction. [Review] [4 refs]. *Nurs Times* 2004;100(12):65-67.
- Dorey G. Is smoking a cause of erectile dysfunction? A literature review. [Review] [53 refs]. *Br J Nurs* 2001;10(7):455-465.
- Dorey G. Conservative treatment of erectile dysfunction. 3: Literature review. [Review] [25 refs]. *Br J Nurs* 2000;9(13):859-863.
- Dorey G. Conservative treatment of erectile dysfunction. 2: Clinical trials. [Review] [16 refs]. *Br J Nurs* 2000;9(12):755-762.
- Dorey G. Conservative treatment of erectile dysfunction. 1: Anatomy/physiology. [Review] [35 refs]. *Br J Nurs* 2000;9(11):691-694.
- Dorey G. Restoring pelvic floor function in men: review of RCTs. [Review] [17 refs]. *Br J Nurs* 2005;14(19):1014-1018, 1020-1.
- Dorey G, Feneley R C, Speakman M J et al. Pelvic floor muscle exercises and manometric biofeedback for erectile dysfunction and postmicturition dribble: three case studies. *Journal of Wound, Ostomy, & Continence Nursing* 2003;30(1):44-51.
- Dorey G, Speakman M J, Feneley R C et al. Pelvic floor exercises for erectile dysfunction. *BJU Int* 2005;96(4):595-597.
- Dorey G, Speakman M, Feneley R et al. Pelvic floor exercises for treating post-micturition dribble in men with erectile dysfunction: a randomized controlled trial. *Urol Nurs* 2004;24(6):490-497.
- Dorey G, Speakman M, Feneley R et al. Randomised controlled trial of pelvic floor muscle exercises and manometric biofeedback for erectile dysfunction. *Br J Gen Pract* 2004;54(508):819-825.
- Dorflinger T, Jensen F S, Krarup T et al. Transurethral prostatectomy compared with incision of the prostate in the treatment of prostatism caused by small benign prostate glands. *Scandinavian Journal of Urology & Nephrology* 1992;26(4):333-338.
- Dorr R T, Lines R, Levine N et al. Evaluation of melanotan-II, a superpotent cyclic melanotropic peptide in a pilot phase-I clinical study. *Life Sci* 1996;58(20):1777-1784.
- Dorrance A M, Lewis R W, Mills T M. Captopril treatment reverses erectile dysfunction in male stroke prone spontaneously hypertensive rats. *Int J Impot Res* 2002;14(6):494-497.
- Dos Reis J M, Glina S, Da Silva M F et al. Penile prosthesis surgery with the patient under local regional anesthesia. *Br J Urol* 1993;150(4):1179-1181.
- Dossenbach Martin, Hodge Andrew, Anders Martin et al. Prevalence of sexual dysfunction in patients with schizophrenia: International variation and underestimation. [References]. *Int J Neuropsychopharmacol* 2005;8(2):195-201.
- Dossey L. Listerine's Long Shadow: Disease Mongering and the Selling of Sickness. *Explore-The Journal of Science & Healing* 2006;2(5):379-385.
- Dossey L. Truth and Healing: A Time for Hard Questions. *Explore-The Journal of Science & Healing* 2005;1(4):235-240.
- Douchez J, Droz J P, Desclaux B et al. Quality of life in long-term survivors of nonseminomatous germ cell testicular tumors. *Br J Urol* 1993;149(3):498-501.
- Douglass M A, Lin J C. Update on the treatment of benign prostatic hyperplasia. *Hosp Formul* 2005;40(2):50-64.

- Doust J, Miller E, Duchesne G et al. A systematic review of brachytherapy. Is it an effective and safe treatment for localised prostate cancer?. [Review] [0 refs]. *Aust Fam Physician* 2004;33(7):525-529.
- Dow J A, Gluck R W, Golimbu M et al. Multiphasic diagnostic evaluation of arteriogenic, venogenic, and sinusoidogenic impotency. Value of noninvasive tests compared with penile duplex ultrasonography. *Urology* 1991;38(5):402-407.
- Drago J R, Badalament R A, Nesbitt J A. Radical prostatectomy 1972-1987 single institutional experience: Comparison of standard radical prostatectomy and nerve-sparing technique. *Urology* 1990;35(5):377-380.
- Drake Virginia K E. Nontraditional psychiatric practice issues: My time in prison with women survivors of IPV. [References]. *Issues Ment Health Nurs* 2007;28(2):231-237.
- Dresser M J, Desai D, Gidwani S et al. Dapoxetine, a novel treatment for premature ejaculation, does not have pharmacokinetic interactions with phosphodiesterase-5 inhibitors. *Int J Impot Res* 2006;18(1):104-110.
- Droste D W, Ritter M A, Dittrich R et al. Arterial hypertension and ischaemic stroke. *Acta Neurol Scand* 2003;107(4):241-251.
- Droupy S, Hessel A, Benoit G et al. Assessment of the functional role of accessory pudendal arteries in erection by transrectal color Doppler ultrasound. *Br J Urol* 1999;162(6):1987-1991.
- Droupy S, Ponsot Y, Giuliano F. How, why and when should urologists evaluate male sexual function?. *Nature Clinical Practice Urology* 2006;3(2):84-94.
- du Plessis S S, de Jongh P S, Franken D R. Effect of acute in vivo sildenafil citrate and in vitro 8-bromo-cGMP treatments on semen parameters and sperm function. *Fertility & Sterility* 2004;81(4):1026-1033.
- Dubbelman Y D, Dohle G R, Schroder F H. Sexual Function Before and After Radical Retropubic Prostatectomy: A Systematic Review of Prognostic Indicators for a Successful Outcome. *Eur Urol* 2006;50(4):711-720.
- Dubocq F, Tefilli M V, Gheiler E L et al. Long-term mechanical reliability of multicomponent inflatable penile prosthesis: Comparison of device survival. *Urology* 1998;52(2):277-281.
- Duby J J, Campbell R K, Setter S M et al. Diabetic neuropathy: An intensive review. *Am J Health Syst Pharm* 2004;61(2):160-176.
- Ducharme Stanley. From the Editor. *Sex Disabil* 2006;24(3):127-129.
- Duckworth K. Running an erectile dysfunction clinic.[see comment]. *Pap Natl Conf Prof Nurses Physicians* 1997;12(11):775-778.
- Dugoua J-J, Mills E, Perri D et al. Safety and efficacy of ginkgo (ginkgo biloba) during pregnancy and lactation. *Can J Clin Pharmacol* 2006;13(3):e277-e284.
- Duncan G G, Philips N, Pickles T. Report on the quality of life analysis from the phase III trial of pion versus photon radiotherapy in locally advanced prostate cancer. *Eur J Cancer* 2000;36(6):759-765.
- Dundar M, Kocak I, Dundar S O et al. Evaluation of side effects of sildenafil in group of young healthy volunteers. *International Urology & Nephrology* 2001;32(4):705-708.
- Dunkel L. Use of aromatase inhibitors to increase final height. *Molecular & Cellular Endocrinology* 2006;254-255:207-216.
- Dunlop John, Marquis Karen L, Lim H K et al. Pharmacological profile of the 5-HT-sub(2c) receptor agonist WAY-163909; therapeutic potential in multiple indications. [References]. *CNS Drug Rev* 2006;12(3-4):167-177.
- Dunn K M, Croft P R, Hackett G I. Association of sexual problems with social, psychological, and physical problems in men and women: a cross sectional population survey. *Journal of Epidemiology & Community Health* 1999;53(3):144-148.
- Dunn K M, Croft P R, Hackett G I. Sexual problems: a study of the prevalence and need for health care in the general population. *Fam Pract* 1998;15(6):519-524.
- Dursteler-MacFarland K M, Stohler R, Moldovanyi A et al. Complaints of heroin-maintained patients: A survey of symptoms ascribed to diacetylmorphine. *Drug & Alcohol Dependence* 2006;81(3):231-239.
- Duschek E J J, Gooren L J, Netelenbos C. Effects of raloxifene on gonadotrophins, sex hormones, bone turnover and lipids in healthy elderly men. *Eur J Endocrinol* 2004;150(4):539-546.
- Dusing R. Sexual dysfunction in male patients with hypertension: influence of antihypertensive drugs. [Review] [75 refs]. *Drugs* 2005;65(6):773-786.
- Dutkiewicz S. Long-term treatment with doxazosin in men with benign prostatic hyperplasia: 10-year follow-up. *International Urology & Nephrology* 2004;36(2):169-173.
- Dutta T C, Eid J F. Vacuum constriction devices for erectile dysfunction: a long-term, prospective study of patients with mild, moderate, and severe dysfunction. *Urology* 1999;54(5):891-893.
- Dvorkin L, Song K Y, Miranda Massari et al. Herbs for benign prostatic hyperplasia. *Ann Pharmacother* 2002;36(9):1443-1452.

- Eardley I. Optimisation of PDE5 Inhibitor Therapy in Men with Erectile Dysfunction: Converting 'Non-Responders' into 'Responders'. *Eur Urol* 2006;50(1):31-33.
- Eardley I. Can an erectogenic pharmacotherapy regimen after radical prostatectomy improve postoperative erectile function?. *Nature Clinical Practice Urology* 2006;3(2):72-73.
- Earle C M, Seah M, Coulden S E et al. The use of the vacuum erection device in the management of erectile impotence. *Int J Impot Res* 1996;8(4):237-240.
- East Marion L, Hofer Heribert, Wickler Wolfgang. The erect 'penis' is a flag of submission in a female-dominated society: Greetings in Serengeti spotted hyenas. *Behav Ecol Sociobiol* 1993;33(6):355-370.
- Eberhard J, Lindstrom E, Holstad M et al. Prolactin level during 5 years of risperidone treatment in patients with psychotic disorders. *Acta Psychiatr Scand* 2007;115(4):268-276.
- Eden C G, Cahill D, Vass J A et al. Laparoscopic radical prostatectomy: The initial UK series. *BJU Int* 2002;90(9):876-882.
- Edmondson J D, Hatcher P A, McGrath R S et al. Noninvasive evaluation of vasculogenic impotence. *Journal of Vascular Technology* 1994;18(3):125-127.
- Eglau Uwe. Brief therapy for sexual dysfunction. *International Forum for Logotherapy* 1992;15(2):108-110.
- Ehrensaft M K, Condra M, Morales A et al. Communication patterns in patients with erectile dysfunction and their partners. *Int J Impot Res* 1994;6(1):25-32.
- Ei-Bahnasawy M S, Gomha M A. Penile fractures: The successful outcome of immediate surgical intervention. *Int J Impot Res* 2000;12(5):273-277.
- Eilenberg K L, Hoover A M, Rutherford M L et al. From informed consent through database lock: An interactive clinical trial conducted using the internet. *Drug Inf J* 2004;38(3):239-251.
- Ekman P. A risk-benefit assessment of treatment with finasteride in benign prostatic hyperplasia. [Review] [32 refs]. *Drug Saf* 1998;18(3):161-170.
- el-Abd S A. Endoscopic treatment of posttraumatic urethral obliteration: experience in 396 patients. *Br J Urol* 1995;153(1):67-71.
- El-Bahrawy M, El-Baz M A, Emam A et al. Noninvasive vacuum constriction device in the management of erectile dysfunction. *International Urology & Nephrology* 1995;27(3):331-333.
- El-Gabry E A, Strup S E, Gomella L G. Deciding on radical prostatectomy: The physician's perspective. *Semin Urol Oncol* 2000;18(3):205-213.
- El-Hakim A, Leung R A, Tewari A. Robotic prostatectomy: A pooled analysis of published literature. *Expert Rev Anticancer Ther* 2006;6(1):11-20.
- El-Latif M A, Makhlof A A, Moustafa Y M et al. Diagnostic value of nitric oxide, lipoprotein(a), and malondialdehyde levels in the peripheral venous and cavernous blood of diabetics with erectile dysfunction. *Int J Impot Res* 2006;18(6):544-549.
- El-Rayes B F, Hussain M H. Hormonal therapy for prostate cancer: Past, present and future. *Expert Rev Anticancer Ther* 2002;2(1):37-47.
- El-Sakka A I. Prevalence of Peyronie's disease among patients with erectile dysfunction. *Eur Urol* 2006;49(3):564-569.
- El-Sakka A I. Lower urinary tract symptoms in patients with erectile dysfunction: is there a vascular association?. *Eur Urol* 2005;48(2):319-325.
- El-Sakka A I. Cardiovascular system as a 'core' of sexual life. *Expert Opin Pharmacother* 2005;6(13):2223-2230.
- El-Sakka A I, Morsy A M. Screening for ischemic heart disease in patients with erectile dysfunction: role of penile Doppler ultrasonography. *Urology* 2004;64(2):346-350.
- El-Sakka A I, Lin C S, Chui R M et al. Effects of diabetes on nitric oxide synthase and growth factor genes and protein expression in an animal model. *Int J Impot Res* 1999;11(3):123-132.
- El-Sakka A I, Rashwan H M, Lue T F. Venous patch graft for Peyronie's disease. Part II: outcome analysis.[erratum appears in *J Urol* 1999 Sep;162(3 Pt 1):809]. *Br J Urol* 1998;160(6:Pt 1):t-3.
- El-Senosy Mohamed, Yousry Rabie, Mohamed Osman et al. Changes in sexual function in epileptics. *Arab Journal of Psychiatry* 1994;5(2):92-101.
- El-Thaher T S, Matalka K Z, Taha H A et al. Ferula harmonis 'zallouh' and enhancing erectile function in rats: Efficacy and toxicity study. *Int J Impot Res* 2001;13(4):247-251.
- Elabbady A, Hassouna M M, Elhilali M. Apomorphine versus mating behavior in testing erectile capabilities of diabetic rats. *Urology* 1995;45(4):715-719.
- Elhanbly S, bdel-Gaber S, Fathy H et al. Erectile dysfunction in smokers: a penile dynamic and vascular study. *J Androl* 2004;25(6):991-995.

- Elhilali M M. Alfuzosin: An α_1 -receptor blocker for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia. *Expert Opin Pharmacother* 2006;7(5):583-596.
- Elhilali M, Emberton M, Matzkin H et al. Long-term efficacy and safety of alfuzosin 10 mg once daily: A 2-year experience in 'real-life' practice. *BJU Int* 2006;97(3):513-519.
- Eliasson T, Abramsson L, Damber J-E. Importance of thermal dose and antenna location in transurethral microwave thermotherapy for benign prostatic hyperplasia. *J Endourol* 1998;12(6):581-589.
- Elist J. Effects of pollen extract preparation Prostat/Poltit on lower urinary tract symptoms in patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome: A randomized, double-blind, placebo-controlled study. *Urology* 2006;67(1):60-63.
- Elliott D S, Barrett D M. Long-term followup and evaluation of primary realignment of posterior urethral disruptions.[see comment]. *Br J Urol* 1997;157(3):814-816.
- Ellison Carol, Rinkleib. Intimacy-based sex therapy: Sexual choreography. [References]. Kleinplatz, Peggy J (Ed) 2001;(2001):375-Routledge.
- Ellison K E, Gandhi G. Optimising the use of beta-adrenoceptor antagonists in coronary artery disease. *Drugs* 2005;65(6):787-797.
- Elves A W, Ahmed M, Abrams P. Computer-assisted learning; experience at the Bristol Urological Institute in the teaching of urology. *Br J Urol* 1997;80 Suppl 3, pp.59-62, 1997 Nov.
- Emberton M, Neal D E, Black N et al. The effect of prostatectomy on symptom severity and quality of life. *Br J Urol* 1996;77(2):233-247.
- Eng T Y, Thomas C R, Herman T S. Progress in the treatment of localized prostate cancer with external beam irradiation. *Expert Rev Anticancer Ther* 2006;6(1):93-108.
- Englert H, Schaefer G, Roll S et al. Prevalence of erectile dysfunction among middle-aged men in a metropolitan area in Germany. *Int J Impot Res* 2007;19(2):183-188.
- Enzlin P, Mak R, Kittel F et al. Sexual functioning in a population-based study of men aged 40-69 years: the good news. *Int J Impot Res* 2004;16(6):512-520.
- Erdogru T, Kadioglu A, Cayan S et al. Does the positive intracavernous papaverine test always indicate a normal penile vascular system?. *Eur Urol* 1997;31(3):323-328.
- Erdogru T, Savas M, Yilmaz N et al. Evaluation of penile hemodynamic status and adjustment of treatment alternatives in Peyronie's disease. *Asian J Androl* 2002;4(3):187-190.
- Erdogru T, Usta M F, Ates M et al. Development of Peyronie's disease during long-term colchicine treatment. *International Urology & Nephrology* 2003;35(2):207-208.
- Eri L M, Tveter K J. Safety, side effects and patient acceptance of the antiandrogen Casodex in the treatment of benign prostatic hyperplasia. *Eur Urol* 1994;26(3):219-226.
- Eri L M, Tveter K J. Safety, side effects and patient acceptance of the luteinizing hormone releasing hormone agonist leuprolide in treatment of benign prostatic hyperplasia. *Br J Urol* 1994;152(2:Pt 1):t-52.
- Erkan E, Muslumanoglu A Y, Oktar T et al. Polymorphism of endothelial nitric oxide synthase gene in patients with erectile dysfunction. *Br J Sex Med* 2006;3(1):69-75.
- Erlichman M, Handelsman H, Hotta S S. Cryosurgery for recurrent prostate cancer following radiation therapy. [Review] [29 refs]. *Health Technology Assessment (Rockville, Md)* 1999;(13):i-v.
- Ernst E, Pittler M H, Wider B et al. Acupuncture: Its evidence-base is changing. *Am J Chin Med* 2007;35(1):21-25.
- Ersay A, Nergis Y, Tok D et al. Intracavernosal anaesthesia: The effect of intracavernosal lidocaine injection on cavernosal tissue. *Acta Anaesthesiol Ital* 1996;47(4):281-286.
- Esen A, Kitapci M, Ergen A et al. Dual radioisotopic study: a technique for the evaluation of vasculogenic impotence. *Br J Urol* 1992;147(1):42-46.
- Esper R J, Nordaby R A, Vilarin-o JO et al. Endothelial dysfunction: A comprehensive appraisal. *Cardiovasc Diabetol* 2006;5, 2006. Article Number
- Esposito K, Ciotola M, Giugliano F et al. Mediterranean diet improves erectile function in subjects with the metabolic syndrome. *Int J Impot Res* 2006;18(4):405-410.
- Esposito K, Giugliano F, Di Palo C et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial.[see comment]. *JAMA* 2004;291(24):2978-2984.
- Estey E H. Modulation of angiogenesis in patients with myelodysplastic syndrome. *Baillieres Best Practice & Research in Clinical Haematology* 2004;17(4 SPEC.ISS.):623-639.
- Ethans K D, Casey A R, Schryvers O I et al. The effects of sildenafil on the cardiovascular response in men with spinal cord injury at or above the sixth thoracic level. *J Spinal Cord Med* 2003;26(3):222-226.

- Evans M F. Critical appraisal: Lose weight to lose erectile dysfunction. *Can Fam Physician* 2005;51(JAN.):47-49.
- Everaerd Walter. Male erectile disorder. O'Donohue, William (Ed); Geer, James H (Ed) 1993;(1993):418
- Evren Cuneyt, Can Suat, Evren Bilge et al. Lifetime posttraumatic stress disorder in Turkish alcohol-dependent inpatients: Relationship with depression, anxiety and erectile dysfunction. [References]. *Psychiatry Clin Neurosci* 2006;60(1):77-84.
- Exaire Murad E, Chavez de, los Rios et al. Lisinopril vs methyl-dopa in essential hypertension: A comparative study. *Invest Med Int* 1992;18(4):163-168.
- Fabbri A, Aversa A, Isidori A. Erectile dysfunction: An overview. *Hum Reprod Update* 1997;3(5):455-466.
- Fabian Jose, Luis. Psychotropic medications and priapism. *Am J Psychiatry* 1993;150(2):349-350.
- Fagan Peter. Psychogenic impotence in relatively young men. Levine, Stephen B (Ed); Risen, Candace B (Ed); Althof, Stanley E (Ed) 2003;(2003):473-Routledge.
- Fagan Peter J. Treatment case: A couple with sexual dysfunction and paraphilia. [References]. Costa, Paul T Jr 1994;(Ed):Thomas-factor.
- Fahn S, Chouinard S. Experience with tranlycypromine in early Parkinson's disease. *J Neural Transm* 1998;Supplementum.52-61.
- Fahrenkrug J. Gut/brain peptides in the genital tract: VIP and PACAP. *Scandinavian Journal of Clinical and Laboratory Investigation Supplement* 2001;61(234):35-39.
- Fainstein Day P, Guitelman M, Artese R et al. Retrospective multicentric study of pituitary incidentalomas. *Pituitary* 2004;7(3):145-148.
- Fallon B. Cadaveric dura mater graft for correction of penile curvature in Peyronie disease. *Urology* 1990;35(2):127-129.
- Fandel T M, Bella A J, Tantiwongse K et al. The effect of intracavernosal growth differentiation factor-5 therapy in a rat model of cavernosal nerve injury. *BJU Int* 2006;98(3):632-636.
- Fanning K D, Lloyd K B. Current pharmacological treatment options for prostate cancer. *P & T* 2002;27(10):500-505.
- Fardella C E, Gloger S. Neurobehavioral and psychological changes induced by hyperthyroidism: Diagnostic and therapeutic implications. *Expert Review of Neurotherapeutics* 2002;2(5):709-716.
- Faria Miguel, Magalhaes-Cardoso Teresa, Lafuente-de-Carvalho Jose-Maria et al. Corpus Cavernosum from Men with Vasculogenic Impotence is Partially Resistant to Adenosine Relaxation due to Endothelial A-sub(2B) Receptor Dysfunction. [References]. *J Pharmacol Exp Ther* 2006;319(1):405-413.
- Fava M, Rankin M. Sexual functioning and SSRIs. [Review] [31 refs]. *Hillside J Clin Psychiatry* 2002;63Suppl-6.
- Febbraro Greg A R. Sexual Arousal Disorders. [References]. McAnulty, Richard D (Ed); Burnette, M 2006;Michele(Ed):2-151.
- Fecik S E. Drug-induced sexual dysfunction. *Medical Update for Psychiatrists* 1998;3(6):176-181.
- Fedele D, Bortolotti A, Coscelli C et al. Erectile dysfunction in type 1 and type 2 diabetics in Italy. On behalf of Gruppo Italiano Studio Deficit Erettile nei Diabetici. *Int J Epidemiol* 2000;29(3):524-531.
- Fedele D, Coscelli C, Cucinotta D et al. Incidence of erectile dysfunction in Italian men with diabetes. *Br J Urol* 2001;166(4):1368-1371.
- Fedele D, Coscelli C, Santeusano F et al. Erectile dysfunction in diabetic subjects in Italy. Gruppo Italiano Studio Deficit Erettile nei Diabetici. *Diabetes Care* 1998;21(11):1973-1977.
- Feher M D. Statin prescribing rises and infarct rates plateau. Why the mismatch?. *British Journal of Cardiology* 2004;11(6):421-423.
- Fehr J L, Alund G, Muhlebach P et al. Significance of cavernosography in standardized cavernosometry. *Urol Int* 1992;49(1):13-18.
- Feigenberg S J, Lee W R, Desilvio M L et al. Health-related quality of life in men receiving prostate brachytherapy on RTOG 98-05. *Int J Radiat Oncol Biol Phys* 2005;62(4):956-964.
- Fernandez De, La Maza S, Conrad S et al. Early clinical experience with water-jet dissection (hydro-jet) during nerve-sparing radical retropubic prostatectomy. *Minimally Invasive Therapy & Allied Technologies: Mitat* 2002;11(5-6):257-264.
- Fernandez H H, Trieschmann M E, Friedman J H. Treatment of psychosis in Parkinson's disease: Safety considerations. *Drug Saf* 2003;26(9):643-659.
- Ferrario C M, Levy P. Sexual dysfunction in patients with hypertension: implications for therapy. [Review] [49 refs]. *J Clin Hypertens* 2002;4(6):424-432.
- Ferraz Marcos, Rochedo Ferraz, Marcia Martins et al. Preventing L-NAME inhibitory effects on rat sexual behavior with hydralazine, isradipine or captopril co-treatment. [References]. *Pharmacology, Biochemistry and Behavior* 2003;75(2):265-272.
- Ferrer E, Moral M A, Bozzo J. The role of statins in erectile dysfunction. *Med Actual* 2007;43(1):55-59.

- Ferri C, Giuggioli D, Cazzato M et al. HCV-related cryoglobulinemic vasculitis: An update on its etiopathogenesis and therapeutic strategies. *Clinical & Experimental Rheumatology* 2003;21(6 SUPPL. 32):S78-S84.
- Ferrini M, Magee T R, Vernet D et al. Aging-related expression of inducible nitric oxide synthase and markers of tissue damage in the rat penis. *Biol Reprod* 2001;64(3):974-982.
- Fietkau R, Riepl M, Kettner H et al. Supportive treatment with megestrol acetate during radio-(chemo-) therapy. A randomized trial. *Sonderb Z Strahlenther Onkol* 1996;172(3):162-168.
- Filippi S, Morelli A, Sandner P et al. Characterization and functional role of androgen-dependent PDE5 activity in the bladder. *Endocrinology* 2007;148(3):1019-1029.
- Fine Reuben. A Little New Light on an Old Profession. *PsycCRITIQUES* 2006;2006 American Psychological Assn.
- Finelli A, Hirshberg E D, Radomski S B. The treatment choice of elderly patients with erectile dysfunction. *Geriatric Nephrology & Urology* 1998;8(1):15-19.
- Finney G, Haynes A M, Cross P et al. Cross-sectional analysis of sexual function after prostate brachytherapy. *Urology* 2005;66(2):377-381.
- Firoozi F, Longhurst P A, White M D. In vivo and in vitro response of corpus cavernosum to phosphodiesterase-5 inhibition in the hypercholesterolaemic rabbit. *BJU Int* 2005;96(1):164-168.
- Fishbain D, Berman K, Kajdasz D K. Duloxetine for neuropathic pain based on recent clinical trials. *Current Pain & Headache Reports* 2006;10(3):199-204.
- Fishel B, Chen J, Alon M et al. The value of testing pudendal nerve conduction in evaluating erectile dysfunction in diabetics. *Int J Impot Res* 2000;12(2):103-105.
- Fisher Jane E, Ed O'Donohue, William T. *Practitioner's guide to evidence-based psychotherapy.* (2006) 2006;vi, 754 pp. New York, NY, US754
- Fitch W P, Easterling W J, Talbert R L et al. Topical verapamil HCl, topical trifluoperazine, and topical magnesium sulfate for the treatment of Peyronie's Disease - A Placebo-Controlled Pilot Study. *Br J Sex Med* 2007;4(2):477-484.
- Fitch William, Tecumseh Sherman. Vocal tract length perception and the evolution of language. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 1995;55(7-B):Jan
- Fitzgerald S W, Erickson S J, Foley W D et al. Color Doppler sonography in the evaluation of erectile dysfunction. [Review] [15 refs]. *Radiographics* 1992;12(1):3-17.
- Fitzgerald S W, Erickson S J, Foley W D et al. Color Doppler sonography in the evaluation of erectile dysfunction: patterns of temporal response to papaverine. *AJR Am J Roentgenol* 1991;American Journal of Roentgenology. 157(2):331-336.
- Fitzpatrick J M, Artibani W. Therapeutic Strategies for Managing BPH Progression. *European Urology Supplements* 2006;5(20):997-1003.
- Flaherty Maria Y. Group treatment of men with erectile dysfunction: An outcome study using physiological, behavioral, and psychological assessments. *Dissertation Abstracts International* 1990;51(3-B):Sep
- Fleshner N, Kulkarni G. Should finasteride be used to prevent prostate cancer?. [Review] [47 refs]. *Curr Treat Options Oncol* 2006;7(5):346-354.
- Fleshner N E, Trachtenberg J. Treatment of advanced prostate cancer with the combination of finasteride plus flutamide: early results. *Eur Urol* 1993;24(Suppl 2):106-112.
- Fletcher A. Quality of life in the management of hypertension. [Review] [21 refs]. *Clinical & Experimental Hypertension (New York)* 1999;21(5-6):961-972.
- Fogari R, Zoppi A. Effect of antihypertensive agents on quality of life in the elderly. [Review] [125 refs]. *Drugs Aging* 2004;21(6):377-393.
- Fogari R, Zoppi A, Poletti L et al. Sexual activity in hypertensive men treated with valsartan or carvedilol: a crossover study. *Am J Hypertens* 2001;14(1):27-31.
- Fogarty J D, Bleustein C B, Hafron J M et al. Cutaneous temperature measurements in men with penile prostheses: a comparison study. *Int J Impot Res* 2005;17(6):506-509.
- Fonseca V, Jawa A. Endothelial and erectile dysfunction, diabetes mellitus, and the metabolic syndrome: Common pathways and treatments?. *Am J Cardiol* 2005;96(12 SUPPL. 2):13M-18M.
- Foreman Mark M, Doherty Paul C. Experimental approaches for the development of pharmacological therapies for erectile dysfunction. Riley, Alan J (Ed); Peet, Malcolm (Ed); Wilson, Catherine (Ed) 1993;(1993):235
- Foresta C, Bettella A, Spolaore D et al. Suppression of the high endogenous levels of plasma FSH in infertile men are associated with improved Sertoli cell function as reflected by elevated levels of plasma inhibin B. *Hum Reprod* 2004;19(6):1431-1437.

- Formenti S C, Lieskovsky G, Simoneau A R et al. Impact of moderate dose of postoperative radiation on urinary continence and potency in patients with prostate cancer treated with nerve sparing prostatectomy. *Br J Urol* 1996;155(2):616-619.
- Formenti S C, Lieskovsky G, Skinner D et al. Update on impact of moderate dose of adjuvant radiation on urinary continence and sexual potency in prostate cancer patients treated with nerve-sparing prostatectomy. *Urology* 2000;56(3):453-458.
- Forssmann W-G, Meyer M, Forssmann K. The renal urodilatin system: Clinical implications. *Cardiovasc Res* 2001;51(3):450-462.
- Foster R S. Early-stage testis cancer. [Review] [21 refs]. *Curr Treat Options Oncol* 2001;2(5):413-419.
- Foster-Schubert K E, Cummings D E. Emerging therapeutic strategies for obesity. *Endocr Rev* 2006;27(7):779-793.
- Fourcade R-O, McLeod D. Tolerability of antiandrogens in the treatment of prostate cancer. *Urooncology* 2004;4(1):5-13.
- Fowler F J, Collins M M, Corkery E W et al. The impact of androgen deprivation on quality of life after radical prostatectomy for prostate carcinoma. *Cancer* 2002;95(2):287-295.
- Fowler C, McAllister W, Plail R et al. Randomised evaluation of alternative electrosurgical modalities to treat bladder outflow obstruction in men with benign prostatic hyperplasia. *Health Technol Assess* 2005;9(4):iii-30.
- Fraiman M C, Lepor H, McCullough A R. Changes in penile morphometrics in men with erectile dysfunction after nerve-sparing radical retropubic prostatectomy. *Mol Urol* 1999;3(2):109-115.
- Frajese G, Lazzari R, Magnani A et al. Neurotransmitter, opiodergic system, steroid-hormone interaction and involvement in the replacement therapy of sexual disorders. *J Steroid Biochem Mol Biol* 1990;37(3):411-419.
- Francavilla S, Properzi G, Bellini C et al. Endothelin-1 in diabetic and nondiabetic men with erectile dysfunction. *Br J Urol* 1997;158(5):1770-1774.
- Francis D A, Christopher A T, Beasley B D. Conservative Treatment of Peripheral Neuropathy and Neuropathic Pain. *Clinics in Podiatric Medicine & Surgery* 2006;23(3):509-530.
- Francis S H, Corbin J D. Phosphodiesterase-5 inhibition: The molecular biology of erectile function and dysfunction. *Urol Clin North Am* 2005;32(4):419-429.
- Francisca E A, d'Ancona F C, Meuleman E J et al. Sexual function following high energy microwave thermotherapy: results of a randomized controlled study comparing transurethral microwave thermotherapy to transurethral prostatic resection. *Br J Urol* 1999;161(2):486-490.
- Frankel S J, Donovan J L, Peters T I et al. Sexual dysfunction in men with lower urinary tract symptoms. *J Clin Epidemiol* 1998;51(8):677-685.
- Frankel S, Smith G D, Donovan J et al. Screening for prostate cancer. *Lancet* 2003;361(9363):1122-1128.
- Franklin S S, Smith D H G, Codispoti J et al. Combination treatment with sustained-release verapamil and indapamide in the treatment of mild-to-moderate hypertension. *Am J Ther* 1996;3(3):229-236.
- Franks S, Jacobs H S. Hyperprolactinaemia. *Clinics in Endocrinology & Metabolism* 1983;12(3):641-668.
- Fransson P, Widmark A. Self-assessed sexual function after pelvic irradiation for prostate carcinoma. Comparison with an age-matched control group. *Cancer* 1996;78(5):1066-1078.
- Frederick Mark. The hypnotherapeutic treatment of impotency: A case study. *Australian Journal of Clinical Hypnotherapy and Hypnosis* 1991;12(1):61-63.
- Freedland S J, Haffner M C, Landis P K et al. Obesity does not adversely affect health-related quality-of-life outcomes after anatomic retropubic radical prostatectomy. *Urology* 2005;65(6):1131-1136.
- Freedman A L, Costa Neto F, Mehringer C M et al. Long-term results of penile vein ligation for impotence from venous leakage. *Br J Urol* 1993;149(5 Pt 2):1301-1303.
- Freundenreich Oliver. Exacerbation of idiopathic priapism with risperidone-citalopram combination. [References]. *Hillside J Clin Psychiatry* 2002;63(3):249-250.
- Freytag F, Schelling A, Meinicke T et al. Comparison of 26-week efficacy and tolerability of telmisartan and atenolol, in combination with hydrochlorothiazide as required, in the treatment of mild to moderate hypertension: a randomized, multicenter study. *Clin Ther* 2001;23(1):108-123.
- Fricker J. The rise and fall of Viagra. *Drug Discov Today* 2001;6(14):704-706.
- Fritsch M J, Bauer M, Partsch C J et al. Endocrine evaluation after endoscopic third ventriculostomy (ETV) in children. *Childs Nerv Syst* 2007;23(6):627-631.
- Froschermaier S E, Werner D, Leike S et al. Enhanced external counterpulsation as a new treatment modality for patients with erectile dysfunction. *Urol Int* 1998;61(3):168-171.

- Frucht S J. Parkinson disease: An update. *Proc Aust Assoc Neurol* 2004;10(4):185-194.
- Fugl-Meyer Kerstin S, Arrhult Helene, Pharmanson Helena et al. A Swedish Telephone Help-line for Sexual Problems: A 5-year Survey. [References]. *Br J Sex Med* 2004;1(3):278-283.
- Fukui M, Kitagawa Y, Ose H et al. Role of endogenous androgen against insulin resistance and athero-sclerosis in men with type 2 diabetes. *Current Diabetes Reviews* 2007;3(1):25-31.
- Funder J W. Eplerenone: Hypertension, heart failure and the importance of mineralocorticoid receptor blockade. *Future Cardiology* 2006;2(5):535-541.
- Fung M M, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: the Rancho Bernardo Study. *J Am Coll Cardiol* 2004;43(8):1405-1411.
- Furst G, Muller-Mattheis V, Cohnen M et al. Venous incompetence in erectile dysfunction: evaluation with color-coded duplex sonography and cavernosometry/-graphy. *Eur Radiol* 1999;9(1):35-41.
- Furtado R N V, Oliveira L M, Natour J. Polyarticular corticosteroid injection versus systemic administration in treatment of rheumatoid arthritis patients: A randomized controlled study. *Br J Rheumatol* 2005;32(9):1691-1698.
- Furusyo N, Hayashi J, Ueno K et al. Human lymphoblastoid interferon treatment for patients with hepatitis C virus-related cirrhosis. *Clin Ther* 1997;19(6):1352-1367.
- Fux R, Morike K, Prohmer A M T et al. Impact of CYP2D6 genotype on adverse effects during treatment with metoprolol: A prospective clinical study. *Clinical Pharmacology & Therapeutics* 2005;78(4):378-387.
- Gacci M, Vittori G, Giubilei G et al. Long-term delayed extrusion of a penile prosthesis. *Arch Ital Urol Androl* 2007;79(1):41-42.
- Gaddam K K, Pratt-Ubunama M N, Calhoun D A. Aldosterone antagonists: Effective add-on therapy for the treatment of resistant hypertension. *Expert Review of Cardiovascular Therapy* 2006;4(3):353-359.
- Gades N M, Nehra A, Jacobson D J et al. Association between smoking and erectile dysfunction: a population-based study. *Am J Epidemiol* 2005;161(4):346-351.
- Gall H, Sparwasser C H, Stief C G et al. Diagnosis of venous incompetence in erectile dysfunction. Comparative study of cavernosography and Doppler ultrasound. *Urology* 1990;35(3):235-238.
- Galle G, Trummer H. The etiology of erectile dysfunction and mechanisms by which drugs improve erection. *Med Actual* 2003;39(3):193-201.
- Gallen I, Carter C. Prospective audit of the introduction of insulin glargine (Lantus) into clinical practice in type 1 diabetes. *Practical Diabetes International* 2004;21(3):110-114.
- Gallo L, Perdona S, Autorino R et al. Vesicourethral anastomosis during radical retropubic prostatectomy: does the number of sutures matter?. *Urology* 2007;69(3):547-551.
- Game X, Moscovici J, Game L et al. Evaluation of sexual function in young men with spina bifida and myelomeningocele using the International Index of Erectile Function. *Urology* 2006;67(3):566-570.
- Ganabathi K, Dmochowski R, Zimmern P E et al. Peyronie's disease: surgical treatment based on penile rigidity. *Br J Urol* 1995;153(3:Pt 1):t-6.
- Ganem J P, Lucey D T, Janosko E O et al. Unusual complications of the vacuum erection device. [Review] [17 refs]. *Urology* 1998;51(4):627-631.
- Gannon Kenneth, Glover Lesley, Abel Paul et al. Masculinity, infertility, stigma and media reports. [References]. *Soc Sci Med* 2004;59(6):1169-1175.
- Ganz P. Erectile dysfunction: Pathophysiologic mechanisms pointing to underlying cardiovascular disease. *Am J Cardiol* 2005;96(12 SUPPL. 2):8M-12M.
- Ganz P A, Greendale G A. Female sexual desire--beyond testosterone. *J Natl Cancer Inst* 2007;99(9):659-661.
- Ganzarain Ramon. Group-as-a-whole dynamics in work with traumatized patients: Technical strategies, their rationales, and limitations. [References]. Klein, Robert H (Ed); Schermer, Victor L (Ed) 2000;(2000):364
- Garban H, Marquez D, Cai L et al. Restoration of normal adult penile erectile response in aged rats by long-term treatment with androgens. *Biol Reprod* 1995;53(6):1365-1372.
- Garban H, Marquez D, Magee T et al. Cloning of rat and human inducible penile nitric oxide synthase. Application for gene therapy of erectile dysfunction. *Biol Reprod* 1997;56(4):954-963.
- Garber B. Inflatable penile prostheses for the treatment of erectile dysfunction. *Expert Review of Medical Devices* 2005;2(3):341-350.
- Garber B B. Outpatient inflatable penile prosthesis insertion. *Urology* 1997;49(4):600-603.
- Garcia J M, Li H, Mann D et al. Hypogonadism in male patients with cancer. *Cancer* 2006;106(12):2583-2591.

- Garcia-Campayo Javier, Sanz-Carrillo C, Lobo A. Orgasmic sexual experiences as a side effect of fluoxetine: A case report. *Acta Psychiatr Scand* 1995;91(1):69-70.
- Gardner D M, Baldessarini R J, Waraich P. Modern antipsychotic drugs: A critical overview. *CMAJ: Canadian Medical Association Journal* 2005;172(13):1703-1711.
- Garg G, Singh D, Saraf S et al. Management of benign prostate hyperplasia: An overview of a-adrenergic antagonist. *Biol Pharm Bull* 2006;29(8):1554-1558.
- Garippa Philip A, Sanders Nina. Resolution of erectile dysfunction and inhibited male orgasm in a single homosexual male and transfer of inhibited male orgasm cure to his partner: A case report. *J Sex Marital Ther* 1997;23(2):126-130.
- Garko S B, Ogunsina M O, Danbauchi S S. Sexual dysfunction in hypertensive patients: Implications for therapy. *Annals of African Medicine* 2005;4(2):46-51.
- Garnick M B, Fair W R. Prostate cancer: emerging concepts. Part II. [Review] [60 refs]. *Ann Intern Med* 1996;125(3):205-212.
- Garver D L. Evolution of antipsychotic intervention in the schizophrenic psychosis. *Curr Drug Targets* 2006;7(9):1205-1215.
- Gastal E L, Henry M, Beker A R et al. Sexual behavior of donkey jacks: Influence of ejaculatory frequency and season. *Theriogenology* 1996;46(4):593-603.
- Gasteiger R. Safe operation of chemical plants methodology and practice of risk prevention. *Journal of Occupational Accidents* 1990;13(1-2):145-156.
- Gaston K E, Ornstein D K. Pharmacotherapy for biochemical recurrences after therapy for localised prostate cancer. [Review] [117 refs]. *Expert Opin Pharmacother* 2002;3(6):657-669.
- Gazzaruso C, Giordanetti S, De Amici E et al. Relationship between erectile dysfunction and silent myocardial ischemia in apparently uncomplicated type 2 diabetic patients.[see comment]. *Circulation* 2004;110(1):22-26.
- Gazzaruso C, Pujia A, Solerte S B et al. Erectile dysfunction and angiographic extent of coronary artery disease in type II diabetic patients. *Int J Impot Res* 2006;18(3):311-315.
- Gee W F, Holtgrewe H L, Albertsen P C et al. Practice trends of American urologists in the treatment of impotence, incontinence and infertility. *Br J Urol* 1996;156(5):1778-1780.
- Gelbard M K, James K, Riach P et al. Collagenase versus placebo in the treatment of Peyronie's disease: A double-blind study. *Br J Urol* 1993;149(1):56-58.
- Gelenberg A J, Trivedi M H, Rush A J et al. Randomized, placebo-controlled trial of nefazodone maintenance treatment in preventing recurrence in chronic depression. *Biol Psychiatry* 2003;54(8):806-817.
- Gemery J M, Nangia A K, Mamourian A C et al. Digital three-dimensional modelling of the male pelvis and bicycle seats: impact of rider position and seat design on potential penile hypoxia and erectile dysfunction. *BJU Int* 2007;99(1):135-140.
- George A J. The actions and side effects of Anabolic Steroids in sport and social abuse. *Andrologie* 2003;13(4):354-380.
- George C, Grippat J, Safar M. Second line treatment of essential hypertension after beta-blockade. A randomised trial in 558 patients initially treated with bisoprolol 10mg. *DRUG INVEST* 1990;2(3):150-154.
- George V K, Erkhan S, Dhabuwala C B. Follow-up with Mentor two-piece inflatable penile prosthesis. *Int J Impot Res* 1995;7(1):17-21.
- George W H, Davis K C, Norris J et al. Alcohol and erectile response: the effects of high dosage in the context of demands to maximize sexual arousal. *Experimental & Clinical Psychopharmacology* 2006;14(4):461-470.
- Gerber G S, Fitzpatrick J M. The role of a lipido-sterolic extract of *Serenoa repens* in the management of lower urinary tract symptoms associated with benign prostatic hyperplasia. *BJU Int* 2004;94(3):338-344.
- Gerber H R. Intrathecal morphine for chronic benign pain. *Baillieres Best Practice & Research in Clinical Anaesthesiology* 2003;17(3):429-442.
- Gerhard I, Roth B, Eggert-Kruse W et al. Effects of kallikrein on sperm motility, capillary tube test, and pregnancy rate in an AIH program. *Arch Androl* 1990;24(2):129-145.
- Gerstenberg T C, Nordling J, Hald T et al. Evaluation of patients with suspected neurogenic impotence. *Neurourology & Urodynamics* 1990;9(2):216-217.
- Ghanem H, Anis T. Preference studies are of value to the field of sexual medicine: Con. *Current Sexual Health Reports* 2006;3(1):9-12.
- Ghaziuddin Neera, Alessi Norman E. An open clinical trial of trazodone in aggressive children. *J Child Adolesc Psychopharmacol* 1992;2(4):291-297.
- Ghofrani H A, Osterloh I H, Grimminger F. Sildenafil: From angina to erectile dysfunction to pulmonary hypertension and beyond. *Nat Rev Genet* 2006;5(8):689-702.

- Ghofrani H A, Pepke-Zaba J, Barbera J A et al. Nitric oxide pathway and phosphodiesterase inhibitors in pulmonary arterial hypertension. *J Am Coll Cardiol* 2004;43(12 SUPPL.):68S-72S.
- Ghofrani H A, Voswinkel R, Reichenberger F et al. Differences in hemodynamic and oxygenation responses to three different phosphodiesterase-5 inhibitors in patients with pulmonary arterial hypertension: a randomized prospective study. *J Am Coll Cardiol* 2004;44(7):1488-1496.
- Gholami S S, Gonzalez-Cadavid N F, Lin C-S et al. Peyronie's disease: A review. *Br J Urol* 2003;169(4):1234-1241.
- Gholami S S, Rogers R, Chang J et al. The effect of vascular endothelial growth factor and adeno-associated virus mediated brain derived neurotrophic factor on neurogenic and vasculogenic erectile dysfunction induced by hyperlipidemia. *Br J Urol* 2003;169(4):1577-1581.
- Giagulli V A, Carbone D. Hormonal control of inhibin B in men. *J Endocrinol Invest* 2006;29(8):706-713.
- Gibbons C H, Freeman R. Treatment options for autonomic neuropathies. *Curr Treat Options Neurol* 2006;8(2):119-132.
- Giembycz M A. Life after PDE4: Overcoming adverse events with dual-specificity phosphodiesterase inhibitors. *Curr Opin Pharmacol* 2005;5(3 SPEC. ISS.):238-244.
- Gilbert P, Sparwasser C, Beckert R et al. Venous surgery in erectile dysfunction. The role of dorsal-penile-vein ligation and spongiosolysis for impotence. [Review] [26 refs]. *Urol Int* 1992;49(1):40-47.
- Gilbey S G. Neuropathy and foot problems in diabetes. *Clin Med (Northfield Il)* 2004;4(4):318-323.
- Gillatt D. Antiandrogen treatments in locally advanced prostate cancer: Are they all the same?. *Journal of Cancer Research & Clinical Oncology* 2006;132(SUPPL.1):S17-S26.
- Gilling P J, Kennett K M, Fraundorfer M R. Holmium laser resection v transurethral resection of the prostate: results of a randomized trial with 2 years of follow-up. *J Endourol* 2000;14(9):757-760.
- Gindin Leon, Roberto Resnicoff, Diana E-Mail et al. Unconsummated marriages: A separate and different clinical entity. [References]. *J Sex Marital Ther* 2002;28(Suppl1):85-99.
- Gingell C. Use of intracavernosal alprostadil in erectile dysfunction. *Hospital Medicine (London)* 1998;59(10):777
- Ginsberg David L. Aripiprazole-induced recurrent priapism. [References]. *Primary Psychiatry* 2006;13(11):28-29.
- Giovannoni M P, Vergelli C, Biancalani C et al. Novel pyrazolopyrimidopyridazinones with potent and selective phosphodiesterase 5 (PDE5) inhibitory activity as potential agents for treatment of erectile dysfunction. *J Med Chem* 2006;49(17):5363-5371.
- Giraldi A, Wyllie M, Wagner G. Abanoquil, a new alpha-1 adrenoceptor antagonist. In vitro and in vivo effect on erectile tissue. *Int J Impot Res* 2000;12 Suppl 1S37-S40.
- Gitlin Michael J. Effects of depression and antidepressants on sexual functioning. *Bull Menninger Clin* 1995;59(2):232-248.
- Giuberti A, Manganini V, Picozzi S C et al. Complete genital prosthetization in patients treated with bilateral orchiectomy for metachronous testicular cancer. *Arch Ital Urol Androl* 2007;79(1):26-29.
- Giuliano F. Editorial Comment on: Peripheral Mechanisms of Erectile Dysfunction in a Rat Model of Chronic Cocaine Use. *Eur Urol* 2007;
- Giuliano F. Impact of medical treatments for benign prostatic hyperplasia on sexual function. [Review] [23 refs]. *BJU Int* 2006;97 Suppl 234-38.
- Giuliano F, Allard J. Apomorphine SL (Uprima): Preclinical and clinical experiences learned from the first central nervous system-acting ED drug. *Int J Impot Res* 2002;14(SUPPL. 1):S53-S56.
- Giuliano F, Clement P. Serotonin and Premature Ejaculation: From Physiology to Patient Management. *Eur Urol* 2006;50(3):454-466.
- Giuliano F, Hultling C, El Masry W S et al. Sildenafil citrate (VIAGRA): a novel oral treatment for erectile dysfunction caused by traumatic spinal cord injury. *Int J Clin Pract* 1999;Supplement.102-106.
- Giuliano F, Kaplan S A, Cabanis M J et al. Hemodynamic interaction study between the alpha1-blocker alfuzosin and the phosphodiesterase-5 inhibitor tadalafil in middle-aged healthy male subjects. *Urology* 2006;67(6):1199-1204.
- Giuliano Francois, Rampin Olivier, E-Mail Address et al. Neural control of erection. [References]. *Physiol Behav* 2004;83(2):189-201.
- Gjertson C K, Walmsley K, Kaplan S A. Benign prostatic hyperplasia: Now we can begin to tailor treatment. *Cleve Clin J Med* 2004;71(11):857-880.
- Gladstone David. Review of Madhouse: A Tragic Tale of Megalomania and Modern Medicine. *Hist Psychiatry* 2006;17(4):499-500.
- Gleave M, Evans C P. What's hot in the prostate?. *Prostate Cancer & Prostatic Diseases* 2003;6(4):268-271.

- Gleave M, Qian J, Andreou C et al. The effects of the dual 5 α -reductase inhibitor dutasteride on localized prostate cancer - Results from a 4-month pre-radical prostatectomy study. *Prostate Suppl* 2006;66(15):1674-1685.
- Glick H A, McCarron T J, Althof S E et al. Construction of scales for the Center for Marital and Sexual Health (CMASH) Sexual Functioning Questionnaire. *J Sex Marital Ther* 1997;23(2):103-117.
- Glimelius B, Steineck G. Low evidence of radiation therapy in prostate cancer: A plea for intensified scientific activity. *Acta Oncol (Madr)* 2004;43(4):311-315.
- Glina S. Testosterone and erectile dysfunction. *The Journal of Mens Health & Gender* 2004;1(4):407-412.
- Glina S, Silva M F, Puech-Leao P et al. Veno-occlusive dysfunction of corpora cavernosa: comparison of diagnostic methods. *Int J Impot Res* 1995;7(1):1-10.
- Goadsby P J. Recent advances in the diagnosis and management of migraine. *Br Med J* 2006;332(7532):25-29.
- Godschalk M F, Unice K A, Bergner D et al. A trial study: The effect of low dose human chorionic gonadotropin on the symptoms of benign prostatic hyperplasia. *Br J Urol* 2003;170(4 I):1264-1269.
- Goetz L L, Stiens S A. Abdominal electric stimulation facilitates penile vibratory stimulation for ejaculation after spinal cord injury: a single-subject trial. *Archives of Physical Medicine & Rehabilitation* 2005;86(9):1879-1883.
- Review.**
- Alboni P, Bettiol K, Fuca G et al. Sexual activity with and without the use of sildenafil: risk of cardiovascular events in patients with heart disease. [Review] [41 refs]. *Italian Heart Journal: Official Journal of the Italian Federation of Cardiology* 2004;5(5):343-349.
- Alexander W D. The diabetes physician and an assessment and treatment programme for male erectile impotence. *Diabet Med* 1990;7(6):540-543.
- Althof Stanley E, Seftel Allen D. The evaluation and management of erectile dysfunction. *Psychiatr Clin North Am* 1995;18(1):171-192.
- Altwein J E, Thon W F. Oral treatment of erectile dysfunction: Background, spectrum and limitations. *Aktuel Urol* 1999;30(7):449-460.
- Anderson P C B, Gommersall L, Hayne D et al. New phosphodiesterase inhibitors in the treatment of erectile dysfunction. *Expert Opin Pharmacother* 2004;5(11):2241-2249.
- Anderson T R, Goldberg J F, Harrow M. A review of medication side effects and treatment adherence in bipolar disorder. *Primary Psychiatry* 2004;11(9):48-54.
- Andersson K-E, Schroder A. Therapeutic strategies for drug treatment of stress urinary incontinence. *Drug Discovery Today: Therapeutic Strategies* 2004;1(2):259-265.
- Anonymous. New oral drugs for erectile dysfunction. [Review] [21 refs]. *Drug & Therapeutics Bulletin* 2004;42(7):49-52.
- Anonymous. Oral agents are successful in the treatment of erectile dysfunction in patients with cardiovascular disease. *Drugs & Therapy Perspectives* 2005;21(6):
- Anonymous. Phosphodiesterase type 5 (PDE5) inhibitors: Looking beyond erectile dysfunction. *British Journal of Cardiology* 2003;10(SUPPL. 4):S1-S8.
- Anonymous. In erectile disorders: A narrow therapeutic margin. *Prescrire Int* 2002;11(59):76-79.
- Anonymous. Tadalafil. Slightly more convenient, but poorly assessed in organic disorders. *Prescrire Int* 2003;12(68):213-215.
- Anonymous. Sildenafil and erectile dysfunction. Helpful. *Prescrire Int* 1998;7(38):163-165.
- Archer S L, Gragasin F S, Webster L et al. Aetiology and management of male erectile dysfunction and female sexual dysfunction in patients with cardiovascular disease. *Drugs Aging* 2005;22(10):823-844.
- Ashton A K, D'Mello D A, Dantz B et al. Treatment regimens for managing depression in family practice. *J Fam Pract* 2003;52(SUPPL.):S48-S60.
- Atala A, Amin M. Current concepts in the treatment of genitourinary tract disorders in the older individual. [Review] [87 refs]. *Drugs Aging* 1991;1(3):176-193.
- Aung H H, Dey L, Rand V et al. Alternative therapies for male and female sexual dysfunction. *Am J Chin Med* 2004;32(2):161-173.
- Aversa A, Bruzziches R, Spera G. A rationale for the use of testosterone 'salvage' in treatment of men with erectile dysfunction failing phosphodiesterase inhibitors. *Endocr Pract* 2005;15(2):99-105.
- Aversa A, Pili M, Fabbri A et al. Erectile dysfunction: Expectations beyond phosphodiesterase Type 5 inhibition. *J Endocrinol Invest* 2004;27(2):192-206.
- Bain J. Epidemiology, evaluation and diagnosis of andropause. *Geriatrics and Aging* 2003;6(10 SUPPL.):4-8.

- Baldwin D S. Sexual dysfunction associated with antidepressant drugs. [Review] [96 refs]. *Expert Opin Drug Saf* 2004;3(5):457-470.
- Bancroft J. A history of sexual medicine in the United Kingdom. *Br J Sex Med* 2005;2(4):569-574.
- Basu A, Ryder R E. New treatment options for erectile dysfunction in patients with diabetes mellitus. [Review] [88 refs]. *Drugs* 2004;64(23):2667-2688.
- Beckman T J, Mynderse L A. Evaluation and medical management of benign prostatic hyperplasia. *Mayo Clin Proc* 2005;80(10):1356-1362.
- Beckman T J, bu-Lebdeh H S, Mynderse L A. Evaluation and medical management of erectile dysfunction. [Review] [34 refs]. *Mayo Clin Proc* 2006;81(3):385-390.
- Bella A J, Brock G B. Tadalafil in the treatment of erectile dysfunction. [Review] [32 refs]. *Curr Urol Rep* 2003;4(6):472-478.
- Bella A J, Brock G B. Intracavernous pharmacotherapy for erectile dysfunction. *Endocrine* 2004;23(2-3):149-155.
- Bella A J, Brant W O, Brock G B. Contemporary intracavernous pharmacotherapy for erectile dysfunction in the aging male. *Aging Health* 2006;2(4):559-570.
- Bellinghieri G, Santoro D, Lo Forti B et al. Erectile dysfunction in uremic dialysis patients: Diagnostic evaluation in the sildenafil era. *Am J Kidney Dis* 2001;38(4 SUPPL. 1):S115-S117.
- Bernstein A J, Peters K M. Expanding indications for neuromodulation. *Urol Clin North Am* 2005;32(1):59-63.
- Beutel M. Psychosomatic aspects in the diagnosis and treatment of erectile dysfunction. [Review] [40 refs]. *Andrologia* 1999;31 Suppl 137-44.
- Bhugra D, Crowe M. Physical treatments of erectile disorders. *Int Rev Psychiatry* 1995;7(2):217-223.
- Blanker Marco H, Verhagen Arianne P. Lipid-lowering drugs and erectile dysfunction. [References]. *Fam Pract* 2002;19(5):567
- Brant W O, Bella A J, Lue T F. Erectile and sexual dysfunction in the aging diabetic male. *Aging Health* 2006;2(6):1025-1034.
- Briganti A, Salonia A, Gallina A et al. Emerging oral drugs for erectile dysfunction. [Review] [83 refs]. *Expert Opinion on Emerging Drugs* 2004;9(1):179-189.
- Brock G. Oral agents: First-line therapy for erectile dysfunction. *European Urology Supplements* 2002;1(8):12-18.
- Brock G B. Tadalafil: a new agent for erectile dysfunction. [Review] [12 refs]. *Can J Urol* 2003;10Suppl-22.
- Brock G B, Bochinski D. Modern pharmacotherapy for erectile dysfunction: evolving concepts with central and peripheral acting agents. [Review] [40 refs]. *Curr Opin Urol* 2001;11(6):625-630.
- Brock G B, Lue T F. Drug-induced male sexual dysfunction. An update. [Review] [88 refs]. *Drug Saf* 1993;8(6):414-426.
- Broderick G A. Intracavernous pharmacotherapy: Treatment for the aging erectile response. *Urol Clin North Am* 1996;23(1):111-126.
- Broderick G A. Changing practice patterns in erectile dysfunction: a diagnostic algorithm for the new millennium. [Review] [42 refs]. *Adv Ren Replace Ther* 1999;6(4):314-326.
- Broderick G A. Evidence based assessment of erectile dysfunction. [Review] [62 refs]. *Int J Impot Res* 1998;10 Suppl 2S64-S73.
- Brotans F B, Campos J C, Gonzalez-Correales R et al. Core document on erectile dysfunction: Key aspects in the care of a patient with erectile dysfunction. *Int J Impot Res* 2004;16(SUPPL. 2):S26-S39.
- Burnett A L. Phosphodiesterase 5 mechanisms and therapeutic applications. *Am J Cardiol* 2005;96(12 SUPPL. 2):
- Burns-Cox N, Gingell C. Medical treatment of erectile dysfunction. [Review] [64 refs]. *Postgrad Med J* 1998;74(872):336-342.
- Butler R N, Lewis M I, Hoffman E et al. Love and sex after 60: how to evaluate and treat the impotent older man. A roundtable discussion: Part 2.[see comment]. *Geriatrics* 1994;49(10):27-32.
- Buvat J. Androgen therapy with dehydroepiandrosterone. [Review] [89 refs]. *World J Urol* 2003;21(5):346-355.
- Carbone D J, Seftel A D. Erectile dysfunction. Diagnosis and treatment in older men. [Review] [33 refs]. *Geriatrics* 2002;57(9):18-24.
- Carrier S. Pharmacology of phosphodiesterase 5 inhibitors. [Review] [21 refs]. *Can J Urol* 2003;10Suppl-6.
- Carrier S, Zvara P, Lue T F. Erectile dysfunction. *Endocrinology & Metabolism Clinics of North America* 1994;23(4):773-782.
- Carson C C. Cardiac safety in clinical trials of phosphodiesterase 5 inhibitors. *Am J Cardiol* 2005;96(12 SUPPL. 2):

- Carson C C. Erectile dysfunction: Evaluation and new treatment options. *Psychosom Med* 2004;66(5):664-671.
- Carson C C. Long-term use of sildenafil. *Expert Opin Pharmacother* 2003;4(3):397-405.
- Carson C C. Penile prosthesis implantation: surgical implants in the era of oral medication. [Review] [36 refs]. *Urol Clin North Am* 2005;32(4):503-509.
- Carson C C. Oral and injectable medications for the treatment of erectile dysfunction. [Review] [54 refs]. *Curr Urol Rep* 2000;1(4):307-312.
- Carson C C, Lue T F. Phosphodiesterase type 5 inhibitors for erectile dysfunction. *BJU Int* 2005;96(3):257-280.
- Carson C C. Cardiac safety in clinical trials of phosphodiesterase 5 inhibitors. [Review] [25 refs]. *Am J Cardiol* 2005;96(12B):37M-41M.
- Carson C C, Hubbard J S, Wallen E. Erectile dysfunction and treatment of carcinoma of the prostate. [Review] [52 refs]. *Curr Urol Rep* 2005;6(6):461-469.
- Carson C C, Porst Nehra, Althof Meuleman. Erectile dysfunction in the 21st century: Whom we can treat, whom we cannot treat and patient education. *Int J Impot Res* 2002;14(SUPPL. 1):S29-S34.
- Carson C, Giuliano F, Goldstein I et al. The 'effectiveness' scale-therapeutic outcome of pharmacologic therapies for ED: an international consensus panel report. [Review] [7 refs]. *Int J Impot Res* 2004;16(3):207-213.
- Champion H C. Erectile dysfunction and cardiovascular disease: Carrots, sticks, and better men's health. *Advanced Studies in Medicine* 2006;6(4):163-170.
- Chandra Singh J, Devasia A, Gnanaraj L et al. Erectile dysfunction. *Natl Med J India* 2005;18(3):139-143.
- Chaudhuri A, Wiles P. Optimal treatment of erectile failure in patients with diabetes. [Review] [42 refs]. *Drugs* 1995;49(4):548-554.
- Cheitlin M D. Should the patient with coronary artery disease use sildenafil?. [Review] [25 refs]. *Prev Cardiol* 2003;6(3):161-165.
- Cheitlin M D. Sexual activity and cardiovascular disease. *Am J Cardiol* 2003;92(9 SUPPL. 1):3M-8M.
- Chew K K. Intracavernosal injection therapy. Does it still have a role in erectile dysfunction?. [Review] [21 refs]. *Aust Fam Physician* 2001;30(1):43-46.
- Chu N V, Edelman S V. Erectile dysfunction and diabetes. [Review] [32 refs]. *Curr Diab Rep* 2002;2(1):60-66.
- Corbin J D, Francis S H, Webb D J. Phosphodiesterase type 5 as a pharmacologic target in erectile dysfunction. *Urology* 2002;60(2 SUPPL. 2):4-11.
- Costabile R A. Transurethral therapy for the treatment of erectile dysfunction: Infant or dinosaur?. *Mol Urol* 1999;3(2):135-139.
- Costabile R A. Alprostadil for the treatment of erectile dysfunction. *Expert Opin Investig Drugs* 1999;8(6):877-884.
- Courmoyer Barry. Male erectile difficulty: Crisis intervention and short-term treatment. Roberts, Albert R (Ed) 1990;(1990):treatment-278.
- Courtois F J, Charvier K F, Leriche A et al. Clinical approach to erectile dysfunction in spinal cord injured men. A review of clinical and experimental data. [Review] [60 refs]. *Paraplegia* 1995;33(11):628-635.
- Crum N F, Furtek K J, Olson P E et al. A review of hypogonadism and erectile dysfunction among HIV-infected men during the pre- and post-HAART eras: Diagnosis, pathogenesis, and management. *AIDS Patient Care & Stds* 2005;19(10):655-671.
- Cummings M H. The impact of erectile dysfunction and its treatment with phosphodiesterase type-5 (PDE5) inhibitors in patients with diabetes. *Practical Diabetes International* 2004;21(6):225-230.
- Dal Piaz V, Castellana M C, Vergelli C et al. Synthesis and evaluation of some pyrazolo[3,4-d]pyridazinones and analogues as PDE 5 inhibitors potentially useful as peripheral vasodilator agents. *Journal of Enzyme Inhibition & Medicinal Chemistry* 2002;17(4):227-233.
- Davidson Julian M, Rosen Raymond C. Hormonal determinants of erectile function. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- DeWire D M. Evaluation and treatment of erectile dysfunction. [Review] [35 refs]. *Am Fam Physician* 1996;53(6):2101-2108.
- Dinsmore W. Treatment of erectile dysfunction. *Int J STD AIDS* 2004;15(4):215-221.
- Dinsmore W W. Available and future treatments for erectile dysfunction. [Review] [23 refs]. *Clin Cornerstone* 2005;7(1):37-45.
- DiSanto M E. Contractile mechanisms in diabetes-related erectile dysfunction. *Curr Pharm Des* 2005;11(31):3995-4010.
- Doggrell S. Do vardenafil and tadalafil have advantages over sildenafil in the treatment of erectile dysfunction?. *Int J Impot Res* 2007;19(3):281-295.

- Douglass M A, Lin J C. Update on the treatment of benign prostatic hyperplasia. *Hosp Formul* 2005;40(2):50-64.
- Droupy S, Ponsot Y, Giuliano F. How, why and when should urologists evaluate male sexual function?. *Nature Clinical Practice Urology* 2006;3(2):84-94.
- Duckworth K. Running an erectile dysfunction clinic.[see comment]. *Pap Natl Conf Prof Nurses Physicians* 1997;12(11):775-778.
- Dunsmuir W D, Holmes S A. The aetiology and management of erectile, ejaculatory, and fertility problems in men with diabetes mellitus. [Review] [96 refs]. *Diabet Med* 1996;13(8):700-708.
- Eardley I. Vardenafil: a new oral treatment for erectile dysfunction. [Review] [20 refs]. *Int J Clin Pract* 2004;58(8):801-806.
- Eardley I, Cartledge J. Tadalafil (Cialis) for men with erectile dysfunction.[see comment]. *Int J Clin Pract* 2002;56(4):300-304.
- Ebert T. Clinical experiences with testosterone therapy: Prostate safety. *Aging Male* 2004;7(4):304-311.
- Ebert T, Jockenhovel F, Morales A et al. The current status of therapy for symptomatic late-onset hypogonadism with transdermal testosterone gel. *Eur Urol* 2005;47(2):137-146.
- Eid J F. Sildenafil citrate: current clinical experience. [Review] [19 refs]. *Int J Impot Res* 2000;12Suppl-6.
- Eilenberg K L, Hoover A M, Rutherford M L et al. From informed consent through database lock: An interactive clinical trial conducted using the internet. *Drug Inf J* 2004;38(3):239-251.
- Emmick J T, Stuewe S R, Mitchell M. Overview of the cardiovascular effects of tadalafil. *Eur Heart J Suppl* 2002;4(H):H32-H47.
- Everaerd Walter. Male erectile disorder. O'Donohue, William (Ed); Geer, James H (Ed) 1993;(1993):418
- Fabbri A, Aversa A, Isidori A. Erectile dysfunction: An overview. *Hum Reprod Update* 1997;3(5):455-466.
- Fagan Peter. Psychogenic impotence in relatively young men. Levine, Stephen B (Ed); Risen, Candace B (Ed); Althof, Stanley E (Ed) 2003;(2003):473-Routledge.
- Fazio L, Brock G. Erectile dysfunction: Management update. *CMAJ: Canadian Medical Association Journal* 2004;170(9):1429-1437.
- Feret B. Apomorphine: A sublingual dopamine agonist for the treatment of erectile dysfunction. *Hosp Formul* 2000;35(7):573-579.
- Ferrario C M, Levy P. Sexual dysfunction in patients with hypertension: implications for therapy. [Review] [49 refs]. *J Clin Hypertens* 2002;4(6):424-432.
- Foreman Mark M, Doherty Paul C. Experimental approaches for the development of pharmacological therapies for erectile dysfunction. Riley, Alan J (Ed); Peet, Malcolm (Ed); Wilson, Catherine (Ed) 1993;(1993):235
- Fricker J. The rise and fall of Viagra. *Drug Discov Today* 2001;6(14):704-706.
- Galle G, Trummer H. The etiology of erectile dysfunction and mechanisms by which drugs improve erection. *Med Actual* 2003;39(3):193-201.
- Garber B. Inflatable penile prostheses for the treatment of erectile dysfunction. *Expert Review of Medical Devices* 2005;2(3):341-350.
- Garcia-Reboll L, Mulhall J P, Goldstein I. Drugs for the treatment of impotence. [Review] [98 refs]. *Drugs Aging* 1997;11(2):140-151.
- Gerber H R. Intrathecal morphine for chronic benign pain. *Baillieres Best Practice & Research in Clinical Anaesthesiology* 2003;17(3):429-442.
- Ghofrani H A, Pepke-Zaba J, Barbera J A et al. Nitric oxide pathway and phosphodiesterase inhibitors in pulmonary arterial hypertension. *J Am Coll Cardiol* 2004;43(12 SUPPL.):68S-72S.
- Gingell C. Use of intracavernosal alprostadil in erectile dysfunction. *Hospital Medicine (London)* 1998;59(10):777
- Gingell J C. New developments in self-injection therapy for erectile dysfunction. [Review] [33 refs]. *Br J Urol* 1998;81(4):599-603.
- Gitlin Michael J. Effects of depression and antidepressants on sexual functioning. *Bull Menninger Clin* 1995;59(2):232-248.
- Giuliano F. Apomorphine SL: Evolution of a centrally acting treatment for erectile dysfunction. *European Urology Supplements* 2002;1(3):1-3.
- Giuliano F. Phosphodiesterase type 5 inhibition in erectile dysfunction: An overview. *Eur Heart J Suppl* 2002;4(H):H7-H12.
- Giuliano F, Varanese L. Tadalafil: A novel treatment for erectile dysfunction. *Eur Heart J Suppl* 2002;4(H):H24-H31.
- Gjertson C K, Walmsley K, Kaplan S A. Benign prostatic hyperplasia: Now we can begin to tailor treatment. *Cleve Clin J Med* 2004;71(11):857-880.
- Gleave M, Evans C P. What's hot in the prostate?. *Prostate Cancer & Prostatic Diseases* 2003;6(4):268-271.

- Glina S. Testosterone and erectile dysfunction. *The Journal of Mens Health & Gender* 2004;1(4):407-412.
- Godschalk M F, Sison A, Mulligan T. Diagnosis and therapy of erectile dysfunction. *Med Actual* 1997;33(7):475-483.
- Godschalk Michael F, Sison Alfredo, Mulligan Thomas. Management of erectile dysfunction by the geriatrician. *J Am Geriatr Soc* 1997;45(10):1240-1246.
- Goldenberg M M. Pharmaceutical-approval update. *P & T* 2005;30(7):414-415.
- Goldstein I. A clinical paradigm for the combined management of androgen insufficiency and erectile dysfunction. *Endocrinol Metab Clin North Am* 2007;36(2):435-452.
- Goldstein I, Carson C, Rosen R et al. Vasomax for the treatment of male erectile dysfunction. *World J Urol* 2001;19(1):51-56.
- Goldstein Irwin. Diagnosis of erectile dysfunction. *Sex Disabil* 2004;22(2):121-130.
- Gontero P, Kirby R. Proerectile pharmacological prophylaxis following nerve-sparing radical prostatectomy (NSRP). *Prostate Cancer & Prostatic Diseases* 2004;7(3):223-226.
- Gonzalez R R, Kaplan S A. Tadalafil for the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia. [Review] [36 refs]. *Expert Opinion On Drug Metabolism & Toxicology* 2006;2(4):609-617.
- Gonzalez-Cadavid N F, Rajfer J. Mechanisms of, and novel pharmacological approaches to, Peyronie's disease. *Drug Discovery Today: Disease Mechanisms* 2004;1(1):99-104.
- Gonzalez-Cadavid N F, Rajfer J. Therapy of erectile dysfunction: Potential future treatments. *Endocrine* 2004;23(2-3):167-176.
- Gooren L J G, Saad F. Recent insights into androgen action on the anatomical and physiological substrate of penile erection. *Asian J Androl* 2006;8(1):3-9.
- Graber Benjamin. Medical aspects of sexual arousal disorders. O'Donohue, William (Ed); Geer, James H (Ed) 1993;(1993):418
- Graul A I. The year's new drugs. *Drug News Perspect* 2003;16(1):22-39.
- Greco E A, Spera G, Aversa A. Combining testosterone and PDE5 inhibitors in erectile dysfunction: basic rationale and clinical evidences.[see comment]. [Review] [53 refs]. *Eur Urol* 2006;50(5):940-947.
- Gregoire Alain. New treatments for erectile impotence. *Br J Psychiatry Suppl* 1992;160(Mar.):315-326.
- Greiner K A, Weigel J W. Erectile dysfunction.[see comment]. *Am Fam Physician* 1996;54(5):1675-1682.
- Grossman A, Barenboim E, Azaria B et al. Oral drug therapy for erectile dysfunction: Overview and aeromedical implications. *Aviation Space & Environmental Medicine* 2004;75(11):997-1000.
- Guay A T. Lecture 5: Sexual dysfunction in the diabetic patient. *Int J Impot Res* 2001;13(SUPPL. 5):S47-S50.
- Guay A T. Erectile dysfunction. Are you prepared to discuss it?. [Review] [12 refs]. *Postgrad Med* 133;97(4):127-130.
- Guirguis Waguih. Oral treatment of erectile dysfunction: From herbal remedies to designer drugs. *J Sex Marital Ther* 1998;24(2):69-73.
- Guirguis Waguih R. The problem of the single impotent man. *Int Rev Psychiatry* 1995;7(2):191-194.
- Gupta M, Kovar A, Meibohm B. The clinical pharmacokinetics of phosphodiesterase-5 inhibitors for erectile dysfunction. *J Clin Pharmacol* 2005;45(9):987-1003.
- Hackett G I. Patient preferences in treatment of erectile dysfunction: The continuing importance of patient education. *Clin Cornerstone* 2005;7(1):57-64.
- Hafez E S, Hafez S D. Erectile dysfunction: anatomical parameters, etiology, diagnosis, and therapy. [Review] [59 refs]. *Arch Androl* 2005;51(1):15-31.
- Hafron J, Christ G J. Novel therapeutic strategies for the treatment of erectile dysfunction. *Drug Discovery Today: Therapeutic Strategies* 2004;1(2):249-257.
- Hale T M, Hannan J L, Heaton J P W et al. Common therapeutic strategies in the management of sexual dysfunction and cardiovascular disease. *Current Drug Targets - Cardiovascular & Haematological Disorders* 2005;5(2):185-195.
- Hall M C. Management of erectile dysfunction after radical prostatectomy. [Review] [46 refs]. *Semin Urol Oncol* 1995;13(3):215-223.
- Handelsman D J, Liu P Y. Andropause: Invention, prevention, rejuvenation. *Trends in Endocrinology & Metabolism* 2005;16(2):39-45.
- Handelsman H. Diagnosis and treatment of impotence. [Review] [171 refs]. *Health Technol Assess Rep* 1990;(2):1-23.
- Harvey Kenneth V, Balon Richard. Clinical implications of antidepressant drug effects on sexual function. *Ann Clin Psychiatry* 1995;7(4):189-201.

- Hatch J P. Psychophysiological aspects of sexual dysfunction. [Review] [88 refs]. *Arch Sex Behav* 1981;10(1):49-64.
- Hatzichristou D G, Pescatori E S. Current treatments and emerging therapeutic approaches in male erectile dysfunction. *BJU International - Supplement* 2001;88(3):11-17.
- Hatzimouratidis K, Hatzichristou D G. Treatment options for erectile dysfunction in patients failing oral drug therapy. *Eau Update Series* 2004;2(2):75-83.
- Hayes A, Kochar M S. Erectile dysfunction in patients with hypertension: Management tactics. *Consultant* 2004;44(12):1534-1540.
- Heaton J P. Apomorphine: an update of clinical trial results. *Int J Impot Res* 2000;12Suppl-73.
- Heaton J P W. Characterising the benefit of apomorphine SL (Uprima) as an optimised treatment for representative populations with erectile dysfunction. *Int J Impot Res* 2001;13(SUPPL. 3):S35-S39.
- Hedelin H, Stroberg P. Treatment for erectile dysfunction based on patient-reported outcomes: To every man the PDE5 inhibitor that he finds superior. *Drugs* 2005;65(16):2245-2251.
- Hedlund H, Hedlund P. Pharmacotherapy in erectile dysfunction agents for self-injection programs and alternative application models. [Review] [78 refs]. *Scandinavian Journal of Urology & Nephrology Supplementum* 1996;179:129-138.
- Herschorn S. Cardiovascular safety of PDE5 inhibitors. [Review] [15 refs]. *Can J Urol* 2003;10Suppl-8.
- Heyns C F. Triptorelin in the treatment of prostate cancer: Clinical efficacy and tolerability. *Am J Cancer* 2005;4(3):169-183.
- Hijazi R A, Cunningham G R. Andropause: is androgen replacement therapy indicated for the aging male?. [Review] [123 refs]. *Annu Rev Med* 2005;56:117-137.
- Hijazi R A, Betancourt-Albrecht M, Cunningham G R. Gonadal and erectile dysfunction in diabetics. *Med Clin North Am* 2004;88(4):933-945.
- Hirooka Y, Shimokawa H. Therapeutic potential of rho-kinase inhibitors in cardiovascular diseases. [Review] [76 refs]. *American Journal of Cardiovascular Drugs* 2005;5(1):31-39.
- Hood S, Kirby M. PDE-5 inhibitors - A summary. *British Journal of Diabetes & Vascular Disease* 2004;4(6):383-386.
- Hood S, Kirby M. Risk factor assessment of erectile dysfunction. *British Journal of Diabetes & Vascular Disease* 2004;4(3):157-161.
- Howes L, Martin J, Kritharides L. Diltiazem-mediated inhibition of sildenafil metabolism may promote nitrate-induced hypotension [1] (multiple letters). *Intern Med J* 2001;31(6):373-375.
- Hutter A M. Role of the Cardiologist: Clinical Aspects of Managing Erectile Dysfunction. *Clin Cardiol* 2004;27(4 SUPPL.):I3-17.
- Incrocci L. Radiotherapeutic treatment of Peyronie's disease. *Expert Review of Pharmacoeconomics & Outcomes Research* 2004;4(2):235-242.
- Incrocci L, Slob A K, Levendag P C. Sexual (dys)function after radiotherapy for prostate cancer: a review. [Review] [131 refs]. *Int J Radiat Oncol Biol Phys* 2002;52(3):681-693.
- Intili H. Factors in predicting initial in-office therapeutic dosages of alprostadil for the treatment of organic impotence. *Urol Nurs* 1998;18(2):111-113.
- Jackson G. Phosphodiesterase type 5 inhibition in cardiovascular disease: Experimental models and potential clinical applications. *Eur Heart J Suppl* 2002;4(H):H19-H23.
- Jackson G, Gillies H, Osterloh I. Past, present, and future: a 7-year update of Viagra (sildenafil citrate). [Review] [128 refs]. *Int J Clin Pract* 2005;59(6):680-691.
- Jannini E A, Lenzi A, Wagner G. New perspectives in the pharmacotherapy of erectile dysfunction. *IDrugs* 2003;6(12):1165-1172.
- Jeon Y H, Heo Y-S, Kim C M et al. Phosphodiesterase: Overview of protein structures, potential therapeutic applications and recent progress in drug development. *Cellular & Molecular Life Sciences* 2005;62(11):1198-1220.
- Jiang W, Guan J, Macielag M J et al. Pyrroloquinolone PDE5 inhibitors with improved pharmaceutical profiles for clinical studies on erectile dysfunction. *J Med Chem* 2005;48(6):2126-2133.
- Jin L, Linder A E, Mills T M et al. Inhibition of the tonic contraction in the treatment of erectile dysfunction. *Expert Opin Ther Targets* 2003;7(2):265-276.
- Jnnemann K P. How effective are PDE-S inhibitors?. *Journal fur Urologie und Urogynakologie* 2003;10(4):16-19.
- Jockenhovel F. Testosterone therapy - What, when and to whom?. *Aging Male* 2004;7(4):319-324.
- Johansen K L. Treatment of hypogonadism in men with chronic kidney disease. *Advances in Chronic Kidney Disease* 2004;11(4):348-356.
- Kalsi J S, Kell P D. Update on oral treatments for male erectile dysfunction. [Review] [53 refs]. *Journal of the European Academy of Dermatology & Venereology* 2004;18(3):267-274.

- Kalsi J S, Bahadur G, Muneer A et al. Novel PDE5 inhibitors for the treatment of male erectile dysfunction. *Reprod Biomed Online* 2003;7(4):456-461.
- Kantor J, Bilker W B, Glasser D B et al. Prevalence of erectile dysfunction and active depression: an analytic cross-sectional study of general medical patients. *Am J Epidemiol* 2002;156(11):1035-1042.
- Kaplan S A. Editorial: Benign prostatic hyperplasia management - Statistical significance may not translate into clinical relevance. *Br J Urol* 2004;171(3):1207-1208.
- Kaufman J M. The effect of androgen supplementation therapy on the prostate. *Aging Male* 2003;6(3):166-174.
- Kaufman J M, Vermeulen A. The decline of androgen levels in elderly men and its clinical and therapeutic implications. *Endocr Rev* 2005;26(6):833-876.
- Kendirci M, Hellstrom W J G. Current concepts in the management of erectile dysfunction in men with prostate cancer. *Clinical Prostate Cancer* 2004;3(2):87-92.
- Kendirci M, Bejma J, Hellstrom W J G. Update on erectile dysfunction in prostate cancer patients. *Curr Opin Urol* 2006;16(3):186-195.
- Kendirci M, Walls M M, Hellstrom W J. Central nervous system agents in the treatment of erectile dysfunction. [Review] [137 refs]. *Urol Clin North Am* 2005;32(4):487-501.
- Khan M A, Mikhailidis D P, Morgan R J. Sildenafil: A urologist's view. *Current Medical Research & Opinion, Supplement* 1999;16(1):s48-s58.
- Khan M A, Thompson C S, Sullivan M E et al. The role of prostaglandins in the aetiology and treatment of erectile dysfunction. [Review] [83 refs]. *Prostaglandins Leukotrienes & Essential Fatty Acids* 1999;60(3):169-174.
- Kim S, Narayanan S, Song J C. Tadalafil: An oral selective phosphodiesterase 5 inhibitor for treatment of erectile dysfunction. *Hosp Formul* 2002;37(6):289-296.
- Kim Y C, Yoo M, Lee M G. DA-8159: Erectogenic. *Drugs of the Future* 2005;30(7):678-682.
- Kirby M. Management of erectile dysfunction in men with cardiovascular conditions. *British Journal of Cardiology* 2003;10(4):305-307.
- Kirby M, Kirby R. The management of hypertension in patients with benign prostatic hyperplasia and erectile dysfunction. *British Journal of Cardiology* 2005;12(2):107-116.
- Kloner R. Erectile dysfunction and hypertension. *Int J Impot Res* 2007;19(3):296-302.
- Kloner R A. Sex and the patient with cardiovascular risk factors: focus on sildenafil. [Review] [37 refs]. *Am J Med* 2000;109Suppl-21S.
- Kloner R A. Novel Phosphodiesterase Type 5 Inhibitors: Assessing Hemodynamic Effects and Safety Parameters. *Clin Cardiol* 2004;27(4 SUPPL.):I20-I25.
- Kloner R A. Erectile dysfunction and cardiovascular risk factors. *Hospital Practice (Office Edition)* 2001;36(8):41-51.
- Kloner R A. Pharmacology and drug interaction effects of the phosphodiesterase 5 inhibitors: Focus on β -blocker interactions. *Am J Cardiol* 2005;96(12 SUPPL. 2):
- Kloner R, Padma-Nathan H. Erectile dysfunction in patients with coronary artery disease. [Review] [40 refs]. *Int J Impot Res* 2005;17(3):209-215.
- Koppiker N, Boolell M, Price D. Recent advances in the treatment of erectile dysfunction in patients with diabetes mellitus. [Review] [111 refs]. *Endocr Pract* 2003;9(1):52-63.
- Korenman S G. New insights into erectile dysfunction: A practical approach. *Am J Med* 1998;105(2):135-144.
- Kuan J, Brock G. Selective phosphodiesterase type 5 inhibition using tadalafil for the treatment of erectile dysfunction. *Expert Opin Investig Drugs* 2002;11(11):1605-1613.
- Kubin M, Wagner G, Fugl-Meyer A R. Epidemiology of erectile dysfunction. *Int J Impot Res* 2003;15(1):63-71.
- Kulkarni S K, Patil C S. Phosphodiesterase 5 enzyme and its inhibitors: Update on pharmacological and therapeutical aspects. *Methods & Findings in Experimental & Clinical Pharmacology* 2004;26(10):789-799.
- Kuritzky L. Noninvasive management of lower urinary tract symptoms and sexual dysfunction associated with benign prostatic hyperplasia in the primary care setting. *Compr Ther* 2005;31(3):194-208.
- Kuthe A. Phosphodiesterase 5 inhibitors in male sexual dysfunction. *Curr Opin Urol* 2003;13(5):405-410.
- Labbate L A, Croft H A, Oleshansky M A. Antidepressant-related erectile dysfunction: management via avoidance, switching antidepressants, antidotes, and adaptation. [Review] [82 refs]. *Hillside J Clin Psychiatry* 2003;64Suppl-9.

- Lau D H, Mumtaz F H, Thompson C S et al. Erectile dysfunction: A need for greater awareness. *Journal of the Royal Society for the Promotion of Health* 2004;124(5):214-216.
- Lauterbach E C. The neuropsychiatry of Parkinson's disease and related disorders. *Psychiatr Clin North Am* 2004;27(4):801-825.
- Lazarou S, Morgentaler A. Hypogonadism in the man with erectile dysfunction: what to look for and when to treat. [Review] [40 refs]. *Curr Urol Rep* 2005;6(6):476-481.
- Ledda A. Erectile dysfunction: intracavernous treatment. [Review] [12 refs]. *Current Medical Research & Opinion* 2000;16 Suppl 1s59-s62.
- Lee-Chiong T L. Parasomnias and other sleep-related movement disorders. *Primary Care; Clinics in Office Practice* 2005;32(2):415-434.
- Leiblum Sandra R, Rosen Raymond C. Couples therapy for erectile disorders: Conceptual and clinical considerations. *J Sex Marital Ther* 1991;17(2):147-159.
- Lepor H. Radical prostatectomy: Status and opportunities for improving outcomes. *Cancer Invest* 2004;22(3):435-444.
- Levine L A. Diagnosis and treatment of erectile dysfunction. [Review] [32 refs]. *Am J Med* 2000;109Suppl-12S.
- Levine L A. Erectile dysfunction following treatment of prostate cancer: New insights and therapeutic options. *The Journal of Mens Health & Gender* 2004;1(4):328-333.
- Levine Laurence A E. Erectile dysfunction following treatment of prostate cancer: new insights and therapeutic options. [References]. *Journal of Men's Health & Gender* 2004;1(4):328-333.
- Levy A, Crowley T, Gingell C. Non-surgical management of erectile dysfunction. [Review] [103 refs]. *Clin Endocrinol (Oxf)* 2000;52(3):253-260.
- Lewis J M, Osbourne A L M, O'Leary M P. Erectile dysfunction. *J Med Liban* 2004;52(4):213-216.
- Lewis J, Helfrick B, Marzucco J. Clinical conversations: intraurethral alprostadil (MUSE). Interview by Patricia Bates. *Urol Nurs* 1997;17(4):159-161.
- Lewis R. Review of intraurethral suppositories and iontophoresis therapy for erectile dysfunction. [Review] [18 refs]. *Int J Impot Res* 2000;12Suppl-90.
- Linsenmeyer T A. Evaluation and treatment of erectile dysfunction following spinal cord injury: a review. [Review] [65 refs]. *J Am Paraplegia Soc* 1991;14(2):43-51.
- Lischer G H, Nehra A. Therapies for neurologic erectile dysfunction. *Expert Review of Neurotherapeutics* 2003;3(5):641-648.
- Lording D W. Erectile dysfunction: Update on oral therapies. *Med Today* 2003;4(5):58-66.
- Lue T F. Topical and oral agents for erectile dysfunction. *J Formos Med Assoc* 1999;98(4):233-241.
- Lue T F, Lee K L. Pharmacotherapy for erectile dysfunction. [Review] [45 refs]. *Chin Med J* 2000;113(4):291-298.
- Maan Z, Arya M, Patel H R H. Priapism - A review of the medical management. *Expert Opin Pharmacother* 2003;4(12):2271-2277.
- Magoha G A. Management of male erectile dysfunction: a review.[see comment]. [Review] [55 refs]. *East Afr Med J* 1998;75(11):623-627.
- Mak K Y. Management of sexual dysfunction in primary care. *Hong Kong Practitioner* 2004;26(12):527-532.
- Marshall V L, Grosset D G. GPI-1485 Guilford. *Curr Opin Investig Drugs* 2004;5(1):107-112.
- Martin W J, MacIntyre D E. Melanocortin receptors and erectile function. *Eur Urol* 2004;45(6):706-713.
- Martin-Morales A, Rosen R C. Effective treatment of erectile dysfunction with vardenafil. *Med Actual* 2003;39(1):51-59.
- Masson P, Lambert S M, Brown M et al. PDE-5 inhibitors: current status and future trends. [Review] [80 refs]. *Urol Clin North Am* 2005;32(4):511-525.
- Matfin G. New treatments for erectile dysfunction. *Sexuality, Reproduction & Menopause* 2003;1(1):40-45.
- Matfin G, Jawa A, Fonseca V A. Erectile dysfunction: Interrelationship with the metabolic syndrome. *Curr Diab Rep* 2005;5(1):64-69.
- McCullough A R. An Update on the PDE-5 Inhibitors (PDE-5i). *J Androl* 2003;24(6 SUPPL.):S52-S58.
- McCullough A R. Prevention and management of erectile dysfunction following radical prostatectomy. [Review] [67 refs]. *Urol Clin North Am* 2001;28(3):613-627.
- McKay D. Nutrients and botanicals for erectile dysfunction: examining the evidence. *Altern Med Rev* 2004;9(1):4-16.
- McLeod A L, McKenna C J, Northridge D B. Myocardial infarction following the combined recreational use of Viagra and cannabis. *Clin Cardiol* 2002;25(3):133-134.

- McMahon C G. New treatment options for erectile dysfunction. [Review] [10 refs]. *Aust Fam Physician* 1999;28(8):783-787.
- McMahon C G. Current concepts in the management of post-radical prostatectomy impotence. *Curr Opin Urol* 1998;8(6):535-540.
- Mealy N E. Apomorphine hydrochloride, new formulations. *Drugs of the Future* 2004;29(6):627-628.
- Meuleman E J H. Review of tadalafil in the treatment of erectile dysfunction. *Expert Opin Pharmacother* 2003;4(11):2049-2056.
- Meuleman E J H, Hedlund Pryor, Nehra Althof et al. Prevalence of erectile dysfunction: Need for treatment?. *Int J Impot Res* 2002;14(SUPPL. 1):S22-S28.
- Meyer J J. Impotence. Assessment in the private-practice office. *Postgrad Med* 1994;84(2):87-91.
- Michel M C. Lower Urinary Tract Disorders - Ray Fuller Symposium Physiology, Pharmacology and Therapeutic Approaches 6-7 July 2002, San Francisco, CA, USA. *IDrugs* 2002;5(8):792-796.
- Michelakis E, Tymchak W, Archer S. Sildenafil: from the bench to the bedside. [Review] [10 refs]. *CMAJ Canadian Medical Association Journal* 2000;163(9):1171-1175.
- Mikhail N. Management of erectile dysfunction by the primary care physician. *Cleve Clin J Med* 2005;72(4):293-311.
- Minhas S, Kalsi J S, Ralph D J. Cialis (tadalafil): a new treatment for erectile dysfunction. [Review] [13 refs]. *Hospital Medicine (London)* 2003;64(10):589-592.
- Mitka M. Researchers Seek New Uses for Sildenafil. *J Am Med Assoc* 2003;289(21):2784-2786.
- Mobley D F, Baum N. Medical management of benign prostatic hyperplasia in older adults. *Geriatrics and Aging* 2004;7(6):23-28.
- Mohan R, Bhugra D. Literature update: A critical review. *Sexual & Relationship Therapy* 2005;20(1):115-122.
- Mohr David C, Beutler Larry E. Erectile dysfunction: A review of diagnostic and treatment procedures. *Clin Psychol Rev* 1990;10(1):123-150.
- Monga M, Bernie J, Rajasekaran M. Male infertility and erectile dysfunction in spinal cord injury: a review. [Review] [86 refs]. *Archives of Physical Medicine & Rehabilitation* 1999;80(10):1331-1339.
- Montague D K, Angermeier K W. Current status of penile prosthesis implantation. [Review] [55 refs]. *Curr Urol Rep* 2000;1(4):291-296.
- Montorsi F. Tolerability and safety of apomorphine SL (Ixense (TM)). [Review] [9 refs]. *Int J Impot Res* 2003;15Suppl-9.
- Montorsi F. Oral pharmacotherapy for erectile dysfunction: A personal view of experiences with three different drugs. *The Journal of Mens Health & Gender* 2004;1(1):29-31.
- Montorsi F. The role of apomorphine SL in the treatment of erectile dysfunction. *European Urology Supplements* 2002;1(3):4-11.
- Montorsi F, Oettel M. Testosterone and sleep-related erections: an overview*. [Review] [142 refs]. *Br J Sex Med* 2005;2(6):771-784.
- Montorsi F, Corbin J, Phillips S. Review of phosphodiesterases in the urogenital system: New directions for therapeutic intervention. *Br J Sex Med* 2004;1(3):322-336.
- Montorsi F, Guazzoni G, Rigatti P et al. Pharmacological management of erectile dysfunction. [Review] [59 refs]. *Drugs* 1995;50(3):465-479.
- Montorsi F, Kuritzky L, Sadovsky R et al. Frequently asked questions about tadalafil for treating men with erectile dysfunction. *The Journal of Mens Health & Gender* 2005;2(1):141-157.
- Montorsi F, Padma-Nathan H, Glina S. Erectile function and assessments of erection hardness correlate positively with measures of emotional well-being, sexual satisfaction, and treatment satisfaction in men with erectile dysfunction treated with sildenafil citrate (Viagra). [Review] [45 refs]. *Urology* 2006;68(3 Suppl):26-37.
- Montorsi F, Salonia A, Deho' F et al. Pharmacological management of erectile dysfunction. [Review] [52 refs]. *BJU Int* 2003;91(5):446-454.
- Montorsi F, Salonia A, Zanoni M et al. Counselling the patient with prostate cancer about treatment-related erectile dysfunction. *Curr Opin Urol* 2001;11(6):611-617.
- Montouris G, Morris G L. Reproductive and sexual dysfunction in men with epilepsy. *Epilepsy Behav* 2005;7(SUPPL. 2):S7-S14.
- Moore C R, Wang R. Pathophysiology and treatment of diabetic erectile dysfunction. [Review] [84 refs]. *Asian J Androl* 2006;8(6):675-684.
- Morales A. Yohimbine in erectile dysfunction: would an orphan drug ever be properly assessed?. [Review] [43 refs]. *World J Urol* 2001;19(4):251-255.
- Morales A. Erectile dysfunction: An overview. *Clin Geriatr Med* 2003;19(3):529-538.
- Morales A. Testosterone replacement: when is there a role?. [Review] [39 refs]. *Int J Impot Res* 2000;12 Suppl 4S112-S118.

- Morales A, Heaton J P. Hormonal erectile dysfunction. Evaluation and management. *Urol Clin North Am* 2001;28(2):279-288.
- Morales A, Heaton J P. Hypogonadism and erectile dysfunction: pathophysiological observations and therapeutic outcomes. [Review] [24 refs]. *BJU Int* 2003;92(9):896-899.
- Morales A, Porst W. Developmental status of topical therapies for erectile and ejaculatory dysfunction. *Int J Impot Res* 2000;12(SUPPL. 4):S80-S85.
- Moreland R B, Nakane M, Hsieh G et al. Prospectives for pharmacotherapy of male erectile dysfunction. *Current Opinion in Central & Peripheral Nervous System Investigational Drugs* 2000;2(3):283-302.
- Morelli A, Vignozzi L, Filippi S et al. Erectile dysfunction: Molecular biology, pathophysiology and pharmacological treatment. *Minerva Urol Nefrol* 2005;57(2):85-90.
- Morley J E, Perry H M. Androgen treatment of male hypogonadism in older males. [Review] [72 refs]. *Journal of Steroid Biochemistry & Molecular Biology* 2003;85(2-5):367-373.
- Moyad M A. Promoting general health during androgen deprivation therapy (ADT): A rapid 10-step review for your patients. *Urol Oncol* 2005;23(1):56-64.
- Mulcahy J J. Erectile function after radical prostatectomy. [Review] [27 refs]. *Semin Urol Oncol* 2000;18(1):71-75.
- Mulhall J P. Understanding erectile dysfunction medication preference studies. [Review] [42 refs]. *Curr Opin Urol* 2004;14(6):367-373.
- Mulhall J P. Current concepts in erectile dysfunction. *Am J Manag Care* 2000;6(12:Suppl):Suppl-31.
- Mulhall J P. Intracavernosal injection therapy: a practical guide. *Tech Urol* 1997;3(3):129-134.
- Mulhall J P, Montorsi F. Evaluating preference trials of oral phosphodiesterase 5 inhibitors for erectile dysfunction. *Eur Urol* 2006;49(1):30-37.
- Muller S C, el-Damanhoury H, Ruth J et al. Hypertension and impotence. *Eur Urol* 1991;19(1):29-34.
- Mulligan T, Katz P G. Urologic considerations in geriatric erectile failure. [Review] [55 refs]. *Clin Geriatr Med* 1991;7(1):73-84.
- Mulligan T, Teitelman J. Geriatric sexual dysfunction. [Review] [15 refs]. *Va Med Q* 1991;118(2):97-99.
- Mulligan T, Reddy S, Gulur P V et al. Disorders of male sexual function. *Clin Geriatr Med* 2003;19(3):473-481.
- Murray F T, Geisser M E, Cohen M S et al. Evaluation and treatment of sexual dysfunction in men with diabetes mellitus. [Review] [21 refs]. *J Fla Med Assoc* 1991;78(11):757-761.
- Nehra A. Selecting therapy for maintaining sexual function in patients with benign prostatic hyperplasia. *BJU Int* 2005;96(3):237-243.
- Nehra A. Treatment of endocrinologic male sexual dysfunction. [Review] [22 refs]. *Mayo Clin Proc* 2000;75 SupplS40-S45.
- Nehra A, Kulaksizoglu H. Combination therapy for erectile dysfunction: where we are and what's in the future. [Review] [30 refs]. *Curr Urol Rep* 2002;3(6):467-470.
- Nehra A, Moreland R B. Neurologic erectile dysfunction. *Urol Clin North Am* 2001;28(2):289-308.
- Nehra A, Steers W D, Althof S E et al. Third international conference on the management of erectile dysfunction: Linking pathophysiology and therapeutic response. *Br J Urol* 2003;170(2 II):S3-S5.
- Noss M B, Christ G J, Melman A. Sildenafil: A new oral therapy for erectile dysfunction. *Med Actual* 1999;35(3):211-217.
- Nurnberg H G. Managing treatment-emergent sexual dysfunction associated with serotonergic antidepressants: before and after sildenafil. *J Psychiatr.Pract.* 2001;7(2):92-108.
- Nutt D, Johnson F N. Potential applications of venlafaxine. *Reviews in Contemporary Pharmacotherapy* 1998;9(5):321-331.
- O'Farrell Timothy J. Sexual functioning of male alcoholics. Collins, R 1990;Lorraine(Ed):Kenneth-271.
- O'Keefe M, Hunt D K. Assessment and treatment of impotence. [Review] [104 refs]. *Med Clin North Am* 1995;79(2):415-434.
- O'Leary M. Erectile dysfunction.[update in Clin Evid. 2002 Dec;(8):872-80; PMID: 15259177]. [Review] [19 refs]. *Clin Evid* 2002;(7):796-803.
- Olin J W, Jang J, Jaff M R et al. The top 12 advances in vascular medicine. *Journal of Endovascular Therapy: Official Journal of the International Society of Endovascular Specialists* 2004;11(SUPPL. 2):II21-II31.
- Opsomer R J. Treatment of Erectile Dysfunction. *Acta Clin Belg* 2002;57(5):272-276.
- Owens J. David Brown: Proteomicsin drug discovery. *Drug Discovery Today Targets* 2003;2(4):134-137.

- Padma-Nathan H. Efficacy and tolerability of tadalafil, a novel phosphodiesterase 5 inhibitor, in treatment of erectile dysfunction. [Review] [20 refs]. *Am J Cardiol* 2003;92(9A):19M-25M.
- Padma-Nathan H. A new era in the treatment of erectile dysfunction. *Am J Cardiol* 1999;84(5B):18N-23N.
- Padma-Nathan H. Sildenafil citrate (Viagra(TM)): An update. *Mol Urol* 1999;3(2):127-134.
- Padma-Nathan H. Sildenafil citrate (Viagra) treatment for erectile dysfunction: An updated profile of response and effectiveness. *Int J Impot Res* 2006;18(5):423-431.
- Padma-Nathan H, Giuliano F. Oral drug therapy for erectile dysfunction. *Urol Clin North Am* 2001;28(2):321-334.
- Padma-Nathan Harin, Christ George, Adaikan Ganesan et al. Pharmacotherapy for Erectile Dysfunction. [References]. *Br J Sex Med* 2004;1(2):128-140.
- Pedersen Beth L, Mohl Bo. Behind every penis is a man. *Nord Sexol* 1991;9(4):226-231.
- Penedo F J, Dahn J R. Prostate cancer and QOL: Impact of treatment, disease burden and psychosocial interventions. *Expert Review of Pharmacoeconomics & Outcomes Research* 2004;4(5):525-535.
- Peterson Frederick L J. The assessment and treatment of erection dysfunction. Vandecreek, Leon (Ed); Jackson, Thomas L (Ed) 2000;(2000):18-71.
- Pomeroy J M, Rabasseda X. Tadalafil, a further innovation in the treatment of sexual dysfunction. [Review] [39 refs]. *Med Actual* 2003;39(2):103-113.
- Porst H. The rationale for prostaglandin E1 in erectile failure: a survey of worldwide experience. [Review] [219 refs]. *Br J Urol* 1996;155(3):802-815.
- Porst H. Restoring a normal sexual response: The ultimate goal of erectile dysfunction therapy. *European Urology Supplements* 2002;1(8):19-24.
- Porst H, Pryor Heaton, Nehra. Current perspectives on intracavernosal pharmacotherapy for erectile dysfunction. *Int J Impot Res* 2000;12(SUPPL. 4):S91-S100.
- Potts Annie, Grace Victoria, Gavey Nicola et al. "Viagra stories": Challenging 'erectile dysfunction'. [References]. *Soc Sci Med* 2004;59(3):489-499.
- Pryor J L, Redmon B, Wilson Wyllie et al. New therapies and delivery mechanisms for treatment of erectile dysfunction. *Int J Impot Res* 2000;12(SUPPL. 4):S158-S162.
- Pryor J P. Safety of sildenafil. [Review] [25 refs]. *Curr Opin Urol* 2000;10(6):613-615.
- Pryor J P. Pharmacotherapy of erectile dysfunction. *Sexual & Relationship Therapy* 2002;17(4):389-400.
- Raeburn J N. Erectile dysfunction. *Cme Bulletin Endocrinology & Diabetes* 2000;3(2):52-55.
- Ramos A S, Samsó J V. Specific aspects of erectile dysfunction in spinal cord injury. [Review] [22 refs]. *Int J Impot Res* 2004;16 Suppl 2S42-S45.
- Ramsay LE, Yeo WW, Jackson PR. Thiazide diuretics: first-line therapy for hypertension. [Review]. *Journal of Hypertension - Supplement* 1992;10(3):S29-S32.
- Reckelhoff J F, Yanes L L, Iliescu R et al. Testosterone supplementation in aging men and women: Possible impact on cardiovascular-renal disease. *American Journal of Physiology - Renal Physiology* 2005;289(5 58-5):F941-F948.
- Reffellmann T, Kloner R A. Pharmacotherapy of erectile dysfunction: Focus on cardiovascular safety. *Expert Opin Drug Saf* 2005;4(3):531-540.
- Reffellmann T, Kloner R A. Sexual function in hypertensive patients receiving treatment. *Vascular Health & Risk Management* 2006;2(4):447-455.
- Reffellmann T, Kloner R A. Cardiovascular effects of phosphodiesterase 5 inhibitors. *Curr Pharm Des* 2006;12(27):3485-3494.
- Reisner G S. Impotence. *Aust Fam Physician* 1993;22(8):1393-1397.
- Renshaw Domeena C. Sexuality. Sadavoy, Joel (Ed); Lazarus, Lawrence W (Ed); Jarvik, Lissy F (Ed) 1991;(1991):770
- Rhoden E L, Morgentaler A. Erectile Dysfunction. *J Long Term Eff Med Implants* 2003;13(6):519-528.
- Rhoden Ernani, Luis Morgentaler, Abraham E-Mail et al. Risks of Testosterone-Replacement Therapy and Recommendations for Monitoring. [References]. *N Engl J Med* 2004;350(5):482-492.
- Riley A J. Yohimbine in the treatment of erectile disorder. [Review] [38 refs]. *Br J Clin Pract* 1994;48(3):133-136.
- Riley Alan J, Peet Malcolm, Wilson Catherine. *Sexual pharmacology*. Refuat Hapeh Vehashinayim 1993;xii, 235 pp. New York, NY, US235
- Rodriguez J J, Al Dashti R, Schwarz E R. Linking erectile dysfunction and coronary artery disease. *Int J Impot Res* 2005;17(SUPPL. S1):

- Roehrborn C G, McNicholas T. The Management of Prostatic Obstruction: How to Determine the Best Options?. *European Urology Supplements* 2003;2(8):13-19.
- Rogers Z R. Priapism in sickle cell disease. *Hematology - Oncology Clinics of North America* 2005;19(5):917-928.
- Rosen R C, McKenna K E. PDE-5 inhibition and sexual response: pharmacological mechanisms and clinical outcomes. [Review] [165 refs]. *Annu Rev Sex Res* 2002;1336-88.
- Rosen R C, Giuliano F, Carson C C. Sexual dysfunction and lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). *Eur Urol* 2005;47(6):824-837.
- Rosenberg K P. Sildenafil. *J Sex Marital Ther* 1999;25(4):271-279.
- Rotella D P. Tadalafil Lilly ICOS. [Review] [38 refs]. *Curr Opin Investig Drugs* 2003;4(1):60-65.
- Rotella D P. Phosphodiesterase 5 inhibitors: current status and potential applications. [Review] [55 refs]. *Nat Rev Genet* 2002;Drug(9):674-682.
- Roy J B. Advances in the management of impotence. [Review] [19 refs]. *J Okla State Med Assoc* 1998;91(1):14-16.
- rruda-Olson A M, Pellikka P A. Appropriate use of exercise testing prior to administration of drugs for treatment of erectile dysfunction. [Review] [47 refs]. *Herz* 2003;28(4):291-297.
- Rushton David N. Sexual and sphincter dysfunction. Bradley, Walter G (Ed); Daroff, Robert B (Ed); Fenichel, Gerald M (Ed); Marsden, C 1991;David(Ed):1-391.
- Russell S T, Khandheria B K, Nehra A. Erectile dysfunction and cardiovascular disease. *Mayo Clin Proc* 2004;79(6):782-794.
- Sadovsky R, Dhindsa S, Margo K. Testosterone deficiency: Which patients should you screen and treat?. *J Fam Pract* 2007;56(5):S1-S21.
- Sadovsky R, Miller T, Moskowitz M et al. Three-year update of sildenafil citrate (Viagra) efficacy and safety. *Int J Clin Pract* 2001;55(2):115-128.
- Saenz de, Tejada I, Angulo J et al. Pathophysiology of erectile dysfunction. *Br J Sex Med* 2005;2(1):26-39.
- Sandel M, Elizabeth. Traumatic brain injury. Sipski, Marca L (Ed); Alexander, Craig J (Ed) 1997;(1997):651
- Schover Leslie R. Erectile failure and chronic illness. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Schubert M, Jockenhovel F. Late-onset hypogonadism in the aging male (LOH): definition, diagnostic and clinical aspects. *J Endocrinol Invest* 2005;28(3 Suppl):23-27.
- Schubert M, Zitzmann M, Yassin A. Intramuscular testosterone undecanoate for the treatment of male hypogonadism-review of recent data. *The Journal of Mens Health & Gender* 2006;3(4):356-362.
- Schulman C C. Lower urinary tract symptoms/benign prostatic hyperplasia: minimizing morbidity caused by treatment. [Review] [45 refs]. *Urology* 2003;62(3:Suppl 1):Suppl-33.
- Schultheiss D. Regenerative medicine in andrology: Tissue engineering and gene therapy as potential treatment options for penile deformations and erectile dysfunction. *Eur Urol* 2004;46(2):162-169.
- Seftel A. Testosterone replacement therapy for male hypogonadism: Part III. Pharmacologic and clinical profiles, monitoring, safety issues, and potential future agents. *Int J Impot Res* 2007;19(1):2-24.
- Seftel A D. Phosphodiesterase type 5 inhibitors: Molecular pharmacology and interactions with other phosphodiesterases. *Curr Pharm Des* 2005;11(31):4047-4058.
- Seftel A D. Tadalafil: A long-acting PDE5 inhibitor for the management of erectile dysfunction. *Therapy* 2004;1(2):185-196.
- Seftel A D, Farber J, Fletcher J et al. A three-part study to investigate the incidence and potential etiologies of tadalafil-associated back pain or myalgia. *Int J Impot Res* 2005;17(5):455-461.
- Seftel A D, Mohammed M A, Althof S E. Erectile dysfunction: Etiology, evaluation, and treatment options. *Med Clin North Am* 2004;88(2):387-416.
- Segraves R T. New treatment for erectile dysfunction. [Review] [38 refs]. *Curr Psychiatry Rep* 2000;2(3):206-210.
- Segraves R T. Treatment of erectile dysfunction: A psychiatric perspective. *Primary Psychiatry* 2004;11(12):58-68.
- Segraves R T, Segraves K B. Pharmacotherapy for sexual disorders: Advantages and pitfalls. *Sexual & Marital Therapy* 1998;13(3):295-309.
- Segraves R, Taylor Althof, Stanley. Psychotherapy and pharmacotherapy of sexual dysfunctions. Nathan, Peter E (Ed); Gorman, Jack M (Ed) 1998;(1998):594
- Senn S. Individual response to treatment: Is it a valid assumption?. *Br Med J* 2004;329(7472):966-968.
- Shabsigh R. Therapy of ED: PDE-5 inhibitors. *Endocrine* 2004;23(2-3):135-141.
- Shabsigh R, Anastasiadis A G. Erectile Dysfunction. *Annu Rev Med* 2003;54(pp 153-168):-168.

- Shabsigh R, Rajfer J, Aversa A et al. The evolving role of testosterone in the treatment of erectile dysfunction. *Int J Clin Pract* 2006;60(9):1087-1092.
- Sharlip I. Diagnosis and treatment of premature ejaculation: The physician's perspective. *Br J Sex Med* 2005;2(SUPPL. 2):103-109.
- Sharlip I D. Does natural erectile function improve following intracavernous injections of vasoactive drugs?. [Review] [12 refs]. *Int J Impot Res* 1997;9(4):193-196.
- Sharlip I D. Evaluation and nonsurgical management of erectile dysfunction. *Urol Clin North Am* 1998;25(4):647-659.
- Shinlapawittayatorn K, Chattipakorn S, Chattipakorn N. Effect of sildenafil citrate on the cardiovascular system. *Brazilian Journal of Medical & Biological Research* 2005;38(9):1303-1311.
- Simonsen U. Interactions between drugs for erectile dysfunction and drugs for cardiovascular disease. [Review] [121 refs]. *Int J Impot Res* 2002;14(3):178-188.
- Singh J C, Devasia A, Gnanaraj L et al. Erectile dysfunction. [Review] [21 refs]. *Natl Med J India* 2005;18(3):139-143.
- Smith David M, Levitte Susan S. Association of fluoxetine and return of sexual potency in three elderly men. *Hillside J Clin Psychiatry* 1993;54(8):317-319.
- Snow K J. Erectile dysfunction: A review and update. *Hosp Formul* 2004;39(5):261-268.
- Solomon H, DeBusk R F, Jackson G. Erectile dysfunction: The need to be evaluated, the right to be treated. *Am Heart J* 2005;150(4):620-626.
- Sommer F, Engelmann U. Future options for combination therapy in the management of erectile dysfunction in older men. *Drugs Aging* 2004;21(9):555-564.
- Sperling H, Lummen G, Schneider T et al. [New treatment options for erectile dysfunction. Pharmacologic and nonpharmacologic options]. *Herz* 2003;28(4):314-324.
- Stahl Stephen M. How psychiatrists can build new therapies for impotence. *Hillside J Clin Psychiatry* 1998;59(2):47-48.
- Steers W D. Viability and safety of combination drug therapies for erectile dysfunction. [Review] [20 refs]. *Br J Urol* 2003;170(2 Pt 2):t-3.
- Steers W D, Rosen R, Andersson K-E et al. Viability and safety of combination drug therapies for erectile dysfunction. *Br J Urol* 2003;170(2 II):S20-S23.
- Stenager Egon, Stenager Elsebeth, Nylev Jensen et al. Sexual problems in multiple sclerosis. *Int J Adolesc Med Health* 1994;7(2):95-105.
- Stimmel G L, Gutierrez M A. Pharmacologic treatment strategies for sexual dysfunction in patients with epilepsy and depression. *CNS Spectr* 2006;11(SUPPL. 9):31-37.
- Sui Z. Phosphodiesterase-5 inhibitors for male erectile dysfunction. *Expert Opinion on Therapeutic Patents* 2003;13(9):1373-1388.
- Susman E. American Urological Association - 97th Annual Meeting: Progress in sexual dysfunction: 25-30 May 2002, Orlando, FL, USA. *IDrugs* 2002;5(7):666-669.
- Swerdloff R S, Wang C. Androgens and the ageing male. *Best Practice & Research Clinical Endocrinology & Metabolism* 2004;18(3):349-362.
- Telang D J, Farah R N. Management of impotence after treatment of carcinoma of the prostate. [Review] [16 refs]. *Henry Ford Hosp Med J* 1992;40(1-2):111-113.
- Teloken C. Management of erectile dysfunction secondary to treatment for localized prostate cancer. [Review] [42 refs]. *Cancer Control* 2001;8(6):540-545.
- Temel Y, Hafizi S, Beuls E et al. The supraspinal network in the control of erection. *Expert Opin Ther Targets* 2005;9(5):941-954.
- Tenover J S. Prevalence and management of mild hypogonadism: Introduction. *Int J Impot Res* 2003;15(SUPPL. 4):S1-S2.
- Thachil A, Bhugra D. Literature update: A critical review. *Sexual & Relationship Therapy* 2005;20(4):457-464.
- Thomas J A. Pharmacological aspects of erectile dysfunction. *Jpn J Pharmacol* 2002;89(2):101-112.
- Tilton Margaret C. Diabetes and amputation. Sipski, Marca L (Ed); Alexander, Craig J (Ed) 1997;(1997):651
- Toda N, Ayajiki K, Okamura T. Nitric oxide and penile erectile function. *Pharmacol Ther* 2005;106(2):233-266.
- Toone Brian K. Sexual dysfunction. Keshavan, Matcheri S (Ed); Kennedy, John S (Ed) 1992;(1992):339
- Tran D, Howes L G. Cardiovascular safety of sildenafil. [Review] [38 refs]. *Drug Saf* 2003;26(7):453-460.

- Uckert S, Stief C G, Jonas U. Current and future trends in the oral pharmacotherapy of male erectile dysfunction. *Expert Opin Investig Drugs* 2003;12(9):1521-1533.
- Utida C, Truzzi J C, Bruschini H et al. Male infertility in spinal cord trauma. [Review] [64 refs]. *International Braz J Urol* 2005;31(4):375-383.
- Vale J. Erectile dysfunction following radical therapy for prostate cancer. *Radiotherapy & Oncology* 2000;57(3):301-305.
- Vardi Y, Gruenwald I. Cardiovascular effects of oral pharmacotherapy in erectile dysfunction. *Current Medical Research & Opinion, Supplement* 1999;16(1):s42-s47.
- Vickers M A, Satyanarayana R. Phosphodiesterase type 5 inhibitors for the treatment of erectile dysfunction in patients with diabetes mellitus. *Int J Impot Res* 2002;14(6):466-471.
- Vinik A, Richardson D. Erectile dysfunction in diabetes. *Diabetes Reviews* 1998;6(1):16-33.
- Vinik A I, Mehrabyan A. Diabetic neuropathies. *Med Clin North Am* 2004;88(4):947-999.
- Vitezic D, Pelcic J M. Erectile dysfunction: oral pharmacotherapy options. [Review] [72 refs]. *International Journal of Clinical Pharmacology & Therapeutics* 2002;40(9):393-403.
- Wakley Gill. The management of impotence in general practice. Lincoln, Rosemarie (Ed) 1992;(1992):193
- Waldinger Marcel D. Use of psychoactive agents in the treatment of sexual dysfunction. *CNS Drugs* 1996;6(3):204-216.
- Wespes E. Intracavernous injection as an option for aging men with erectile dysfunction. [Review] [21 refs]. *Aging Male* 2002;5(3):177-180.
- Wessells H, Blevins J E, Vanderah T W. Melanocortinergic control of penile erection. *Peptides* 2005;26(10):1972-1977.
- wey R B. Autonomic dysfunction in Parkinson's disease. *Neurol Clin* 2004;22(3 SUPPL.):S127-S139.
- Wierman M E, Cassel C K. Erectile dysfunction: A multifaceted disorder. *Hospital Practice (Office Edition)* 1998;33(10):65-90.
- Williams G. Erectile dysfunction-advances. [Review] [4 refs]. *Br J Gen Pract* 1991;235(1499):114-118.
- Witherington R. Vacuum devices for the impotent. [Review] [11 refs]. *J Sex Marital Ther* 1991;17(2):69-80.
- Wright P J. Comparison of phosphodiesterase type 5 (PDE5) inhibitors. [Review] [59 refs]. *Int J Clin Pract* 2006;60(8):967-975.
- Young J M. Vardenafil. *Expert Opin Investig Drugs* 2002;11(10):1487-1496.
- Zonszein J. Diagnosis and management of endocrine disorders of erectile dysfunction. *Urol Clin North Am* 1995;22(4):789-802.
- Guideline.**
- Anonymous. American association of clinical endocrinologists medical guidelines for clinical practice for the evaluation and treatment of male sexual dysfunction: A couple's problem - 2003 update. *Endocr Pract* 2003;9(1):77-94.
- Conway A J, Handelsman D J, Lording D W et al. Use, misuse and abuse of androgens. The Endocrine Society of Australia consensus guidelines for androgen prescribing. [erratum appears in *Med J Aust* 2000 Apr 3;172(7):334]. *Med J Aust* 2000;172(5):220-224.
- Hatzichristou D G, Bertero E B, Goldstein I. Decision making in the evaluation of impotence: The patient profile- oriented algorithm. *Sexuality & Disability* 1994;12(1):29-37.
- Hatzichristou D, Rosen R C, Broderick G et al. Clinical evaluation and management strategy for sexual dysfunction in men and women. *Br J Sex Med* 2004;1(1):49-56.
- Hirsch M, Donatucci C, Glina S et al. Standards for clinical trials in male sexual dysfunction: Erectile dysfunction and rapid ejaculation. *Br J Sex Med* 2004;1(1):87-91.
- Jackson G, Betteridge J, Dean J et al. A systematic approach to erectile dysfunction in the cardiovascular patient: A consensus treatment - Update 2002. *Int J Clin Pract* 2002;56(9):663-671.
- Lewis R W, Fugl-Meyer K S, Bosch R et al. Epidemiology/risk factors of sexual dysfunction. *Br J Sex Med* 2004;1(1):35-39.
- Lue T F, Giuliano F, Montorsi F et al. Summary on the recommendations on sexual dysfunctions in men. *Br J Sex Med* 2004;1(1):6-23.
- Montague D K, Barada J H, Belker A M et al. Clinical guidelines panel on erectile dysfunction: summary report on the treatment of organic erectile dysfunction. The American Urological Association. *Br J Urol* 1996;156(6):2007-2011.
- Perlis Roy H, Fava Maurizio, Nierenberg Andrew A et al. Strategies for treatment of SSRI-associated sexual dysfunction: A survey of an academic psychopharmacology practice. [References]. *Harv Rev Psychiatry* 2002;10(2):109-114.
- Wespes E, Amar E, Hatzichristou D et al. Guidelines on erectile dysfunction. *Eur Urol* 2002;41(1):1-5.

Wincze John P, Carey Michael P. Sexual dysfunction: A guide for assessment and treatment. 1991;xii-212.

Comment/opinion piece.

Akhtar Qureshi N, li Al-Habeeb T, Sayeed Al-Ghamdy Y. Sildenafil citrate (Viagra(TM)): Pros and cons!. Saudi Pharmaceutical Journal 1999;7(4):192-200.

Anonymous. Editor's comment. BJU Int 2002;89(9):i-ii.

Aversa A, Fabbri A. New oral agents for erectile dysfunction: What is changing in our practice?. Asian J Androl 2001;3(3):175-179.

Bahnson R R. Papaverine hydrochloride in peripheral blood and the degree of penile erection: Editorial comment. Br J Urol 1990;143(6):1137

Bancroft J. Hormones and human sexual behavior. J Sex Marital Ther 1984;10(1):3-21.

Bancroft J. Are the effects of androgens on male sexuality noradrenergically mediated? Some consideration of the human. Neuroscience & Biobehavioral Reviews 1995;19(2):325-330.

Benet A E, Sharaby J S, Melman A. Male erectile dysfunction assessment and treatment options. [Review] [15 refs]. Compr Ther 1994;20(12):669-673.

Braunstein G D. Endocrine causes of impotence. Optimistic outlook for restoration of potency. Postgrad Med 1983;74(4):207-217.

Carosa E, Lombardo F, Martini P et al. The therapeutic dilemma: How to use tadalafil. International Journal of Andrology Supplement 2005;28(2):74-80.

Carosa E, Volpe R, Martini P et al. Psychosocial issues of ART in aging male. [Review] [37 refs]. J Endocrinol Invest 2005;28(3 Suppl):117-121.

Cartledge J, Eardley I. Sildenafil. Expert Opin Pharmacother 1999;1(1):137-147.

Cohan P, Korenman S G. Commentary: Erectile dysfunction. Journal of Clinical Endocrinology & Metabolism 2001;86(6):2391-2394.

Dinsmore W W. Clinical aspects of erectile dysfunction. Int J STD AIDS 1996;7(Suppl 3):2-4.

Eardley I. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil: Editorial comment. Eur Urol 2004;45(4):507-508.

El-Sakka A I. Cardiovascular system as a 'core' of sexual life. Expert Opin Pharmacother 2005;6(13):2223-2230.

Fabbri A, Aversa A. The therapeutic dilemma: How to use short-acting PDE5 inhibitor drugs. International Journal of Andrology Supplement 2005;28(2):69-73.

Frajese G, Pozzi F. New achievements and pharmacotherapeutic approaches to impotence in the elderly. Aging-Clinical & Experimental Research 2003;15(3):222-233.

Gold Mark S, Frost-Pineda Kimberly, Carnes Patrick J. Depression-Related Improvement With Vardenafil for Erectile Response. [References]. Am J Psychiatry 2006;163(8):1449

Gonzalez-Cadavid N F, Rajfer J. Therapeutic stimulation of penile nitric oxide synthase (NOS) and related pathways. Med Actual 2000;36(2-3):163-174.

Gooren L. Testosterone supplementation: Why and for whom?. Aging Male 2003;6(3):184-199.

Hall Kathryn S K, Leiblum Sandra R. Sexual dysfunction. Thase, Michael E (Ed); Edelstein, Barry A (Ed); Hersen, Michel (Ed) 1990;(1990):684

Holmes S. Treatment of male sexual dysfunction. Br Med Bull 2000;56(3):798-808.

Horrigan Joseph P, Barnhill L, Jarrett. "Priapism associated with venlafaxine use": Comment. Journal of the American Academy of Child & Adolescent Psychiatry 2000;39(1):16-17.

Incrocci L. Can you still have a sexual life after prostate cancer?. Br J Sex Med 2006;3(SUPPL. 2):86

Israel M. Viagra: The first oral treatment for impotence. Can Pharm J 1998;261(7005):164-165.

Jefferson James W. "Psychotropic medications and their effects on sexual function: Diagnosis, biology, and treatment approaches": Comment. Hillside J Clin Psychiatry 1995;56(11):536-537.

Jockenhovel F, Kaufman J M, Mickisch G H et al. The good, the bad, and the unknown of late onset hypogonadism: The urological perspective. The Journal of Mens Health & Gender 2005;2(3):292-301.

Kalsi J S, Cellek S, Muneer A et al. Current oral treatments for erectile dysfunction. Expert Opin Pharmacother 2002;3(11):1613-1629.

Koeneman K S, Mulhall J P, Goldstein I. Sexual health for the man at midlife: In-office workup. Geriatrics 1997;52(9):76-86.

Kulkarni S K, Reddy D S. Pharmacotherapy of male erectile dysfunction with sildenafil. Indian J Pharmacol 1998;30(6):367-378.

Lakin M. The evaluation and nonsurgical management of impotence. Semin Nephrol 1994;14(6):544-550.

- Leungwattanakij S, Flynn V, Hellstrom W J G. Intracavernosal injection and intraurethral therapy for erectile dysfunction. *Urol Clin North Am* 2001;28(2):343-354.
- Lewis J H. Treatment options for men with sexual dysfunction. *J ET Nurs* 1992;19(4):131-142.
- Liss H K, Elmore J G. Radical prostatectomy versus watchful waiting.[comment]. *N Engl J Med* 2005;353(12):1298-1300.
- Lue T F. The clinical evaluation of the patient presenting with erectile dysfunction: What is reasonable? Editorial comment. *Br J Urol* 1990;144(5):1310
- Lue T F, Khoury S. Comments on the Second International Consultation on Erectile and Sexual Dysfunctions. *Br J Sex Med* 2004;1(1):4-5.
- Lue T, Goldstein I, Traish A. Comparison of oral and intracavernosal vasoactive agents in penile erection. [Review] [35 refs]. *Int J Impot Res* 2000;12Suppl-88.
- Marks L S. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: A randomized controlled trial: Editorial comment 1. *Urology* 2003;62(1):125-126.
- Meinhardt W. Vardenafil: A viewpoint. *Drugs Aging* 2002;19(3):228-229.
- Melman A, Christ G J. The hemodynamics of erection and the pharmacotherapies of erectile dysfunction. *Heart Dis* 2002;4(4):252-264.
- Meuleman E J. Editorial comment. *Eur Urol* 2005;47(4):529
- Mikhailidis D P, Khan M A, Milonis H J et al. The treatment of hypertension in patients with erectile dysfunction. *Current Medical Research & Opinion, Supplement* 1999;16(1):s31-s36.
- Mobley D F, Baum N. When patients request the impotence pill: Tips for office evaluation and treatment. *Postgrad Med* 1998;104(2):55-66.
- Montague D K. Editorial: Medical therapies for erectile dysfunction. *Br J Urol* 1999;162(3 I):732
- Morales A. Yohimbine in erectile dysfunction: The facts. *Int J Impot Res* 2000;12(SUPPL. 1):S70-S74.
- Morales A, Buvat J, Gooren L J et al. Endocrine aspects of sexual dysfunction in men. *Br J Sex Med* 2004;1(1):69-81.
- Morgentaler A. Male impotence. *Lancet* 1999;354(9191):1713-1718.
- Novak A, Brod M, Elbers J. Andropause and quality of life: findings from patient focus groups and clinical experts. *Maturitas* 2002;43(4):231-237.
- Nurnberg H G, Hensley P L. Selective phosphodiesterase type-5 inhibitor treatment of serotonergic reuptake inhibitor antidepressant-associated sexual dysfunction: A review of diagnosis, treatment, and relevance. *CNS Spectr* 2003;8(3):194-202.
- Perimenis P. Editorial comment on the manuscript entitled 'comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction'. *Expert Opin Pharmacother* 2005;6(1):1-2.
- Rivas David A, Chancellor Michael B. Management of erectile dysfunction. Sipski, Marca L (Ed); Alexander, Craig J (Ed) 1997;(1997):651
- Rivera R, Cohen M S. Erectile dysfunction: Which medical option for which patient?. *Consultant* 2006;46(10):1187-1195.
- Sadovsky R, Dunn M, Grobe B M. Erectile dysfunction: The primary care practitioner's view. *Am J Manag Care* 1999;5(3):333-341.
- Sampaio F. Combination of phosphodiesterase-5 inhibitors and alpha-blockers in patients with benign prostatic hyperplasia: Treatments of lower urinary tract symptoms, erectile dysfunction, or both? Editorial comment. *International Braz J Urol* 2006;32(1):114
- Segraves R T. Pharmacologic management of sexual dysfunction: Benefits and limitations. *CNS Spectr* 2003;8(3):225-229.
- Slob A K. Age, libido, and male sexual function. *Prostate Suppl* 2000;45(SUPPL. 10):9-13.
- Star C H, Hobdy-Henderson K C, Mulhall J P. New and Emerging Therapies for Erectile Dysfunction. *Drug Topics* 2000;144(SUPPL. JUNE):3-14.
- Steers W D. The future direction of neuro-urology drug research. *Current Opinion in Central & Peripheral Nervous System Investigational Drugs* 2000;2(3):268-282.
- Stein Michael. Viagra and cluster headache. *Headache: The Journal of Head and Face Pain* 1999;39(1):58-59.
- Stern M F. Erectile dysfunction in older men. *Topics in Geriatric Rehabilitation* 1997;12(4):40-52.
- Studd J W W, Cronje W H. Androgens and libido: A case for men and women. *J Br Menopause Soc* 2001;7(SUPPL. 2):19-21.
- Swerdlow R. Testosterone levels in benign prostatic hyperplasia: Sexual function and response to therapy with dutasteride: Commentary. *Nature Clinical Practice Urology* 2006;3(10):528-529.

Tan R S. Novel treatment options for overlapping yet distinct erectile dysfunction and andropause syndromes. *Curr Opin Investig Drugs* 2003;4(4):435-438.

Tan R S, Pu S J. Is it andropause? Recognizing androgen deficiency in aging men.[see comment]. *Postgrad Med* 2004;115(1):62-66.

Thomas A M, LoPiccolo J. Sexual functioning in persons with diabetes: Issues in research, treatment, and education. *Clin Psychol Rev* 1994;14(1):61-86.

Trost L, Kendirci M, Hellstrom W J G. Erectile dysfunction in the aging man: Current options for treatment. *Aging Health* 2006;2(1):71-86.

Walsh P C. Re: Quality of life: radical prostatectomy versus radiation therapy for prostate cancer.[comment]. *Br J Urol* 1996;155(6):2038-2039.

Wang X-W. Weige. Treatment of erectile dysfunction. *Drugs of the Future* 1999;24(7):747-749.

Wyllie M G. Clinical trials design: protocols and endpoints. *Int J Impot Res* 2000;12Suppl-8.

Letter to the editor

Anonymous. Bashing beta blockers' bad rap. *Harv Heart Lett* 2002;13(2):7

Garg R, Karlawish J H T, Casarett D et al. Sildenafil for diabetic men with erectile dysfunction [3] (multiple letters). *J Am Med Assoc* 1999;282(10):939-941.

Gould D. Letter to the Editor [2]. *Int J Impot Res* 1999;11(4):237-238.

Malozowski S, Sahlroot J T, Herrmann H C. Hemodynamic effects of sildenafil [2] (multiple letters). *N Engl J Med* 2000;343(13):967-968.

Pomara G, Morelli G. Re: Tadalafil has no detrimental effect on human spermatogenesis or reproductive hormones [14] (multiple letters). *Br J Urol* 2004;171(6 I):2390-2391.

Rosen R. Editorial comment. *Eur Urol* 2004;46(6):774-775.

Wicker P A, Siegel R, Marks L S. Treatment of erectile dysfunction with sildenafil [1] (multiple letters). *Urology* 1999;53(5):1070-1071.

Not an original study.

Althof Stanley E, O' Leary, Michael P et al. Self-Esteem, Confidence, and Relationships in Men Treated with Sildenafil Citrate for Erectile Dysfunction. [References]. *J Gen Intern Med* 2006;21(10):1069-1074.

Anon Anonymous. Sildenafil: an oral drug for impotence. *Med Lett Drugs Ther* 1998;40(1026):51-52.

Aversa A, Bruzziches R, Pili M et al. Phosphodiesterase 5 inhibitors in the treatment of erectile dysfunction. *Curr Pharm Des* 2006;12(27):3467-3484.

Bach Dilello, Amy K. The enhancing effects of manualized treatment for erectile dysfunction among men using sildenafil: A preliminary investigation. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2003;64(5-B):2003, pp

Banner Linda L. The effects of collaborative care in the treatment of erectile dysfunction (ED): An integrative treatment protocol (ITP). *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2001;61(12-B):2001, pp

Barrett Peter. Impotence: The referred patient. Lincoln, Rosemarie (Ed) 1992;(1992):193

Broderick G A, Donatucci C F, Hatzichristou D et al. Efficacy of tadalafil in men with erectile dysfunction naive to phosphodiesterase 5 inhibitor therapy compared with prior responders to sildenafil citrate. *Br J Sex Med* 2006;3(4):668-675.

Campbell H E. Clinical monograph for drug formulary review: erectile dysfunction agents. [Review] [64 refs]. *Journal of Managed Care Pharmacy* 2005;11(2):151-171.

Carey Michael P, Lantinga Larry J, Krauss Dennis J. Male erectile disorder. Hersen, Michel (Ed); Ammerman, Robert T (Ed) 1994;(1994):512

Delate T, Simmons V A, Motheral B R. Patterns of use of sildenafil among commercially insured adults in the United States: 1998-2002. *Int J Impot Res* 2004;16(4):313-318.

Ganem J P, Lucey D T, Janosko E O et al. Unusual complications of the vacuum erection device. [Review] [17 refs]. *Urology* 1998;51(4):627-631.

Kachhi P N, Henderson S O. Priapism after androstenedione intake for athletic performance enhancement. *Ann Emerg Med* 2000;35(4):391-393.

Kloner R A, Jackson G, Hutter A M et al. Cardiovascular safety update of Tadalafil: retrospective analysis of data from placebo-controlled and open-label clinical trials of Tadalafil with as needed, three times-per-week or once-a-day dosing. *Am J Cardiol* 2006;97(12):1778-1784.

Leiblum Sandra R, Rosen Raymond C. Principles and practice of sex therapy (3rd ed.). (2000) 2000;xiv, 514 pp. New York, NY, US514

Melman A, Serels S, Morales Wessells et al. Priapism. *Int J Impot Res* 2000;12(SUPPL. 4):S133-S139.

- Musacchio Najah S, Hartrich Molly, Garofalo Robert et al. Erectile Dysfunction and Viagra Use: What's up with College-Age Males? [References]. *J Adolesc Health* 2006;39(3):452-454.
- Oettel M. Report on the satellite symposium, the role of testosterone in erectile function, held at the 7th congress of the European society for sexual medicine (5-8 December 2004, London UK). *The Journal of Mens Health & Gender* 2005;2(2):263-265.
- Padma-Nathan H, Christ G, Adaikan G et al. Pharmacotherapy for erectile dysfunction. *Br J Sex Med* 2004;1(2):128-140.
- Pescatori E S, Drei B, Morgia G et al. Salvaging the oral treatment failure patient. *Current Sexual Health Reports* 2006;3(1):20-24.
- Rosen Raymond C. Medical and psychological interventions for erectile dysfunction: Toward a combined treatment approach. Leiblum, Sandra R (Ed); Rosen, Raymond C (Ed) 2000;(2000):514
- Salem E A, Kendirci M, Hellstrom W J G. Drug evaluation: Udenafil, a long-acting PDE5 inhibitor for erectile dysfunction. *Curr Opin Investig Drugs* 2006;7(7):661-669.
- Sam R, Patel P. Sildenafil in dialysis patients. *Int J Artif Organs* 2006;29(3):264-268.
- Segraves Taylor, Althof Stanley. Psychotherapy and pharmacotherapy for sexual dysfunctions. [References]. Nathan, Peter E (Ed); Gorman, Jack M (Ed) 2002;(2002):681
- Sobel R E, Cappelleri J C. NAION and treatment of erectile dysfunction: Reply from Pfizer [13]. *Br J Ophthalmol* 2006;90(7):927
- Steidle C P, Stecher V J, Pace C et al. Correlation of improved erectile function and rate of successful intercourse with improved emotional well-being assessed with the Self-Esteem And Relationship questionnaire in men treated with sildenafil for erectile dysfunction and stratified by age. *Current Medical Research & Opinion* 2006;22(5):939-948.
- Weeks Gerald R, Gambescia Nancy. Erectile dysfunction: Integrating couple therapy, sex therapy, and medical treatment. (2000) 2000;xii, 201 pp. New York, NY, US201
- Wlasowicz Grace, Saidel. Emotional and functional coping outcomes of men receiving pharmacologic erection therapy for impotence. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2002;62(8-B):Mar
- Wysowski D K, Swann J. Use of medications for erectile dysfunction in the United States, 1996 through 2001. *Br J Urol* 2003;169(3):1040-1042.
- Not an english publication.**
- Albaugh J A. Intracavernosal injection algorithm. *Urol Nurs* 2006;26(6):449-453.
- Amr M M, Abbas E Z, El-Samra M et al. Neuropsychiatric syndromes and occupational exposure to zinc phosphide in Egypt. *Environ Res* 1997;73(1-2):200-206.
- Baker Christine D. A cognitive-behavioural model for the formulation and treatment of sexual dysfunction. Ussher, Jane M (Ed); Baker, Christine D (Ed) 1993;(1993):272
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. [German]. *Urologe (Ausg 1048;A)*.(9):1045-1046.
- Buvat J, Amar E, Cambau O et al. Double-blind multicenter study comparing Alprostadil Alfadex with moxislyte chlorhydrate in patients with chronic erectile dysfunction. *Andrologie* 1998;8(2):204-212.
- Carlsen J E, Kober L, Torp-Pedersen C T et al. The optimal dosage of bendrofluazide in hypertension. A randomized double-blind dosage-response investigation. OPTIMAL DOSIS AF BENDROFLUMETIAZID VED HYPERTENSION. EN RANDOMISERET DOBBELTBLIND DOSIS-RESPONSUNDERSOGELSE. *UGESKR LAEG* 1990;152(42):3072-3075.
- Carmignani G, Oneto F. Medical therapy of prostate carcinoma. *Minerva Urol Nefrol* 2004;56(2):147-163.
- Chueh S C, Yu H J, Chiu T Y et al. Treating benign prostatic hyperplasia with finasteride in Chinese men: one-year experience. *J Formos Med Assoc* 1996;95(8):650-652.
- Cushman W C, Cohen J D, Jones R P et al. Comparison of the fixed combination of enalapril/diltiazem ER and their monotherapies in stage 1 to 3 essential hypertension. *American journal of hypertension : journal of the American Society of Hypertension* 1998;11(1 Pt 1):23-30.
- East Marion L, Hofer Heribert, Wickler Wolfgang. The erect 'penis' is a flag of submission in a female-dominated society: Greetings in Serengeti spotted hyenas. *Behav Ecol Sociobiol* 1993;33(6):355-370.
- Fietkau R, Riepl M, Kettner H et al. Supportive treatment with megestrol acetate during radio-(chemo-) therapy. A randomized trial. *Sonderb Z Strahlenther Onkol* 1996;172(3):162-168.
- Furusyo N, Hayashi J, Ueno K et al. Human lymphoblastoid interferon treatment for patients with hepatitis C virus-related cirrhosis. *Clin Ther* 1997;19(6):1352-1367.

- Gupta A, Cohen B H, Ruggieri P et al. Phase I study of thalidomide for the treatment of plexiform neurofibroma in neurofibromatosis 1. *Neurology* 2003;60(1):130-132.
- Hampson S, Kessel D. Colour Doppler and cavernosometry in the evaluation of impotence [abstract]. *Br-J-Radiol* 1991;64
- Lai X P. [Treatment of 76 cases of impotence by acupuncture and point injection]. *Shanghai Journal of Acupuncture and Moxibustion* 1994;13(1):14
- Lepola U, Heikkinen H, Rimon R et al. Clinical evaluation of alprazolam in patients with panic disorder: A double-blind comparison with imipramine. *Hum Psychopharmacol* 1990;5(2):159-163.
- Merkel C, Marin R, Enzo E et al. Randomised trial of nadolol alone or with isosorbide mononitrate for primary prophylaxis of variceal bleeding in cirrhosis. *Lancet* 1996;348(9043):1677-1681.
- Nickel J C. Placebo therapy of benign prostatic hyperplasia: a 25-month study. *Canadian PROSPECT Study Group. Br J Urol* 1998;81(3):383-387.
- Ribq N, Rajmil O, Bassas L et al. Response to intracavernosal administration of three different drugs in the same group of patients with erectile dysfunction. *Arch Esp Urol* 2001;54(4):355-359.
- Rosen R C, Fisher W A, Beneke M et al. The COUPLES-project: a pooled analysis of patient and partner treatment satisfaction scale (TSS) outcomes following vardenafil treatment. *BJU Int* 2007;99(4):849-859.
- Rowland David L, Haensel Stefan M, Blom Jan H et al. Penile sensitivity in men with premature ejaculation and erectile dysfunction. *J Sex Marital Ther* 1993;19(3):189-197.
- Samli M M, Dincel C. Terazosin and doxazosin in the treatment of BPH: Results of a randomized study with crossover in non-responders. *Urol Int* 2004;73(2):125-129.
- Sanchez D J, Rodriguez P L, Navarro A et al. Comparative treatment of primary hypercholesterolemia with lovostatin or bezafibrate. Randomized and double blind study. *TRATAMIENTO COMPARATIVO DE LA HIPERCOLESTEROLEMIA PORIMARIA CON LOVOSTATINA Y BEZAFIBRATO. ENSAYO RANDOMIZADO Y A DOBLE CIEGO. REV 1991;ESP. CARDIOL.* 44(4):251-257.
- Summerbell C D, Youle M, McDonald V et al. Megestrol acetate vs cyproheptadine in the treatment of weight loss associated with HIV infection. *Int J STD AIDS* 1992;3(4):278-280.
- Swindle R, Cameron A, Rosen R. A 15-item short form of the Psychological and Interpersonal Relationship Scales. *Int J Impot Res* 2006;18(1):82-88.
- Unger T. Lessons from ALLHAT: Are low budget diuretics first line therapy in hypertension?. *Z Kardiol* 2004;93(5):349-356.
- Van D V L L, Brouwer J, Portegies M et al. Effect and safety of bisoprolol (Emcor (R)) and isosorbidedinitrate in the treatment of angina pectoris. *DE EFFECTIVITEIT EN VEILIGHEID VAN BISOPROLOL (EMCOR (R)) EN ISOSORBIDEDINITRATEN BIJ DE BEHANDELING VAN ANGINA PECTORIS. Belg Tijdschr Geneesk 1993;THER. GENEESM. ONDERZ.* 18(5):138-141.
- Velasco M, Urbina A, Silva H et al. A double-blind, parallel, comparative evaluation of amlodipine vs. captopril in the monotherapeutic treatment of mild and moderate essential hypertension. *J Cardiovasc Pharmacol* 1991;17(SUPPL. 1):S19-S21.
- Yeni E, Unal D, Verit A et al. Minimal transurethral prostatectomy plus bladder neck incision versus standard transurethral prostatectomy in patients with benign prostatic hyperplasia: a randomised prospective study. *Urol Int* 2002;69(4):283-286.
- Not a relevant study.**
- Annual update 2004/2005 - Treatment of genitourinary disorders. *Drugs of the Future* 2005;30(9):931-934.
- Abrams J. Time course of the interaction between tadalafil and nitrates.[comment]. *J Am Coll Cardiol* 2004;43(11):2150-2151.
- Adaikan P G, Chong Y S, Chew S S L et al. Male sexual dysfunction. *Curr Obstet Gynaecol* 2000;10(1):23-28.
- Adams M A, Perdok R J, Padley R J et al. Safety and tolerability of apomorphine SL in men with cardiovascular disorders. *European Urology Supplements* 2002;1(3):28-32.
- Ahl J, Kinon B J, Liu-Seifert H. Sexual dysfunction associated with neuroleptic-induced hyperprolactinemia improves with reduction in prolactin levels. *Ann N Y Acad Sci* 2004;1032(pp 289-290):-290.
- Ahuja S K, Krane N K, Hellstrom W J. Penile prostheses in the management of impotence in patients with end-stage renal disease. *J La State Med Soc* 1998;150(1):32-34.
- Akbari F, Alavi M, Esteghamati A et al. Effect of renal transplantation on sperm quality and sex hormone levels. *BJU Int* 2003;92(3):281-283.

- Akkus E, Kadioglu A, Esen A et al. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. *Eur Urol* 2002;41(3):298-304.
- Alexandre B, Lemaire A, Desvieux P et al. Intracavernous injections of prostaglandin E1 for erectile dysfunction: patient satisfaction and quality of sex life on long-term treatment. *Br J Sex Med* 2007;4(2):426-431.
- Alfonso A, Rieniets K I, Vigersky R A. Incidence and clinical significance of elevated macroprolactin levels in patients with hyperprolactinemia. *Endocr Pract* 2006;12(3):275-280.
- Alvizatos G, Skolarikos A, Laguna P. Recent data upon impotence, incontinence and quality of life issues concerning radical prostatectomy. [Review] [74 refs]. *Arch Esp Urol* 2003;56(3):321-330.
- Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.
- Althof S E. Quality of life and erectile dysfunction. *Urology* 2002;59(6):803-810.
- Althof S E, Corty E W, Levine S B et al. EDITS: development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. *Urology* 1999;53(4):793-799.
- Althof Stanley E, Turner Louisa A. Self-injection therapy and external vacuum devices in the treatment of erectile dysfunction: Methods and outcome. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Altwein J E, Keuler F U. Oral treatment of erectile dysfunction with apomorphine SL. [Review] [34 refs]. *Urol Int* 2001;67(4):257-263.
- Anderson R A, Bancroft J, Wu F C. The effects of exogenous testosterone on sexuality and mood of normal men. *Journal of Clinical Endocrinology & Metabolism* 1992;75(6):1503-1507.
- Anderson R A, Martin C W, Kung A W et al. 7Alpha-methyl-19-nortestosterone maintains sexual behavior and mood in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 1999;84(10):3556-3562.
- Anderson R A, Wallace A M, Sattar N et al. Evidence for tissue selectivity of the synthetic androgen 7 alpha-methyl-19-nortestosterone in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 2003;88(6):2784-2793.
- Andersson K-E. Pharmacology of penile erection. *Pharmacol Rev* 2001;53(3):417-450.
- Andolsek K M. Alprostadil for the treatment of erectile dysfunction. *Am Fam Physician* 1997;55(5):1902-1903.
- Andriole G, Bruchofsky N, Chung L W K et al. Dihydrotestosterone and the prostate: The scientific rationale for 5a-reductase inhibitors in the treatment of benign prostatic hyperplasia. *Br J Urol* 2004;172(4 I):1399-1403.
- Anonymous. Tadalafil: new preparation. Slightly more convenient, but poorly assessed in organic disorders. *Prescrire Int* 2003;12(68):213-215.
- Anonymous. Tadalafil (cialis) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1172):101-102.
- Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.
- Anonymous. First study of Viagra in black men demonstrates effective, well-tolerated treatment. *Urol Nurs* 2002;22(4):285-286.
- Anonymous. Study shows patients taking vardenafil consistently completed sexual intercourse. *Urol Nurs* 2001;21(6):413-414.
- Anonymous. Apomorphine (TAP holdings). 6a beta-aporphine-10,11-diol hydrochloride hemihydrate, apomorphine hydrochloride, spontane, Uprima. *Drugs in R & D* 1999;2(6):415-416.
- Anonymous. Intraurethral alprostadil for impotence. *Medical Letter on Drugs & Therapeutics* 1997;39(997):32
- Anonymous. Treatment for impotence gains FDA approval. *Am J Health Syst Pharm* 1995;52(19):2078-2079.
- Anonymous. Intracavernous injection of alprostadil for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 1995;37(958):83-84.
- Anonymous. Vardenafil works for 10 hours. *Can Pharm J* 2005;275(7360):133
- Anonymous. Treatment duration of action is important in ED. *Can Pharm J* 2004;273(7330):878
- Anonymous. Dutasteride. *Prescrire Int* 2004;13(73):183
- Anonymous. Erratum: Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo controlled, crossover study (*Indian Journal of Pharmacology* (2004) vol. 37 (5) (317)). *Indian J Pharmacol* 2004;36(6):391
- Anonymous. Partnership struck between Bayer and Schering. *Nat Rev Genet* 2004;3(10):819
- Anonymous. Erectile dysfunction drugs may reduce fertility but help depression. *Can Pharm J* 2004;272(7294):439

- Anonymous. Sildenafil appears safe and effective for some heart failure patients. *Can Pharm J* 2004;272(7290):310
- Anonymous. What to do when oral treatment fails?. *Int J Impot Res* 2003;15(SUPPL. 7):S30-S32.
- Anonymous. Oral drug treatment of erectile dysfunction. *Int J Impot Res* 2003;15(SUPPL. 7):S27-S29.
- Anonymous. Counselling and increased dose of sildenafil improves response in ED. *British Journal of Diabetes & Vascular Disease* 2003;3(6):445
- Anonymous. Improve erectile function early after prostatectomy. *Med Today* 2003;4(11):8-9.
- Anonymous. Recent FDA approval of new erectile dysfunction drug provides first challenge to sildenafil. *Geriatrics and Aging* 2003;6(8):11
- Anonymous. Inhaled apomorphine promising for erectile dysfunction treatment. *Can Pharm J* 2003;271(7261):170
- Anonymous. Transurethral alprostadil. *Prescrire Int* 2002;11(61):144
- Anonymous. IDdb News focus. *Current Drug Discovery* 2003;(pp 10-13):-13.
- Anonymous. Vardenafil prolongs improved erectile function in diabetics. *Cardiology Review* 2002;19(10):38-39.
- Anonymous. Erectile dysfunction treated effectively with tadalafil. *Economics of Neuroscience* 2001;3(11):19
- Anonymous. New erectile dysfunction drug useful in diabetes. *Can Pharm J* 2001;267(7173):669
- Anonymous. Erectile dysfunction - Alprostadil. *Manuf Chem Aerosol News* 2001;72(11):21
- Anonymous. Erectile dysfunction - Vardenafil. *Manuf Chem Aerosol News* 2001;72(6):25
- Anonymous. FDA approves oral therapy for erectile dysfunction. *Am J Health Syst Pharm* 1998;55(10):981-984.
- Anonymous. Sildenafil Viagra(R) UK-92480: Treatment of erectile dysfunction phosphodiesterase V inhibitor. *Drugs of the Future* 1998;23(2):242-243.
- Anonymous. Intracavernosal alprostadil for erectile dysfunction. *Hospital Practice (Office Edition)* 1996;31(8):136-137.
- Anonymous. Intracavernous alprostadil: Effective therapy for erectile dysfunction. *Drugs & Therapy Perspectives* 1996;7(6):1-5.
- Anonymous. Heart drug with 'viagra side-effect'. *Indian J Med Sci* 1999;53(5):236
- Anonymous. What to do if Viagra won't do. *Harvard Mens Health Watch* 2005;9(10):4-8.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: intracavernous injection of prostaglandin E1. *JAMA* 1991;265(24):3321-3323.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: papaverine and phentolamine. *JAMA* 1990;264(6):752-754.
- Ansong K S, Punwaney R B. An assessment of the clinical relevance of serum testosterone level determination in the evaluation of men with low sexual drive. *Br J Urol* 1999;162(3 I):719-721.
- Ansong K S, Lewis C, Jenkins P et al. Epidemiology of erectile dysfunction: a community-based study in rural New York State. *Ann Epidemiol* 2000;10(5):293-296.
- Arafa M, Eid H, Shamloul R. Significance of phentolamine redosing during prostaglandin E1 penile color Doppler ultrasonography in diagnosis of vascular erectile dysfunction. *Int J Urol* 2007;14(5):476-477.
- Araujo A B, O'Donnell A B, Brambilla D J et al. Prevalence and incidence of androgen deficiency in middle-aged and older men: Estimates from the Massachusetts male aging study. *Journal of Clinical Endocrinology & Metabolism* 2004;89(12):5920-5926.
- Araujo Andre B, Durante Richard, Feldman Henry A et al. The relationship between depressive symptoms and male erectile dysfunction: Cross-sectional results from the Massachusetts male aging study. *Psychosom Med* 1998;60(4):458-465.
- Arnavaz A, Aurich A, Weissenborn K et al. Effect of sildenafil (Viagra) on cerebral blood flow velocity: a pilot study. *Psychiatry Res* 2003;122(3):207-209.
- Arnold R, Beer D, Bhalay G et al. 8-Aryl xanthines potent inhibitors of phosphodiesterase 5. *Bioorg Med Chem Lett* 2002;12(18):2587-2590.
- Aronson J K. Features of this month's Journal. *Br J Clin Pharmacol* 2003;55(4):327-328.
- Arslan D, Esen A A, Secil M et al. A new method for the evaluation of erectile dysfunction: sildenafil plus Doppler ultrasonography. *Br J Urol* 2001;166(1):181-184.
- Arthur R. Cardiovascular disorders and erectile dysfunction. *British Journal of Cardiology* 2002;9(3):144-145.

- Ashok S, Sigman M. Bioavailable testosterone should be used for the determination of androgen levels in infertile men. *Br J Urol* 2007;177(4):1443-1446.
- Ashton A K, Jamerson B D, Weinstein W L et al. Antidepressant-related adverse effects impacting treatment compliance: Results of a patient survey. *Current Therapeutic Research, Clinical & Experimental* 2005;66(2):96-106.
- Atala A. What's new in urology. *J Am Coll Surg* 2004;199(3):446-461.
- Atikeler M K, Gecit I, Senol F A. Optimum usage of prilocaine-lidocaine cream in premature ejaculation. *Andrologia* 2002;34(6):356-359.
- Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: quetiapine-induced sexual dysfunctions. *Int J Impot Res* 2005;17(2):201-203.
- Avasthi A, Basu D, Kulhara P et al. Psychosexual dysfunction in Indian male patients: Revisited after seven years. *Arch Sex Behav* 1994;23(6):685-695.
- Aversa A, Mazzilli F, Rossi T et al. Effects of sildenafil (Viagra) administration on seminal parameters and post-ejaculatory refractory time in normal males. *Hum Reprod* 2000;15(1):131-134.
- Aydin S, Unal D, Erol H et al. Multicenter clinical evaluation of the aetiology of erectile dysfunction: a survey report. *International Urology & Nephrology* 2001;32(4):699-703.
- Ayub W, Fletcher S. End-stage renal disease and erectile dysfunction. Is there any hope?. *Nephrology Dialysis Transplantation* 2000;15(10):1525-1528.
- Bagatell C J, Heiman J R, Rivier J E et al. Effects of endogenous testosterone and estradiol on sexual behavior in normal young men. [erratum appears in *J Clin Endocrinol Metab* 1994 Jun;78(6):1520]. *Journal of Clinical Endocrinology & Metabolism* 1994;78(3):711-716.
- Baggaley M R, Hirst J F, Watson J P. Outcome of patients referred to a psychosexual clinic with erectile failure. *Sexual & Marital Therapy* 1996;11(2):123-130.
- Bai W J, Zhu J C, Jiang H et al. [A comparative study of different vasoactive drugs in the treatment of impotence]. *Chinese Journal of Urology* 1992;13(6):453-455.
- Bailey J, Evans J P, Hardy M et al. Synopsis: 2005 Annual Meeting of the American Society of Andrology. *J Androl* 2005;26(6):678-688.
- Bain J. Andropause. Testosterone replacement therapy for aging men. [Review] [55 refs]. *Can Fam Physician* 2001;47:91-97.
- Balon Richard. Sildenafil and sexual dysfunction associated with antidepressants. [References]. *J Sex Marital Ther* 1999;25(4):259-264.
- Bancroft J, Gutierrez P. Erectile dysfunction in men with and without diabetes mellitus: a comparative study. [see comment]. *Diabet Med* 1996;13(1):84-89.
- Bancroft J, Munoz M, Beard M et al. The effects of a new alpha-2 adrenoceptor antagonist on sleep and nocturnal penile tumescence in normal male volunteers and men with erectile dysfunction. *Psychosom Med* 1995;57(4):345-356.
- Baniel J, Israilov S, Segenreich E et al. Comparative evaluation of treatments for erectile dysfunction in patients with prostate cancer after radical retropubic prostatectomy. *BJU Int* 2001;88(1):58-62.
- Barnas J, Parker M, Guhring P et al. The utility of tamsulosin in the management of orgasm-associated pain: a pilot analysis. [see comment]. *Eur Urol* 2005;47(3):361-365.
- Barqawi A, O'Donnell C, Kumar R et al. Correlation between LUTS (AUA-SS) and erectile dysfunction (SHIM) in an age-matched racially diverse male population: data from the Prostate Cancer Awareness Week (PCAW). *Int J Impot Res* 2005;17(4):370-374.
- Bartlik Barbara D, Kaplan Peter, Kaplan Helen S. Psychostimulants apparently reverse sexual dysfunction secondary to selective serotonin re-uptake inhibitors. *J Sex Marital Ther* 1995;21(4):264-271.
- Bayes M, Rabasseda X, Prous J R. Gateways to Clinical Trials. *Methods & Findings in Experimental & Clinical Pharmacology* 2004;26(9):723-753.
- bdel-Khalek M, El-Hammady S, Ibrahim el. A 4-year follow-up of a randomized prospective study comparing transurethral electrovaporization of the prostate with neodymium: YAG laser therapy for treating benign prostatic hyperplasia. *BJU Int* 2003;91(9):801-805.
- Beal K, Mears J G. Short report: Penile lymphoma following local injections for erectile dysfunction. *Leuk Lymphoma* 2001;42(1-2):247-249.
- Beard S, Hunn A, Wight J. Treatments for spasticity and pain in multiple sclerosis: A systematic review. *Health Technol Assess* 2003;7(40):111p
- Beasley C M, Mitchell M I, Dmitrienko A A et al. The combined use of ibutilide as an active control with intensive electrocardiographic sampling and signal averaging as a sensitive method to assess the effects of tadalafil on the human QT interval. [see comment]. *J Am Coll Cardiol* 2005;46(4):678-687.
- Becher E, Glina S. Erectile dysfunction in Latin America and treatment with sildenafil citrate (Viagra): Introduction. *Int J Impot Res* 2002;14(SUPPL. 2):S1-S2.

- Bella A J, Brock G B. Tadalafil: A comprehensive update. *Journal of Drug Evaluation* 2004;2(8):225-246.
- Benson G S. The clinical evaluation of the patient presenting with erectile dysfunction: what is reasonable?. [Review] [27 refs]. *Semin Urol* 1990;8(2):94-99.
- Beretta G, Saltarelli O, Marzotto M et al. Transcutaneous minoxidil in the treatment of erectile dysfunctions in spinal cord injured men. *Acta Eur Fertil* 1993;24(1):27-30.
- Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;
- Bestane W J, Bestane M C, Ramos N A. Prospective study of sodium nitroprusside in pharmacologically induced erection. *Braz J Urol* 2001;27(2):155-158.
- Beutel M E, Wiltink J, Hauck E W et al. Correlations between hormones, physical, and affective parameters in aging urologic outpatients. *Eur Urol* 2005;47(6):749-755.
- Bhatia M S, Malik S C. Dhat syndrome--a useful diagnostic entity in Indian culture. *Br J Psychiatry* 1991;159(Nov.):691-695.
- Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.
- Bivalacqua T J, Hellstrom W J G. Potential application of gene therapy for the treatment of erectile dysfunction. *J Androl* 2001;22(2):183-190.
- Black A M, Day A G, Morales A. The reliability of clinical and biochemical assessment in symptomatic late-onset hypogonadism: Can a case be made for a 3-month therapeutic trial?. *BJU Int* 2004;94(7):1066-1070.
- Blander D S, Sanchez-Ortiz R F, Broderick G A. Sex inventories: can questionnaires replace erectile dysfunction testing?. *Urology* 1999;54(4):719-723.
- Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329
- Boccon Gibod L. Is transurethral needle ablation a safe and effective treatment for lower urinary tract symptoms secondary to BPH?. *Nature Clinical Practice Urology* 2004;1(1):24-25.
- Bochinski D J, Dean R C, Lue T F. Erectile dysfunction and priapism. *Nat Clin Pract Urol* 2004;1(1):49-53.
- Bodie J A, Beeman W W, Monga M. Psychogenic erectile dysfunction. *Int J Psychiatry Med* 2003;33(3):273-293.
- Bodie J, Lewis J, Schow D et al. Laboratory evaluations of erectile dysfunction: an evidence based approach. *Br J Urol* 2003;169(6):2262-2264.
- Bodner D R, Leffler B, Frost F. The role of intracavernous injection of vasoactive medications for the restoration of erection in spinal cord injured males: a three year follow up. *Paraplegia* 1992;30(2):118-120.
- Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.
- Boolell M, Allen M J, Ballard S A et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int J Impot Res* 1996;8(2):47-52.
- Boshier A, Wilton L V, Shakir S A W. Evaluation of the safety of sildenafil for male erectile dysfunction: Experience gained in general practice use in England in 1999. *BJU Int* 2004;93(6):796-801.
- Bouloux P. Testim 1% testosterone gel for the treatment of male hypogonadism. [Review] [33 refs]. *Clin Ther* 2005;27(3):286-298.
- Boydak B, Nalbantgil S, Fici F et al. A randomised comparison of the effects of nebivolol and atenolol with and without chlorthalidone on the sexual function of hypertensive men. *Clinical Drug Investigation* 2005;25(6):409-416.
- Braatvedt G D. Outcome of managing impotence in clinical practice. *N Z Med J* 1999;112(1092):272-274.
- Brake M, Loertzer H, Horsch R et al. Treatment of Peyronie's disease with local interferon-alpha 2b. *BJU Int* 2001;87(7):654-657.
- Bratus D, Hlebic G, Hajdinjak T. 16905960 of erectile dysfunction. *Croat Med J* 2007;48(1):76-80.
- Brazil M. Viagra for broken hearts?. *Nat Rev Genet* 2005;4(3):190
- Brennemann W, Kohler W, Zierz S et al. Testicular dysfunction in adrenomyeloneuropathy. *Eur J Endocrinol* 1997;137(1):34-39.
- Brennemann W, Stitz B, Van Ahlen H et al. Treatment of idiopathic erectile dysfunction in men with the opiate antagonist naltrexone--a double-blind study. *J Androl* 1993;14(6):407-410.
- Briganti A, Chun F K H, Salonia A et al. A comparative review of apomorphine formulations for erectile dysfunction: Recommendations for use in the elderly. *Drugs Aging* 2006;23(4):309-319.

- Briganti A, Salonia A, Gallina A et al. Drug insight: Oral phosphodiesterase type 5 inhibitors for erectile dysfunction. *Nature Clinical Practice Urology* 2005;2(5):239-247.
- Briganti A, Salonia A, Zanni G et al. Erectile dysfunction and radical prostatectomy: An update. *Eau Update Series* 2004;2(2):84-92.
- Brindis R G, Kloner R A. Sildenafil in patients with cardiovascular disease. [Review] [33 refs]. *Am J Cardiol* 2003;92(9A):26M-36M.
- Brixius K, Middeke M, Lichtenthal A et al. Nitric oxide, erectile dysfunction and beta-blocker treatment (MR NOED study): Benefit of nebivolol versus metoprolol in hypertensive men. *Clinical & Experimental Pharmacology & Physiology* 2007;34(4):327-331.
- Broderick G A, Allen G, McClure R D. Vacuum tumescence devices: the role of papaverine in the selection of patients. *Br J Urol* 1991;145(2):284-286.
- Brooks D P, Giuliano F. Genitourinary diseases. *Drug Discovery Today: Therapeutic Strategies* 2005;2(1):iii-iv.
- Brown J S, Wessells H, Chancellor M B et al. Urologic complications of diabetes. *Diabetes Care* 2005;28(1):177-185.
- Buchholz N P, Weuste R, Mattarelli G et al. Post-vasectomy erectile dysfunction. *J Psychosom Res* 1994;38(7):759-762.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. *Urologe* 2005;Ausg. A. 44(9):1045-1046, 1048-51.
- Buena F, Swerdloff R S, Steiner B S et al. Sexual function does not change when serum testosterone levels are pharmacologically varied within the normal male range. *Fertility & Sterility* 1993;59(5):1118-1123.
- Bukofzer S, Livesey N. Safety and tolerability of apomorphine SL (Uprima). *Int J Impot Res* 2001;13(SUPPL. 3):S40-S44.
- Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.
- Burnett A L. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: A randomized controlled trial: Editorial comment 2. *Urology* 2003;62(1):126
- Burnett A L. Vasoactive pharmacotherapy to cure erectile dysfunction: fact or fiction?. [Review] [45 refs]. *Urology* 2005;65(2):224-230.
- Burnett A L. The impact of sildenafil on molecular science and sexual health. *Eur Urol* 2004;46(1):9-14.
- Burns-Cox N, Gingell C. The andropause: fact or fiction?. [Review] [49 refs]. *Postgrad Med J* 1997;73(863):553-556.
- Buvat J. Hyperprolactinemia and sexual function in men: a short review. [Review] [26 refs]. *Int J Impot Res* 2003;15(5):373-377.
- Buvat J, Boujadoue G. Testosterone replacement therapy in the ageing man. *The Journal of Mens Health & Gender* 2005;2(4):396-399.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Campbell M. Beneficial cardiovascular effects and safety of sildenafil reported in trio of studies. *Cardiology Review* 2001;18(6):27
- Cappelleri J C, Siegel R L, Glasser D B et al. Relationship between patient self-assessment of erectile dysfunction and the sexual health inventory for men. *Clin Ther* 2001;23(10):1707-1719.
- Cara A M, Lopes-Martins R A B, Antunes E et al. The role of histamine in human penile erection. *Br J Urol* 1995;75(2):220-224.
- Carani C, Bancroft J, Granata A et al. Testosterone and erectile function, nocturnal penile tumescence and rigidity, and erectile response to visual erotic stimuli in hypogonadal and eugonadal men. *Psychoneuroendocrinology* 1992;17(6):647-654.
- Carani C, Scuteri A, Marrama P et al. The effects of testosterone administration and visual erotic stimuli on nocturnal penile tumescence in normal men. *Horm Behav* 1990;24(3):435-441.
- Cardenas D D, Ditunno J, Graziani V et al. Phase 2 trial of sustained-release fampridine in chronic spinal cord injury. *Proc Annu Clin Spinal Cord Inj Conf* 2007;45(2):158-168.
- Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.
- Carey Michael P, Wincze John P, Meisler Andrew W. Sexual dysfunction: Male erectile disorder. Barlow, David H (Ed) 1993;(1993):534
- Carosa E, Benvenega S, Trimarchi F et al. Sexual inactivity results in reversible reduction of LH bioavailability. *Int J Impot Res* 2002;14(2):93-99.
- Carson C C. PNU-83757: a new agent for the treatment of erectile dysfunction.[comment]. *Curr Urol Rep* 2002;3(6):465-466.

- Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.
- Carson C C, Hatzichristou D G, Carrier S. Erratum: Erectile response with vardenafil in sildenafil nonresponders: A multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial (*BJU International* (2004) 94 (1301-1309)). *BJU Int* 2005;96(3):466
- Carson C C, Rajfer J, Eardley I et al. The efficacy and safety of tadalafil: an update. *BJU Int* 2004;93(9):1276-1281.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Caspi A, Goldenberg M M. Sildenafil: A new drug treatment for male erectile dysfunction. *P & T* 1998;23(5):
- Cawello W, Schweer H, Dietrich B et al. Pharmacokinetics of prostaglandin E1 and its main metabolites after intracavernous injection and short-term infusion of prostaglandin E1 in patients with erectile dysfunction. *Br J Urol* 1997;158(4):1403-1407.
- Cecchi M, Sepich C A, Felipetto R et al. Vacuum constriction device and topical minoxidil for management of impotence. *Arch Esp Urol* 1995;48(10):1058-1059.
- Chaiban J T, Azar S T. Erectile dysfunction in diabetic patients. *J Med Liban* 2004;52(4):217-219.
- Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.
- Chatterjee R, Andrews H O, McGarrigle H H et al. Cavernosal arterial insufficiency is a major component of erectile dysfunction in some recipients of high-dose chemotherapy/chemoradiotherapy for haematological malignancies. *Bone Marrow Transplant* 2000;25(11):1185-1189.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Chaudhuri T K, Fink S, Burger R H et al. Nuclear penogram: Non-invasive technique to monitor and record effect of pharmacologically-induced penile erection in impotence therapy. *Urology* 1990;35(1):98
- Cheitlin M D, Hutter A M, Brindis R G et al. Use of sildenafil (Viagra) in patients with cardiovascular disease. *Circulation* 1999;99(1):168-177.
- Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.
- Chen J, Greenstein A, Kaver I et al. Use of automatic insulin injector for intracorporeal injection in erectile dysfunction. *Br J Urol* 1994;152(2):461-462.
- Chen J, Mabjeesh N J, Greenstein A. Sildenafil versus the vacuum erection device: patient preference. *Br J Urol* 2001;166(5):1779-1781.
- Chen J, Wollman Y, Chernichovsky T et al. Effect of oral administration of high-dose nitric oxide donor L-arginine in men with organic erectile dysfunction: results of a double-blind, randomized, placebo-controlled study. *BJU Int* 1999;83(3):269-273.
- Chen K-C, Minor T X, Rahman N U et al. The additive erectile recovery effect of brain-derived neurotrophic factor combined with vascular endothelial growth factor in a rat model of neurogenic impotence. *BJU Int* 2005;95(7):1077-1080.
- Chen K-K, Jiann B-P, Lin J S N et al. Erratum: Efficacy and safety of on-demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study (*Journal of Sexual Medicine* vol. 1 (2)). *Br J Sex Med* 2005;2(1):158
- Cheng J Y W, Ng E M L, Chen R Y L et al. Prevalence of erectile dysfunction in Asian populations: A meta-analysis. *Int J Impot Res* 2007;19(3):229-244.
- Chew K K. Prevalence of hypogonadism in the aging male and male erectile dysfunction in Asia-Pacific countries. *Asian J Androl* 2003;5(2):171-172.
- Chew K K, Stuckey B G. Clinical course of penile fibrosis in intracavernosal prostaglandin E1 injection therapy: a follow-up of 44 patients. *Int J Impot Res* 2003;15(2):94-98.
- Chew K K, Stuckey B G A. Use of transurethral alprostadil (MUSE) (prostaglandin E1) for glans tumescence in a patient with penile prosthesis. *Int J Impot Res* 2000;12(3):195-196.
- Chew K K, Stuckey B G A, Thompson P L. Erectile dysfunction, sildenafil and cardiovascular risk. *Med J Aust* 2000;172(6):279-283.
- Chia S. Management of premature ejaculation -- a comparison of treatment outcome in patients with and without erectile dysfunction. *Int J Androl* 2002;25(5):301-305.

- Chinegwundoh F, Anie K A. Treatments for priapism in boys and men with sickle cell disease. [Review] [16 refs]. *Cochrane Database Syst Rev* 2004;(4):CD004198
- Chiu K C, Cohan P, Martinez D et al. Adrenal insufficiency after medical therapy for prolactin and adrenocorticotrophic hormone co-producing pituitary macroadenoma without hypercortisolism. *Endocr Pract* 2001;11(6):443-446.
- Chiu Y J, Reid I A. Effect of sildenafil on renin secretion in human subjects. *Experimental biology and medicine (Maywood, NJ)* 2002;227(8):620-625.
- Christ B, Brockmeier D, Hauck E W et al. Interactions of sildenafil and tacrolimus in men with erectile dysfunction after kidney transplantation. *Urology* 2001;58(4):589-593.
- Christ G J, Melman A. The application of gene therapy to the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):111-112.
- Chue P. Gabapentin treatment for premature ejaculation [3]. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 2004;49(9):644-645.
- Cimentepe E, Unsal A, Saglam R. Randomized clinical trial comparing transurethral needle ablation with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: results at 18 months. *J Endourol* 2003;17(2):103-107.
- Clark C. Erectile dysfunction and other problems. *Can Pharm J* 2004;272(7299):608-610.
- Clark R V, Hermann D J, Cunningham G R et al. Marked Suppression of Dihydrotestosterone in Men with Benign Prostatic Hyperplasia by Dutasteride, a Dual 5 α -Reductase Inhibitor. *Journal of Clinical Endocrinology & Metabolism* 2004;89(5):2179-2184.
- Claro J A, Passerotti C C, Figueiredo Neto A C et al. An alternative non-invasive treatment for Peyronie's disease. *International Braz J Urol* 2004;30(3):199-204.
- Clough J. CNS-targeted sexual dysfunction drug for men and women. *Drug Discov Today* 2002;7(9):492-494.
- Coelho O R. Tolerability and safety profile of sildenafil citrate (Viagra) in Latin American patient populations. *Int J Impot Res* 2002;14(Suppl 2):54-59.
- Coker C, Bettocchi C, Pryor J. Caverject, a new licensed prostaglandin preparation for use in erectile dysfunction. *J Androl* 1994;15(6 SUPPL.):71S
- Coleman C I, Carabino J M, Vergara C M et al. Vardenafil. *Hosp Formul* 2003;38(3):131-148.
- Collazos J, Martinez E, Mayo J et al. Sexual dysfunction in HIV-infected patients treated with highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2002;31(3):322-326.
- Colp G M, Scropo F I. Can self-directed pelvic floor exercises improve erectile function?. *Nature Clinical Practice Urology* 2005;2(3):128-129.
- Conti C R, Pepine C J, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. *Am J Cardiol* 1999;83(5A):29C-34C.
- Contreras L N, Masini A M, Danna M M et al. Glucocorticoids: their role on gonadal function and LH secretion. *Minerva Endocrinol* 1996;21(2):43-46.
- Cooper A J, Losztyn S, Russell N C et al. Medroxyprogesterone acetate, nocturnal penile tumescence, laboratory arousal, and sexual acting out in a male with schizophrenia. *Arch Sex Behav* 1990;19(4):361-372.
- Cormio L, Nisen H, Ruutu M et al. Etilefrine in the prevention of prolonged erection after diagnostic pharmacological stimulation. *Ann Chir Gynaecol* 1996;85(3):247-250.
- Corona G, Mannucci E, Fisher A D et al. Effect of hyperprolactinemia in male patients consulting for sexual dysfunction. *Br J Sex Med* 2007;4(5):1485-1493.
- Corona G, Mannucci E, Petrone L et al. ANDROTEST: a structured interview for the screening of hypogonadism in patients with sexual dysfunction. *Br J Sex Med* 2006;3(4):706-715.
- Corona G, Mannucci E, Petrone L et al. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. *Int J Impot Res* 2006;18(2):190-197.
- Corona G, Mannucci E, Schulman C et al. Psychobiologic correlates of the metabolic syndrome and associated sexual dysfunction. *Eur Urol* 2006;50(3):595-604.
- Creasey G H. Lecture 6: restoration of male sexual function following spinal cord injury. *Int J Impot Res* 2000;12 Suppl 3S54-S55.
- Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.
- Crum-Cianflone N F, Bavaro M, Hale B et al. Erectile dysfunction and hypogonadism among men with HIV. *AIDS Patient Care & Stds* 2007;21(1):9-19.
- Culha M, Mutlu N, Acar O et al. Patient-partner satisfaction with intracavernous medication supported with oral agents in selected cases of Peyronie's disease: A ten-month follow-up study. *International Urology & Nephrology* 1999;31(2):257-262.

- Curran M, Keating G. Tadalafil.[erratum appears in *Drugs*. 2003;63(23):2703]. [Review] [31 refs]. *Drugs* 2003;63(20):2203-2212.
- Curri S B, Menchini Fabris F. Evidence and results obtained with a new Trans-Epidermal Barrier (T.E.B.) drug in the medical treatment of vascular impotence. *Boll Chim Farm* 1996;135(5):316-334.
- Cyranoski D. Malaysian researchers bet big on home-grown Viagra. *Nat Med* 2005;11(9):912
- Czuriga I, Riecanaky I, Bodnar J et al. Comparison of the New Cardioselective Beta-Blocker Nebivolol with Bisoprolol in Hypertension: The Nebivolol, Bisoprolol Multicenter Study (NEBIS). *Cardiovascular Drugs & Therapy* 2003;17(3):257-263.
- Dang G, Matern R, Bivalacqua T J et al. Intralesional interferon-alpha-2B injections for the treatment of Peyronie's disease. *South Med J* 2004;97(1):42-46.
- Davis B E, Weigel J W, Whitford C S. Treatment of male impotence: a new option. *Kans Med* 1990;91(12):325-326.
- Davis J M. American College of Neuropsychopharmacology - 43rd annual meeting. 12-16 December 2004, San Juan, Puerto Rico. *IDrugs* 2005;8(2):100-103.
- Davis M E, Brewster M E. Cyclodextrin-based pharmaceuticals: Past, present and future. *Nat Rev Genet* 2004;3(12):1023-1035.
- De Meyer J M, Oosterlinck W. Influence of the method of intracavernous injection on penile rigidity: a possible pharmacokinetic explanation. *Urology* 1997;49(2):248-252.
- De Tejada I. Vardenafil Duration of Action. *Eur Urol* 2006;50(5):901-902.
- De Tejada I, Garvey D S, Schroeder J D et al. Design and evaluation of nitrosylated alpha-adrenergic receptor antagonists as potential agents for the treatment of impotence. *Journal of Pharmacology & Experimental Therapeutics* 1999;290(1):121-128.
- Degirmenci B, Acar M, Albayrak R et al. Effects of sildenafil citrate (Viagra) on renal arteries: An evaluation with Doppler ultrasound. *Urol Int* 2006;77(2):170-172.
- Del Popolo G, Li Marzi V, Mondaini N et al. Time/duration effectiveness of sildenafil versus tadalafil in the treatment of erectile dysfunction in male spinal cord-injured patients. *Proc Annu Clin Spinal Cord Inj Conf* 2004;42(11):643-648.
- Delizonna L L, Wincze J P, Litz B T et al. A comparison of subjective and physiological measures of mechanically produced and erotically produced erections (or, is an erection an erection?). *J Sex Marital Ther* 2001;27(1):21-31.
- Denisov M F, Davis J M, Brecher M. Re: Prolactin levels and adverse events in patients treated with risperidone [8] (multiple letters). *J Clin Psychopharmacol* 2002;22(5):538-540.
- Derby C A, Araujo A B, Johannes C B et al. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 2000;12(4):197-204.
- Derby C A, Barbour M M, Hume A L et al. Drug therapy and prevalence of erectile dysfunction in the Massachusetts Male Aging Study cohort. *Pharmacotherapy* 2001;21(6):676-683.
- Derouet H, Nolden W, Jost W H et al. Treatment of erectile dysfunction by an external ischiocavernous muscle stimulator. *Eur Urol* 1998;34(4):355-359.
- Desouza C, Parulkar A, Lumpkin D et al. Acute and prolonged effects of sildenafil on brachial artery flow-mediated dilatation in type 2 diabetes.. *Diabetes Care* 2002;25(8):1336-1339.
- Dietzen C J, Lloyd L K. Complications of intracavernous injections and penile prostheses in spinal cord injured men. *Archives of Physical Medicine & Rehabilitation* 1992;73(7):652-655.
- Dinelli N, Salintri G, Pomara G et al. Role of pharmacologic rehabilitation in the recovery of sexual function following radical prostatectomy. *Minerva Urol Nefrol* 2005;57(4):325-329.
- Dinsmore W W. Medical treatment of impotence with papaverine and phentolamine intracavernosal injection. *Ulster Med J* 1990;59(2):174-176.
- Dinsmore W W, Gingell C, Hackett G et al. Treating men with predominantly nonpsychogenic erectile dysfunction with intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector system: a multicentre double-blind placebo-controlled study. *BJU Int* 1999;83(3):274-279.
- Djavan B, Milani S, Fong Y K. Dutasteride: A novel dual inhibitor of 5 α -reductase for benign prostatic hyperplasia. *Expert Opin Pharmacother* 2005;6(2):311-317.
- Doggrell S A. Comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction. *Expert Opin Pharmacother* 2005;6(1):75-84.
- Donatucci C F, Lue T F. Erectile dysfunction in men under 40: etiology and treatment choice. *Int J Impot Res* 1993;5(2):97-103.
- Doumas M, Tsakiris A, Douma S et al. Beneficial effects of switching from beta-blockers to nebivolol on the erectile function of hypertensive patients. *Asian J Androl* 2006;8(2):177-182.

- Dundar S O. Visual loss associated with erectile dysfunction drugs. *Can J Ophthalmol* 2007;42(1):10-12.
- Dupont Simon. Multiple sclerosis and sexual functioning: A review. *Clin Rehabil* 1995;9(2):135-141.
- Durackova Z, Trebaticky B, Novotny V et al. Lipid metabolism and erectile function improvement by Pycnogenol, extract from the bark of *Pinus pinaster* in patients suffering from erectile dysfunction - A pilot study. *Adv Food Nutr Res* 2003;23(9):1189-1198.
- Eandi J A, Yao A P, Javidan J. Penile paraffinoma: the delayed presentation. *Int Urol Nephrol* 2007;
- Eardley I. New oral therapies for the treatment of erectile dysfunction. *Br J Urol* 1998;81(1):122-127.
- Earle C M, Keogh E J, Ker J K et al. The role of intracavernosal vasoactive agents to overcome impotence due to spinal cord injury. *Paraplegia* 1992;30(4):273-276.
- Earle C M, Stuckey B G, Ching H L et al. The incidence and management of priapism in Western Australia: a 16 year audit. *Int J Impot Res* 2003;15(4):272-276.
- Edwards G, Muirhead G J. *British Journal of Clinical Pharmacology: Introduction*. *Br J Clin Pharmacol* 2002;53(SUPPL. 1):1S-3S.
- Ekmekcioglu O, Inci M, Demirci D et al. Effects of sildenafil citrate on ejaculation latency, detumescence time, and refractory period: placebo-controlled, double-blind, crossover laboratory setting study. *Urology* 2005;65(2):347-352.
- Ekselius L, Von Knorring L. Effect on sexual function of long-term treatment with selective serotonin reuptake inhibitors in depressed patients treated in primary care. *J Clin Psychopharmacol* 2001;21(2):154-160.
- El Malik E M A. Erectile dysfunction: An update of diagnosis and management. *Qatar Medical Journal* 2000;9(2):9-17.
- El-Bahnasawy M S, El-Assmy A, Dawood A et al. Effect of the use of internal iliac artery for renal transplantation on penile vascularity and erectile function: A prospective study. *Br J Urol* 2004;172(6 I):2335-2339.
- El-Rufaie Omer E F, Bener Abdulbari, Abuzeid Mohamed S O et al. Sexual dysfunction among type II diabetic men: A controlled study. *J Psychosom Res* 1997;43(6):605-612.
- El-Sakka A I. Penile axial rigidity and Doppler ultrasonography parameters in patients with erectile dysfunction: association with type 2 diabetes. *Urology* 2003;62(3):525-531.
- Emilien G. Alprox-TD NexMed Inc. *Current Opinion in Central & Peripheral Nervous System Investigational Drugs* 2000;2(3):311-320.
- Ende A R, Lo Re V, DiNubile M J et al. Erectile dysfunction in an urban HIV-positive population. *AIDS Patient Care & Stds* 2006;20(2):75-78.
- Engelhardt P F, Daha L K, Zils T et al. Acupuncture in the treatment of psychogenic erectile dysfunction: first results of a prospective randomized placebo-controlled study. *Int J Impot Res* 2003;15(5):343-346.
- Engelson E S, Pi-Sunyer F X, Kotler D P. Effects of megestrol acetate therapy on body composition and circulating testosterone concentrations in patients with AIDS. *Int J STD AIDS* 1995;9(9):1107-1108.
- Engl T, Beecken W-D, Wolfram M et al. Urotharmacology: Current and future strategies in the treatment of erectile dysfunction and benign prostate hyperplasia. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(10):527-533.
- English J C, King D H C, Foley J P. Penile shaft hypopigmentation: Lichen sclerosus occurring after the initiation of alprostadil intracavernous injections for erectile dysfunction. *J Am Acad Dermatol* 1998;39(5 I):801-803.
- Ensign C. First-line therapies for erectile dysfunction. [Review] [8 refs]. *JAAPA* 2001;14(10):17-20.
- Erdogru T, Kocak T, Serdaroglu P et al. Evaluation and therapeutic approaches of voiding and erectile dysfunction in neurological Behcet's syndrome. *Br J Urol* 1999;162(1):147-153.
- Ernst E. Chinese herbal medicines for consumers in the West. *Focus on Alternative & Complementary Therapies* 2005;10(2):94-97.
- Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol*. 1998;159(2):433-436.
- Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.
- Esposito K, Giugliano F, Martedi E et al. High proportions of erectile dysfunction in men with the metabolic syndrome. *Diabetes Care* 2005;28(5):1201-1203.
- Evans M F. Viagra! Are we ready?. *Can Fam Physician* 1998;44:2103-2105.
- Fagan Peter J, Blum Lois H. Issues in the psychotherapeutic treatment of sexual dysfunction following radical retropubic prostatectomy. Rosen, Raymond C (Ed); Leiblum, Sandra R (Ed) 1995;(1995):400

- Fagan T C, Buttler S, Marbury T et al. Cardiovascular safety of sublingual apomorphine in patients on stable doses of oral antihypertensive agents and nitrates. *Am J Cardiol* 2001;88(7):760-766.
- Faiman C. Endocrine causes of impotence. *Cleve Clin J Med* 1993;60(6):428-429.
- Fazeli-Matin S, Montague D K, Angermeier K W et al. Penile fracture after intracavernous injection therapy. *Br J Urol* 1998;159(6):2094
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.
- Fedele D, Lamonica M, Bax G. Experience with sildenafil in diabetes. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):49-52.
- Fekete F, Fabian E. [Effectiveness and adverse effects of sildenafil in erectile dysfunction]. *Orv.Hetil.* 2000;141(3):115-118.
- Feldman H A, Goldstein I, Hatzichristou D G et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *Br J Urol* 1994;151(1):54-61.
- Feldman H A, Johannes C B, Derby C A et al. Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study. *Prev Med* 2000;30(4):328-338.
- Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.
- Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.
- Finkbeiner A. Random musing about a little blue pill. *J Ark Med Soc* 1998;95(3):100-101.
- Fishbain David A. Impact of sildenafil on male erectile disorder due to psychological factors. *Can J Psychiatry* 2000;45(1):85-86.
- Fisher W A, Rosen R C, Eardley I et al. The Multinational Men's Attitudes to Life Events and Sexuality (MALES) Study Phase II: Understanding PDE5 inhibitor treatment seeking patterns, among men with erectile dysfunction. *Br J Sex Med* 2004;1(2):150-160.
- Flack J M. The effect of doxazosin on sexual function in patients with benign prostatic hyperplasia, hypertension, or both.[see comment]. [Review] [47 refs]. *Int J Clin Pract* 2002;56(7):527-530.
- Foresta C, Caretta N, Rossato M et al. Role of androgens in erectile function. *Br J Urol* 2004;171(6 Pt 1):2358-2362.
- Foulks C J, Cushner H M. Sexual dysfunction in the male dialysis patient: pathogenesis, evaluation, and therapy. [Review] [105 refs]. *Am J Kidney Dis* 1986;8(4):211-222.
- Frank T. Tadalafil (Cialis-Lilly). *Consultant Pharmacist* 2004;19(4):280-281.
- Frank T. Vardenafil (Levitra-Bayer) GSK. *Consultant Pharmacist* 2004;19(4):278-280.
- Franzen D, Metha A, Seifert N et al. Effects of beta-blockers on sexual performance in men with coronary heart disease. A prospective, randomized and double blinded study. *Int J Impot Res* 2001;13(6):348-351.
- Fraunfelder F W, Fraunfelder F T. Scientific Challenges in Postmarketing Surveillance of Ocular Adverse Drug Reactions. *Am J Ophthalmol* 2007;143(1):
- Freemantle N. Valuing the effects of sildenafil in erectile dysfunction. *Br Med J* 2000;320(7243):1156-1157.
- Freytag S O, Stricker H, Pegg J et al. Phase I Study of Replication-Competent Adenovirus-Mediated Double-Suicide Gene Therapy in Combination with Conventional-Dose Three-Dimensional Conformal Radiation Therapy for the Treatment of Newly Diagnosed, Intermediate- to High-Risk Prostate Cancer. *Cancer Res* 2003;63(21):7497-7506.
- Fu Q, Yao D-H, Jiang Y-Q. Effect of sodium nitroprusside on hemodynamics of corpus cavernosum in Chinese. *Asian J Androl* 2001;3(4):311-313.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Fulgram P F, Cochran J S, Denman J L et al. Re: Disappointing initial results with transurethral alprostadil for erectile dysfunction in a urology practice setting [5]. *Br J Urol* 1999;162(4):1390
- Gallo L, Perdona S, Autorino R et al. Recovery of erection after pelvic urologic surgery: our experience. *Int J Impot Res* 2005;17(6):484-493.
- Gerstenbluth R E, Maniam P N, Corty E W et al. Prostate-specific antigen changes in hypogonadal men treated with testosterone replacement. *J Androl* 2002;23(6):922-926.
- Ghezzi A, Malvestiti G M, Baldini S et al. Erectile impotence in multiple sclerosis: A neurophysiological study. *J Neurol* 1995;242(3):123-126.

- Giammusso B, Gattuso U, Vanaclocha V et al. Percutaneous lumbar sympathectomy in the treatment of erectile dysfunction secondary to cavernous adrenergic hypertone: initial results of an original technique. *Arch Ital Urol Androl* 2005;77(1):5-9.
- Giampietro O, Ferdeghini M, Cerri M et al. Evaluation of the hypothalamic-pituitary-testicular interaction in diabetic males. *European J Lab Med* 1994;2(2):83-89.
- Gillies H C, Roblin D, Jackson G. Coronary and systemic hemodynamic effects of sildenafil citrate: From basic science to clinical studies in patients with cardiovascular disease. *Int J Cardiol* 2002;86(2-3):131-141.
- Ginsberg D L. Gabapentin treatment of premature ejaculation. *Primary Psychiatry* 2004;11(12):20-21.
- Ginsberg D L. Vardenafil treatment of sertraline-induced sexual dysfunction. *Primary Psychiatry* 2004;11(11):23-24.
- Ginsberg David L. Sildenafil-dihydrocodeine interaction results in prolonged erections. [References]. *Primary Psychiatry* 2003;10(2):23
- Ginzburg R, Wong Y, Fader J S. Effect of bupropion on sexual dysfunction. *Ann Pharmacother* 2005;39(12):2096-2099.
- Giuberti A, Picozzi S C, Mazza L et al. Testosterone supplementation in hypogonadal men: our personal experience. *Arch Ital Urol Androl* 2005;77(4):191-193.
- Giuliano F. Control of penile erection by the melanocortineric system: Experimental evidences and therapeutic perspectives. *J Androl* 2004;25(5):683-691.
- Giuliano F, Allard J, Rampin O et al. Pro-erectile effect of systemic apomorphine: Existence of a spinal site of action. *Br J Urol* 2002;167(1):402-406.
- Giuliano F, Hultling C, El Masry W S et al. Randomized trial of sildenafil for the treatment of erectile dysfunction in spinal cord injury. Sildenafil Study Group. *Ann Neurol*. 1999;46(1):15-21.
- Giuliano F, Pena B M, Mishra A et al. Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction. *Qual Life Res* 2001;10(4):359-369.
- Giuliano Francois, Pena Beatrice, Mishra Avani et al. "Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction": Erratum. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 2002;11(6):613-670.
- Gladh Y M, Rahgozar M, Hammar M L et al. Prevalence of symptoms possibly related to PADAM, in a Swedish population aged 55, 65 and 75 years. *Maturitas* 2005;50(3):161-166.
- Glasser S P. Revisiting erectile dysfunction in cardiovascular patients. *Cardiology Review* 2003;20(12):42-43.
- Glasser S P. Safety of PDE 5 inhibition in patients with cardiovascular disease. *Cardiology Review* 2002;19(11):32-33.
- Glenn D R J, McClure N, Lewis S E M. The hidden impact of diabetes on male sexual dysfunction and fertility. *Hum Fertil* 2003;6(4):174-179.
- Goldenberg M M. Safety and efficacy of sildenafil citrate in the treatment of male erectile dysfunction. *Clin Ther.* 1998;20(6):1033-1048.
- Goldstein I. Oral phentolamine: an alpha-1, alpha-2 adrenergic antagonist for the treatment of erectile dysfunction. [Review] [9 refs]. *Int J Impot Res* 2000;12Suppl-80.
- Gontero P, Fontana F, Zitella A et al. A prospective evaluation of efficacy and compliance with a multistep treatment approach for erectile dysfunction in patients after non-nerve sparing radical prostatectomy. *BJU Int* 2005;95(3):359-365.
- Gore J L, Swerdloff R S, Rajfer J. Androgen deficiency in the etiology and treatment of erectile dysfunction. *Urol Clin North Am* 2005;32(4):457-468.
- Govier F E, McClure R D, Kramer-Levien D. Endocrine screening for sexual dysfunction using free testosterone determinations. *Br J Urol* 1996;156(2 Pt 1):405-408.
- Graul A, Castaner J. Phentolamine Mesilate. Treatment of erectile dysfunction. *Drugs of the Future* 1998;23(7):725-728.
- Graul A I. Latest findings on the diagnosis and treatment of erectile dysfunction. *Drug News Perspect* 1996;9(9):572-575.
- Gray P B, Singh A B, Woodhouse L J et al. Dose-dependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. *Journal of Clinical Endocrinology & Metabolism* 2005;90(7):3838-3846.
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.
- Green H J, Pakenham K I, Headley B C et al. Coping and health-related quality of life in men with prostate cancer randomly assigned to hormonal medication or close monitoring. *Psychooncology* 2002;11(5):401-414.
- Green J S A, Holden S T R, Ingram P et al. An investigation of erectile dysfunction in Gwent, Wales. *BJU Int* 2001;88(6):551-553.

- Greenstein A, Plymate S R, Katz P G. Visually stimulated erection in castrated men. *Br J Urol* 1995;153(3:Pt 1):t-2.
- Gresser U, Gleiter C H. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil--review of the literature. [Review] [92 refs]. *Eur J Med Res* 2002;7(10):435-446.
- Gross A J, Sauerwein D H, Kutzenberger J et al. Penile prostheses in paraplegic men. *Br J Urol* 1996;78(2):262-264.
- Grover J K, Vats V, Ajeeta. Sildenafil (Viagra(TM)). *Medico-Legal Update* 1998;3(1-2):67-78.
- Grugni G, Carani C, Maestroni G et al. Melatonin levels in psychogenic impotence. *Hormone & Metabolic Research* 1994;26(9):440-441.
- Grunwald J E, Jacob S S, Siu K et al. Acute effects of sildenafil citrate (Viagra) on intraocular pressure in open-angle glaucoma. *Am J Ophthalmol* 2001;132(6):872-874.
- Gryglewska B, Grodzicki T. Betaxolol in elderly patients in primary care. *New Medicine* 2003;6(4):108-111.
- Guay A T, Sabharwal P, Varma S et al. Delayed diagnosis of psychological erectile dysfunction because of the presence of macroprolactinemia. *Journal of Clinical Endocrinology & Metabolism* 1996;81(7):2512-2514.
- Guay D R P. Geriatric pharmacotherapy updates. *American Journal Geriatric Pharmacotherapy* 2004;2(1):81-87.
- Guirguis W R, Maytom M C, Orr M et al. SILDENAFIL FOR ERECTILE DYSFUNCTION - A ONE-YEAR STUDY. 151st Annual Meeting of the American Psychiatric Association 1998;Toronto, Ontario, Canada. 30th May-4th June. 1998. Issue No. 63, 1998.
- Guo Y L, Zhu J C, Pan T M et al. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction. *Chinese Journal of Urology* 2001;22(7):389-394.
- Gupta N, Sawlani K K, Tripathi A K. Appropriate use of sildenafil citrate in male erectile dysfunction.[see comment]. [Review] [52 refs]. *J Assoc Physicians India* 2001;49:889-896.
- Gupta S, Salimpour P, Saenz de et al. A possible mechanism for alteration of human erectile function by digoxin: inhibition of corpus cavernosum sodium/potassium adenosine triphosphatase activity. *Br J Urol* 1998;159(5):1529-1536.
- Hackett G I. The treatment of patients with diabetes. *Int J STD AIDS* 1996;7(Suppl 3):24-26.
- Haensel S M, Klem T M, Hop W C et al. Fluoxetine and premature ejaculation: a double-blind, crossover, placebo-controlled study. *J Clin Psychopharmacol* 1998;18(1):72-77.
- Haensel S M, Rowland D L, Kallan K T. Clomipramine and sexual function in men with premature ejaculation and controls. *Br J Urol* 1996;156(4):1310-1315.
- Hamed S, Mohamed K, El-taher A et al. The sexual and reproductive health in men with generalized epilepsy: A multidisciplinary evaluation. *Int J Impot Res* 2006;18(3):287-295.
- Hammadeh M Y, Philp T. Transurethral electrovaporization of the prostate (TUVP) is effective, safe and durable. [Review] [28 refs]. *Prostate Cancer & Prostatic Diseases* 2003;6(2):121-126.
- Hammadeh M Y, Madaan S, Hines J et al. 5-year outcome of a prospective randomized trial to compare transurethral electrovaporization of the prostate and standard transurethral resection. *Urology* 2003;61(6):1166-1171.
- Hanash K A. Comparative results of goal oriented therapy for erectile dysfunction.. *Br J Urol* 1997;157(6):2135-2138.
- Harman S M. Testosterone, Sexuality, and Erectile Function in Aging Men. *J Androl* 2003;24(6 SUPPL.):S42-S45.
- Hartmann Uwe, Langer Dieter. Combination of psychosexual therapy and intrapenile injections in the treatment of erectile dysfunctions: Rationale and predictors of outcome. *J Sex Educ Ther* 1993;19(1):1-12.
- Harwood P J, Grotz M, Eardley I et al. Erectile dysfunction after fracture of the pelvis. *Journal of Bone & Joint Surgery - British Volume* 2005;87(3):281-290.
- Haslam M T. A trial of idazoxan and yohimbine in erectile dysfunction. *Sex Marital Ther* 1992;7(3):261-266.
- Hatzichristou D G. Sildenafil citrate: lessons learned from 3 years of clinical experience. [Review] [60 refs]. *Int J Impot Res* 2002;14Suppl-52.
- Hatzichristou D G. Current treatment and future perspectives for erectile dysfunction. [Review] [85 refs]. *Int J Impot Res* 1998;10Suppl-13.
- Hatzimouratidis K, Hatzichristou D. Testosterone and erectile function: an unresolved enigma. *Eur Urol* 2007;52(1):26-28.
- Hatzimouratidis K, Hatzichristou D. Phosphodiesterase Type 5 Inhibitors: The Day After. *Eur Urol* 2007;51(1):75-89.
- Hatzimouratidis K, Hatzichristou D G. A comparative review of the options for treatment of erectile dysfunction: Which treatment for which patient?. *Drugs* 2005;65(12):1621-1650.

- Hawton Keith, Catalan Jose, Fagg Joan. Sex therapy for erectile dysfunction: Characteristics of couples, treatment outcome, and prognostic factors. *Arch Sex Behav* 1992;21(2):161-175.
- Hazell P. Review of new compounds available in Australia for the treatment of attention-deficit hyperactivity disorder. *Australasian Psychiatry* 2004;12(4):369-375.
- He X Q, Hong B F, Wang X X et al. Evaluation of efficacy and safety of oral sildenafil citrate therapy for men with erectile dysfunction. *Pharmaceutical Journal of Chinese Peoples Liberation Army* 2002;18(4):205-208.
- Heaton J. New classification system for erectile dysfunction therapies. *J Androl* 1998;19(4):399-404.
- Heaton J P. Key issues from the clinical trials of apomorphine SL. *World J Urol* 2001;19(1):25-31.
- Heaton J P W, Altwein J E. The role of apomorphine SL in the treatment of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):36-38.
- Heaton J P W, Wagner Porst, Eid Wyllie. Apomorphine: An update of clinical trial results. *Int J Impot Res* 2000;12(SUPPL. 4):S67-S73.
- Heaton J P, Dean J, Sleep D J. Sequential administration enhances the effect of apomorphine SL in men with erectile dysfunction. *Int J Impot Res* 2002;14(1):61-64.
- Hellstrom W J G, Kendirci M. Type 5 Phosphodiesterase Inhibitors: Curing Erectile Dysfunction. *Eur Urol* 2006;49(6):942-945.
- Hellstrom W J, Overstreet J W, Yu A et al. Tadalafil has no detrimental effect on human spermatogenesis or reproductive hormones.[see comment]. *Br J Urol* 2003;170(3):887-891.
- Hellstrom Wayne J G, Egan Robert A, McGee Hall T et al. "Visual field defect and intracerebral hemorrhage associated with use of vardenafil (Levitra)": Comment and Reply. [References]. *Neurology* 2006;66(2):293-294.
- Herrmann H C, Chang G, Klugherz B D et al. Hemodynamic effects of sildenafil in men with severe coronary artery disease.[see comment]. *N Engl J Med* 2000;342(22):1622-1626.
- Hirshkowitz M, Moore C A, O'Connor S et al. Androgen and sleep-related erections. *J Psychosom Res* 1997;42(6):541-546.
- Hirst J F, Watson J P. Referrals aged 60+ to an inner-city psychosexual dysfunction clinic. *Sexual & Marital Therapy* 1996;11(2):131-146.
- Hofner K, Claes H, De Reijke T M et al. Tamsulosin 0.4 mg once daily: effect on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. *Eur Urol* 1999;36(4):335-341.
- Hollander J B, Gonzalez J, Norman T. Patient satisfaction with pharmacologic erection program. *Urology* 1992;39(5):439-441.
- Holt S. Natural approaches to promote sexual function: Part 1: Viagra versus a natural approach. *Alternative & Complementary Therapies* 1999;5(4):204-208.
- Holtkamp M, Weissinger F, Meierkord H. Erectile dysfunction with topiramate. *Epilepsia* 2005;46(1):166-167.
- Hong B, Ji Y H, Hong J H et al. A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report.[see comment]. *Br J Urol* 2002;168(5):2070-2073.
- Hopps C V, Mulhall J P. Novel agents for sexual dysfunction. *BJU Int* 2003;92(6):534-538.
- Horita H, Sato Y, Adachi H et al. Effects of levodopa on nocturnal penile tumescence: a preliminary study. *J Androl* 1998;19(5):619-624.
- Howes O D, Wheeler M J, Pilowsky L S et al. Sexual function and gonadal hormones in patients taking antipsychotic treatment for schizophrenia or schizoaffective disorder. *Hillside J Clin Psychiatry* 2007;68(3):361-367.
- Howes Oliver D, Smith Shubulade, Aitchison Kathy J E. Comments on "Prolactin Levels and Erectile Function in Patients Treated With Risperidone." [References]. *J Clin Psychopharmacol* 2005;25(4):393-394.
- Huang S T, Hsieh M L. Different hemodynamic responses by color Doppler ultrasonography studies between sildenafil non-responders and responders. *Asian J Androl* 2007;9(1):129-133.
- Huang W J, Chen K K, Chang L S. Correlation between voiding and erectile function in patients with symptomatic benign prostatic hyperplasia. *Journal of the Chinese Medical Association: JCMA* 2005;68(4):178-182.
- Hubler J, Szanto A, Konyves K. Methylene blue as a means of treatment for priapism caused by intracavernous injection to combat erectile dysfunction. *International Urology & Nephrology* 2003;35(4):519-521.
- Hultling C. Partners' perceptions of the efficacy of sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Clin Pract* 1999;Supplement.102-108.
- Hummel S, Paisley S, Morgan A et al. Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: A systematic review. *Health Technol Assess* 2003;7(33):157p

- Hunter R H, Joy C B, Kennedy E et al. Risperidone versus typical antipsychotic medication for schizophrenia.[update of Cochrane Database Syst Rev. 2000;(2):CD000440; PMID: 10796543]. [Review] [105 refs]. Cochrane Database Syst Rev 2003;(2):CD000440
- Hyer S L, Duckworth K, Jones C. Managing erectile disorders in diabetes: The one stop andrology clinic. *Practical Diabetes International* 1998;15(8):225-226.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Israilov S, Baniel J, Shmueli J et al. Treatment program for erectile dysfunction in patients with cardiovascular diseases. *Am J Cardiol* 2004;93(6):689-693.
- Jackson G. Erectile dysfunction and cardiovascular disease.[see comment]. [Review] [46 refs]. *Int J Clin Pract* 1999;53(5):363-368.
- Jackson G. Treatment of erectile dysfunction in patients with cardiovascular disease: Guide to drug selection. *Drugs* 2004;64(14):1533-1545.
- Jackson G. Vardenafil - PDE5 inhibitor number 3. *Int J Clin Pract* 2004;58(3):229
- Jackson G. PDE5 inhibitors: Looking beyond ED. *Int J Clin Pract* 2003;57(3):159-160.
- Jackson G. Sildenafil (Viagra): New data, new confidence in treating erectile dysfunction in the cardiovascular patient. *Int J Clin Pract* 2002;56(2):75
- Jackson G. Phosphodiesterase 5 inhibition: Effects on the coronary vasculature. *Int J Clin Pract* 2001;55(3):183-188.
- Jackson G. The metabolic syndrome and erectile dysfunction: multiple vascular risk factors and hypogonadism. *Eur Urol* 2006;50(3):426-427.
- Jackson G, Montorsi P, Cheitlin M D. Cardiovascular safety of sildenafil citrate (Viagra): an updated perspective. [Review] [52 refs]. *Urology* 2006;68(3 Suppl):47-60.
- Jackson G, Sweeney M, Osterloh I H. Sildenafil citrate (Viagra(TM)): A cardiovascular overview. *British Journal of Cardiology* 1999;6(6):325-334.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- James J S. Frequent urination, leg cramps, leg weakness, erection difficulties: HIV myelopathy amino acid study. *AIDS Treat News* 2000;(344):3-4.
- Jani A B. The effectiveness of combining hormone therapy and radiotherapy in the treatment of prostate cancer. *Expert Opin Pharmacother* 2004;5(12):2469-2477.
- Jani A B, Kao J, Heimann R et al. Hormone therapy and radiotherapy for early prostate cancer: A utility-adjusted number needed to treat (NNT) analysis. *Int J Radiat Oncol Biol Phys* 2005;61(3):687-694.
- Jarow J P, Nana-Sinkam P, Sabbagh M et al. Outcome analysis of goal directed therapy for impotence. *Br J Urol* 1996;155(5):1609-1612.
- Jeong S-J, Park K, Moon J-D et al. Bicycle saddle shape affects penile blood flow. *Int J Impot Res* 2002;14(6):513-517.
- Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.
- Jordan G H. What's new in urology. *J Am Coll Surg* 2003;197(3):444-457.
- Kadioglu A, Erdogru T, Tellaloglu S. Evaluation of penile arteries in papaverine-induced erection with color Doppler ultrasonography. *Arch Esp Urol* 1995;48(6):654-658.
- Kamel H K, Morley J E. The management of erectile dysfunction. *Reproductive Medicine Review* 2001;9(1):35-47.
- Kang B J, Lee S J, Kim M D et al. A placebo-controlled, double-blind trial of Ginkgo biloba for antidepressant-induced sexual dysfunction. *Hum Psychopharmacol* 2002;17(6):279-284.
- Kaplan S A, Meehan A G, Shah A. The age related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Br J Urol* 2006;176(4 Pt 1):1524-1527.
- Karlawish J H, Casarett D. Sildenafil for diabetic men with erectile dysfunction.[comment]. *JAMA* 1999;282(10):940-941.
- Kassouf W, Carrier S. A comparison of the International Index of Erectile Function and erectile dysfunction studies.. *BJU Int* 2003;91(7):667-669.
- Kaufman J M, Hatzichristou D G, Mulhall J P et al. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *Br J Urol* 1994;151(3):612-618.
- Keijzers G B. Aviptadil (Senatek). [Review] [36 refs]. *Curr Opin Investig Drugs* 2001;2(4):545-549.
- Keles I, Aydin G, Orkun S et al. Two clinical problems in elderly men: osteoporosis and erectile dysfunction. *Arch Androl* 2005;51(3):177-184.

- Kell P. Cardiovascular safety of sildenafil. *Int J STD AIDS* 2002;13(7):439-443.
- Keoghane S R, Sullivan M E, Miller M A W. The aetiology, pathogenesis and management of priapism. *BJU Int* 2002;90(2):149-154.
- Kerfoot W W, Park H Y, Schwartz L B et al. Characterization of calcium channel blocker induced smooth muscle relaxation using a model of isolated corpus cavernosum. *Br J Urol* 1993;150(1):249-252.
- Kernohan A F, McIntyre M, Hughes D M et al. An oral yohimbine/L-arginine combination (NMI 861) for the treatment of male erectile dysfunction: a pharmacokinetic, pharmacodynamic and interaction study with intravenous nitroglycerine in healthy male subjects. *Br J Clin Pharmacol* 2005;59(1):85-93.
- Khalaf I M, Levinson I P. Erectile dysfunction in the Africa/Middle East Region: Epidemiology and experience with sildenafil citrate (Viagra). *Int J Impot Res* 2003;15(SUPPL. 1):S1-S2.
- Khan L A. Sildenafil citrate (Viagra). *JK Pract* 2001;8(1):52-53.
- Khan M A, Raistrick M, Mikhailidis D P et al. MUSE: clinical experience. *Current Medical Research & Opinion* 2002;18(2):64-67.
- Kilic S, Ergin H, Baydinc Y C. Venlafaxine extended release for the treatment of patients with premature ejaculation: a pilot, single-blind, placebo-controlled, fixed-dose crossover study on short-term administration of an antidepressant drug. *Int J Androl* 2005;28(1):47-52.
- Kilic S, Salih M, Anafarta K et al. Adenosine: a new agent in the diagnosis of impotence. *Int J Impot Res* 1994;6(4):191-198.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Kim N N. Phosphodiesterase type 5 inhibitors: A biochemical and clinical correlation survey. *Int J Impot Res* 2003;15(SUPPL. 5):S13-S19.
- Kim N N, Dhir V, Azadzi K M et al. Pilot study of the endothelin-A receptor selective antagonist BMS-193884 for the treatment of erectile dysfunction. *J Androl* 2001;23(1):76-83.
- Kim S C, Seo K K, Lee S K et al. Comparison of the synergistic effects of tamsulosin versus phentolamine on penile erection: In vitro and in vivo studies. *Urol Res* 1999;27(6):437-444.
- Kim S C, Seo K K, Park B D et al. Risk factors for an early increase in dose of vasoactive agents for intracavernous pharmacotherapy. *Urol Int* 2000;65(4):204-207.
- Kimoto Y, Sakamoto S, Fujikawa K et al. Up-titration of vardenafil dose from 10 mg to 20 mg improved erectile function in men with spinal cord injury. *Int J Urol* 2006;13(11):1428-1433.
- Kirby R S. Report from London. *Prostate Cancer & Prostatic Diseases* 2005;8(4):299
- Kirby R S, Andersen M, Gratzke P et al. A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. *BJU Int* 2001;87(3):192-200.
- Kirby R S, O'Leary M P, Carson C. Efficacy of extended-release doxazosin and doxazosin standard in patients with concomitant benign prostatic hyperplasia and sexual dysfunction. *BJU Int* 2005;95(1):103-109.
- Kiriakova N, Kiriakov A, Schneider E et al. Therapeutic effect of essential phospholipids on functional sexual disorders in males. *Journal of the European Academy of Dermatology & Venereology* 1998;11(2):191-193.
- Kleinberg D L, Davis J M, De Coster R et al. Prolactin levels and adverse events in patients treated with risperidone.[see comment]. *J Clin Psychopharmacol* 1999;19(1):57-61.
- Kley H K, Stremmel W, Kley J B et al. Testosterone treatment of men with idiopathic hemochromatosis. *Clin Investig* 1992;70(7):566-572.
- Kloner R A. Cardiovascular risk and sildenafil. [Review] [27 refs]. *Am J Cardiol* 2000;86(2A):57F-61F.
- Kloner R A, Zusman R M. Cardiovascular effects of sildenafil citrate and recommendations for its use. [Review] [21 refs]. *Am J Cardiol* 1999;84(5B):11N-17N.
- Kloner R A, Brindis R G, Cheitlin M D et al. Roundtable discussion: Tadalafil study group. *Am J Cardiol* 2003;92(9 SUPPL. 1):58M-65M.
- Kloner R A, Hutter A M, Emmick J T et al. Time course of the interaction between tadalafil and nitrates.[see comment]. *J Am Coll Cardiol* 2003;42(10):1855-1860.
- Kloner R A, Jackson G, Emmick J T et al. Interaction between the phosphodiesterase 5 inhibitor, tadalafil and 2 alpha-blockers, doxazosin and tamsulosin in healthy normotensive men. *Br J Urol* 2004;172(5:Pt 1):t-40.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil in patients on common antihypertensive therapies. [Review] [5 refs]. *Am J Cardiol* 2003;92(9A):47M-57M.

- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil. [Review] [12 refs]. *Am J Cardiol* 2003;92(9A):37M-46M.
- Klotz T, Mathers M J, Braun M et al. Effectiveness of oral L-arginine in first-line treatment of erectile dysfunction in a controlled crossover study. *Urol Int* 1999;63(4):220-223.
- Knegtering R, Castelein S, Bous H et al. A Randomized Open-Label Study of the Impact of Quetiapine Versus Risperidone on Sexual Functioning. *J Clin Psychopharmacol* 2004;24(1):56-61.
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Knoll L D, Benson R C, Bilhartz D L et al. A randomized crossover study using yohimbine and isoxsuprine versus pentoxifylline in the management of vasculogenic impotence. *Br J Urol* 1996;155(1):144-146.
- Kobayashi T, Okuno H, Nishiyama H et al. Adult-onset idiopathic hypogonadotropic hypogonadism presented with erectile and ejaculatory disorder. *Int J Urol* 2002;9(10):604-606.
- Kramer-Levien D J. Papaverine--the medical implant. *AUAA J* 1987;7(4):13-Jun.
- Krause W, Mueller U, Mazur A. Measurement of steroid levels in saliva in a population-based survey of lifestyle, medical conditions, marriage, sex life and hormone status in aging men: A feasibility study. *Aging Male* 2002;5(4):203-215.
- Kriston L, Harms A, Berner M M. A meta-regression analysis of treatment effect modifiers in trials with flexible-dose oral sildenafil for erectile dysfunction in broad-spectrum populations. *Int J Impot Res* 2006;18(6):559-565.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Kuba R, Pohanka M, Zakopcan J et al. Sexual dysfunctions and blood hormonal profile in men with focal epilepsy. *Epilepsia* 2006;47(12):2135-2140.
- Kukreja R C, Ockaili R, Salloum F et al. Cardioprotection with phosphodiesterase-5 inhibition - A novel preconditioning strategy. *Journal of Molecular & Cellular Cardiology* 2004;36(2):165-173.
- Kunelius P, Hakkinen J, Lukkarinen O. Is high-dose yohimbine hydrochloride effective in the treatment of mixed-type impotence? A prospective, randomized, controlled double-blind crossover study. *Urology* 1997;49(3):441-444.
- Kupez D. Alprostadil for the treatment of erectile dysfunction. *J Am Acad Nurse Pract* 1996;21(5):143-145.
- Kupelian V, Shabsigh R, Travison T G et al. Is there a relationship between sex hormones and erectile dysfunction? Results from the Massachusetts Male Aging Study. *Br J Urol* 2006;176(6 Pt 1):2584-2588.
- Kvistborg A, Halse J, Bakke S et al. Long-term treatment of macroprolactinomas with CV 205-502. *Acta Endocrinol (Copenh)* 1993;128(4):301-307.
- La Pera G, Franco Giannotti C, Taggi F et al. Prevalence of sexual disorders in those young males who later become drug abusers. *J Sex Marital Ther* 2003;29(2):149-156.
- La Vignera S, Calogero A E, Cannizzaro M A et al. Erectile vascular dysfunction and analysis of the risk factors related to it. Clinical experience. *Minerva Endocrinol* 2007;32(1):17-21.
- Labbate Lawrence A. "Sex and serotonin reuptake inhibitor antidepressants": Erratum. *Psychiatr Ann* 1999;29(12):683
- Labbate Lawrence A, Croft Harry A, Oleshansky Marvin A E. Antidepressant-Related Erectile Dysfunction: Management via Avoidance, Switching Antidepressants, Antidotes, and Adaptation. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl 10):11-19.
- Labbate Lawrence A, Grimes Jamie, Hines Alan et al. Sexual dysfunction induced by serotonin reuptake antidepressants. *J Sex Marital Ther* 1998;24(1):3-12.
- Lamberg L. New drug for erectile dysfunction boon for many, 'viagravation' for some. *J Am Med Assoc* 1998;280(10):867-869.
- Larson T R. Current treatment options for benign prostatic hyperplasia and their impact on sexual function. *Urology* 2003;61(4):692-698.
- Lasaponara F, Paradiso M, Milan M G et al. Erectile dysfunction after kidney transplantation: our 22 years of experience.[see comment]. *Transplant Proc* 2004;36(3):502-504.
- Laties A, Sharlip I. Ocular safety in patients using sildenafil citrate therapy for erectile dysfunction. [Review] [81 refs]. *Br J Sex Med* 2006;3(1):12-27.
- Laties A M, Zrenner E. Viagra (sildenafil citrate) and ophthalmology. *Progress in Retinal & Eye Research* 2002;21(5):485-506.
- Laties A M, Fraunfelder F T, Flach A J et al. Ocular safety of Viagra, (sildenafil citrate). *Trans Am Ophthalmol Soc* 1999;97(pp 115-128):-128.
- Latini D M, Penson D F, Lubeck D P et al. Longitudinal differences in disease specific quality of life in men with erectile dysfunction: Results from the exploratory comprehensive evaluation of erectile dysfunction study. *Br J Urol* 2003;169(4):1437-1442.

- Laumann Edward O, West Suzanne, Glasser Dale et al. Prevalence and Correlates of Erectile Dysfunction by Race and Ethnicity Among Men Aged 40 or Older in the United States: From the Male Attitudes Regarding Sexual Health Survey. [References]. *Br J Sex Med* 2007;4(1):57-65.
- Lawless C, Cree J. Oral medications in the management of erectile dysfunction. [Review] [15 refs]. *J Am Board Fam Pract* 1998;11(4):307-314.
- Lawless C, Force R W. Sildenafil for erectile dysfunction. *J Fam Pract* 1998;47(2):97-98.
- Lawrence I G, Price D E, Howlett T A et al. Correcting impotence in the male dialysis patient: experience with testosterone replacement and vacuum tumescence therapy. *Am J Kidney Dis* 1998;31(2):313-319.
- Lea A P, Bryson H M, Balfour J A. Intracavernous alprostadil. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in erectile dysfunction. [Review] [123 refs]. *Drugs Aging* 1996;8(1):56-74.
- Lebret T, Herve J M, Gorny P et al. Efficacy and safety of a novel combination of L-arginine glutamate and yohimbine hydrochloride: a new oral therapy for erectile dysfunction. *Eur Urol* 2002;41(6):608-613.
- Lee W R. The role of androgen deprivation therapy combined with prostate brachytherapy. [Review] [31 refs]. *Urology* 2002;60(3:Suppl 1):Suppl-44.
- Lehmann K, Casella R, Blochlinger A et al. Reasons for discontinuing intracavernous injection therapy with prostaglandin E1 (alprostadil). *Urology* 1999;53(2):397-400.
- Lehmann K, John H, Kacl G et al. Variable response to intracavernous prostaglandin E1 testing for erectile dysfunction. *Urology* 1999;54(3):539-543.
- Lenze E J, Karp J F, Mulsant B H et al. Somatic symptoms in late-life anxiety: Treatment issues. *Journal of Geriatric Psychiatry & Neurology* 2005;18(2):89-96.
- Lenzi A. The role of the medical andrologist in the assisted reproduction era. *J Endocrinol Invest* 2003;26(3):268-273.
- Leslie S J, Atkins G, Oliver J J et al. No adverse hemodynamic interaction between sildenafil and red wine. *Clinical Pharmacology & Therapeutics* 2004;76(4):365-370.
- Levien T, Baker D E. Lepirudin and sildenafil citrate. *Hosp Pharm* 1998;33(12):1524-1552.
- Levine S B. A slightly different idea. *Arch Sex Behav* 2005;34(1):38-39.
- Levy M M. Benefits being missed [5]. *Can Pharm J* 2005;274(7334):109.
- Lewis R L, Sadovsky R, Eardley I et al. The efficacy of tadalafil in clinical populations. *Br J Sex Med* 2005;2(4):517-531.
- Lexchin J. New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?. *Can Fam Physician* 2002;48(SEPT.):1487-1492.
- Li J Y, Li X Y, Li M et al. Decline of serum levels of free testosterone in aging healthy Chinese men. *Aging Male* 2005;8(3-4):203-206.
- Licht M R. Use of oral sildenafil (Viagra) in the treatment of erectile dysfunction. [Review] [13 refs]. *Compr Ther* 1999;25(2):90-94.
- Lim P H C, Man K L, Foo C N et al. Clinical efficacy and safety of sildenafil citrate (Viagra) in a multi-racial population in Singapore: A retrospective study of 1520 patients. *Int J Urol* 2002;9(6):308-315.
- Lim P H C, Moorthy P, Benton K G F. The clinical safety of Viagra. *Ann N Y Acad Sci* 2002;962(pp 378-388):-388.
- Limoge J P, Olins E, Henderson D et al. Minimally invasive therapies in the treatment of erectile dysfunction in anticoagulated cases: a study of satisfaction and safety. *Br J Urol* 1996;155(4):1276-1279.
- Lin C-S, Xin Z-C, Lin G et al. Phosphodiesterases as therapeutic targets. *Urology* 2003;61(4):685-691.
- Lincoln T M. Cyclic GMP and phosphodiesterase 5 inhibitor therapies: What's on the horizon. *Mol Pharmacol* 2004;66(1):11-13.
- Lindsey I. What is the incidence of sexual dysfunction in males following rectal excision for benign and malignant diseases?. *National Research Register* 2000;2000.
- Linnet O I, Neff L L. Intracavernous prostaglandin E1 in erectile dysfunction. *Clin Investig* 1994;72(2):139-149.
- Linnebur S A. Pharmacotherapy update: What's new about old medications. *Annals of Long Term Care* 2004;12(9):34-44.
- Lipshultz L I. Injection therapy for erectile dysfunction. *N Engl J Med* 1996;334(14):913-914.
- Lipshultz L I, Kim E D. Treatment of erectile dysfunction in men with diabetes. *J Am Med Assoc* 1999;281(5):465-466.
- Llisterri J L, Lozano Vidal J V, Aznar Vicente J et al. Sexual dysfunction in hypertensive patients treated with losartan. *Am J Med Sci* 2001;321(5):336-341.

- Long R L, Sherman L S, Lombardi T J. A goal-oriented, cost-effective approach to the diagnosis and treatment of 24 male erectile dysfunction. [Review] [24 refs]. *J Ky Med Assoc* 1995;93(11):500-508.
- Loudon Julia B. Potential confusion between erectile dysfunction and premature ejaculation: An evaluation of men presenting with erectile difficulty at a sex therapy clinic. *Sexual & Marital Therapy* 1998;13(4):397-403.
- Lu J, SJ Fan J, Zhu J et al. The prospective and randomized control study of Viagra combined with Andriol in the treatment of ED in the aging male. *Chinese Journal of Andrology* 2003;17(3):194-196.
- Lue T F. Erectile dysfunction. *N Engl J Med* 2000;342(24):1802-1813.
- Lue T F. Impotence after radical pelvic surgery: physiology and management. [Review] [56 refs]. *Urol Int* 1991;46(3):259-265.
- Lukkarinen O, Tonttila P, Hellstrom P et al. Non-prosthetic surgery in the treatment of erectile dysfunction. A retrospective study of 45 impotent patients in the University of Oulu. *Scandinavian Journal of Urology & Nephrology* 1998;32(1):42-46.
- Lunenfeld B. Androgen therapy in the aging male. [Review] [110 refs]. *World J Urol* 2003;21(5):292-305.
- Maan Z, Arya M, Shergill I et al. Peyronie's disease: An update of the medical management. *Expert Opin Pharmacother* 2004;5(4):799-805.
- Maas R, Schwedhelm E, Albsmeier J et al. The pathophysiology of erectile dysfunction related to endothelial dysfunction and mediators of vascular function. *Vasc Med* 2002;7(3):213-225.
- Mahmud A, Hennessy M, Feely J. Effect of sildenafil on blood pressure and arterial wave reflection in treated hypertensive men. *J Hum Hypertens* 2001;15(10):707-713.
- Maier U, Koinig G. Andrological findings in young patients under long-term antidepressive therapy with clomipramine. *Psychopharmacology (Berl)* 1994;116(3):357-359.
- Mak R, De Backer G, Kornitzer M et al. Prevalence and correlates of erectile dysfunction in a population-based study in Belgium. *Eur Urol* 2002;41(2):132-138.
- Manasia P, Pomerol J, Ribe N et al. Comparison of the efficacy and safety of 90 mg versus 20 mg fluoxetine in the treatment of premature ejaculation. *Br J Urol* 2003;170(1):164-165.
- Manecke R G, Mulhall J P. Medical treatment of erectile dysfunction. [Review] [69 refs]. *Ann Med* 1999;31(6):388-398.
- Manganiello V. International Journal of Impotence Research: Editorial commentary. *Int J Impot Res* 2004;16(SUPPL. 1):S1-S3.
- Mann K, Klingler T, Noe S et al. Effects of yohimbine on sexual experiences and nocturnal penile tumescence and rigidity in erectile dysfunction. *Arch Sex Behav* 1996;25(1):1-16.
- Mann R D. Introduction - Tadalafil. *Journal of Drug Evaluation* 2004;2(8):223
- Mann R D. Executive summary sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):221-223.
- Manning M, Junemann K P, Scheepe J R et al. Long-term followup and selection criteria for penile revascularization in erectile failure.[see comment]. *Br J Urol* 1998;160(5):1680-1684.
- Marberger M, Roehrborn C G, Marks L S et al. Relationship among serum testosterone, sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. *Journal of Clinical Endocrinology & Metabolism* 2006;91(4):1323-1328.
- Margel D, Tal R, Livne P M et al. Predictors of erectile function improvement in obstructive sleep apnea patients with long-term CPAP treatment. *Int J Impot Res* 2005;17(2):186-190.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- Marquer C, Bressolle F. Moxisylyte: A review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic use in impotence. *Fundam Clin Pharmacol* 1998;12(4):377-387.
- Martin D J, Badwan K, Parker M et al. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. *Br J Urol* 2002;168(6):2483-2485.
- Martins F E, Reis J P. Visual erotic stimulation test for initial screening of psychogenic erectile dysfunction: a reliable noninvasive alternative?. *Br J Urol* 1997;157(1):134-139.
- Masand P S, Ashton A K, Gupta S et al. Sustained-release bupropion for selective serotonin reuptake inhibitor-induced sexual dysfunction: a randomized, double-blind, placebo-controlled, parallel-group study.[see comment]. *Am J Psychiatry* 2001;158(5):805-807.

- Matthew A G, Goldman A, Trachtenberg J et al. Sexual dysfunction after radical prostatectomy: Prevalence, treatments, restricted use of treatments and distress. *Br J Urol* 2005;174(6):2105-2110.
- Maytom M C, Derry F A, Dinsmore W W et al. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord*. 1999;37(2):110-116.
- McCarthy Barry W. Relapse prevention strategies and techniques with erectile dysfunction. *J Sex Marital Ther* 2001;27(1):1-8.
- McClellan K J, Goa K L. Transdermal testosterone. [Review] [17 refs]. *Drugs* 1998;55(2):253-258.
- McClure R D. Endocrine evaluation and therapy of erectile dysfunction. [Review] [77 refs]. *Urol Clin North Am* 1988;15(1):53-64.
- McConnell J D, Roehrborn C G, Bautista O M et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
- McCullough A R, Barada J H, Fawzy A et al. Achieving treatment optimization with sildenafil citrate (Viagra) in patients with erectile dysfunction. *Urology* 2002;60(2 Suppl 2):28-38.
- McKinlay J B. The worldwide prevalence and epidemiology of erectile dysfunction. [Review] [17 refs]. *Int J Impot Res* 2000;12Suppl-S11.
- McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992;9:265A
- McMahon C G. Nonsurgical treatment of cavernosal venous leakage. *Urology* 1997;49(1):97-100.
- McMahon C G. Treatment of Erectile Dysfunction with Chronic Dosing of Tadalafil. *Eur Urol* 2006;50(2):215-217.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- McMahon C G, Stuckey B G A, Andersen M et al. Efficacy of sildenafil citrate (viagra) in men with premature ejaculation. *Br J Sex Med* 2005;2(3):368-375.
- Mealy N E. NBI-69733. *Drugs of the Future* 2004;29(6):642
- Mealy N E. GPI-1485. *Drugs of the Future* 2004;29(6):640
- Mealy N E. EMR-62203. *Drugs of the Future* 2004;29(6):639
- Mealy N E. Dasantafil. *Drugs of the Future* 2004;29(6):633
- Mealy N E. DA-8159. *Drugs of the Future* 2004;29(6):631
- Mealy N E. Avanafil. *Drugs of the Future* 2004;29(6):628-629.
- Mealy N E. Alprostadil cream. *Drugs of the Future* 2004;29(6):626-627.
- Mealy N E, Bayes M. PT-141. *Drugs of the Future* 2004;29(11):1177
- Mealy N E, Bayes M. ABT-724. *Drugs of the Future* 2005;30(9):935
- Mehdiyev T V. Intracavernous injection probe of vasoactive preparations in the diagnosis of erectile dysfunctions in patients with diabetes mellitus. *Azerbaijzhanskii Meditsinskii Zhurnal* 2002;(pp 17-19):-19.
- Meinhardt W, Kropman R F, Vermeij P et al. The influence of medication on erectile function. *Int J Impot Res* 1997;9(1):17-26.
- Melman A, Bar-Chama N, McCullough A et al. The first human trial for gene transfer therapy for the treatment of erectile dysfunction: preliminary results. *Eur Urol* 2005;48(2):314-318.
- Mendelson W B, Gujavarty K, Slintak C et al. Reported sexual dysfunction in obstructive sleep apnea patients. *Ann Clin Psychiatry* 1990;2(2):93-101.
- Merrick G S, Wallner K E, Butler W M. Minimizing prostate brachytherapy-related morbidity. *Urology* 2003;62(5):786-792.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Meyhoff H H, Rosenkilde P, Bodker A. Non-invasive management of impotence with transcutaneous nitroglycerin. *Br J Urol* 1992;69(1):88-90.
- Migliari R, Muscas G, Usai E. Effect of Casodex on sleep-related erections in patients with advanced prostate cancer. *Br J Urol* 1992;148(2 I):338-341.
- Mikhail N. Efficacy and safety of sildenafil in patients with congestive heart failure [7]. *Arch Intern Med* 2004;164(18):2067-2068.
- Millard R J, Stricker P D, Lynch W J et al. Risks of self-injection therapy for impotence. *Med J Aust* 1996;165(2):117-118.
- Miller D C, Wei J T, Dunn R L et al. Use of medications or devices for erectile dysfunction among long-term prostate cancer treatment survivors: potential influence of sexual motivation and/or indifference. *Urology* 2006;68(1):166-171.

- Miller N, Smolkin M E, Bissonette E et al. Undetectable prostate specific antigen at 6-12 months: a new marker for early success in hormonally treated patients after prostate brachytherapy. *Cancer* 2005;103(12):2499-2506.
- Mills R D, Sethia K K. Maximisation of the erectile response in the investigation of impotence. *Int J Impot Res* 1999;11(1):29-32.
- Mills T M, Lewis R W. The role of androgens in the erectile response: A 1999 perspective. *Mol Urol* 1999;3(2):75-80.
- Milman H A, Arnold S B, Rivera-Miranda G et al. Neurologic, psychological, and aggressive disturbances with sildenafil. *Ann Pharmacother* 2002;36(7-8):1129-1134.
- Mirone V G, Stief C G. Efficacy of apomorphine SL in erectile dysfunction.[erratum appears in *BJU Int* 2002 Jan;89(1):140]. [Review] [11 refs]. *BJU Int* 2001;88(Suppl 3):25-29.
- Mittleman M A, Glasser D B, Orazem J. Clinical trials of sildenafil citrate (Viagra) demonstrate no increase in risk of myocardial infarction and cardiovascular death compared with placebo. *Int J Clin Pract* 2003;57(7):597-600.
- Mittleman M M, Rosen R C. Evaluating clinical trial design results and analysis of drug treatments for erectile dysfunction. *Int J Impot Res* 2003;15(4):x-xiii.
- Miwa Y, Kaneda T, Yokoyama O. Correlation between the Aging Males' Symptoms Scale and sex steroids, gonadotropins, dehydroepiandrosterone sulfate, and growth hormone levels in ambulatory men. *Br J Sex Med* 2006;3(4):723-726.
- Mohr B A, Bhasin S, Link C L et al. The effect of changes in adiposity on testosterone levels in older men: longitudinal results from the Massachusetts Male Aging Study. *Eur J Endocrinol* 2006;155(3):443-452.
- Montejo A L, Llorca G, Izquierdo J A et al. Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction.[see comment]. *Hillside J Clin Psychiatry* 2001;62Suppl-21.
- Montejo-Gonzalez A L, Llorca G, Izquierdo J A et al. SSRI-induced sexual dysfunction: fluoxetine, paroxetine, sertraline, and fluvoxamine in a prospective, multicenter, and descriptive clinical study of 344 patients. *Journal of Sex and Marital Therapy* 1997;23(3):176-194.
- Montorsi F. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil: Editorial comment. *Eur Urol* 2004;45(4):508-509.
- Montorsi F, Althof S E. Partner responses to sildenafil citrate (Viagra) treatment of erectile dysfunction. *Urology* 2004;63(4):762-767.
- Montorsi F, Burnett A L. Erectile dysfunction after radical prostatectomy. *BJU Int* 2004;93(1):1-2.
- Montorsi F, Briganti A, Salonia A et al. Current and Future Strategies for Preventing and Managing Erectile Dysfunction Following Radical Prostatectomy. *Eur Urol* 2004;45(2):123-133.
- Montorsi F, Briganti A, Salonia A et al. Can Phosphodiesterase Type 5 Inhibitors Cure Erectile Dysfunction?. *Eur Urol* 2006;49(6):979-986.
- Montorsi F, Guazzoni G, Bocciardi A et al. Improved minimally-invasive assessment of penile haemodynamics: the combination of colour Doppler sonography and injection-stimulation test. *Int J Impot Res* 1995;7(1):33-40.
- Montorsi F, Perani D, Anchisi D et al. Brain activation patterns during video sexual stimulation following the administration of apomorphine: results of a placebo-controlled study. *Eur Urol* 2003;43(4):405-411.
- Montorsi F, Salonia A, Briganti A et al. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47(5):612-621.
- Montorsi F, Strambi L F, Guazzoni G et al. Effect of yohimbine-trazodone on psychogenic impotence: a randomized, double-blind, placebo-controlled study. *Urology* 1994;44(5):732-736.
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol*. 2002;26
- Morales A. Men's aging and sexual disorders: An update on diagnosis and treatment. *Rev Endocr Metab Disord* 2005;6(2):85-92.
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Morales Alvaro, Condra Michael, Heaton Jeremy P et al. Impotence: Organic factors and management approach. *Sexual & Marital Therapy* 1991;6(2):97-106.
- Moreira E D, Lbo C F, Diament A et al. Incidence of erectile dysfunction in men 40 to 69 years old: results from a population-based cohort study in Brazil. *Urology* 2003;61(2):431-436.
- Moreira E D, Lisboa Lobo C F, Villa M et al. Prevalence and correlates of erectile dysfunction in Salvador, northeastern Brazil: a population-based study. *Int J Impot Res* 2002;14Suppl-9.
- Morley John E, Kaiser Fran E. Aging and sexuality. Vellas, Bruno (Ed); Albareda, J 1992;-L(Ed):1992-165.

- Mulhall J P. Deciphering erectile dysfunction drug trials. [Review] [35 refs]. *Br J Urol* 2003;170(2 Pt 1):353-358.
- Mulhall J P. Sublingual apomorphine for the treatment of erectile dysfunction. [Review] [22 refs]. *Expert Opin Investig Drugs* 2002;11(2):295-302.
- Mulhall J P, bdel-Moneim A, Abobakr R et al. Improving the accuracy of vascular testing in impotent men: correcting hemodynamic alterations using a vasoactive medication re-dosing schedule. *Br J Urol* 2001;166(3):923-926.
- Mulhall J P, Daller M, Traish A M et al. Intracavernosal forskolin: Role in management of vasculogenic impotence resistant to standard 3-agent pharmacotherapy. *Br J Urol* 1997;158(5):1752-1759.
- Mulhall J P, Levine L A, Junemann K P. Erection hardness: a unifying factor for defining response in the treatment of erectile dysfunction. [Review] [37 refs]. *Urology* 2006;68(3 Suppl):17-25.
- Mulligan T, Schmitt B. Testosterone for erectile failure. *J Gen Intern Med* 1993;8(9):517-521.
- Mulligan T, Frick M F, Zuraw Q C et al. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 2006;60(7):762-769.
- Muneer A, Ralph D J, Minhas S. Sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):225-246.
- Munoz M, Bancroft J, Beard M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 2. The erectile response to erotic stimuli in men with erectile dysfunction, in relation to age and in comparison with normal volunteers. *Psychopharmacology (Berl)* 1994;115(4):471-477.
- Munoz M, Bancroft J, Turner M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 1. The erectile response to erotic stimuli in volunteers. *Psychopharmacology (Berl)* 1994;115(4):463-470.
- Murphy A M, O'Leary M. Failure of the Ambicor inflatable penile prosthesis to deflate. *Int J Impot Res* 2005;17(3):291-292.
- Murphy J C, Srinivas S, Terris M K. Flutamide administration at 500 mg daily has similar effects on serum testosterone to 750 mg daily. *J Androl* 2004;25(4):630-634.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nakata M, Takashima S, Kaminou T et al. Embolotherapy for venous impotence: use of ethanol. *Journal of Vascular & Interventional Radiology* 2000;11(8):1053-1057.
- Nakonezny P A, Byerly M J, Rush A J. The relationship between serum prolactin level and sexual functioning among male outpatients with schizophrenia or schizoaffective disorder: A randomized double-blind trial of risperidone vs. quetiapine. *J Sex Marital Ther* 2007;33(3):203-216.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Nandwani R, Gourlay Y. Possible interaction between sildenafil and HIV combination therapy [1]. *Lancet* 1999;353(9155):840
- Narayan P, Trachtenberg J, Lepor H et al. A dose-response study of the effect of flutamide on benign prostatic hyperplasia: results of a multicenter study. *Urology* 1996;47(4):497-504.
- Neese Leah E, Schover Leslie R, Klein Eric A et al. Finding help for sexual problems after prostate cancer treatment: A phone survey of men's and women's perspectives. [References]. *Psychooncology* 2003;12(5):463-473.
- Nehra A, Blute M L, Barrett D M et al. Rationale for combination therapy of intraurethral prostaglandin E(1) and sildenafil in the salvage of erectile dysfunction patients desiring noninvasive therapy. *Int J Impot Res* 2002;14(Suppl 1):38-42.
- Neumeyer K, Kirkpatrick P. Tadalafil and vardenafil. *Nat Rev Genet* 2004;3(4):295-296.
- Nicolosi A, Moreira E D, Shirai M et al. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology* 2003;61(1):201-206.
- Nieschlag E, Swerdloff R, Behre H M et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *Int J Androl* 2005;28(3):125-127.
- Nurnberg H G, Hensley P L. Sildenafil citrate for the management of antidepressant-associated erectile dysfunction. *Hillside J Clin Psychiatry* 2003;64Suppl-5.
- Nurnberg H G, Gelenberg A, Hargreave T B et al. Efficacy of sildenafil citrate for the treatment of erectile dysfunction in men taking serotonin reuptake inhibitors. *Am J Psychiatry* 2001;158(11):1926-1928.
- Nurnberg H G, Seidman S N, Gelenberg A J et al. Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. *Urology* 2002;60(2 Suppl 2):58-66.

- Nurnberg H, George. Erectile Dysfunction and Comorbid Depression: Prevalence, Treatment Strategies, and Associated Medical Conditions. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl10):3-4.
- Nurnberg H, George Hensley, Paula L et al. Sildenafil in the treatment of sexual dysfunction induced by selective serotonin reuptake inhibitors: An overview. [References]. *CNS Drugs* 2000;13(5):321-335.
- O'Sullivan J D. Apomorphine as an alternative to sildenafil in Parkinson's disease. [References]. *Journal of Neurology, Neurosurgery & Psychiatry* 2002;72(5):681
- O'Sullivan J D, Hughes A J. Apomorphine-induced penile erections in Parkinson's disease. *Mov Disord* 1998;13(3):536-539.
- Oefelein M G. Time to normalization of serum testosterone after 3-month luteinizing hormone-releasing hormone agonist administered in the neoadjuvant setting: implications for dosing schedule and neoadjuvant study consideration.[see comment]. *Br J Urol* 1998;160(5):1685-1688.
- Ohebshalom M, Mulhall J P. Transdermal and topical pharmacotherapy for male sexual dysfunction. *Expert Opinion on Drug Delivery* 2005;2(1):115-120.
- Ojumu A, Dobs A S. Is Hypogonadism a Risk Factor for Sexual Dysfunction?. *J Androl* 2003;24(6 SUPPL.):S46-S51.
- Onu P E. Depot medroxyprogesterone in the management of benign prostatic hyperplasia. *Eur Urol* 1995;28(3):229-235.
- Opsomer R J, Wese F X, De Groote P et al. The external vacuum device in the management of erectile dysfunction. *Acta Urol Belg* 1997;65(4):13-16.
- Ormod D, Easthope S E, Figgitt D P. Vardenafil.[erratum appears in *Drugs Aging* 2002;19(11):886]. [Review] [30 refs]. *Drugs Aging* 2002;19(3):217-227.
- Osterloh I H, Riley A. Clinical update on sildenafil citrate. [Review] [58 refs]. *Br J Clin Pharmacol* 2002;53(3):219-223.
- Osterloh I H, Collins M, Wicker P et al. Sildenafil citrate (VIAGRA): overall safety profile in 18 double-blind, placebo controlled, clinical trials. [Review] [0 refs]. *Int J Clin Pract* 1999;Supplement.102-105.
- Owens J. Seeking selectivity. *Nat Rev Genet* 2005;4(2):106
- Ozbek E, Yurekli M, Soyly A et al. The role of adrenomedullin in varicocele and impotence. *BJU Int* 2000;86(6):694-698.
- Ozdel O, Oguzhanoglu A, Oguzhanoglu N K et al. A follow-up study of male sexual disorders: The neurophysiological assessments, anxiety-depression levels, and response to fluoxetine treatment [10]. *J Clin Psychopharmacol* 2004;24(4):461-463.
- Padma-Nathan H, Eardley I, Kloner R A et al. A 4-year update on the safety of sildenafil citrate (Viagra). [Review] [88 refs]. *Urology* 2002;60(2:Suppl 2):Suppl-90.
- Pagani E, Glina S, Puech-Leao P et al. Anxiety and high plasma catecholamines do not impair pharmacologically-induced erection of psychogenic erectile dysfunctional patients. *Int J Impot Res* 2003;15(4):282-286.
- Paice Judith A, Penn Richard D, Ryan Will G. Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. *J Pain Symptom Manage* 1994;9(2):126-131.
- Paick J S, Yang J H, Kim S W et al. Severity of erectile dysfunction in married impotent patients: interrelationship with anthropometry, hormones, metabolic profiles and lifestyle. *Int J Urol* 2007;14(1):48-53.
- Paick J S, Yang J H, Kim S W et al. The role of prolactin levels in the sexual activity of married men with erectile dysfunction. *BJU Int* 2006;98(6):1269-1273.
- Paick S H, Meehan A, Lee M et al. The relationship among lower urinary tract symptoms, prostate specific antigen and erectile dysfunction in men with benign prostatic hyperplasia: results from the proscar long-term efficacy and safety study. *Br J Urol* 2005;173(3):903-907.
- Palha A P, Gomes F A, Martins A S et al. [Clinical, multicentric, and open study to evaluate the efficacy of and tolerance to sildenafil in patients with erectile dysfunction]. *Acta Med Port.* 2002;15(4):249-256.
- Pan C C, Lin J S N, Wong W S. Comparison of effect on erection between vacuum constriction devices and intra-cavernous injection of prostaglandin E1. *Asian J Surg* 1997;20(2):162-166.
- Papatsoris A G, Deliveliotis C, Singer C et al. Erectile dysfunction in Parkinson's disease. *Urology* 2006;67(3):447-451.
- Parazzini F, Menchini Fabris F, Bortolotti A et al. Frequency and determinants of erectile dysfunction in Italy. *Eur Urol* 2000;37(1):43-49.
- Paris G, Sponsel W E, Sandoval S S et al. Sildenafil increases ocular perfusion. *Int Ophthalmol* 2001;23(4-6):355-358.
- Parker C. The Scandinavian Prostate Cancer Group Study: The case for conservative management. *BJU Int* 2005;96(7):952-953.

- Parsons J K, Marschke P, Maples P et al. Effect of methylprednisolone on return of sexual function after nerve-sparing radical retropubic prostatectomy. *Urology* 2004;64(5):987-990.
- Patankar M. Sildenafil citrate. *J Indian Med Assoc* 2000;98(12):
- Patterson D, Kloner R, Effron M et al. The effect of tadalafil on the time to exercise-induced myocardial ischaemia in subjects with coronary artery disease. *Br J Clin Pharmacol* 2005;60(5):459-468.
- Pegge N C, Twomey A M, Vaughton K et al. The role of endothelial dysfunction in the pathophysiology of erectile dysfunction in diabetes and in determining response to treatment. *Diabet Med* 2006;23(8):873-878.
- Penninga E, Jensen B A, Hansen P B et al. Anagrelide treatment in 52 patients with chronic myeloproliferative diseases. *Clinical & Laboratory Haematology* 2004;26(5):335-340.
- Penson D F, Feng Z, Kuniyuki A et al. General quality of life 2 years following treatment for prostate cancer: what influences outcomes? Results from the prostate cancer outcomes study. [see comment]. *Am J Clin Oncol* 2003;21(6):1147-1154.
- Perez Martin A, Skinner Eila C, Meyerowitz Beth E E. Sexuality and intimacy following radical prostatectomy: Patient and partner perspectives. [References]. *Health Psychol* 2002;21(3):288-293.
- Perimenis P, Athanasopoulos A, Papathanasopoulos P et al. Gabapentin in the management of the recurrent, refractory, idiopathic priapism. *Int J Impot Res* 2004;16(1):84-85.
- Pescatori E S, Calpista A, Artibani W et al. Self-injection devices for intracavernosal pharmacotherapy: operational classification and safety considerations. *Int J Impot Res* 1996;8(2):53-57.
- Pescatori E S, Silingardi V, Galeazzi G M et al. Audiovisual sexual stimulation by virtual glasses is effective in inducing complete cavernosal smooth muscle relaxation: a pharmacocavernosometric study. *Int J Impot Res* 2000;12(2):83-88.
- Phelps J S, Jain A, Monga M. The PsychoedPlusMed approach to erectile dysfunction treatment: the impact of combining a psychoeducational intervention with sildenafil. *J Sex Marital Ther* 2004;30(5):305-314.
- Philipp M, Kohnen R, Benkert O. A comparison study of moclobemide and doxepin in major depression with special reference to effects on sexual dysfunction. *Int Clin Psychopharmacol* 1993;7(3-4):149-153.
- Philipp M, Tiller J W G, Baier D et al. Comparison of moclobemide with selective serotonin reuptake inhibitors (SSRIs) on sexual function in depressed adults. *Eur Neuropsychopharmacol* 2000;10(5):305-314.
- Phillips B G, Kato M, Pesek C A et al. Sympathetic activation by sildenafil. [see comment]. *Circulation* 2000;102(25):3068-3073.
- Pirotte B, de Tullio P, Antoine M-H et al. New insights into the development of ATP-sensitive potassium channel openers. *Expert Opinion on Therapeutic Patents* 2005;15(5):497-504.
- Pisters L L, von Eschenbach A C, Scott S M et al. The efficacy and complications of salvage cryotherapy of the prostate. *J Urol* 1997;157(3):921-925.
- Pittler M, Ernst E. Trials have shown yohimbine is effective for erectile dysfunction [14]. *Br Med J* 1998;317(7156):478
- Polak K, Wimpissinger B, Berisha F et al. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. *Invest Ophthalmol Vis Sci* 2003;44(11):4872-4876.
- Pollack Mark H, Reiter Stewart, Hammerness Paul. Genitourinary and sexual adverse effects of psychotropic medication. *Int J Psychiatry Med* 1992;22(4):305-327.
- Pomara G, Morelli G, Montorsi F et al. Re: Montorsi F, Salonia A, Briganti A, Barbieri L, Zanni G, Surdi N, Cestari A, Montorsi P, Rigatti P. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47:612-21 (multiple letters). *Eur Urol* 2005;48(2):345-346.
- Pomerantz J M. Viagra and medical necessity. *Drug Benefit Trends* 2002;14(10):33+40
- Pommerville P. Drug treatments for erectile dysfunction: An update. *Geriatrics and Aging* 2004;7(6):10-16.
- Pommerville P J. From bedside to bed. Recovery of sexual function after prostate cancer. *Can Fam Physician* 2005;51(JULY):941-943+948.
- Porst H. IC351 (tadalafil, Cialis): update on clinical experience. [Review] [12 refs]. *Int J Impot Res* 2002;14Suppl-64.
- Porst H. Phosphodiesterase type-5 inhibitors: A critical comparative analysis. *Eau Update Series* 2004;2(2):56-63.
- Porst H C. Re-dosing of prostaglandin-E1 versus prostaglandin-E1 plus phentolamine in male erectile dysfunction: a dynamic color power Doppler study. *Int J Impot Res* 2000;12(2):134-135.

- Porst H, Giuliano F, Glina S et al. Evaluation of the Efficacy and Safety of Once-a-Day Dosing of Tadalafil 5 mg and 10 mg in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial. *Eur Urol* 2006;50(2):351-359.
- Pouaha J, Martin S, Reichert-Penetrat S et al. Thalidomide and sexual dysfunction in men.[comment]. *Br J Dermatol* 2002;146(6):1112-1113.
- Power-Smith Parsley. Beneficial sexual side-effects from fluoxetine. *Br J Psychiatry Suppl* 1994;164 Feb 1994, 249-250. [http249-250](http://249-250).
- Pradeep C, Car N, Metelko Z. Impotence in diabetic men. *Diabetol Croat* 1996;25(2):61-68.
- Pratt-Ubunama M N, Nishizaka M K, Calhoun D A. Aldosterone antagonism: An emerging strategy for effective blood pressure lowering. *Curr Hypertens Rep* 2005;7(3):186-192.
- Preskorn S H. Duloxetine. *Journal of Psychiatric Practice* 2004;10(6):375-385.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Prins J, Blanker M H, Bohnen A M et al. Prevalence of erectile dysfunction: A systematic review of population-based studies. *Int J Impot Res* 2002;14(6):422-432.
- Priyadarshi S. Oral terbutaline in the management of pharmacologically induced prolonged erection. *Int J Impot Res* 2004;16(5):424-426.
- Pryor J. Vardenafil: update on clinical experience. [Review] [10 refs]. *Int J Impot Res* 2002;14(Suppl-9).
- Pryor J P. Orgasmic and ejaculatory dysfunction. *Sexual & Relationship Therapy* 2002;17(1):87-95.
- Qian L X, Wu H F, Xu H et al. Multi-center Evaluation of Efficacy and Safety of Oral Mesylate Phentolamine for the Treatment of Erectile Dysfunction. *Int J Androl* 2001;7(5):302-305.
- Quinn M J, Jefferson K, Persad R. Benign prostatic hyperplasia and sexual dysfunction [3] (multiple letters). *Lancet* 2003;361(9368):1562
- Quirk J, Thornton M, Neumeyer K et al. Cardiology and vascular disorders. *Nat Rev Genet* 2004;3(7 SUPPL.):S12-S17.
- Radomski S B, Herschorn S, Rangaswamy S. Topical minoxidil in the treatment of male erectile dysfunction. *Br J Urol* 1994;151(5):1225-1226.
- Ramasubbu R. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Reffellmann T, Kloner R A. Effects of sildenafil on myocardial infarct size, microvascular function, and acute ischemic left ventricular dilation. *Cardiovasc Res* 2003;59(2):441-449.
- Reyes J A, Tan D A, Quimpo J A et al. The Philippine Male Aging Survey. *Aging Male* 2004;7(3):227-235.
- Rhoden E L, Estrada C, Levine L et al. The value of pituitary magnetic resonance imaging in men with hypogonadism.[see comment]. *Br J Urol* 2003;170(3):795-798.
- Richardson J D. Intracorporeal injections for the treatment of impotence. *Med J Aust* 1991;155(10):688
- Richter S, Vardi Y, Ringel A et al. Intracavernous injections: still the gold standard for treatment of erectile dysfunction in elderly men. *Int J Impot Res* 2001;13(3):172-175.
- Riley Alan. Oral treatments for erectile dysfunction. *Int J STD AIDS* 1996;7(Suppl 3):16-18.
- Rizvi K, Hampson J P, Harvey J N. Do lipid-lowering drugs cause erectile dysfunction? A systematic review.[see comment]. [Review] [35 refs]. *Fam Pract* 2002;19(1):95-98.
- Roach M, Winter K, Michalski J M et al. Penile bulb dose and impotence after three-dimensional conformal radiotherapy for prostate cancer on RTOG 9406: findings from a prospective, multi-institutional, phase I/II dose-escalation study. *Int J Radiat Oncol Biol Phys* 2004;60(5):1351-1356.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Roizenblatt S, Guilleminault C, Poyares D et al. A double-blind, placebo-controlled, crossover study of sildenafil in obstructive sleep apnea. *Arch Intern Med* 2006;166(16):1763-1767.

- Rojewski M T, Korper S, Schrezenmeier H. Arsenic trioxide therapy in acute promyelocytic leukemia and beyond: From bench to bedside. *Leuk Lymphoma* 2004;45(12):2387-2401.
- Rosano G M, Marazzi G, Patrizi R et al. Comparison of trimetazidine plus sildenafil to chronic nitrates in the control of myocardial ischemia during sexual activity in patients with coronary artery disease. *Am J Cardiol* 2005;95(3):327-331.
- Rosas-Vargas H, Coral-Vazquez R M, Tapia R et al. Glu298Asp endothelial nitric oxide synthase polymorphism is a risk factor for erectile dysfunction in the Mexican Mestizo population. *J Androl* 2004;25(5):728-732.
- Rose V L. Sildenafil in the treatment of erectile dysfunction. *Am Fam Physician* 1998;58(1):268
- Rosen R C, Kostis J B. Overview of phosphodiesterase 5 inhibition in erectile dysfunction. *Am J Cardiol* 2003;92(9 SUPPL. 1):9M-18M.
- Rosen R C, Lane R M, Menza M. Effects of SSRIs on sexual function: a critical review.[see comment]. [Review] [255 refs]. *J Clin Psychopharmacol* 1999;19(1):67-85.
- Rosen R C, Shabsigh R, Kuritzky L et al. The efficacy of tadalafil in improving sexual satisfaction and overall satisfaction in men with mild, moderate, and severe erectile dysfunction: A retrospective pooled analysis of data from randomized, placebo-controlled clinical trials. *Current Medical Research & Opinion* 2005;21(11):1701-1709.
- Rosen Raymond C. Erectile dysfunction: The medicalization of male sexuality. *Clin Psychol Rev* 1996;16(6):497-519.
- Rosen Raymond C, Leiblum Sandra R. Treatment of male erectile disorder: Current options and dilemmas. *Sexual & Marital Therapy* 1993;8(1):5-8.
- Rosen Raymond C, Leiblum Sandra, Risa. Erectile disorders: An overview of historical trends and clinical perspectives. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Rosenthal B D, May N R, Metro M J et al. Adjunctive use of AndroGel (testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone. *Urology* 2006;67(3):571-574.
- Rowland D L, Greenleaf W J, Dorfman L J et al. Aging and sexual function in men. *Arch Sex Behav* 1993;22(6):545-557.
- Rowland D L, Kallan K, Slob A K. Yohimbine, erectile capacity, and sexual response in men. *Arch Sex Behav* 1997;26(1):49-62.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382
- Ruof J, Graf-Morgenstern M, Muller M J. Quality of life in patients with erection difficulties: Evaluation of a German version of the "Quality of life measure for men with erection difficulties" (QoL-Med). *Aktuel Urol* 2001;32(1):21-26.
- Ryder R E, Close C F, Moriarty K T et al. Impotence in diabetes: aetiology, implications for treatment and preferred vacuum device. *Diabet Med* 1992;9(10):893-898.
- Saad F, Grahl A S, Aversa A et al. Effects of testosterone on erectile function: implications for the therapy of erectile dysfunction. *BJU Int* 2007;99(5):988-992.
- Saad F, Hoesl C E, Oettel M et al. Dehydroepiandrosterone treatment in the aging male - What should the urologist know?. *Eur Urol* 2005;48(5):724-733.
- Sadock Virginia A. A sexually compulsive male with erectile dysfunction treated with Viagra: Discussion. *Journal of Sex Education & Therapy* 1998;23(4):275-277.
- Safarinejad M R. Prevalence and risk factors for erectile dysfunction in a population-based study in Iran. *Int J Impot Res* 2003;15(4):246-252.
- Sairam K, Kulinskaya E, Boustead G B et al. Prevalence of undiagnosed prostate cancer in men with erectile dysfunction. *BJU Int* 2002;89(3):261-263.
- Sak S C, Eardley I. What is the relationship between benign prostatic hyperplasia and sexual function?. *Sexual & Relationship Therapy* 2004;19(4):431-443.
- Sakamoto H, Shimada M, Yoshida H. Hemodynamic evaluation of the penile arterial system in patients with erectile dysfunction using power doppler imaging. *Urology* 2002;60(3):480-484.
- Saks Bonnie R. A sexually compulsive male with erectile dysfunction treated with Viagra: Case report. *Journal of Sex Education & Therapy* 1998;23(4):271-274.
- Salonia A, Barbieri L, Chen J et al. Comparison of the effect of sildenafil and apomorphine SL on nocturnal erections in healthy volunteers: a placebo-controlled study. *Eur Urol* 2005;47(4):524-529.
- Salonia A, Maga T, Colombo R et al. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. *Br J Urol* 2002;168(6):2486-2489.
- Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr.Med Res Opin.* 2003;19(4):241-262.

- Salonia Andrea, Briganti Alberto, Montorsi Piero et al. Safety and tolerability of oral erectile dysfunction treatments in the elderly. [References]. *Drugs and Aging* 2005;22(4):323-338.
- Samarasinghe Y, Rivas-Toro H. HEART UK 18th annual medical and scientific meeting: From diabetes to mixed hyperlipidaemias. *British Journal of Cardiology* 2004;11(5):364-365.
- Sathe R S, Komisaruk B R, Ladas A K et al. Naltrexone-induced augmentation of sexual response in men. *Arch Med Res* 2001;32(3):221-226.
- Sato Y, Horita H, Adachi H et al. Effect of oral administration of prostaglandin E1 on erectile dysfunction. *Br J Urol* 1997;80(5):772-775.
- Sato Y, Suzuki N, Adachi H et al. Evaluation of the alleviative action of neurotrophin for penile pain associated with intracavernous injection of prostaglandin E1 assessed using the visual analogue scale. *Int J Impot Res* 1998;10(1):1-3.
- Savoca G, Silvestre G, Belgrano E. Intracavernosal injection therapy and surgical therapy in diabetic patients with erectile dysfunction. [Review] [26 refs]. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):53-57.
- Scalvini T, Martini P R, Obici L et al. Infertility and Hypergonadotropic Hypogonadism as First Evidence of Hereditary Apolipoprotein A-I Amyloidosis. *Br J Urol* 2007;
- Schiavi Raul C, Schanzer Harry, Sozio Giampaolo et al. Erectile function and penile blood pressure in diabetes mellitus. *J Sex Marital Ther* 1994;20(2):119-124.
- Schimmer A D, Ali V, Stewart A K et al. Male sexual function after autologous blood or marrow transplantation. *Biology of Blood & Marrow Transplantation* 2001;7(5):279-283.
- Scholz M, Strum S. Re: Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: results of a prospective, randomized trial.[comment]. *Br J Urol* 1999;161(6):1914-1915.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266
- Schrader S, Mills A, Schepeler M et al. Improvement in sexual functioning and satisfaction in nonresponders to testosterone gel: clinical effectiveness in hypogonadal, HIV-positive males. *Clin Cornerstone* 2005;7 Suppl 4S26-S31.
- Schroder F H, Whelan P, De Reijke T M et al. Metastatic prostate cancer treated by flutamide versus cyproterone acetate. Final analysis of the "European Organization for Research and Treatment of Cancer" (EORTC) Protocol 30892. *Eur Urol* 2004;45(4):457-464.
- Schultheiss D, Stief C G. Physiology and pathophysiology of erection: Consequences for present medical therapy of erectile dysfunction. *Andrologia* 1999;31(SUPPL. 1):59-64.
- Schwartz E J, Wong P, Graydon R J. Sildenafil preserves intracorporeal smooth muscle after radical retropubic prostatectomy. *Br J Urol* 2004;171(2 I):771-774.
- Seftel A. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(6):2297-2300.
- Seftel A. Effect of lifestyle changes on erectile dysfunction in obese men. A randomized controlled trial. *Br J Urol* 2005;173(2):544-545.
- Seftel A D. From aspiration to achievement: Assessment and noninvasive treatment of erectile dysfunction in aging men. *J Am Geriatr Soc* 2005;53(1):119-130.
- Seftel A D. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(4 I):1364-1366.
- Segraves R T. Pharmacological enhancement of human sexual behavior. *Journal of Sex Education & Therapy* 1991;17(4):283-289.
- Segraves R, Taylor. Two additional uses for sildenafil in psychiatric patients. [References]. *J Sex Marital Ther* 1999;25(4):265-266.
- Segraves Robert, Taylor Segraves, Kathleen Blindt et al. Sexual function in patients taking bupropion sustained release. *Hillside J Clin Psychiatry* 1995;56(8):374
- Seidman Stuart N. Exploring the relationship between depression and erectile dysfunction in aging men. *Hillside J Clin Psychiatry* 2002;63(Suppl5):5-12.
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Seyam R M, Albakry A, Ghobish A et al. Prevalence of erectile dysfunction and its correlates in Egypt: a community-based study. *Int J Impot Res* 2003;15(4):237-245.
- Shabbir M, Mikhailidis D M, Morgan R J. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors.[comment]. *Current Medical Research & Opinion* 2004;20(5):603-606.
- Shabbir M, Shah J S, Kirby R S. Cardiac failure and benign prostatic hyperplasia: Management of common comorbidities. *BJU Int* 2005;95(3):278-280.

- Shabsigh R. Testosterone therapy in erectile dysfunction. [Review] [34 refs]. *Aging Male* 2004;7(4):312-318.
- Shabsigh R. Testosterone therapy in erectile dysfunction and hypogonadism. *Br J Sex Med* 2005;2(6):785-792.
- Shabsigh R. Hypogonadism and erectile dysfunction: The role for testosterone therapy. *Int J Impot Res* 2003;15(SUPPL. 4):S9-S13.
- Shabsigh R, Katz M, Yan G et al. Cardiovascular issues in hypogonadism and testosterone therapy. [Review] [44 refs]. *Am J Cardiol* 2005;96(12B):67M-72M.
- Shakir S A W, Wilton L V, Boshier A et al. Cardiovascular events in users of sildenafil: Results from first phase of prescription event monitoring in England. *Br Med J* 2001;322(7287):651-652.
- Shamloul R. Management of honeymoon impotence. *Br J Sex Med* 2006;3(2):361-366.
- Shamloul R, El-Dakhly M, Ghanem H et al. Intracavernous chlorpromazine versus phentolamine: A double-blind clinical comparative study. *Br J Sex Med* 2004;1(3):310-313.
- Shamloul R, Ghanem H M, Salem A et al. The value of penile duplex in the prediction of intracavernous drug-induced priapism. *Int J Impot Res* 2004;16(1):78-79.
- Shamsa A, Motavalli S M, Aghdam B. Erectile function in end-stage renal disease before and after renal transplantation. *Transplant Proc* 2005;37(7):3087-3089.
- Sharlip I D. Editorial comment. *International Braz J Urol* 2005;31(4):354-355.
- Sharlip I D. Can self-injection therapy cure impotence?. [Review] [7 refs]. *Advances in Experimental Medicine & Biology* 1997;43383-86.
- Shimon I, Lubina A, Gorfine M et al. Feedback inhibition of gonadotropins by testosterone in men with hypogonadotropic hypogonadism: comparison to the intact pituitary-testicular axis in primary hypogonadism. *J Androl* 2006;27(3):358-364.
- Siegel R L, Dubin N H, Andrade J R. Sildenafil citrate and sperm function [3] (multiple letters). *American Journal of Obstetrics & Gynecology* 2001;184(4):777-778.
- Sighinolfi M C, de Stefani S, Mofferdin A et al. Intracavernous prostaglandin E1 infusion in diabetes with associated ischemic necrosis of the glans penis. *Br J Urol* 2004;171(6 I):2380
- Silvestri A, Galetta P, Cerquetani E et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo.[see comment]. *Eur Heart J* 2003;24(21):1928-1932.
- Singer Carlos, Weiner William J, Sanchez-Ramos J et al. Sexual function in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry* 1991;54(10):942
- Sipski M, Alexander C, Guo X et al. Cardiovascular effects of sildenafil in men with SCIs at and above T6. *Topics in Spinal Cord Injury Rehabilitation* 2003;8(3):26-34.
- Siraj Q H, Bomanji J, Akhtar M A et al. Quantitation of pharmacologically-induced penile erections: The value of radionuclide phallography in the objective evaluation of erectile haemodynamics. *Nucl Med Commun* 1990;11(6):445-458.
- Slob A K, Dohle G R, Incrocci L. 'Sildenafil and pharmaco-penile duplex ultrasonography' by Speel et al: Inconclusive results. *Int J Impot Res* 2002;14(2):136-137.
- Slob A, Koos Steyvers, Christel L et al. Routine psychophysiological screening of 384 men with erectile dysfunction. *J Sex Marital Ther* 1998;24(4):273-279.
- Smith K J, Roberts M S. The cost-effectiveness of sildenafil. *Ann Intern Med* 2000;132(12):933-937.
- Smith K M, Romanelli F. Recreational use and misuse of phosphodiesterase 5 inhibitors. [Review] [56 refs]. *Journal of the American Pharmacists Association: JAPhA* 2005;45(1):63-72.
- Sobh M A, Abd el, Hamid I et al. Effect of erythropoietin on sexual potency in chronic haemodialysis patients. A preliminary study. *Scand J Urol Nephrol* 1992;26(2):181-185.
- Sogari P R, Teloken C, Souto C A. Atropine role in the pharmacological erection test: study of 228 patients.. *Br J Urol* 1997;158(5):1760-1763.
- Sohle G R. Re: The age-related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Eur Urol* 2007;51(5):1440
- Sohn Michael, Sikora Richard. Ginkgo biloba extract in the therapy of erectile dysfunction. *Journal of Sex Education & Therapy* 1991;17(1):53-61.
- Solursh L, Solursh D S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *International Journal of Adolescent Medicine & Health* 1994;7(2):119-124.

- Solursh Lionel P, Solursh Diane S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *Int J Adolesc Med Health* 1994;7(2):119-124.
- Sonda L P, Mazo R, Chancellor M B. The role of yohimbine for the treatment of erectile impotence. *J Sex Marital Ther* 1990;16(1):15-21.
- Sonksen J, Biering-Sorensen F. Transcutaneous nitroglycerin in the treatment of erectile dysfunction in spinal cord injured. *Paraplegia* 1992;30(8):554-557.
- Sorbera L A, Martin L, Rabasseda X et al. Vardenafil. Treatment of erectile dysfunction. Phosphodiesterase 5 inhibitor. *Drugs of the Future* 2001;26(2):141-144.
- Sparwasser C, Drescher P, Pust R A et al. Long-term results of therapy with intracavernous injections and penile venous surgery in chronic erectile dysfunction. *Scand J Urol Nephrol Suppl* 1994;157(Suppl):107-112.
- Speakman M T, Kloner R A. Viagra and cardiovascular disease. *Journal of Cardiovascular Pharmacology & Therapeutics* 1999;4(4):259-267.
- Srilatha B, Adaikan P G, Chong Y S. Relevance of oestradiol-testosterone balance in erectile dysfunction patients' prognosis. *Singapore Med J* 2007;48(2):114-118.
- Stas S N, Anastasiadis A G, Fisch H et al. Urologic aspects of andropause. *Urology* 2003;61(2):261-266.
- Steers W D. Tachyphylaxis and phosphodiesterase type 5 inhibitors.[comment]. *Br J Urol* 2002;168(1):207
- Steers W D. Viagra - After one year. *Urology* 1999;54(1):12-17.
- Steidle C, Witt M A, Matrisciano J et al. Sexual functioning and satisfaction in nonresponders to testosterone gel: Potential effectiveness of retreatment in hypogonadal males. *Clin Cornerstone* 2005;7 Suppl 4S20-S25.
- Steiger A, Holsboer F, Benkert O. Studies of nocturnal penile tumescence and sleep electroencephalogram in patients with major depression and in normal controls. *Acta Psychiatr Scand* 1993;87(5):358-363.
- Steiger Axel, Benkert O, Holsboer F. Effects of long-term treatment with the MAO-A inhibitor moclobemide on sleep EEG and nocturnal hormonal secretion in normal men. *Neuropsychobiology* 1994;30(2-3):101-105.
- Stief C G, Uckert S, Jonas U. Strategies in the oral pharmacotherapy of male erectile dysfunction viewed from bench and bedside (Part II). *The Journal of Mens Health & Gender* 2005;2(3):325-332.
- Stief C G, Uckert S, Becker A J et al. The effect of the specific phosphodiesterase (PDE) inhibitors on human and rabbit cavernous tissue in vitro and in vivo. *Br J Urol* 1998;159(4):1390-1393.
- Stief C, Padley R J, Perdok R J et al. Cross-study review of the clinical efficacy of apomorphine SL 2 and 3 mg: Pooled data from three placebo-controlled, fixed-dose crossover studies. *European Urology Supplements* 2002;1(3):12-20.
- Stolk E A, Busschbach J J, Caffa M et al. Cost utility analysis of sildenafil compared with papaverine-phenolamine injections.[see comment]. *BMJ* 2000;320(7243):1165-1168.
- Strachan M W, Teoh W L, Don-Wauchope A C et al. Clinical and radiological features of patients with macroprolactinaemia. *Clin Endocrinol (Oxf)* 2003;59(3):339-346.
- Strahilevitz J, Rahav G, Schroers H-J et al. An outbreak of Phialemonium infective endocarditis linked to intracavernous penile injections for the treatment of impotence. *Clin Infect Dis* 2005;40(6):781-786.
- Stroberg P, Murphy A, Costigan T. Switching patients with erectile dysfunction from sildenafil citrate to tadalafil: results of a European multicenter, open-label study of patient preference. *Clin Ther* 2003;25(11):2724-2737.
- Struthers A D. Aldosterone blockade in heart failure. *J Renin Angiotensin Aldosterone Syst* 2004;5(SUPPL. 1):S23-S27.
- Stuckey B G A. Tadalafil phase 3 experience. *European Urology Supplements* 2002;1(8):25-30.
- Suetomi T, Endo F, Takeshima H et al. Evaluation of the effectiveness of sildenafil using questionnaire methods versus audio-visual sexual stimulation. *Int J Urol* 2005;12(4):369-373.
- Suzuki F, Shimizu C, Umetsu M et al. Adult-onset idiopathic hypogonadotropic hypogonadism due to isolated pituitary gonadotropin deficiency. *Adv Intern Med* 2004;43(7):571-574.
- Svartberg J, Aasebo U, Hjalmsarsen A et al. Testosterone treatment improves body composition and sexual function in men with COPD, in a 6-month randomized controlled trial.. *Respir Med* 2004;98(9):906-913.
- Swartz D A, Todd M W. Intracavernous papaverine and glaucoma.[see comment]. *JAMA* 1990;264(5):570
- Szucs A, Janszky J, Barsi P et al. Sleep-related painful erection is associated with neurovascular compression of basal forebrain [5]. *J Neurol* 2002;249(4):486-487.
- T'Sjoen G, Feyen E, De Kuyper P et al. Self-referred patients in an aging male clinic: much more than androgen deficiency alone. *Aging Male* 2003;6(3):157-165.

- Tam S W, Worcel M, Wyllie M. Yohimbine: a clinical review. [Review] [152 refs]. *Pharmacol Ther* 2001;91(3):215-243.
- Tarhan F, Canguven O, Kuyumcuoglu U. Intracavernous sodium nitroprusside (SNP) versus papaverine/phentolamine in erectile dysfunction: a comparative study of short-term efficacy and side-effects.[comment]. *Br J Sex Med* 2006;3(2):377
- Tarhan F, Kuyumcuoglu U, Kolsuz A et al. Effect of intracavernosal sodium nitroprusside in impotence. *Urol Int* 1996;56(4):211-214.
- Tas A, Dilek K, Gullulu M et al. Treatment of erectile dysfunction in hemodialysis patients and effects of sildenafil [abstract]. XXXVIII Congress of the European Renal Association European Dialysis & Transplant Association June 24-27 2003;2001, Vienna, Austria 131p. 2003.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Teillac P, Bono A V, Irani J et al. The role of luteinizing hormone-releasing hormone therapy in locally advanced prostate cancer and biochemical failure: Considerations for optimal use. *Clin Ther* 2005;27(3):273-285.
- Teloken P E, Smith E B, Lodowsky C et al. Defining association between sleep apnea syndrome and erectile dysfunction. *Urology* 2006;67(5):1033-1037.
- Thadani U, Smith W, Nash S et al. The effect of vardenafil, a potent and highly selective phosphodiesterase-5 inhibitor for the treatment of erectile dysfunction, on the cardiovascular response to exercise in patients with coronary artery disease. *J Am Coll Cardiol* 2002;40(11):2006-2012.
- Thaveundayil J X, Hambalek R, Ng Ying et al. Prolonged penile erections induced by hydroxyzine: Possible mechanism of action. *Neuropsychobiology* 1994;30(1):4-6.
- Thrasher J B. What's new in urology. *J Am Coll Surg* 2005;201(3):438-448.
- Tindall B, Forde S, Goldstein D et al. Sexual dysfunction in advanced HIV disease. *AIDS Care* 1994;6(1):105-107.
- Tomlinson J. Viagra and its use in cardiovascular disease.[erratum appears in *J Hum Hypertens* 2000 Apr;14(4):283]. [Review] [11 refs]. *J Hum Hypertens* 1999;13(9):593-594.
- Tomova A, Kumanov P. Are dehydroepiandrosterone sulphate and lipids associated with erectile dysfunction? [References]. *Maturitas* 2005;50(4):294-299.
- Tordjman G. NO/Pg E1: a new association in the treatment of erectile impotence. *Contracept Fertil Sex (Paris)* 1993;21, pp.509-510, 1993.
- Tosti A, Pazzaglia M, Soli M et al. Evaluation of sexual function with an international index of erectile function in subjects taking finasteride for androgenetic alopecia.[see comment]. *Arch Dermatol* 2004;140(7):857-858.
- Traish A M, Goldstein I, Kim N N. Testosterone and erectile function: from basic research to a new clinical paradigm for managing men with androgen insufficiency and erectile dysfunction. *Eur Urol* 2007;52(1):54-70.
- Trinchieri A, Nicola M, Masini F et al. Prospective comprehensive assessment of sexual function after retropubic non nerve sparing radical prostatectomy for localized prostate cancer. *Arch Ital Urol Androl* 2005;77(4):219-223.
- Truss M C, Becker A J, Djamilian M H et al. Role of the nitric oxide donor linsidomine chlorhydrate (SIN-1) in the diagnosis and treatment of erectile dysfunction. *Urology* 1994;44(4):553-556.
- Tsai S K, Hong C Y. Intracavernosal metaraminol for treatment of intraoperative penile erection. *Postgrad Med J* 1990;66(780):831-833.
- Tsujimura A, Matsumiya K, Matsuoka Y et al. Bioavailable testosterone with age and erectile dysfunction. *Br J Urol* 2003;170(6 Pt 1):2345-2347.
- Tuzgen S, Karamehmetoglu S S, Karacan I et al. Use of sildenafil in the treatment of erectile dysfunction in patients with spinal cord injury. *Neurosurgery Quarterly* 2006;16(1):40-43.
- Tzivoni D, Klein J, Hisdai D et al. The Israel Heart Society expert consensus document: The cardiac patient and sexual activity in the era of sildenafil (Viagra). *Israel Medical Association Journal: Imaj* 2000;2(1):63-65.
- Unnikrishnan A G, Rajaratnam S, Seshadri M S et al. The 'hook effect' on serum prolactin estimation in a patient with macroprolactinoma. *Neurol India* 2001;49(1):78-80.
- Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Uygur M C, Arik A I, Altug U et al. Effects of the 5 alpha-reductase inhibitor finasteride on serum levels of gonadal, adrenal, and hypophyseal hormones and its clinical significance: a prospective clinical study. *Steroids* 1998;63(4):208-213.
- Valdevenito R, Melman A. Intracavernous self-injection pharmacotherapy program: analysis of results and complications. *Int J Impot Res* 1994;6(2):81-91.

- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy.[comment]. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Jonker-Pool G et al. Sexual functioning in testosterone-supplemented patients treated for bilateral testicular cancer. *Br J Urol* 1997;79(3):461-467.
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Dijk M, Skrekas T, De La et al. The association between lower urinary tract symptoms and sexual dysfunction: Fact or fiction?. *Curr Opin Urol* 2005;15(1):39-44.
- Van Moorselaar J. LUTS and Sexual Dysfunction: Implications for Management of BPH. *European Urology Supplements* 2003;2(10):13-20.
- Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
- Vatansever H S, Kaykcioglu O, Gumus B. Histopathologic effect of chronic use of sildenafil citrate on the choroid & retina in male rats. *Indian J Med Res* 2003;117(MAY):211-215.
- Verit A, Oguz H. Ophthalmic aspects of erectile dysfunction drugs [3]. *Am J Ophthalmol* 2006;141(3):598
- Vick R N, Benevides M, Patel M et al. The efficacy, safety and tolerability of intracavernous PNU-83757 for the treatment of erectile dysfunction.. *Br J Urol* 2002;167(6):2618-2623.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Vickers M A, Wright E A. Erectile dysfunction in the patient with diabetes mellitus. *Am J Manag Care* 2004;10(1 SUPPL.):S3-S11.
- Vidal J, Curcoll L, Roig T et al. Intracavernous pharmacotherapy for management of erectile dysfunction in multiple sclerosis patients. *Rev Neurol* 1995;23(120):269-271.
- Vinik A I, Maser R E, Mitchell B D et al. Diabetic autonomic neuropathy. [Review] [192 refs]. *Diabetes Care* 2003;26(5):1553-1579.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.
- Vitezic D. A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction. [Review] [72 refs]. *Drug Saf* 2001;24(4):255-265.
- Vlachopoulos C, Hirata K, O'Rourke M F. Effect of sildenafil on arterial stiffness and wave reflection. *Vasc Med* 2003;8(4):243-248.
- Vogt H J, Brandl P, Kockott G et al. Double-blind, placebo-controlled safety and efficacy trial with yohimbine hydrochloride in the treatment of nonorganic erectile dysfunction. *Int J Impot Res* 1997;9(3):155-161.
- Wagner G, Mulhall J. Pathophysiology and diagnosis of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):3-10.
- Wagner G, Rabkin J, Rabkin R. Effects of testosterone replacement therapy on sexual interest, function, and behavior in HIV+ men. *J Sex Res* 1997;34(1):27-33.
- Wagner Gorm, Kaplan Helen, Singer. The new injection treatment for impotence: Medical and psychological aspects. *Refuat Hapeh Vehashinayim* 1993;x, 210 pp. Philadelphia, PA, US210
- Wagrell L, Schelin S, Nordling J et al. Three-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomized multicenter study. *Urology* 2004;64(4):698-702.
- Wald M, Seftel A D, Ross L S et al. Computational models for detection of erectile dysfunction. *Br J Urol* 2005;173(1):167-170.
- Waldbaum R S. The safety of PDE5 inhibitors in ED treatment: Putting cardiovascular concerns to rest. *Cardiology Review* 2005;22(9):23-24.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Wang Z, Liu B C, Chen B et al. Randomized controlled study on erectile dysfunction treated by trazodone. *Chinese Journal of Andrology* 2002;16(3):236-238.
- Ware J, Catesby Rose F, Vincent McBrayer et al. The acute effects of nefazodone, trazodone and buspirone on sleep and sleep-related penile tumescence in normal subjects. *Sleep: Journal of Sleep Research & Sleep Medicine* 1994;17(6):544-550.
- Watanabe T, Chancellor M B, Rivas D A et al. Epidemiology of current treatment for sexual dysfunction in spinal cord injured men in the USA model spinal cord injury centers. *J Spinal Cord Med* 1996;19(3):186-189.

- Webb D J, Freestone S, Allen M J et al. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. *Am J Cardiol* 1999;83(5A):21C-28C.
- Webb D J, Muirhead G J, Wulff M et al. Sildenafil citrate potentiates the hypotensive effects of nitric oxide donor drugs in male patients with stable angina. *J Am Coll Cardiol* 2000;36(1):25-31.
- Wegner H E H, Knispel H H, Meier T et al. Nitric oxide donor, linsidomine chlorhydrate (SIN-1), in the diagnosis and treatment of erectile dysfunction: Critical appraisal and review of the literature. *International Urology & Nephrology* 1995;27(5):621-628.
- Weinhardt L S, Carey M P. Prevalence of erectile disorder among men with diabetes mellitus: Comprehensive review, methodological critique, and suggestions for future research. *J Sex Res* 1996;33(3):205-214.
- Weinsaft J W, Hickey K, Bokhari S et al. Effects of tadalafil on myocardial blood flow in patients with coronary artery disease. *Coron Artery Dis* 2006;17(6):493-499.
- Weiske W-H. Invasive diagnosis and therapy - Are they still reasonable in the age of sildenafil?. *Andrologia* 1999;31(SUPPL. 1):95-97.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Wessells H, Fuciarelli K, Hansen J et al. Synthetic melanotropic peptide initiates erections in men with psychogenic erectile dysfunction: double-blind, placebo controlled crossover study. *Br J Urol* 1998;160(2):389-393.
- Wessells H, Gralnek D, Dorr R et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000;56(4):641-646.
- Wheatley D. Triple-blind, placebo-controlled trial of Ginkgo biloba in sexual dysfunction due to antidepressant drugs. *Hum Psychopharmacol* 2004;19(8):545-548.
- Wilke D R, Parker C, Andonowski A et al. Testosterone and erectile function recovery after radiotherapy and long-term androgen deprivation with luteinizing hormone-releasing hormone agonists. *BJU Int* 2006;97(5):963-968.
- Williams G. Male erectile dysfunction. *Prescribers' Journal* 2000;40(1):49-58.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):
- Wilt T J, Fink H A. Is antidepressant plus sildenafil a recipe for priapism?. *Postgrad Med* 2004;116(6):11-12.
- Witt Deborah K. Yohimbine for erectile dysfunction. *J Fam Pract* 1998;46(4):282-283.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wyllie M G. The hunt for pink Viagra. *BJU Int* 2005;95(1):181-182.
- Wyllie M G. Let's hope for more in 2004. *BJU Int* 2004;93(1):175-176.
- Wyllie M G. The Second International Consultation on Erectile Dysfunction: Highlights from the pharmaceutical industry. *BJU Int* 2003;92(6):645-646.
- Wyllie M G. The genesis of a phytopharmaceutical industry (Mark II). *BJU Int* 2003;91(7):721-722.
- Yajima T, Yajima Y, Koppiker N et al. No clinically important effects on intraocular pressure after short-term administration of sildenafil citrate (Viagra). *Am J Ophthalmol* 2000;129(5):675-676.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yaman O, Tokatli Z, Akand M et al. Characteristics of sildenafil erections in healthy young men. *Asian J Androl* 2005;7(4):395-398.
- Yamanaka M, Shirai M, Shiina H et al. Vascular endothelial growth factor restores erectile function through inhibition of apoptosis in diabetic rat penile crura. *Br J Urol* 2005;173(1):318-323.
- Yan J Y, Yang W Z. A comparative effects of Sildenafil and Yohimbine for the treatment of erectile dysfunction. *Chinese Journal of Andrology* 2000;14(2):103-105.
- Yarkony G M. Enhancement of sexual function and fertility in spinal cord-injured males. [Review] [40 refs]. *Am J Phys Med Rehabil* 1990;69(2):81-87.
- Yassin A A, Saad F. Treatment of sexual dysfunction of hypogonadal patients with long-acting testosterone undecanoate (Nebido). [Review] [25 refs]. *World J Urol* 2006;24(6):639-644.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.

- Yasumoto R, Nishisaka N, Sakakura T et al. Ethanol embolization for impotent patients with venous leakage: A new technique and initial results. *Minimally Invasive Therapy & Allied Technologies: Mitat* 1996;5(6):564-566.
- Yeager J, Beihn R M. Retention and migration of alprostadil cream applied topically to the glans meatus for erectile dysfunction. *Int J Impot Res* 2005;17(1):91-95.
- Youssef A F, Fort F L, Ronsen B et al. Evaluation of apomorphine HCl effects on reproductive endpoints: Studies in male rats and dogs. *J Toxicol Sci* 1999;51(2):273-279.
- Zaslau S, Nicolis C, Galea G et al. A simplified pharmacologic erection program for patients with spinal cord injury. *J Spinal Cord Med* 1999;22(4):303-307.
- Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200
- Zhao L. Clinical observation on the therapeutic effects of heavy moxibustion plus point-injection in treatment of impotence. *J Tradit Chin Med* 2004;24(2):126-127.
- Zhigang Long, Xiaowei Liu, Shengbo Lu. Therapy of impotence with traditional Chinese medicine. *Journal of Sex Education & Therapy* 1994;20(2):140-143.
- Ziegler D. Management of erectile dysfunction in diabetic patients. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):58-65.
- Zini Dante, Carani Cesare, Baldini Augusto et al. Sexual behavior of men with isolated hypogonadotropic hypogonadism or prepubertal anterior panhypopituitarism. *Horm Behav* 1990;24(2):174-185.
- Zlotta A R, Teillac P, Raynaud J P et al. Evaluation of male sexual function in patients with Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), Tamsulosin or Finasteride. *Eur Urol* 2005;48(2):269-276.
- Zusman R M. Cardiovascular data on sildenafil citrate: introduction.[erratum appears in *Am J Cardiol* 1999 Jul 15;84(2):244]. *Am J Cardiol* 1999;83(5A):1C-2C.
- Zusman R M, Morales A, Glasser D B et al. Overall cardiovascular profile of sildenafil citrate. [Review] [33 refs]. *Am J Cardiol* 1999;83(5A):35C-44C.
- Zusman R M, Prisant L M, Brown M J. Effect of sildenafil citrate on blood pressure and heart rate in men with erectile dysfunction taking concomitant antihypertensive medication. *Sildenafil Study Group. J Hypertens* 2000;18(12):1865-1869.
- Observational injection study with < 6 months followup in duration.**
- Bancroft J, Smith G, Munoz M et al. Erectile response to visual erotic stimuli before and after intracavernosal papaverine, and its relationship to nocturnal penile tumescence and psychometric assessment. *Br J Urol* 1991;68(6):629-638.
- Beretta G, Marzotto M, Zanollo A et al. Office treatment: intracavernous injections of prostaglandin E1 (PG E1) and improvement of spontaneous erections. *Acta Eur Fertil* 1991;22(4):221-223.
- Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.
- Brown S L, Haas C A, Koehler M et al. Hepatotoxicity related to intracavernous pharmacotherapy with papaverine. *Urology* 1998;52(5):844-847.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Chun S S, Fenemore J, Heaton J P et al. Enhancement of erectile responses to vasoactive drugs by a variable amplitude oscillation device. *Int J Impot Res* 1996;8(4):221-225.
- Dinsmore W W, Alderdice D K. Vasoactive intestinal polypeptide and phentolamine mesylate administered by autoinjector in the treatment of patients with erectile dysfunction resistant to other intracavernosal agents. *Br J Urol* 1998;81(3):437-440.
- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Goonawardena S A, de Silva W A, Ketheeswaran T. Pharmacologically induced penile erections in the assessment and treatment of erectile impotence: a preliminary study of 100 patients. *Ceylon Med J* 1997;42(2):72-74.
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.
- Kadioglu A, Erdogru T, Tellaloglu S. Combined intracavernous injection of papaverine and stimulation (CIS) test. *J Androl* 1994;15 Suppl50S-53S.

- Katlowitz N M, Albano G J, Morales P et al. Potentiation of drug-induced erection with audiovisual sexual stimulation. *Urology* 1993;41(5):431-434.
- Katlowitz N, Albano G J, Patsias G et al. Effect of multidose intracorporeal injection and audiovisual sexual stimulation in vasculogenic impotence. *Urology* 1993;42(6):695-697.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Mansi M K, Alkhdair W K, Huraid S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *Br J Urol* 1998;159(6):1927-1930.
- McMahon C G. A pilot study of the role of intracavernous injection of vasoactive intestinal peptide (VIP) and phentolamine mesylate in the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(4):233-236.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Mirone V, Imbimbo C, Fabrizio F et al. Ketanserin plus prostaglandin E1 (PGE-1) as intracavernosal therapy for patients with erectile dysfunction unresponsive to PGE-1 alone. *Br J Urol* 1996;77(5):736-739.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Pagani E, Puech-Leao P, Glina S et al. The value of a second injection on the pharmaco-induced erection test. *Int J Impot Res* 1997;9(3):167-168.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Rodilla F, Fuentes M D, Chuan P et al. Penile self-injection for impotence in patients after radical cystectomy. *Journal of Clinical Pharmacy & Therapeutics* 1994;19(6):359-360.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266.
- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Stief C G, Holmquist F, Djamilian M et al. Preliminary results with the nitric oxide donor linsidomine chlorhydrate in the treatment of human erectile dysfunction. *Br J Urol* 1992;148(5):1437-1440.
- Stief C G, Wetterauer U, Schaebdsau F H et al. Calcitonin-gene-related peptide: a possible role in human penile erection and its therapeutic application in impotent patients. *Br J Urol* 1991;146(4):1010-1014.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Weiss J N, Ravalli R, Badlani G H. Intracavernous pharmacotherapy in psychogenic impotence. *Urology* 1991;37(5):441-443.
- Observational injection study > or = to 6 months in duration.**
- al-Juburi A Z, O'Donnell P D. Follow up outcome of intracavernous papaverine. *J Ark Med Soc* 1990;86(10):383-385.
- Armstrong D K, Convery A G, Dinsmore W W. Reasons for patient drop-out from an intracavernous auto-injection programme for erectile dysfunction. *Br J Urol* 1994;74(1):99-101.
- Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.

- Chen J, Godschalk M F, Katz P G et al. Incidence of penile pain after injection of a new formulation of prostaglandin E1.[see comment]. *Br J Urol* 1995;154(1):77-79.
- Chen J, Godschalk M F, Katz P G et al. Combining intracavernous injection and external vacuum as treatment for erectile dysfunction.[see comment]. *Br J Urol* 1995;153(5):1476-1477.
- Cooper A J. Evaluation of I-C papaverine in patients with psychogenic and organic impotence. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1991;36(8):574-578.
- Dhabuwala C B, Kerkar P, Bhutwala A et al. Intracavernous papaverine in the management of psychogenic impotence. *Arch Androl* 1990;24(2):185-191.
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.
- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Godschalk M, Gheorghiu D, Chen J et al. Long-term efficacy of a new formulation of prostaglandin E1 as treatment for erectile failure.. *Br J Urol* 1996;155(3):915-917.
- Govier F E, McClure R D, Weissman R M et al. Experience with triple-drug therapy in a pharmacological erection program.[see comment]. *Br J Urol* 1993;150(6):1822-1824.
- Incrocci L, Hop W C, Slob A K. Visual erotic and vibrotactile stimulation and intracavernous injection in screening men with erectile dysfunction: a 3 year experience with 406 cases. *Int J Impot Res* 1996;8(4):227-232.
- Irwin M B, Kata E J. High attrition rate with intracavernous injection of prostaglandin E1 for impotency. *Urology* 1994;43(1):84-87.
- Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.
- Kattan S A. The acceptance of satisfaction of Saudi males to vasoactive autoinjection intracavernous therapy, external negative pressure device and penile prosthesis in the treatment of erectile dysfunction. *Ann Saudi Med* 2002;22(3-4):149-152.
- Knispel H H, Huland H. Influence of cause on choice of therapy in 174 patients with erectile dysfunction. *Br J Urol* 1992;147(5):1274-1276.
- Lim P H, Ng F C. Erectile dysfunction in Singapore men: presentation, diagnosis, treatment and results. *Ann Acad Med Singapore* 1992;21(2):248-253.
- Lottman P E, Hendriks J C, Vrugink P A et al. The impact of marital satisfaction and psychological counselling on the outcome of ICI-treatment in men with ED. *Int J Impot Res* 1998;10(2):83-87.
- Lundberg L, Olsson J-O, Kihl B. Long-term experience of self-injection therapy with prostaglandin E1 for erectile dysfunction. *Scand J Urol Nephrol* 1996;30(5):395-397.
- Maniam P, Seftel A D, Corty E W et al. Nocturnal penile tumescence activity unchanged after long-term intracavernous injection therapy. *Br J Urol* 2001;165(3):830-832.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993;42(5):554-558.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Four-drug intracavernous therapy for impotence due to corporeal veno-occlusive dysfunction. *Br J Urol* 1993;149(5 Pt 2):1291-1295.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Intracavernous vasoactive pharmacotherapy: the impact of a new self-injection device.[see comment]. *Br J Urol* 1993;150(6):1829-1832.
- Mulhall J P, Jahoda A E, Cairney M et al. The causes of patient dropout from penile self-injection therapy for impotence. *Br J Urol* 1999;162(4):1291-1294.
- Mulhall J P, Land S, Parker M et al. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *Br J Sex Med* 2005;2(4):532-542.
- Perimenis P, Athanasopoulos A, Geramoutsos I et al. The incidence of pharmacologically induced priapism in the diagnostic and therapeutic management of 685 men with erectile dysfunction. *Urol Int* 2001;66(1):27-29.
- Rowland D L, Boedhoe H S M, Dohle G et al. Intracavernosal self-injection therapy in men with erectile dysfunction: Satisfaction and attrition in 119 patients. *Int J Impot Res* 1999;11(3):145-151.

Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.

Speckens A E, Kattemolle M R, Hengeveld M W et al. A prospective long-term follow-up study of patients evaluated for erectile dysfunction: outcome and associated factors. *Int J Impot Res* 1995;7(2):101-110.

Tariq S H, Haleem U, Omran M L et al. Erectile dysfunction: Etiology and treatment in young and old patients. *Clin Geriatr Med* 2003;19(3):539-551.

Turner L A, Althof S E. The clinical effectiveness of self-injection and external vacuum devices in the treatment of erectile dysfunction: a six-month comparison. *Psychiatr Med* 1992;10(2):283-293.

Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196

Weidner W, Schroeder-Printzen I, Fischer C et al. Experience in the treatment of erectile dysfunction using the intracavernosal self-injection of papaverine: Results of a prospective study after a median follow-up of 42 months involving 135 patients and 10766 injections. *World J Urol* 1992;10(3):179-182.

Weiss J N, Badlani G H, Ravalli R et al. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6(3):171-174.

Not relevant by study design.

Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.

Anderson D C, Seifert C F. Topical nitrate treatment of impotence. [Review] [17 refs]. *Ann Pharmacother* 1993;27(10):1203-1205.

Anonymous. Sildenafil for erectile dysfunction. *Drug Ther.Bull* 1998;36(11):81-84.

Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.

Anonymous. Vasoactive intestinal peptide/phentolamine. *Invicorp, vasopotin. Drugs in R & D* 1999;2(6):436-438.

Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;

Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329

Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.

Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.

Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.

Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.

Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.

Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.

Chiang H-S, Kao Y H, Sheu M T. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995;24(5):767-769.

Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.

Derry F, Hultling C, Seftel A D et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. *Urology* 2002;60(2 Suppl 2):49-57.

Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol.* 1998;159(2):433-436.

Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.

Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.

Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.

- Hellstrom W J. Vardenafil: a new approach to the treatment of erectile dysfunction. [Review] [37 refs]. *Curr Urol Rep* 2003;4(6):479-487.
- Holmes S. Tadalafil: a new treatment for erectile dysfunction. *BJU Int* 2003;91(6):466-468.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- Keating G M, Scott L J. Vardenafil: a review of its use in erectile dysfunction. *Drugs* 2003;63(23):2673-2703.
- Keating G M, Scott L J. Spotlight on vardenafil in erectile dysfunction. *Drugs Aging* 2004;21(2):135-140.
- Kloner R A. Cardiovascular effects of the 3 phosphodiesterase-5 inhibitors approved for the treatment of erectile dysfunction. [Review] [57 refs]. *Circulation* 2004;110(19):3149-3155.
- Langtry H D, Markham A. Sildenafil: a review of its use in erectile dysfunction. *Drugs* 1999;57(6):967-989.
- Lewis R W. Intraurethral and topical agents. *Med Actual* 2000;36(2-3):113-119.
- Licht M R, Schover L R. Sildenafil (Viagra) for treating male erectile dysfunction. *Cleve Clin J Med* 1998;65(6):
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- McMahon C G. Topiglan: MacroChem. *Curr Opin Investig Drugs* 2002;3(4):602-606.
- Mikhail N. Does Testosterone Have a Role in Erectile Function?. *Am J Med* 2006;119:373-382.
- Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *Br J Sex Med* 2005;2(5):658-667.
- Moore R A, Derry S, McQuay H J. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. [Review] [77 refs]. *BMC Urol* 2005;5:18
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol.* 2002;26
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Padma-Nathan H, Eardley I, Kloner R A et al. A 4-year update on the safety of sildenafil citrate (Viagra). [Review] [88 refs]. *Urology* 2002;60(2:Suppl 2):Suppl-90.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Sommer F, Engelmann U. Vardenafil: Bayer Yakuhin. *Curr Opin Investig Drugs* 2002;3(4):607-613.
- Sternbach Harvey. Age-associated testosterone decline in men: Clinical issues for psychiatry. *Am J Psychiatry* 1998;155(10):1310-1318.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Tomsak R. PDE5 inhibitors and permanent visual loss. *Int J Impot Res* 2005;17(6):547-549.
- Tran D, Howes L G. Cardiovascular safety of sildenafil. *Drug Saf* 2003;26(7):453-460.
- Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Uygur M C, Arik A I, Altug U et al. Effects of the 5 alpha-reductase inhibitor finasteride on serum levels of gonadal, adrenal, and hypophyseal hormones and its clinical significance: a prospective clinical study. *Steroids* 1998;63(4):208-213.
- Valdevenito R, Melman A. Intracavernous self-injection pharmacotherapy program: analysis of results and complications. *Int J Impot Res* 1994;6(2):81-91.
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy.[comment]. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy. *Lancet* 2000;356(9224):169

- van Basten J P, Van Driel M F, Jonker-Pool G et al. Sexual functioning in testosterone-supplemented patients treated for bilateral testicular cancer. *Br J Urol* 1997;79(3):461-467.
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Dijk M, Skrekas T, De La et al. The association between lower urinary tract symptoms and sexual dysfunction: Fact or fiction?. *Curr Opin Urol* 2005;15(1):39-44.
- Van Moorselaar J. LUTS and Sexual Dysfunction: Implications for Management of BPH. *European Urology Supplements* 2003;2(10):13-20.
- Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
- Vatansever H S, Kayikcioglu O, Gumus B. Histopathologic effect of chronic use of sildenafil citrate on the choroid & retina in male rats. *Indian J Med Res* 2003;117(MAY):211-215.
- Verit A, Oguz H. Ophthalmic aspects of erectile dysfunction drugs [3]. *Am J Ophthalmol* 2006;141(3):598
- Vick R N, Benevides M, Patel M et al. The efficacy, safety and tolerability of intracavernous PNU-83757 for the treatment of erectile dysfunction.. *Br J Urol* 2002;167(6):2618-2623.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Vickers M A, Wright E A. Erectile dysfunction in the patient with diabetes mellitus. *Am J Manag Care* 2004;10(1 SUPPL.):S3-S11.
- Vidal J, Curcoll L, Roig T et al. Intracavernous pharmacotherapy for management of erectile dysfunction in multiple sclerosis patients. *Rev Neurol* 1995;23(120):269-271.
- Vinik A I, Maser R E, Mitchell B D et al. Diabetic autonomic neuropathy. [Review] [192 refs]. *Diabetes Care* 2003;26(5):1553-1579.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.
- Vitezic D. A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction. [Review] [72 refs]. *Drug Saf* 2001;24(4):255-265.
- Vlachopoulos C, Hirata K, O'Rourke M F. Effect of sildenafil on arterial stiffness and wave reflection. *Vasc Med* 2003;8(4):243-248.
- Vogt H J, Brandl P, Kockott G et al. Double-blind, placebo-controlled safety and efficacy trial with yohimbine hydrochloride in the treatment of nonorganic erectile dysfunction. *Int J Impot Res* 1997;9(3):155-161.
- Wagner G, Mulhall J. Pathophysiology and diagnosis of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):3-10.
- Wagner G, Rabkin J, Rabkin R. Effects of testosterone replacement therapy on sexual interest, function, and behavior in HIV+ men. *J Sex Res* 1997;34(1):27-33.
- Wagner Gorm, Kaplan Helen, Singer. The new injection treatment for impotence: Medical and psychological aspects. *Refuat Hapeh Vehashinayim* 1993;x, 210 pp. Philadelphia, PA, US210
- Wagrell L, Schelin S, Nordling J et al. Three-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomized multicenter study. *Urology* 2004;64(4):698-702.
- Wald M, Seftel A D, Ross L S et al. Computational models for detection of erectile dysfunction. *Br J Urol* 2005;173(1):167-170.
- Waldbaum R S. The safety of PDE5 inhibitors in ED treatment: Putting cardiovascular concerns to rest. *Cardiology Review* 2005;22(9):23-24.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Wang Z, Liu B C, Chen B et al. Randomized controlled study on erectile dysfunction treated by trazodone. *Chinese Journal of Andrology* 2002;16(3):236-238.
- Ware J, Catesby Rose F, Vincent McBrayer et al. The acute effects of nefazodone, trazodone and buspirone on sleep and sleep-related penile tumescence in normal subjects. *Sleep: Journal of Sleep Research & Sleep Medicine* 1994;17(6):544-550.
- Watanabe T, Chancellor M B, Rivas D A et al. Epidemiology of current treatment for sexual dysfunction in spinal cord injured men in the USA model spinal cord injury centers. *J Spinal Cord Med* 1996;19(3):186-189.
- Webb D J, Freestone S, Allen M J et al. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. *Am J Cardiol* 1999;83(5A):21C-28C.

- Webb D J, Muirhead G J, Wulff M et al. Sildenafil citrate potentiates the hypotensive effects of nitric oxide donor drugs in male patients with stable angina. *J Am Coll Cardiol* 2000;36(1):25-31.
- Wegner H E H, Knispel H H, Meier T et al. Nitric oxide donor, linsidomine chlorhydrate (SIN-1), in the diagnosis and treatment of erectile dysfunction: Critical appraisal and review of the literature. *International Urology & Nephrology* 1995;27(5):621-628.
- Weinhardt L S, Carey M P. Prevalence of erectile disorder among men with diabetes mellitus: Comprehensive review, methodological critique, and suggestions for future research. *J Sex Res* 1996;33(3):205-214.
- Weinsaft J W, Hickey K, Bokhari S et al. Effects of tadalafil on myocardial blood flow in patients with coronary artery disease. *Coron Artery Dis* 2006;17(6):493-499.
- Weiske W-H. Invasive diagnosis and therapy - Are they still reasonable in the age of sildenafil?. *Andrologia* 1999;31(SUPPL. 1):95-97.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Wessells H, Fuciarelli K, Hansen J et al. Synthetic melanotropic peptide initiates erections in men with psychogenic erectile dysfunction: double-blind, placebo controlled crossover study. *Br J Urol* 1998;160(2):389-393.
- Wessells H, Gralnek D, Dorr R et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000;56(4):641-646.
- Wheatley D. Triple-blind, placebo-controlled trial of Ginkgo biloba in sexual dysfunction due to antidepressant drugs. *Hum Psychopharmacol* 2004;19(8):545-548.
- Wilke D R, Parker C, Andonowski A et al. Testosterone and erectile function recovery after radiotherapy and long-term androgen deprivation with luteinizing hormone-releasing hormone agonists. *BJU Int* 2006;97(5):963-968.
- Williams G. Male erectile dysfunction. *Prescribers' Journal* 2000;40(1):49-58.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):
- Wilt T J, Fink H A. Is antidepressant plus sildenafil a recipe for priapism?. *Postgrad Med* 2004;116(6):11-12.
- Witt Deborah K. Yohimbine for erectile dysfunction. *J Fam Pract* 1998;46(4):282-283.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wyllie M G. The hunt for pink Viagra. *BJU Int* 2005;95(1):181-182.
- Wyllie M G. Let's hope for more in 2004. *BJU Int* 2004;93(1):175-176.
- Wyllie M G. The Second International Consultation on Erectile Dysfunction: Highlights from the pharmaceutical industry. *BJU Int* 2003;92(6):645-646.
- Wyllie M G. The genesis of a phytopharmaceutical industry (Mark II). *BJU Int* 2003;91(7):721-722.
- Yajima T, Yajima Y, Koppiker N et al. No clinically important effects on intraocular pressure after short-term administration of sildenafil citrate (Viagra). *Am J Ophthalmol* 2000;129(5):675-676.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yaman O, Tokatli Z, Akand M et al. Characteristics of sildenafil erections in healthy young men. *Asian J Androl* 2005;7(4):395-398.
- Yamanaka M, Shirai M, Shiina H et al. Vascular endothelial growth factor restores erectile function through inhibition of apoptosis in diabetic rat penile crura. *Br J Urol* 2005;173(1):318-323.
- Yan J Y, Yang W Z. A comparative effects of Sildenafil and Yohimbine for the treatment of erectile dysfunction. *Chinese Journal of Andrology* 2000;14(2):103-105.
- Yarkony G M. Enhancement of sexual function and fertility in spinal cord-injured males. [Review] [40 refs]. *Am J Phys Med Rehabil* 1990;69(2):81-87.
- Yassin A A, Saad F. Treatment of sexual dysfunction of hypogonadal patients with long-acting testosterone undecanoate (Nebido). [Review] [25 refs]. *World J Urol* 2006;24(6):639-644.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.
- Yasumoto R, Nishisaka N, Sakakura T et al. Ethanol embolization for impotent patients with venous leakage: A new technique and initial results. *Minimally Invasive Therapy & Allied Technologies: Mitat* 1996;5(6):564-566.
- Yeager J, Beihn R M. Retention and migration of alprostadil cream applied topically to the glans meatus for erectile dysfunction. *Int J Impot Res* 2005;17(1):91-95.

Youssef A F, Fort F L, Ronsen B et al. Evaluation of apomorphine HCl effects on reproductive endpoints: Studies in male rats and dogs. *J Toxicol Sci* 1999;51(2):273-279.

Zaslau S, Nicolis C, Galea G et al. A simplified pharmacologic erection program for patients with spinal cord injury. *J Spinal Cord Med* 1999;22(4):303-307.

Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200

Zhao L. Clinical observation on the therapeutic effects of heavy moxibustion plus point-injection in treatment of impotence. *J Tradit Chin Med* 2004;24(2):126-127.

Zhigang Long, Xiaowei Liu, Shengbo Lu. Therapy of impotence with traditional Chinese medicine. *Journal of Sex Education & Therapy* 1994;20(2):140-143.

Ziegler D. Management of erectile dysfunction in diabetic patients. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):58-65.

Zini Dante, Carani Cesare, Baldini Augusto et al. Sexual behavior of men with isolated hypogonadotropic hypogonadism or prepubertal anterior panhypopituitarism. *Horm Behav* 1990;24(2):174-185.

Zlotta A R, Teillac P, Raynaud J P et al. Evaluation of male sexual function in patients with Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), Tamsulosin or Finasteride. *Eur Urol* 2005;48(2):269-276.

Zusman R M. Cardiovascular data on sildenafil citrate: introduction.[erratum appears in *Am J Cardiol* 1999 Jul 15;84(2):244]. *Am J Cardiol* 1999;83(5A):1C-2C.

Zusman R M, Morales A, Glasser D B et al. Overall cardiovascular profile of sildenafil citrate. [Review] [33 refs]. *Am J Cardiol* 1999;83(5A):35C-44C.

Zusman R M, Prisant L M, Brown M J. Effect of sildenafil citrate on blood pressure and heart rate in men with erectile dysfunction taking concomitant antihypertensive medication. Sildenafil Study Group. *J Hypertens* 2000;18(12):1865-1869.

Observational injection study with < 6 months followup in duration.

Bancroft J, Smith G, Munoz M et al. Erectile response to visual erotic stimuli before and after intracavernosal papaverine, and its relationship to nocturnal penile tumescence and psychometric assessment. *Br J Urol* 1991;68(6):629-638.

Beretta G, Marzotto M, Zanollo A et al. Office treatment: intracavernous injections of prostaglandin E1 (PG E1) and improvement of spontaneous erections. *Acta Eur Fertil* 1991;22(4):221-223.

Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.

Brown S L, Haas C A, Koehler M et al. Hepatotoxicity related to intracavernous pharmacotherapy with papaverine. *Urology* 1998;52(5):844-847.

Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.

Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.

Chun S S, Fenemore J, Heaton J P et al. Enhancement of erectile responses to vasoactive drugs by a variable amplitude oscillation device. *Int J Impot Res* 1996;8(4):221-225.

Dinsmore W W, Alderdice D K. Vasoactive intestinal polypeptide and phentolamine mesylate administered by autoinjector in the treatment of patients with erectile dysfunction resistant to other intracavernosal agents. *Br J Urol* 1998;81(3):437-440.

Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.

Goonawardena S A, de Silva W A, Ketheeswaran T. Pharmacologically induced penile erections in the assessment and treatment of erectile impotence: a preliminary study of 100 patients. *Ceylon Med J* 1997;42(2):72-74.

Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.

Kadioglu A, Erdogru T, Tellaloglu S. Combined intracavernous injection of papaverine and stimulation (CIS) test. *J Androl* 1994;15 Suppl50S-53S.

Katlowitz N M, Albano G J, Morales P et al. Potentiation of drug-induced erection with audiovisual sexual stimulation. *Urology* 1993;41(5):431-434.

Katlowitz N, Albano G J, Patsias G et al. Effect of multidose intracorporeal injection and audiovisual sexual stimulation in vasculogenic impotence. *Urology* 1993;42(6):695-697.

- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Mansi M K, Alkhudair W K, Huraib S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *Br J Urol* 1998;159(6):1927-1930.
- McMahon C G. A pilot study of the role of intracavernous injection of vasoactive intestinal peptide (VIP) and phentolamine mesylate in the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(4):233-236.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Mirone V, Imbimbo C, Fabrizio F et al. Ketanserin plus prostaglandin E1 (PGE-1) as intracavernosal therapy for patients with erectile dysfunction unresponsive to PGE-1 alone. *Br J Urol* 1996;77(5):736-739.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Pagani E, Puech-Leao P, Glina S et al. The value of a second injection on the pharmaco-induced erection test. *Int J Impot Res* 1997;9(3):167-168.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Rodilla F, Fuentes M D, Chuan P et al. Penile self-injection for impotence in patients after radical cystectomy. *Journal of Clinical Pharmacy & Therapeutics* 1994;19(6):359-360.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266
- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Stief C G, Holmquist F, Djamilian M et al. Preliminary results with the nitric oxide donor linsidomine chlorhydrate in the treatment of human erectile dysfunction. *Br J Urol* 1992;148(5):1437-1440.
- Stief C G, Wetterauer U, Schaebdsau F H et al. Calcitonin-gene-related peptide: a possible role in human penile erection and its therapeutic application in impotent patients. *Br J Urol* 1991;146(4):1010-1014.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Weiss J N, Ravalli R, Badlani G H. Intracavernous pharmacotherapy in psychogenic impotence. *Urology* 1991;37(5):441-443.
- Observational injection study > or = to 6 months in duration.**
- al-Juburi A Z, O'Donnell P D. Follow up outcome of intracavernous papaverine. *J Ark Med Soc* 1990;86(10):383-385.
- Armstrong D K, Convery A G, Dinsmore W W. Reasons for patient drop-out from an intracavernous auto-injection programme for erectile dysfunction. *Br J Urol* 1994;74(1):99-101.
- Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.
- Chen J, Godschalk M F, Katz P G et al. Incidence of penile pain after injection of a new formulation of prostaglandin E1.[see comment]. *Br J Urol* 1995;154(1):77-79.
- Chen J, Godschalk M F, Katz P G et al. Combining intracavernous injection and external vacuum as treatment for erectile dysfunction.[see comment]. *Br J Urol* 1995;153(5):1476-1477.

- Cooper A J. Evaluation of I-C papaverine in patients with psychogenic and organic impotence. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1991;36(8):574-578.
- Dhabuwala C B, Kerkar P, Bhutwala A et al. Intracavernous papaverine in the management of psychogenic impotence. *Arch Androl* 1990;24(2):185-191.
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.
- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Godschalk M, Gheorghiu D, Chen J et al. Long-term efficacy of a new formulation of prostaglandin E1 as treatment for erectile failure.. *Br J Urol* 1996;155(3):915-917.
- Govier F E, McClure R D, Weissman R M et al. Experience with triple-drug therapy in a pharmacological erection program.[see comment]. *Br J Urol* 1993;150(6):1822-1824.
- Incrocci L, Hop W C, Slob A K. Visual erotic and vibrotactile stimulation and intracavernous injection in screening men with erectile dysfunction: a 3 year experience with 406 cases. *Int J Impot Res* 1996;8(4):227-232.
- Irwin M B, Kata E J. High attrition rate with intracavernous injection of prostaglandin E1 for impotency. *Urology* 1994;43(1):84-87.
- Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.
- Kattan S A. The acceptance of satisfaction of Saudi males to vasoactive autoinjection intracavernous therapy, external negative pressure device and penile prosthesis in the treatment of erectile dysfunction. *Ann Saudi Med* 2002;22(3-4):149-152.
- Knispel H H, Huland H. Influence of cause on choice of therapy in 174 patients with erectile dysfunction. *Br J Urol* 1992;147(5):1274-1276.
- Lim P H, Ng F C. Erectile dysfunction in Singapore men: presentation, diagnosis, treatment and results. *Ann Acad Med Singapore* 1992;21(2):248-253.
- Lottman P E, Hendriks J C, Vrugink P A et al. The impact of marital satisfaction and psychological counselling on the outcome of ICI-treatment in men with ED. *Int J Impot Res* 1998;10(2):83-87.
- Lundberg L, Olsson J-O, Kihl B. Long-term experience of self-injection therapy with prostaglandin E1 for erectile dysfunction. *Scand J Urol Nephrol* 1996;30(5):395-397.
- Maniam P, Seftel A D, Corty E W et al. Nocturnal penile tumescence activity unchanged after long-term intracavernous injection therapy. *Br J Urol* 2001;165(3):830-832.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993;42(5):554-558.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Four-drug intracavernous therapy for impotence due to corporeal veno-occlusive dysfunction. *Br J Urol* 1993;149(5 Pt 2):1291-1295.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Intracavernous vasoactive pharmacotherapy: the impact of a new self-injection device.[see comment]. *Br J Urol* 1993;150(6):1829-1832.
- Mulhall J P, Jahoda A E, Cairney M et al. The causes of patient dropout from penile self-injection therapy for impotence. *Br J Urol* 1999;162(4):1291-1294.
- Mulhall J P, Land S, Parker M et al. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *Br J Sex Med* 2005;2(4):532-542.
- Perimenis P, Athanasopoulos A, Geramoutsos I et al. The incidence of pharmacologically induced priapism in the diagnostic and therapeutic management of 685 men with erectile dysfunction. *Urol Int* 2001;66(1):27-29.
- Rowland D L, Boedhoe H S M, Dohle G et al. Intracavernosal self-injection therapy in men with erectile dysfunction: Satisfaction and attrition in 119 patients. *Int J Impot Res* 1999;11(3):145-151.
- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Speckens A E, Kattemolle M R, Hengeveld M W et al. A prospective long-term follow-up study of patients evaluated for erectile dysfunction: outcome and associated factors. *Int J Impot Res* 1995;7(2):101-110.

Tariq S H, Haleem U, Omran M L et al. Erectile dysfunction: Etiology and treatment in young and old patients. *Clin Geriatr Med* 2003;19(3):539-551.

Turner L A, Althof S E. The clinical effectiveness of self-injection and external vacuum devices in the treatment of erectile dysfunction: a six-month comparison. *Psychiatr Med* 1992;10(2):283-293.

Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196

Weidner W, Schroeder-Printzen I, Fischer C et al. Experience in the treatment of erectile dysfunction using the intracavernosal self-injection of papaverine: Results of a prospective study after a median follow-up of 42 months involving 135 patients and 10766 injections. *World J Urol* 1992;10(3):179-182.

Weiss J N, Badlani G H, Ravalli R et al. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6(3):171-174.

Not relevant by study design.

Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.

Anderson D C, Seifert C F. Topical nitrate treatment of impotence. [Review] [17 refs]. *Ann Pharmacother* 1993;27(10):1203-1205.

Anonymous. Sildenafil for erectile dysfunction. *Drug Ther.Bull* 1998;36(11):81-84.

Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.

Anonymous. Vasoactive intestinal peptide/phentolamine. *Invicorp, vasopotin. Drugs in R & D* 1999;2(6):436-438.

Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;

Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329

Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.

Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.

Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.

Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.

Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.

Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.

Chiang H-S, Kao Y H, Sheu M T. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995;24(5):767-769.

Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.

Derry F, Hultling C, Seftel A D et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. *Urology* 2002;60(2 Suppl 2):49-57.

Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol.* 1998;159(2):433-436.

Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.

Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.

Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.

Hellstrom W J. Vardenafil: a new approach to the treatment of erectile dysfunction. [Review] [37 refs]. *Curr Urol Rep* 2003;4(6):479-487.

Holmes S. Tadalafil: a new treatment for erectile dysfunction. *BJU Int* 2003;91(6):466-468.

- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- Keating G M, Scott L J. Vardenafil: a review of its use in erectile dysfunction. *Drugs* 2003;63(23):2673-2703.
- Keating G M, Scott L J. Spotlight on vardenafil in erectile dysfunction. *Drugs Aging* 2004;21(2):135-140.
- Kloner R A. Cardiovascular effects of the 3 phosphodiesterase-5 inhibitors approved for the treatment of erectile dysfunction. [Review] [57 refs]. *Circulation* 2004;110(19):3149-3155.
- Langtry H D, Markham A. Sildenafil: a review of its use in erectile dysfunction. *Drugs* 1999;57(6):967-989.
- Lewis R W. Intraurethral and topical agents. *Med Actual* 2000;36(2-3):113-119.
- Licht M R, Schover L R. Sildenafil (Viagra) for treating male erectile dysfunction. *Cleve Clin J Med* 1998;65(6):
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- McMahon C G. Topiglan: MacroChem. *Curr Opin Investig Drugs* 2002;3(4):602-606.
- Mikhail N. Does Testosterone Have a Role in Erectile Function?. *Am J Med* 2006;119:373-382.
- Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *Br J Sex Med* 2005;2(5):658-667.
- Moore R A, Derry S, McQuay H J. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. [Review] [77 refs]. *BMC Urol* 2005;5:18
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol.* 2002;26
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Padma-Nathan H, Eardley I, Kloner R A et al. A 4-year update on the safety of sildenafil citrate (Viagra). [Review] [88 refs]. *Urology* 2002;60(2:Suppl 2):Suppl-90.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Sommer F, Engelmann U. Vardenafil: Bayer Yakuin. *Curr Opin Investig Drugs* 2002;3(4):607-613.
- Sternbach Harvey. Age-associated testosterone decline in men: Clinical issues for psychiatry. *Am J Psychiatry* 1998;155(10):1310-1318.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Tomsak R. PDE5 inhibitors and permanent visual loss. *Int J Impot Res* 2005;17(6):547-549.
- Tran D, Howes L G. Cardiovascular safety of sildenafil. *Drug Saf* 2003;26(7):453-460.
- Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Not an original study, or population of interest, intervention of interest, or outcome of interest.**
- Abdallah H M. Comparison of Alprostadil (Caverject) and a combination of vasoactive drugs as local injections for the treatment of erectile dysfunction. *Int Urol Nephrol* 1998;30(5):617-620.
- Abrams J. Time course of the interaction between tadalafil and nitrates.[comment]. *J Am Coll Cardiol* 2004;43(11):2150-2151.
- Adaikan P G, Chong Y S, Chew S S L et al. Male sexual dysfunction. *Curr Obstet Gynaecol* 2000;10(1):23-28.
- Adams M A, Perdok R J, Padley R J et al. Safety and tolerability of apomorphine SL in men with cardiovascular disorders. *European Urology Supplements* 2002;1(3):28-32.
- Agelink M W, Schmitz T, Rembrink K et al. Cardiovascular effects of sildenafil citrate (Viagra): a naturalistic cross-over study. *Eur J Med Res* 2001;6(11):459-464.
- Ahuja S K, Krane N K, Hellstrom W J. Penile prostheses in the management of impotence in patients with end-stage renal disease. *J La State Med Soc* 1998;150(1):32-34.

- Aizenberg Dov, Gur Shay, Zemishlany Zvi et al. Mianserin, a 5-HT-sub(2a/2c) and alpha-sub-2 antagonist, in the treatment of sexual dysfunction induced by serotonin reuptake inhibitors. *Clin Neuropharmacol* 1997;20(3):210-214.
- Aizenberg Dov, Weizman Abraham, Barak Yoram et al. Sildenafil for selective serotonin reuptake inhibitor-induced erectile dysfunction in elderly male depressed patients. [References]. *J Sex Marital Ther* 2003;29(4):297-303.
- al-Juburi A Z, O'Donnell P D. Follow up outcome of intracavernous papaverine. *J Ark Med Soc* 1990;86(10):383-385.
- Alvizatos G, Skolarikos A, Laguna P. Recent data upon impotence, incontinence and quality of life issues concerning radical prostatectomy. [Review] [74 refs]. *Arch Esp Urol* 2003;56(3):321-330.
- Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.
- Althof S E, Cappelleri J C, Shpilsky A et al. Treatment responsiveness of the Self-Esteem And Relationship questionnaire in erectile dysfunction. *Urology* 2003;61(5):888-892.
- Althof S E, O'Leary M P, Cappelleri J C et al. Self-esteem, confidence, and relationships in men treated with sildenafil citrate for erectile dysfunction: results of two double-blind, placebo-controlled trials. *J Gen Intern Med* 2006;21(10):1069-1074.
- Altwein J E, Keuler F U. Oral treatment of erectile dysfunction with apomorphine SL. [Review] [34 refs]. *Urol Int* 2001;67(4):257-263.
- Anderson D C, Seifert C F. Topical nitrate treatment of impotence. [Review] [17 refs]. *Ann Pharmacother* 1993;27(10):1203-1205.
- Anderson R A, Bancroft J, Wu F C. The effects of exogenous testosterone on sexuality and mood of normal men. *Journal of Clinical Endocrinology & Metabolism* 1992;75(6):1503-1507.
- Andersson K-E. Pharmacology of penile erection. *Pharmacol Rev* 2001;53(3):417-450.
- Anonymous. Sildenafil and erectile dysfunction: new preparation. *Helpful. Prescrire.Int* 1998;7(38):163-165.
- Anonymous. Sublingual apomorphine: new preparation. In erectile disorders: a narrow therapeutic margin. *Prescrire.Int* 2002;11(59):76-79.
- Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.
- Anonymous. Viagra: a blueprint for safety and reliability. *Johns Hopkins Medical Letter, Health After* 50 2002;14(10):4-5.
- Anonymous. Vasoactive intestinal peptide/phentolamine. *Invicorp, vasopotin. Drugs in R & D* 1999;2(6):436-438.
- Anonymous. Treatment for impotence gains FDA approval. *Am J Health Syst Pharm* 1995;52(19):2078-2079.
- Anonymous. L-arginine. *Altern Med Rev* 2005;10(2):139-147.
- Anonymous. Use of sildenafil for ED classes II and III. *S Afr Med J* 2005;95(1):38
- Anonymous. Patient preference of ED drugs studied. *British Journal of Diabetes & Vascular Disease* 2003;3(6):444
- Anonymous. New drug for erectile dysfunction. *Can Pharm J* 2002;268(7200):756
- Anonymous. Vardenafil improves erectile function in men with diabetes. *Can Pharm J* 2001;267(7155):
- Anonymous. Alprostadil for erectile impotence. *Drug & Therapeutics Bulletin* 1995;33(8):61-62.
- Anonymous. What to do if Viagra won't do. *Harvard Mens Health Watch* 2005;9(10):4-8.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: intracavernous injection of prostaglandin E1. *JAMA* 1991;265(24):3321-3323.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: papaverine and phentolamine. *JAMA* 1990;264(6):752-754.
- Aranda P, Ruilope L M, Calvo C et al. Erectile dysfunction in essential arterial hypertension and effects of sildenafil: results of a Spanish national study. *Am J Hypertens* 2004;17(2):139-145.
- Ardicoglu A, Kocakoc E, Tuygun U O et al. Effectiveness of vardenafil versus papaverine in penile Doppler ultrasonography. *Urol Int* 2005;75(1):75-79.
- Ardicoglu A, Kocakoc E, Yuzgec V et al. Hemodynamic effects of sildenafil citrate (Viagra) on segmental branches of bilateral renal arteries. *International Urology & Nephrology* 2005;37(4):785-789.
- Armstrong D K, Convery A G, Dinsmore W W. Reasons for patient drop-out from an intracavernous auto-injection programme for erectile dysfunction. *Br J Urol* 1994;74(1):99-101.

- Armstrong D K, Convery A, Dinsmore W W. Prostaglandin E1 in the medical management of erectile dysfunction in a genitourinary medicine clinic. *Ulster Med J* 1994;63(1):18-22.
- Arver S, Dobs A S, Meikle A W et al. Improvement of sexual function in testosterone deficient men treated for 1 year with a permeation enhanced testosterone transdermal system. *Br J Urol* 1996;155(5):1604-1608.
- Ashok S, Sigman M. Bioavailable testosterone should be used for the determination of androgen levels in infertile men. *Br J Urol* 2007;177(4):1443-1446.
- Ashton Adam, Keller. Yohimbine in the treatment of male erectile dysfunction. *Am J Psychiatry* 1994;151(9):1397
- Assalian Pierre. Sildenafil for St. John wort-induced sexual dysfunction. [References]. *J Sex Marital Ther* 2000;26(4):357-358.
- Atmaca M, Kuloglu M, Tezcan E. Sildenafil use in patients with olanzapine-induced erectile dysfunction. *Int J Impot Res* 2002;14(6):547-549.
- Aukst-Margetic B, Margetic B. An open-label series using loratadine for the treatment of sexual dysfunction associated with selective serotonin reuptake inhibitors. *Prog Neuropsychopharmacol Biol Psychiatry* 2005;29(5):754-756.
- Aversa A, Bonifacio V, Moretti C et al. Re-dosing of prostaglandin-E1 versus prostaglandin-E1 plus phentolamine in male erectile dysfunction: a dynamic color power Doppler study. *Int J Impot Res* 2000;12(1):33-40.
- Aviv A, Shelef A, Weizman A. An open-label trial of sildenafil addition in risperidone-treated male schizophrenia patients with erectile dysfunction. *Hillside J Clin Psychiatry* 2004;65(1):97-103.
- Ayub W, Fletcher S. End-stage renal disease and erectile dysfunction. Is there any hope?. *Nephrology Dialysis Transplantation* 2000;15(10):1525-1528.
- Bacar M M, Batislam E, Altinok D et al. Sildenafil citrate for penile hemodynamic determination: an alternative to intracavernosal agents in Doppler ultrasound evaluation of erectile dysfunction. *Urology* 2001;57(4):623-626.
- Bach Amy K, Barlow David H, Wincze John P E. The enhancing effects of manualized treatment for erectile dysfunction among men using sildenafil: A preliminary investigation. [References]. *Behav Ther* 2004;35(1):55-73.
- Bai W J, Zhu J C, Jiang H et al. [A comparative study of different vasoactive drugs in the treatment of impotence]. *Chinese Journal of Urology* 1992;13(6):453-455.
- Bain J. Andropause. Testosterone replacement therapy for aging men. [Review] [55 refs]. *Can Fam Physician* 2001;4791-97.
- Balon Richard. Sildenafil and sexual dysfunction associated with antidepressants. [References]. *J Sex Marital Ther* 1999;25(4):259-264.
- Balon Richard. Fluvoxamine-induced erectile dysfunction responding to sildenafil. *J Sex Marital Ther* 1998;24(4):313-317.
- Bancroft J, Gutierrez P. Erectile dysfunction in men with and without diabetes mellitus: a comparative study.[see comment]. *Diabet Med* 1996;13(1):84-89.
- Bancroft J, Smith G, Munoz M et al. Erectile response to visual erotic stimuli before and after intracavernosal papaverine, and its relationship to nocturnal penile tumescence and psychometric assessment. *Br J Urol* 1991;68(6):629-638.
- Baniel J, Israilov S, Engelstein D et al. Three-year outcome of a progressive treatment program for erectile dysfunction with intracavernous injections of vasoactive drugs. *Urology* 2000;56(4):647-652.
- Barrou B, Cuzin B, Malavaud B et al. Early experience with sildenafil for the treatment of erectile dysfunction in renal transplant recipients. *Nephrol.Dial.Transplant.* 2003;18(2):411-417.
- Beal K, Mears J G. Short report: Penile lymphoma following local injections for erectile dysfunction. *Leuk Lymphoma* 2001;42(1-2):247-249.
- Becher E. Topical alprostadil cream for the treatment of erectile dysfunction. [Review] [46 refs]. *Expert Opin Pharmacother* 2004;5(3):623-632.
- Behrend L, Vibe-Petersen J, Perrild H. Sildenafil in the treatment of erectile dysfunction in men with diabetes: demand, efficacy and patient satisfaction. *Int J Impot Res* 2005;17(3):264-269.
- Bell D S H, Cutter G R, Hayne V B et al. Factors predicting efficacy of phentolamine-papaverine intracorporeal injection for treatment of erectile dysfunction in diabetic male. *Urology* 1992;40(1):36-40.
- Benatov R, Reznik I, Zemishlany Z. Sildenafil citrate (Viagra) treatment of sexual dysfunction in a schizophrenic patient. [References]. *Eur Psychiatry* 1999;14(6):353-355.
- Benckroun A, Faik M, Benjelloun S et al. A baseline-controlled, open-label, flexible dose-escalation study to assess the safety and efficacy of sildenafil citrate (Viagra) in patients with erectile dysfunction. *Int J Impot Res* 2003;15(Suppl 1):19-24.
- Benevides M D, Carson C C. Intraurethral application of alprostadil in patients with failed inflatable penile prosthesis. *Br J Urol* 2000;163(3):785-787.

- Beretta G, Marzotto M, Zanollo A et al. Office treatment: intracavernous injections of prostaglandin E1 (PG E1) and improvement of spontaneous erections. *Acta Eur Fertil* 1991;22(4):221-223.
- Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;
- Billington C J, Shafer R B, Morley J E. Effects of opioid blockade with nalmefene in older impotent men. *Life Sci* 1990;47(9):799-805.
- Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.
- Bischoff E. Vardenafil preclinical trial data: Potency, pharmacodynamics, pharmacokinetics, and adverse events. *Int J Impot Res* 2004;16(SUPPL. 1):S34-S37.
- Black A M, Day A G, Morales A. The reliability of clinical and biochemical assessment in symptomatic late-onset hypogonadism: Can a case be made for a 3-month therapeutic trial?. *BJU Int* 2004;94(7):1066-1070.
- Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329
- Blonde L. Sildenafil citrate for erectile dysfunction in men with diabetes and cardiovascular risk factors: a retrospective analysis of pooled data from placebo-controlled trials. *Curr Med Res Opin* 2006;22(11):2111-2120.
- Bocchi E A, Guimaraes G, Mocelin A et al. Sildenafil effects on exercise, neurohormonal activation, and erectile dysfunction in congestive heart failure: a double-blind, placebo-controlled, randomized study followed by a prospective treatment for erectile dysfunction. *Circulation* 2002;106(9):1097-1103.
- Bodansky H J E. Successful tadalafil treatment for erectile dysfunction associated with Charcot-Marie-Tooth syndrome. [References]. *Sexual and Relationship Therapy* 2006;21(1):87-89.
- Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.
- Bouloux P. Testim 1% testosterone gel for the treatment of male hypogonadism. [Review] [33 refs]. *Clin Ther* 2005;27(3):286-298.
- Boyarsky B K, Haque W, Rouleau M R et al. Sexual functioning in depressed outpatients taking mirtazapine. *Depression & Anxiety* 1999;9(4):175-179.
- Braatvedt G D. Outcome of managing impotence in clinical practice. *N Z Med J* 1999;112(1092):272-274.
- Brazil M. Viagra for broken hearts?. *Nat Rev Genet* 2005;4(3):190
- Briganti A, Salonia A, Gallina A et al. Drug insight: Oral phosphodiesterase type 5 inhibitors for erectile dysfunction. *Nature Clinical Practice Urology* 2005;2(5):239-247.
- Brignardello E, Manti R, Papotti M et al. Ectopic secretion of LH by an endocrine pancreatic tumor. *J Endocrinol Invest* 2004;27(4):361-365.
- Brindis R G, Kloner R A. Sildenafil in patients with cardiovascular disease. [Review] [33 refs]. *Am J Cardiol* 2003;92(9A):26M-36M.
- Brisson T E, Broderick G A, Thiel D D et al. Vardenafil rescue rates of sildenafil nonresponders: objective assessment of 327 patients with erectile dysfunction. *Urology* 2006;68(2):397-401.
- Brock G B, McMahon C G, Chen K K et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. *Br J Urol* 2002;168(4 Pt 1):1332-1336.
- Brock G, Chan J, Carrier S et al. The treatment of erectile dysfunction study: focus on treatment satisfaction of patients and partners. *BJU Int* 2007;99(2):376-382.
- Brown S L, Haas C A, Koehler M et al. Hepatotoxicity related to intracavernous pharmacotherapy with papaverine. *Urology* 1998;52(5):844-847.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. *Urologe* 2005;Ausg. A. 44(9):1045-1046, 1048-51.
- Burge M R, Lanzi R A, Skarda S T et al. Idiopathic hypogonadotropic hypogonadism in a male runner is reversed by clomiphene citrate. *Fertility & Sterility* 1997;67(4):783-785.
- Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.
- Burnett A L. Vasoactive pharmacotherapy to cure erectile dysfunction: fact or fiction?. [Review] [45 refs]. *Urology* 2005;65(2):224-230.
- Burns-Cox N, Gingell C. The andropause: fact or fiction?. [Review] [49 refs]. *Postgrad Med J* 1997;73(863):553-556.
- Buvat J. Hyperprolactinemia and sexual function in men: a short review. [Review] [26 refs]. *Int J Impot Res* 2003;15(5):373-377.

- Buvat J, Montorsi F. Safety and tolerability of apomorphine SL in patients with erectile dysfunction. *BJU Int* 2001;88(3):30-35.
- Buvat J, Lemaire A, Ratajczyk J. Acceptance, efficacy and preference of Sildenafil in patients on long term auto-intracavernosal therapy: a study with follow-up at one year. *Int J Impot Res* 2002;14(6):483-486.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Cappelleri J C, Althof S E, Siegel R L et al. Association between the Erectile Dysfunction Inventory of Treatment Satisfaction and the Self-Esteem and Relationship Questionnaire following treatment with sildenafil citrate for men with erectile dysfunction. *Value Health* 2005;8(Suppl 1):54-60.
- Cappelleri J C, Bell S S, Althof S E et al. Comparison between sildenafil-treated subjects with erectile dysfunction and control subjects on the Self-Esteem And Relationship questionnaire. *Br J Sex Med* 2006;3(2):274-282.
- Carani C, Granata A R, Bancroft J et al. The effects of testosterone replacement on nocturnal penile tumescence and rigidity and erectile response to visual erotic stimuli in hypogonadal men. *Psychoneuroendocrinology* 1995;20(7):743-753.
- Carani C, Zini D, Baldini A et al. Effects of androgen treatment in impotent men with normal and low levels of free testosterone. *Arch Sex Behav* 1990;19(3):223-234.
- Caretta N, Palego P, Ferlin A et al. Resumption of spontaneous erections in selected patients affected by erectile dysfunction and various degrees of carotid wall alteration: Role of tadalafil. *Eur Urol* 2005;48(2):326-332.
- Carey F, Quah S P, Dinsmore W. Postal survey to determine how many patients continued to seek treatment with sildenafil following sildenafil trials. *Int J STD AIDS* 2003;14(7):501-502.
- Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.
- Carosa E, Martini P, Brandetti F et al. Type V phosphodiesterase inhibitor treatments for erectile dysfunction increase testosterone levels. *Clin Endocrinol (Oxf)* 2004;61(3):382-386.
- Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.
- Carson C C, Rajfer J, Eardley I et al. The efficacy and safety of tadalafil: an update. *BJU Int* 2004;93(9):1276-1281.
- Caruso S, Intelisano G, Farina M et al. Efficacy and safety of daily intake of apomorphine SL in men affected by erectile dysfunction and mild hyperprolactinemia: a prospective, open-label, pilot study. *Urology* 2003;62(5):922-927.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Chaiban J T, Azar S T. Erectile dysfunction in diabetic patients. *J Med Liban* 2004;52(4):217-219.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Cheitlin M D, Hutter A M, Brindis R G et al. Use of sildenafil (Viagra) in patients with cardiovascular disease. *Circulation* 1999;99(1):168-177.
- Chen J K, Hwang T I, Yang C R. Comparison of effects following the intracorporeal injection of papaverine and prostaglandin E1. *Br J Urol* 1992;69(4):404-407.
- Chen J, Godschalk M F, Katz P G et al. Incidence of penile pain after injection of a new formulation of prostaglandin E1.[see comment]. *Br J Urol* 1995;154(1):77-79.
- Chen J, Godschalk M F, Katz P G et al. Combining intracavernous injection and external vacuum as treatment for erectile dysfunction.[see comment]. *Br J Urol* 1995;153(5):1476-1477.
- Chen J, Godschalk M, Katz P G et al. The lowest effective dose of prostaglandin E1 as treatment for erectile dysfunction.. *Br J Urol* 1995;153(1):80-81.
- Chen J, Mabjeesh N J, Greenstein A et al. Clinical efficacy of sildenafil in patients on chronic dialysis. *Br J Urol* 2001;165(3):819-821.
- Chen J, Sofer M, Kaver I et al. Concomitant use of sildenafil and a vacuum entrapment device for the treatment of erectile dysfunction. *Br J Urol* 2004;171(1):292-295.
- Chen K-K, Jiann B-P, Lin J S N et al. Erratum: Efficacy and safety of on-demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study (*Journal of Sexual Medicine* vol. 1 (2)). *Br J Sex Med* 2005;2(1):158

- Cheng E. Real-life safety and efficacy of vardenafil in the treatment of erectile dysfunction—results from 30,010 U.S. patients. *Br J Sex Med* 2007;4(2):432-439.
- Chew K K. Prevalence of hypogonadism in the aging male and male erectile dysfunction in Asia-Pacific countries. *Asian J Androl* 2003;5(2):171-172.
- Chew K K, Stuckey B G A. Use of transurethral alprostadil (MUSE) (prostaglandin E1) for glans tumescence in a patient with penile prosthesis. *Int J Impot Res* 2000;12(3):195-196.
- Chew K K, Stuckey B G A, Thompson P L. Erectile dysfunction, sildenafil and cardiovascular risk. *Med J Aust* 2000;172(6):279-283.
- Chia S. Management of premature ejaculation -- a comparison of treatment outcome in patients with and without erectile dysfunction. *Int J Androl* 2002;25(5):301-305.
- Chia S J, Ramesh K, Earnest A. Clinical application of prognostic factors for patients with organic causes of erectile dysfunction on 100 mg of sildenafil citrate. *Int J Urol* 2004;11(12):1104-1109.
- Chiang H S, Wen T C, Liang J F. Titration study of MUSE (Medicated Urethral System for Erection) in erectile dysfunction. *J Formos Med Assoc* 2000;99(12):926-930.
- Chiang H-S, Kao Y H, Sheu M T. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995;24(5):767-769.
- Chiang P-H, Tsai E-M, Chiang C-P. The role of trazodone in the treatment of erectile dysfunction. *Kao-Hsiung i Hsueh Ko Hsueh Tsa Chih [Kaohsiung Journal of Medical Sciences]* 1994;10(6):287-294.
- Chinegwundoh F, Anie K A. Treatments for priapism in boys and men with sickle cell disease. [Review] [16 refs]. *Cochrane Database Syst Rev* 2004;(4):CD004198
- Choi H K, Adimoelja A, Kim S C et al. A dose-response study of alprostadil sterile powder (S.Po.) (Caverject) for the treatment of erectile dysfunction in Korean and Indonesian men. *Int J Impot Res* 1997;9(1):47-51.
- Christ B, Brockmeier D, Hauck E W et al. Investigation on interaction between tacrolimus and sildenafil in kidney-transplanted patients with erectile dysfunction. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(3):149-156.
- Christ G J, Melman A. The application of gene therapy to the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):111-112.
- Chun S S, Fenemore J, Heaton J P et al. Enhancement of erectile responses to vasoactive drugs by a variable amplitude oscillation device. *Int J Impot Res* 1996;8(4):221-225.
- Clark C. Erectile dysfunction and other problems. *Can Pharm J* 2004;272(7299):608-610.
- Claro J A, Ximenes S F, Nardoza A et al. Effect of sildenafil in cavernous arteries of patients with erectile dysfunction. *International Braz J Urol* 2003;29(4):320-326.
- Cohen J S. Comparison of FDA reports of patient deaths associated with sildenafil and with injectable alprostadil. *Ann Pharmacother* 2001;35(3):285-288.
- Conti C R, Pepine C J, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. *Am J Cardiol* 1999;83(5A):29C-34C.
- Cooper A J. Evaluation of I-C papaverine in patients with psychogenic and organic impotence. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1991;36(8):574-578.
- Copel L, Katz R, Blachar A et al. Clinical and duplex US assessment of effects of sildenafil on cavernosal arteries of the penis: Comparison with intracavernosal injection of vasoactive agents - Initial experience. *Radiology* 2005;237(3):986-991.
- Corona G, Mannucci E, Fisher A D et al. Effect of hyperprolactinemia in male patients consulting for sexual dysfunction. *Br J Sex Med* 2007;4(5):1485-1493.
- Corona G, Mannucci E, Schulman C et al. Psychobiologic correlates of the metabolic syndrome and associated sexual dysfunction. *Eur Urol* 2006;50(3):595-604.
- Costabile R A, Spevak M, Fishman I J et al. Efficacy and safety of transurethral alprostadil in patients with erectile dysfunction following radical prostatectomy. *Br J Urol* 1998;160(4):1325-1328.
- Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.
- Curran M, Keating G. Tadalafil.[erratum appears in *Drugs*. 2003;63(23):2703]. [Review] [31 refs]. *Drugs* 2003;63(20):2203-2212.
- Dachille G, Pagliarulo V, Ludovico G M et al. Sexual dysfunction in patients under dialytic treatment. *Minerva Urol Nefrol* 2006;58(2):195-200.
- Davis B E, Weigel J W, Whitford C S. Treatment of male impotence: a new option. *Kans Med* 1990;91(12):325-326.

- De Rose A F, Giglio M, Traverso P et al. Combined oral therapy with sildenafil and doxazosin for the treatment of non-organic erectile dysfunction refractory to sildenafil monotherapy. *Int J Impot Res* 2002;14(1):50-53.
- De Meyer J M, Thibo P, Hatzichriston D G. The effect of re-dosing of vasodilators on the intracavernosal pressure and on the penile rigidity. *Eur Urol* 1998;33(3):293-297.
- De Siati M, Saugo M, Franzolin N. The start of pharmacological activity after sublingual administration of sildenafil citrate in 30 patients affected by erectile dysfunction. *Arch Ital Urol Androl* 2003;75(1):18-20.
- Decter R M, Furness P D, Nguyen T A et al. Reproductive understanding, sexual functioning and testosterone levels in men with spina bifida. *Br J Urol* 1997;157(4):1466-1468.
- Derby C A, Araujo A B, Johannes C B et al. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 2000;12(4):197-204.
- Derry F, Hultling C, Seftel A D et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. *Urology* 2002;60(2 Suppl 2):49-57.
- Dhabuwala C B, Kerkar P, Bhutwala A et al. Intracavernous papaverine in the management of psychogenic impotence. *Arch Androl* 1990;24(2):185-191.
- Dinsmore W W. Medical treatment of impotence with papaverine and phentolamine intracavernosal injection. *Ulster Med J* 1990;59(2):174-176.
- Dinsmore W W, Alderdice D K. Vasoactive intestinal polypeptide and phentolamine mesylate administered by autoinjector in the treatment of patients with erectile dysfunction resistant to other intracavernosal agents. *Br J Urol* 1998;81(3):437-440.
- Dizon M N, Vesely D L. Gonadotropin-secreting pituitary tumor associated with hypersecretion of testosterone and hypogonadism after hypophysectomy. *Endocr Pract* 2002;8(3):225-231.
- Doggrell S A. Comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction. *Expert Opin Pharmacother* 2005;6(1):75-84.
- Donatucci C F, Lue T F. Erectile dysfunction in men under 40: etiology and treatment choice. *Int J Impot Res* 1993;5(2):97-103.
- Donatucci C, Eardley I, Buvat J et al. Vardenafil improves erectile function in men with erectile dysfunction irrespective of disease severity and disease classification. *Br J Sex Med* 2004;1(3):301-309.
- Dundar S O, Dayanir Y, Topalolu A et al. Effect of sildenafil on ocular hemodynamics in 3 months regular use. *Int J Impot Res* 2006;18(3):282-286.
- Dundar S O, Topalolu A, Dundar M et al. Effects of sildenafil on blue-on-yellow and white-on-white Humphrey perimetry in 3 months regular use. *Arb Paul Ehrlich Inst Georg Speyer Haus Ferdinand Blum Inst Frankf A M* 2006;20(7):810-813.
- Dunn A. Sildenafil: A new therapy for erectile dysfunction. *Conn Med* 1998;62(7):413-416.
- Dusing R. Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men. *Blood Pressure Supplement* 2003;229-34.
- Eardley I. New oral therapies for the treatment of erectile dysfunction. *Br J Urol* 1998;81(1):122-127.
- El Malik E M A. Erectile dysfunction: An update of diagnosis and management. *Qatar Medical Journal* 2000;9(2):9-17.
- El-Sakka A I. Efficacy of sildenafil citrate in treatment of erectile dysfunction: effect of type 2 diabetes. *Eur Urol* 2004;46(4):503-509.
- El-Sakka A I. Efficacy of sildenafil citrate in treatment of erectile dysfunction: impact of associated premature ejaculation and low desire. *Urology* 2006;68(3):642-647.
- El-Sakka A I, Hassoba H M, Elbakry A M et al. Prostatic specific antigen in patients with hypogonadism: Effect of testosterone replacement. *Br J Sex Med* 2005;2(2):235-240.
- Elhanbly S, Schoor R, Elmogy M et al. What nonresponse to intracavernous injection really indicates: a determination by quantitative analysis. *Br J Urol* 2002;167(1):192-196.
- Engel J D, McVary K T. Transurethral alprostadil as therapy for patients who withdrew from or failed prior intracavernous injection therapy. *Urology* 1998;51(5):687-692.
- Engelhardt P F, Daha L K, Zils T et al. Acupuncture in the treatment of psychogenic erectile dysfunction: first results of a prospective randomized placebo-controlled study. *Int J Impot Res* 2003;15(5):343-346.
- Engelhardt P F, Plas E, Hubner W A et al. Comparison of intraurethral liposomal and intracavernosal prostaglandin-E1 in the management of erectile dysfunction. *Br J Urol* 1998;81(3):441-444.
- Engl T, Beecken W-D, Wolfram M et al. Uropharmacology: Current and future strategies in the treatment of erectile dysfunction and benign prostate hyperplasia. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(10):527-533.

- English J C, King D H C, Foley J P. Penile shaft hypopigmentation: Lichen sclerosus occurring after the initiation of alprostadil intracavernous injections for erectile dysfunction. *J Am Acad Dermatol* 1998;39(5 I):801-803.
- Erbagci A, Yagci F, Sarica K et al. Evaluation and therapeutic regulation of erectile dysfunction with visual stimulation test. An objective approach by using sildenafil citrate test. *Urol.Int* 2002;69(1):21-26.
- Erdogru T, Usta M F, Ceken K et al. Is sildenafil citrate an alternative agent in the evaluation of penile vascular system with color Doppler ultrasound?. *Urol Int* 2002;68(4):255-260.
- Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol.* 1998;159(2):433-436.
- Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.
- Espinoza R, Melchor J L, Gracida C. Sildenafil (Viagra) in kidney transplant recipients with erectile dysfunction. *Transplant Proc* 2002;34(1):408-409.
- Fagelman E, Fagelman A, Shabsigh R. Efficacy, safety, and use of sildenafil in urologic practice. *Urology* 2001;57(6):1141-1144.
- Fava M, Rankin M A, Alpert J E et al. An open trial of oral sildenafilin antidepressant-induced sexual dysfunction. *Psychotherapy & Psychosomatics* 1998;67(6):328-331.
- Fazeli-Matin S, Montague D K, Angermeier K W et al. Penile fracture after intracavernous injection therapy. *Br J Urol* 1998;159(6):2094
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.
- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Feldman R, Meuleman E J, Steers W. Sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: analysis of two flexible dose-escalation studies. Sildenafil Study Group. *Int J Clin Pract* 1999;102(Suppl Jun.):100-102.
- Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.
- Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.
- Fishbain David A. Impact of sildenafil on male erectile disorder due to psychological factors. *Can J Psychiatry* 2000;45(1):85-86.
- Flack J M. The effect of doxazosin on sexual function in patients with benign prostatic hyperplasia, hypertension, or both.[see comment]. [Review] [47 refs]. *Int J Clin Pract* 2002;56(7):527-530.
- Fonseca V, Seftel A, Denne J et al. Impact of diabetes mellitus on the severity of erectile dysfunction and response to treatment: analysis of data from tadalafil clinical trials. *Diabetologia* 2004;47(11):1914-1923.
- Foresta C, Caretta N, Lana A et al. Relationship Between Vascular Damage Degrees and Endothelial Progenitor Cells in Patients with Erectile Dysfunction: Effect of Vardenafil Administration and PDE5 Expression in the Bone Marrow. *Eur Urol* 2007;51(5):1411-1419.
- Foresta C, Ferlin A, De Toni L et al. Circulating endothelial progenitor cells and endothelial function after chronic Tadalafil treatment in subjects with erectile dysfunction. *Int J Impot Res* 2006;18(5):484-488.
- Foulks C J, Cushner H M. Sexual dysfunction in the male dialysis patient: pathogenesis, evaluation, and therapy. [Review] [105 refs]. *Am J Kidney Dis* 1986;8(4):211-222.
- Fox K M, Thadani U, Ma P T et al. Sildenafil citrate does not reduce exercise tolerance in men with erectile dysfunction and chronic stable angina. *Eur Heart J* 2003;24(24):2206-2212.
- Freitas D, Athanazio R, Almeida D et al. Sildenafil improves quality of life in men with heart failure and erectile dysfunction. *Int J Impot Res* 2006;18(2):210-212.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Fugl-Meyer K S, Stothard D, Belger M et al. The effect of tadalafil on psychosocial outcomes in Swedish men with erectile distress: a multicentre, non-randomised, open-label clinical study. *Int J Clin Pract* 2006;60(11):1386-1393.
- Fujisawa M, Sawada K. Clinical efficacy and safety of sildenafil in elderly patients with erectile dysfunction. *Arch Androl* 2004;50(4):255-260.
- Fulgham P F, Cochran J S, Denman J L et al. Disappointing initial results with transurethral alprostadil for erectile dysfunction in a urology practice setting.. *Br J Urol* 1998;160(6 Pt 1):2041-2046.

- Gana T E, Quizon L F, Castell R et al. A dose-response study of alprostadil in patients with erectile dysfunction. *Curr Ther Res Clin Exp* 1996;57(9):700-710.
- Garcia-Bravo A M, Suarez-Hernandez D, Ruiz-Fernandez M A et al. Determination of changes in blood pressure during administration of sildenafil (Viagra) in patients with spinal cord injury and erectile dysfunction. *Proc Annu Clin Spinal Cord Inj Conf* 2006;44(5):301-308.
- Ghanem H, Sherif T, bdel-Gawad T et al. Short term use of intracavernous vasoactive drugs in the treatment of persistent psychogenic erectile dysfunction. *Int J Impot Res* 1998;10(4):211-214.
- Gheorghiu S, Godschalk M, Gentili A et al. Quality of life in patients using self-administered intracavernous injections of prostaglandin E1 for erectile dysfunction. *Br J Urol* 1996;156(1):80-81.
- Giammusso B, Morgia G, Spampinato A et al. Improved pallesthetic sensitivity of pudendal nerve in impotent diabetic patients treated with acetyl-L-carnitine. *Acta Urologica Italica* 1996;10(3):185-187.
- Gil A, Martinez E, Oyaguez I et al. Erectile dysfunction in a primary care setting: results of an observational, no-control-group, prospective study with sildenafil under routine conditions of use. *Int J Impot Res* 2001;13(6):338-347.
- Gilbert H W, Gingell J C. The results of an intracorporeal papaverine clinic. *Sex Marital Ther* 1991;6(1):49-56.
- Gilbert H W, Gillatt D A, Desai K M et al. Intracorporeal papaverine injection in androgen deprived men. *J R Soc Med* 1990;83(3):161
- Gilbert R N, Graham C W, Regan J B. Double-blind- cross-over trial of testosterone enanthate in impotent men with low or low-normal serum testosterone levels. *Br J Urol* 1992;147264
- Gillies H C, Roblin D, Jackson G. Coronary and systemic hemodynamic effects of sildenafil citrate: From basic science to clinical studies in patients with cardiovascular disease. *Int J Cardiol* 2002;86(2-3):131-141.
- Gingell C, Buvat J, Jardin A et al. Sildenafil citrate (VIAGRA(TM)), an oral treatment for erectile function: 1-year, open-label, extension studies. *Int J Clin Pract* 1999;(pp 30-31):-31.
- Ginsberg D L. Vardenafil treatment of sertraline-induced sexual dysfunction. *Primary Psychiatry* 2004;11(11):23-24.
- Ginsberg David L. Sildenafil-dihydrocodeine interaction results in prolonged erections. [References]. *Primary Psychiatry* 2003;10(2):23
- Ginzburg R, Wong Y, Fader J S. Effect of bupropion on sexual dysfunction. *Ann Pharmacother* 2005;39(12):2096-2099.
- Giuliano F, Donatucci C, Montorsi F et al. Vardenafil is effective and well-tolerated for treating erectile dysfunction in a broad population of men, irrespective of age. *BJU Int* 2005;95(1):110-116.
- Giuliano F, Montorsi F, Mirone V et al. Switching from intracavernous prostaglandin E1 injections to oral sildenafil citrate in patients with erectile dysfunction: results of a multicenter European study. The Sildenafil Multicenter Study Group. *Br J Urol* 2000;164(3:Pt 1):t-11.
- Giuliano F, Pena B M, Mishra A et al. Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction. *Qual Life Res* 2001;10(4):359-369.
- Giuliano F, Rubio-Aurioles E, Kennelly M et al. Efficacy and safety of vardenafil in men with erectile dysfunction caused by spinal cord injury. *Neurology* 2006;66(2):210-216.
- Glenn D R J, McClure N, Lewis S E M. The hidden impact of diabetes on male sexual dysfunction and fertility. *Hum Fertil* 2003;6(4):174-179.
- Glina S, Sotomayor M, Gatchalian E et al. Timing of dose relative to sexual intercourse attempt in previous sildenafil citrate users treated with tadalafil. *Br J Sex Med* 2006;3(2):309-319.
- Godschalk M F, Chen J, Katz P G et al. Prostaglandin E1 as treatment for erectile failure in elderly men. *J Am Geriatr Soc* 1994;42(12):1263-1265.
- Godschalk M, Gheorghiu D, Chen J et al. Long-term efficacy of a new formulation of prostaglandin E1 as treatment for erectile failure.. *Br J Urol* 1996;155(3):915-917.
- Gogtay N J, Bichile S K, Pinto C J et al. Erectile dysfunction and sildenafil citrate.[comment]. *J Assoc Physicians India* 2001;49871-872.
- Goldenberg M M. Safety and efficacy of sildenafil citrate in the treatment of male erectile dysfunction. *Clin Ther.* 1998;20(6):1033-1048.
- Goldstein I. Oral phentolamine: an alpha-1, alpha-2 adrenergic antagonist for the treatment of erectile dysfunction. [Review] [9 refs]. *Int J Impot Res* 2000;12Suppl-80.
- Goldstein I. A 36-week, open label, non-comparative study to assess the long-term safety of sildenafil citrate (VIAGRA) in patients with erectile dysfunction. *Int J Clin Pract* 1999;Supplement.102-109.

- Goldstein I, Auerbach S, Padma-Nathan H et al. Axial penile rigidity as primary efficacy outcome during multi-institutional in-office dose titration clinical trials with alprostadil alfadex in patients with erectile dysfunction. Alprostadil Alfadex Study Group. *Int J Impot Res* 2000;12(4):205-211.
- Goldstein I, Kim E, Steers W D et al. Efficacy and safety of tadalafil in men with erectile dysfunction with a high prevalence of comorbid conditions: results from MOMENTUS: multiple observations in men with erectile dysfunction in National Tadalafil Study in the US. *Br J Sex Med* 2007;4(1):166-175.
- Gomery P, Bullock A, McGettigan J et al. Tadalafil is efficacious in Black American and Hispanic men with erectile dysfunction: results from multiple observations in men with erectile dysfunction in national tadalafil study in the US (MOMENTUS). *Int J Impot Res* 2007;19(1):76-83.
- Goonawardena S A, de Silva W A, Ketheeswaran T. Pharmacologically induced penile erections in the assessment and treatment of erectile impotence: a preliminary study of 100 patients. *Ceylon Med J* 1997;42(2):72-74.
- Gore J L, Swerdloff R S, Rajfer J. Androgen deficiency in the etiology and treatment of erectile dysfunction. *Urol Clin North Am* 2005;32(4):457-468.
- Govier F E, McClure R D, Weissman R M et al. Experience with triple-drug therapy in a pharmacological erection program.[see comment]. *Br J Urol* 1993;150(6):1822-1824.
- Greco E A, Pili M, Bruzziches R et al. Testosterone:estradiol ratio changes associated with long-term tadalafil administration: a pilot study. *Br J Sex Med* 2006;3(4):716-722.
- Greco E, Polonio-Balbi P. Penile rigidity in erectile dysfunction treated with alprostadil. *Lancet* 1997;350(9092):1682
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.
- Green B G, Martin S. Clinical assessment of sildenafil in the treatment of neurogenic male sexual dysfunction: After the hype. *NeuroRehabilitation* 2000;15(2):101-105.
- Greenstein A, Mabjeesh N J, Sofer M et al. Does sildenafil combined with testosterone gel improve erectile dysfunction in hypogonadal men in whom testosterone supplement therapy alone failed?[see comment]. *Br J Urol* 2005;173(2):530-532.
- Gresser U, Gleiter C H. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil--review of the literature. [Review] [92 refs]. *Eur J Med Res* 2002;7(10):435-446.
- Gross A J, Sauerwein D H, Kutzenberger J et al. Penile prostheses in paraplegic men. *Br J Urol* 1996;78(2):262-264.
- Grossman E B, Swan S K, Muirhead G J et al. The pharmacokinetics and hemodynamics of sildenafil citrate in male hemodialysis patients. *Kidney Int* 2004;66(1):367-374.
- Grover J K, Vats V, Ajeeta. Sildenafil (Viagra(TM)). *Medico-Legal Update* 1998;3(1-2):67-78.
- Guay A T, Perez J B, Jacobson J et al. Efficacy and safety of sildenafil citrate for treatment of erectile dysfunction in a population with associated organic risk factors.[erratum appears in *J Androl* 2002 Jan-Feb;23(1):113]. *J Androl* 2001;22(5):793-797.
- Guay A T, Perez J B, Velasquez E et al. Clinical experience with intraurethral alprostadil (MUSE) in the treatment of men with erectile dysfunction. A retrospective study. Medicated urethral system for erection. *Eur Urol* 2000;38(6):671-676.
- Guay A T, Spark R F, Jacobson J et al. Yohimbine treatment of organic erectile dysfunction in a dose-escalation trial. *Int J Impot Res* 2002;14(1):25-31.
- Gupta N, Sawlani K K, Tripathi A K. Appropriate use of sildenafil citrate in male erectile dysfunction.[see comment]. [Review] [52 refs]. *J Assoc Physicians India* 2001;49:889-896.
- Gupta Sanjay, Masand Prakash, Ashton Adam K et al. Phenelzine-induced sexual dysfunction treated with sildenafil. *J Sex Marital Ther* 1999;25(2):131-135.
- Gutierrez P, Hernandez P, Mas M. Combining programmed intracavernous PGE1 injections and sildenafil on demand to salvage sildenafil nonresponders.. *Int J Impot Res* 2005;17(4):354-358.
- Hammadeh M Y, Madaan S, Hines J et al. 5-year outcome of a prospective randomized trial to compare transurethral electrovaporization of the prostate and standard transurethral resection. *Urology* 2003;61(6):1166-1171.
- Harding L M, Adeniyi A, Everson R et al. Comparison of a needle-free high-pressure injection system with needle-tipped injection of intracavernosal alprostadil for erectile dysfunction. *Int J Impot Res* 2002;14(6):498-501.
- Harrold L R, Gurwitz J H, Field T S et al. The diffusion of a novel therapy into clinical practice: the case of sildenafil.[see comment]. *Arch Intern Med* 2000;160(22):3401-3405.
- Harwood P J, Grotz M, Eardley I et al. Erectile dysfunction after fracture of the pelvis. *Journal of Bone & Joint Surgery - British Volume* 2005;87(3):281-290.
- Hatzichristou D G. Sildenafil citrate: lessons learned from 3 years of clinical experience. [Review] [60 refs]. *Int J Impot Res* 2002;14Suppl-52.
- Hatzichristou D G. Current treatment and future perspectives for erectile dysfunction. [Review] [85 refs]. *Int J Impot Res* 1998;10Suppl-13.

- Hatzichristou D G, Apostolidis A, Tzortzis V et al. Sildenafil versus intracavernous injection therapy: efficacy and preference in patients on intracavernous injection for more than 1 year. *Br J Urol* 2000;164(4):1197-1200.
- Hatzichristou D, Vardi Y, Papp G et al. Effect of tadalafil on sexual timing behavior patterns in men with erectile dysfunction: integrated analysis of randomized, placebo controlled trials. *Br J Urol* 2005;174(4 Pt 1):1356-1359.
- Hatzimouratidis K, Hatzichristou D. Phosphodiesterase Type 5 Inhibitors: The Day After. *Eur Urol* 2007;51(1):75-89.
- Hatzimouratidis K, Hatzichristou D G. A comparative review of the options for treatment of erectile dysfunction: Which treatment for which patient?. *Drugs* 2005;65(12):1621-1650.
- Hauck E W, Altinkilic B M, Schroeder-Printzen I et al. Prostaglandin E1 long-term self-injection programme for treatment of erectile dysfunction--a follow-up of at least 5 years. *Andrologia* 1999;31(Suppl):Suppl-103.
- He X Q, Hong B F, Wang X X et al. Evaluation of efficacy and safety of oral sildenafil citrate therapy for men with erectile dysfunction. *Pharmaceutical Journal of Chinese Peoples Liberation Army* 2002;18(4):205-208.
- Heaton J P. Key issues from the clinical trials of apomorphine SL. *World J Urol* 2001;19(1):25-31.
- Heaton J P W, Wagner Porst, Eid Wyllie. Apomorphine: An update of clinical trial results. *Int J Impot Res* 2000;12(SUPPL. 4):S67-S73.
- Heaton J P, Lording D, Liu S N et al. Intracavernosal alprostadil is effective for the treatment of erectile dysfunction in diabetic men. *Int J Impot Res* 2001;13(6):317-321.
- Heaton J P, Morales A, Adams M A et al. Recovery of erectile function by the oral administration of apomorphine. *Urology* 1995;45(2):200-206.
- Hellstrom W J. Vardenafil: a new approach to the treatment of erectile dysfunction. [Review] [37 refs]. *Curr Urol Rep* 2003;4(6):479-487.
- Hirsch I H, Schanne F J, Carsello J et al. Sequential penile ultrasound monitoring of patients treated with chronic intracavernous prostaglandin E1. *Urology* 1995;45(6):1037-1041.
- Hirsch I H, Smith R L, Chancellor M B et al. Use of intracavernous injection of prostaglandin E1 for neuropathic erectile dysfunction. *Paraplegia* 1994;32(10):661-664.
- Hollander J B, Gonzalez J, Norman T. Patient satisfaction with pharmacologic erection program. *Urology* 1992;39(5):439-441.
- Holmes S. Tadalafil: a new treatment for erectile dysfunction. *BJU Int* 2003;91(6):466-468.
- Hong E K, Lepor H, McCullough A R. Time dependent patient satisfaction with sildenafil for erectile dysfunction (ED) after nerve-sparing radical retropubic prostatectomy (RRP). *Int J Impot Res* 1999;11(SUPPL. 1):S15-S22.
- Hong J H, Ahn T Y. Oral testosterone replacement in Korean patients with PADAM. *Aging Male* 2002;5(1):52-56.
- Hookes J. Asian Federation of Medicinal Chemistry (AFMC) - Fifth International Medicinal Chemistry Symposium: 14-17 October 2003, Kyoto, Japan. *IDrugs* 2003;6(11):1013-1015.
- Huang S T, Hsieh M L. Different hemodynamic responses by color Doppler ultrasonography studies between sildenafil non-responders and responders. *Asian J Androl* 2007;9(1):129-133.
- Hubler J, Szanto A, Konyves K. Methylene blue as a means of treatment for priapism caused by intracavernous injection to combat erectile dysfunction. *International Urology & Nephrology* 2003;35(4):519-521.
- Hwang T I, Chen H E, Tsai T F et al. Combined use of androgen and sildenafil for hypogonadal patients unresponsive to sildenafil alone. *Int J Impot Res* 2006;18(4):400-404.
- Incrocci L, Hop W C, Slob A K. Visual erotic and vibrotactile stimulation and intracavernous injection in screening men with erectile dysfunction: a 3 year experience with 406 cases. *Int J Impot Res* 1996;8(4):227-232.
- Irwin M B, Kata E J. High attrition rate with intracavernous injection of prostaglandin E1 for impotency. *Urology* 1994;43(1):84-87.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Ismail M, Abbott L, Hirsch I H. Experience with intracavernous PGE-1 in the treatment of erectile dysfunction: dose considerations and efficacy. *Int J Impot Res* 1997;9(1):39-42.
- Israilov S, Niv E, Livne P M et al. Intracavernous injections for erectile dysfunction in patients with cardiovascular diseases and failure or contraindications for sildenafil citrate. *Int J Impot Res* 2002;14(1):38-43.
- Israilov S, Shmueli J, Niv E et al. Evaluation of a progressive treatment program for erectile dysfunction in patients with diabetes mellitus. *Int J Impot Res* 2005;17(5):431-436.

- Jackson G. Sildenafil (Viagra): New data, new confidence in treating erectile dysfunction in the cardiovascular patient. *Int J Clin Pract* 2002;56(2):75
- Jackson G, Keltai M, Csanady M et al. Hemodynamic effects of sildenafil citrate and isosorbide mononitrate in men with coronary artery disease and erectile dysfunction. *Br J Sex Med* 2005;2(3):407-414.
- Jackson G, Kloner R A, Costigan T M et al. Update on clinical trials of tadalafil demonstrates no increased risk of cardiovascular adverse events. *Br J Sex Med* 2004;1(2):161-167.
- Jackson G, Montorsi P, Cheitlin M D. Cardiovascular safety of sildenafil citrate (Viagra): an updated perspective. [Review] [52 refs]. *Urology* 2006;68(3 Suppl):47-60.
- Jacobsen F M. Fluoxetine-induced sexual dysfunction and an open trial of yohimbine.[see comment]. *Hillside J Clin Psychiatry* 1992;53(4):119-122.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- Jarow J P, Burnett A L, Geringer A M. Clinical efficacy of sildenafil citrate based on etiology and response to prior treatment.[see comment]. *Br J Urol* 1999;162(3:Pt 1):t-5.
- Jiann B P, Yu C C, Su C C et al. Rechallenge prior sildenafil nonresponders. *Int J Impot Res* 2004;16(1):64-68.
- Jiann B P, Yu C C, Tsai J Y et al. What to learn about sildenafil in the treatment of erectile dysfunction from 3-year clinical experience. *Int J Impot Res* 2003;15(6):412-417.
- Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.
- John H, Lehmann K, Hauri D. Intraurethral prostaglandin improves quality of vacuum erection therapy. *Eur Urol* 1996;29(2):224-226.
- Juergense P H, Botev R, Wuerth D et al. Erectile dysfunction in chronic peritoneal dialysis patients: incidence and treatment with sildenafil. *Perit Dial Int* 2001;21(4):355-359.
- Kadioglu A, Erdogru T, Tellaloglu S. Combined intracavernous injection of papaverine and stimulation (CIS) test. *J Androl* 1994;15 Suppl50S-53S.
- Kaplan B, Ben-Rafael Z, Peled Y et al. Oral sildenafil may reverse secondary ejaculatory dysfunction during infertility treatment. *Fertility & Sterility* 1999;72(6):1144-1145.
- Kaplan Helen S. The combined use of sex therapy and intrapenile injections in the treatment of impotence. *J Sex Marital Ther* 1990;16(4):195-207.
- Kaplan S A, Reis R B, Kohn I J et al. Combination therapy using oral alpha-blockers and intracavernosal injection in men with erectile dysfunction. *Urology* 1998;52(5):739-743.
- Karabulut A, Peskircioglu L, Ozkardes H et al. Objective penile vascular response to intraurethral prostaglandin E2 (dinoprostone). *Urol Int* 2001;67(2):160-162.
- Kassouf W, Carrier S. A comparison of the International Index of Erectile Function and erectile dysfunction studies.. *BJU Int* 2003;91(7):667-669.
- Katlowitz N M, Albano G J, Morales P et al. Potentiation of drug-induced erection with audiovisual sexual stimulation. *Urology* 1993;41(5):431-434.
- Katlowitz N, Albano G J, Patsias G et al. Effect of multidose intracorporeal injection and audiovisual sexual stimulation in vasculogenic impotence. *Urology* 1993;42(6):695-697.
- Kattan S A. The acceptance of satisfaction of Saudi males to vasoactive autoinjection intracavernous therapy, external negative pressure device and penile prosthesis in the treatment of erectile dysfunction. *Ann Saudi Med* 2002;22(3-4):149-152.
- Kaufman J M, Hatzichristou D G, Mulhall J P et al. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *Br J Urol* 1994;151(3):612-618.
- Keating G M, Scott L J. Vardenafil: a review of its use in erectile dysfunction. *Drugs* 2003;63(23):2673-2703.
- Keating G M, Scott L J. Spotlight on vardenafil in erectile dysfunction. *Drugs Aging* 2004;21(2):135-140.
- Kedia S, Zippe C D, Agarwal A et al. Treatment of erectile dysfunction with sildenafil citrate (Viagra) after radiation therapy for prostate cancer. *Urology* 1999;54(2):308-312.
- Kendirci M, Bivalacqua T J, Hellstrom W J. Vardenafil: a novel type 5 phosphodiesterase inhibitor for the treatment of erectile dysfunction. *Expert Opin Pharmacother* 2004;5(4):923-932.
- Khan M A, Raistrick M, Mikhailidis D P et al. MUSE: clinical experience. *Current Medical Research & Opinion* 2002;18(2):64-67.
- Khan M M, Khwaja M. Open label study of intracavernous injection of alprostadi alphasex in the treatment of erectile dysfunction. *J Postgrad Med Inst* 2005;19(1):52-57.

- Kim E D, McVary K T. Topical prostaglandin-E1 for the treatment of erectile dysfunction.. *Br J Urol* 1995;153(6):1828-1830.
- Kim E D, el-Rashidy R, McVary K T. Papaverine topical gel for treatment of erectile dysfunction. *Br J Urol* 1995;153(2):361-365.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Kim N N, Christianson D W, Traish A M. Role of arginase in the male and female sexual arousal response. *Br J Nutr* 2004;134(10 SUPPL.):2873S-2879S.
- Kim S C, Ahn T Y, Choi H K et al. Multicenter study of the treatment of erectile dysfunction with transurethral alprostadil (MUSE) in Korea. *Int J Impot Res* 2000;12(2):97-101.
- Kim S C, Chang I H, Jeon H J. Preference for oral sildenafil or intracavernosal injection in patients with erectile dysfunction already using intracavernosal injection for > 1 year. *BJU Int* 2003;92(3):277-280.
- Kim S C, Lee S W, Seo K K. Characteristics of pain following intracavernous injection of prostaglandin E1. *J Korean Med Sci* 1997;12(4):327-331.
- Kloner R A. Cardiovascular risk and sildenafil. [Review] [27 refs]. *Am J Cardiol* 2000;86(2A):57F-61F.
- Kloner R A, Zusman R M. Cardiovascular effects of sildenafil citrate and recommendations for its use. [Review] [21 refs]. *Am J Cardiol* 1999;84(5B):11N-17N.
- Kloner R A, Brown M, Prisant L M et al. Effect of sildenafil in patients with erectile dysfunction taking antihypertensive therapy. Sildenafil Study Group. *Am J Hypertens* 2001;14(1):70-73.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil in patients on common antihypertensive therapies. [Review] [5 refs]. *Am J Cardiol* 2003;92(9A):47M-57M.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil. [Review] [12 refs]. *Am J Cardiol* 2003;92(9A):37M-46M.
- Kloner R A, Sadovsky R, Johnson E G et al. Efficacy of tadalafil in the treatment of erectile dysfunction in hypertensive men on concomitant thiazide diuretic therapy. *Int J Impot Res* 2005;17(5):450-454.
- Kloner R A, Sadovsky R, Johnson E G et al. Efficacy of tadalafil in the treatment of erectile dysfunction in hypertensive men on concomitant thiazide diuretic therapy. *Br J Urol* 2006;175(4):1450
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Knispel H H, Huland H. Influence of cause on choice of therapy in 174 patients with erectile dysfunction. *Br J Urol* 1992;147(5):1274-1276.
- Koksal M, Ozdemir H, Kargi S et al. The effects of sildenafil on ocular blood flow. *Acta Ophthalmol Scand* 2005;83(3):355-359.
- Kongkanand A, Opanuraks J, Tantiwongse K et al. Evaluating dose regimens of apomorphine, an open-label study. *Int J Impot Res* 2003;15(Suppl 2):10-12.
- Kongkanand A, Ratana-Olarn K, Wuddhikarn S et al. Evaluation of transurethral alprostadil for safety and efficacy in men with erectile dysfunction. *J Med Assoc Thai* 2002;85(2):223-228.
- Kramer-Levien D J. Papaverine--the medical implant. *AUA J* 1987;7(4):13-Jun.
- Kriston L, Harms A, Berner M M. A meta-regression analysis of treatment effect modifiers in trials with flexible-dose oral sildenafil for erectile dysfunction in broad-spectrum populations. *Int J Impot Res* 2006;18(6):559-565.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Kuba R, Pohanka M, Zakopcan J et al. Sexual dysfunctions and blood hormonal profile in men with focal epilepsy. *Epilepsia* 2006;47(12):2135-2140.
- Kunelius P, Lukkarinen O. Intracavernous self-injection of prostaglandin E1 in the treatment of erectile dysfunction. *Int J Impot Res* 1999;11(1):21-24.
- Kuzmarov I W, Ross D, Skamene A et al. A sexual tune-up program as an adjunct to intracavernous pharmacotherapy. *Can J Hum Sex* 1993;2(4):239-241.
- Labbate Lawrence A, Grimes Jamie B, Hines Alan et al. Bupropion treatment of serotonin reuptake antidepressant-associated sexual dysfunction. *Ann Clin Psychiatry* 1997;9(4):241-245.
- Lakin M M, Montague D K, VanderBrug Medendorp S et al. Intracavernous injection therapy: Analysis of results and complications. *Br J Urol* 1990;143(6):1138-1141.
- Lal S, Kiely M E, Thavundayil J X et al. Effect of bromocriptine in patients with apomorphine-responsive erectile impotence: an open study. *J Psychiatry Neurosci* 1991;16(5):262-266.
- Lance R, Albo M, Costabile R A et al. Oral trazodone as empirical therapy for erectile dysfunction: a retrospective review. *Urology* 1995;46(1):117-120.

- Lane B Z, Ausmundson S J, Butler R S et al. Use of a visual analog scale to assess pain of injection with intracavernous injection therapy. *Br J Sex Med* 2005;2(3):428-431.
- Laties A, Sharlip I. Ocular safety in patients using sildenafil citrate therapy for erectile dysfunction. [Review] [81 refs]. *Br J Sex Med* 2006;3(1):12-27.
- Laties A M, Zrenner E. Viagra (sildenafil citrate) and ophthalmology. *Progress in Retinal & Eye Research* 2002;21(5):485-506.
- Laties A M, Fraunfelder F T, Flach A J et al. Ocular safety of Viagra, (sildenafil citrate). *Trans Am Ophthalmol Soc* 1999;97(pp 115-128):-128.
- Lawless C, Cree J. Oral medications in the management of erectile dysfunction. [Review] [15 refs]. *J Am Board Fam Pract* 1998;11(4):307-314.
- Lawless C, Force R W. Sildenafil for erectile dysfunction. *J Fam Pract* 1998;47(2):97-98.
- Lawrence I G, Price D E, Howlett T A et al. Correcting impotence in the male dialysis patient: experience with testosterone replacement and vacuum tumescence therapy. *Am J Kidney Dis* 1998;31(2):313-319.
- Le Bon O, Lion K, Verbanck P et al. Fluparoxan in male erectile disorder: A case report. *Yakubutsu Seishin Kodo* 1995;9(1):67-68.
- Lea A P, Bryson H M, Balfour J A. Intracavernous alprostadil. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in erectile dysfunction. [Review] [123 refs]. *Drugs Aging* 1996;8(1):56-74.
- Lee J, Pommerville P, Brock G et al. Physician-rated patient preference and patient- and partner-rated preference for tadalafil or sildenafil citrate: results from the Canadian 'Treatment of Erectile Dysfunction' observational study. *BJU Int* 2006;98(3):623-629.
- Lee W R. The role of androgen deprivation therapy combined with prostate brachytherapy. [Review] [31 refs]. *Urology* 2002;60(3:Suppl 1):Suppl-44.
- Levine L A, Latchamsetty K C. Treatment of erectile dysfunction in patients with Peyronie's disease using sildenafil citrate. *Int J Impot Res* 2002;14(6):478-482.
- Levitt E E, Mulcahy J J. The effect of intracavernosal injection of papaverine hydrochloride on orgasm latency. *Br J Sex Med* 1995;21(1):39-42.
- Lewis R L, Sadovsky R, Eardley I et al. The efficacy of tadalafil in clinical populations. *Br J Sex Med* 2005;2(4):517-531.
- Lewis R W. Intraurethral and topical agents. *Med Actual* 2000;36(2-3):113-119.
- Li M K, Lim P H, Wong M Y et al. Transurethral alprostadil for the treatment of erectile dysfunction: results of a multicentre trial. *Ann Acad Med Singapore* 2000;29(6):727-731.
- Lim P H, Ng F C. Erectile dysfunction in Singapore men: presentation, diagnosis, treatment and results. *Ann Acad Med Singapore* 1992;21(2):248-253.
- Lim P H C, Man K L, Foo C N et al. Clinical efficacy and safety of sildenafil citrate (Viagra) in a multi-racial population in Singapore: A retrospective study of 1520 patients. *Int J Urol* 2002;9(6):308-315.
- Liu L C, Wu C C, Liu L H et al. Comparison of the effects of papaverine versus prostaglandin E1 on penile blood flow by color duplex sonography. *Eur Urol* 1991;19(1):49-53.
- Livi U, Faggian G, Sorbara C et al. Use of prostaglandin E1 in the treatment of sexual impotence after heart transplantation: initial clinical experience. *Journal of Heart & Lung Transplantation* 1993;12(3):484-486.
- Lombardo T, Giammusso B, Frontini V et al. Thalassaemic men affected by erectile dysfunction treated with transurethral alprostadil: case report. *Hum Reprod* 2000;15(11):2375-2378.
- Long R L, Sherman L S, Lombardi T J. A goal-oriented, cost-effective approach to the diagnosis and treatment of 24 male erectile dysfunction. [Review] [24 refs]. *J Ky Med Assoc* 1995;93(11):500-508.
- Lottman P E, Hendriks J C, Vrugink P A et al. The impact of marital satisfaction and psychological counselling on the outcome of ICI-treatment in men with ED. *Int J Impot Res* 1998;10(2):83-87.
- Lowentritt B H, Scardino P T, Miles B J et al. Sildenafil citrate after radical retropubic prostatectomy. *Br J Urol* 1999;162(5):1614-1617.
- Lowy M, Collins S, Bloch M et al. Quality of erection questionnaire correlates: change in erection quality with erectile function, hardness, and psychosocial measures in men treated with sildenafil for erectile dysfunction. *Br J Sex Med* 2007;4(1):83-92.
- Lue T F. Impotence after radical pelvic surgery: physiology and management. [Review] [56 refs]. *Urol Int* 1991;46(3):259-265.
- Lukkarinen O, Tonttila P, Hellstrom P et al. Non-prosthetic surgery in the treatment of erectile dysfunction. A retrospective study of 45 impotent patients in the University of Oulu. *Scandinavian Journal of Urology & Nephrology* 1998;32(1):42-46.

- Lundberg L, Olsson J-O, Kihl B. Long-term experience of self-injection therapy with prostaglandin E1 for erectile dysfunction. *Scand J Urol Nephrol* 1996;30(5):395-397.
- Lunenfeld B. Androgen therapy in the aging male. [Review] [110 refs]. *World J Urol* 2003;21(5):292-305.
- Magoa G A. Sildenafil (Viagra) in the treatment of male erectile dysfunction in Nairobi. *East Afr Med J* 2000;77(2):76-79.
- Manecke R G, Mulhall J P. Medical treatment of erectile dysfunction. [Review] [69 refs]. *Ann Med* 1999;31(6):388-398.
- Maniam P, Seftel A D, Corty E W et al. Nocturnal penile tumescence activity unchanged after long-term intracavernous injection therapy. *Br J Urol* 2001;165(3):830-832.
- Mansi M K, Alkhudair W K, Huraib S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *Br J Urol* 1998;159(6):1927-1930.
- Marberger M, Roehrborn C G, Marks L S et al. Relationship among serum testosterone, sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. *Journal of Clinical Endocrinology & Metabolism* 2006;91(4):1323-1328.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- Marks L S, Duda C, Dorey F J et al. Treatment of erectile dysfunction with sildenafil.[see comment]. *Urology* 1999;53(1):19-24.
- Marshall G A, Breza J, Lue T F. Improved hemodynamic response after long-term intracavernous injection for impotence. *Urology* 1994;43(6):844-848.
- Martin-Morales A, Haro J M, Beardsworth A et al. Therapeutic effectiveness and patient satisfaction after 6 months of treatment with tadalafil, sildenafil, and vardenafil: results from the erectile dysfunction observational study (EDOS). *Eur Urol* 2007;51(2):541-550.
- Martin-Morales A, Moncada Iribarren I, Cruz Navarro N et al. [Efficacy and safety of two dosing regimens with Tadalafil in Spanish men with erectile dysfunction: results from the SURE study in 14 European countries]. *Actas Urol Esp* 2006;30(8):791-800.
- Martinez R, Puigvert A, Pomerol J M et al. Clinical experience with apomorphine hydrochloride: the first 107 patients. *Br J Urol* 2003;170(6:Pt 1):t-5.
- Martinez-Jabaloyas J M, Gil-Salom M, Villamon-Fort R et al. Prognostic factors for response to sildenafil in patients with erectile dysfunction. *Eur Urol* 2001;40(6):641-647.
- Martinez-Pineiro L, Cortes R, Cuervo E et al. Prospective comparative study with intracavernous sodium nitroprusside and prostaglandin E1 in patients with erectile dysfunction. *Eur Urol* 1998;34(4):350-354.
- Matthew A G, Goldman A, Trachtenberg J et al. Sexual dysfunction after radical prostatectomy: Prevalence, treatments, restricted use of treatments and distress. *Br J Urol* 2005;174(6):2105-2110.
- Maytom M C, Derry F A, Dinsmore W W et al. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord*. 1999;37(2):110-116.
- McClure R D. Endocrine evaluation and therapy of erectile dysfunction. [Review] [77 refs]. *Urol Clin North Am* 1988;15(1):53-64.
- McClure R D, Oses R, Ernest M L. Hypogonadal impotence treated by transdermal testosterone. *Urology* 1991;37(3):224-228.
- McConnell J D, Roehrborn C G, Bautista O M et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
- McCullough A R, Barada J H, Fawzy A et al. Achieving treatment optimization with sildenafil citrate (Viagra) in patients with erectile dysfunction. *Urology* 2002;60(2 Suppl 2):28-38.
- McCullough A R, Carson C C, Hatzichristou D. A prospective study of the beneficial effects of dose optimization and customized instructions on patient satisfaction with sildenafil citrate (Viagra) for erectile dysfunction. *Urology* 2006;68(3 Suppl):38-46.
- McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992;9:265A
- McMahon C. Efficacy and safety of daily tadalafil in men with erectile dysfunction previously unresponsive to on-demand tadalafil. *Br J Sex Med* 2004;1(3):292-300.
- McMahon C G. High dose sildenafil citrate as a salvage therapy for severe erectile dysfunction. *Int J Impot Res* 2002;14(6):533-538.

- McMahon C G. An attempt to standardize the pharmacological diagnostic screening of vasculogenic impotence with prostaglandin E1. *Int J Impot Res* 1995;7(2):83-90.
- McMahon C G. Topiglan: MacroChem. *Curr Opin Investig Drugs* 2002;3(4):602-606.
- McMahon C G. A pilot study of the role of intracavernous injection of vasoactive intestinal peptide (VIP) and phentolamine mesylate in the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(4):233-236.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- McMahon C G, Samali R, Johnson H. Efficacy, safety and patient acceptance of sildenafil citrate as treatment for erectile dysfunction. *Br J Urol* 2000;164(4):1192-1196.
- McMahon C G, Samali R, Johnson H. Treatment of intracorporeal injection nonresponse with sildenafil alone or in combination with triple agent intracorporeal injection therapy. *Br J Urol* 1997;162(6):1992-1997.
- McMahon C, Lording D, Stuckey B et al. Vardenafil improved erectile function in a "real-life" broad population study of men with moderate to severe erectile dysfunction in Australia and New Zealand. *Br J Sex Med* 2006;3(5):892-900.
- McVary K T, Polepalle S, Riggi S et al. Topical prostaglandin E1 SEPA gel for the treatment of erectile dysfunction.. *Br J Urol* 1999;162(3 Pt 1):732
- Mealy N E. Alprostadil cream. *Drugs of the Future* 2004;29(6):626-627.
- Mealy N E, Bayes M. PT-141. *Drugs of the Future* 2004;29(11):1177
- Mehdiyev T V. Intracavernous injection probe of vasoactive preparations in the diagnosis of erectile dysfunctions in patients with diabetes mellitus. *Azerbaidzhanskii Meditsinskii Zhurnal* 2002;(pp 17-19):-19.
- Meinhardt W, de la, Fuente R B et al. Prostaglandin E1 with phentolamine for the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(1):5-7.
- Meinhardt W, Nijeholt A A, Kropman R F et al. Comparison of a mixture of papaverine, phentolamine and prostaglandin E1 with other intracavernous injections. *Eur Urol* 1994;26(4):319-321.
- Mellinger B C, Fried J J, Darracott Vaughan. Papaverine-induced penile blood flow acceleration in impotent men measured by duplex scanning. *Br J Urol* 1990;144(4):897-899.
- Merrick G S, Butler W M, Lief J H et al. Efficacy of sildenafil citrate in prostate brachytherapy patients with erectile dysfunction. *Urology* 1999;53(6):1112-1116.
- Metaweia B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Meyhoff H H, Rosenkilde P, Bodker A. Non-invasive management of impotence with transcutaneous nitroglycerin. *Br J Urol* 1992;69(1):88-90.
- Mikhail N. Does Testosterone Have a Role in Erectile Function?. *Am J Med* 2006;119:373-382.
- Millard R J, Stricker P D, Lynch W J et al. Risks of self-injection therapy for impotence. *Med J Aust* 1996;165(2):117-118.
- Miller N, Smolkin M E, Bissonette E et al. Undetectable prostate specific antigen at 6-12 months: a new marker for early success in hormonally treated patients after prostate brachytherapy. *Cancer* 2005;103(12):2499-2506.
- Mills T M, Lewis R W. The role of androgens in the erectile response: A 1999 perspective. *Mol Urol* 1999;3(2):75-80.
- Mirone V G, Stief C G. Efficacy of apomorphine SL in erectile dysfunction.[erratum appears in *BJU Int* 2002 Jan;89(1):140]. [Review] [11 refs]. *BJU Int* 2001;88(Suppl 3):25-29.
- Mirone V, Imbimbo C, Fabrizio F et al. Ketanserin plus prostaglandin E1 (PGE-1) as intracavernosal therapy for patients with erectile dysfunction unresponsive to PGE-1 alone. *Br J Urol* 1996;77(5):736-739.
- Mirone V, Palmieri A, Cucinotta D et al. Flexible-dose vardenafil in a community-based population of men affected by erectile dysfunction: a 12-week open-label, multicenter trial. *Br J Sex Med* 2005;2(6):842-847.
- Mittleman M A, Glasser D B, Orazem J. Clinical trials of sildenafil citrate (Viagra) demonstrate no increase in risk of myocardial infarction and cardiovascular death compared with placebo. *Int J Clin Pract* 2003;57(7):597-600.
- Mittleman M A, Maclure M, Glasser D B. Evaluation of acute risk for myocardial infarction in men treated with sildenafil citrate. *Am J Cardiol* 2005;96(3):443-446.
- Moemen M N, Hamed H A, Kamel I I et al. Clinical and sonographic assessment of the side effects of intracavernous injection of vasoactive substances. *Int J Impot Res* 2004;16(2):143-145.

- Moncada I, Jara J, Subira D et al. Efficacy of sildenafil citrate at 12 hours after dosing: re-exploring the therapeutic window. *Eur Urol* 2004;46(3):357-360.
- Montorsi F, Althof S E. Partner responses to sildenafil citrate (Viagra) treatment of erectile dysfunction. *Urology* 2004;63(4):762-767.
- Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *Br J Sex Med* 2005;2(5):658-667.
- Montorsi F, Althof S E, Sweeney M et al. Treatment satisfaction in patients with erectile dysfunction switching from prostaglandin E(1) intracavernosal injection therapy to oral sildenafil citrate. *Int J Impot Res* 2003;15(6):444-449.
- Montorsi F, Briganti A, Salonia A et al. Can Phosphodiesterase Type 5 Inhibitors Cure Erectile Dysfunction?. *Eur Urol* 2006;49(6):979-986.
- Montorsi F, Guazzoni G, Barbieri L et al. The effect of intracorporeal injection plus genital and audiovisual sexual stimulation versus second injection on penile color Doppler sonography parameters. *Br J Urol* 1996;155(2):536-540.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993;42(5):554-558.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Four-drug intracavernous therapy for impotence due to corporeal veno-occlusive dysfunction. *Br J Urol* 1993;149(5 Pt 2):1291-1295.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Intracavernous vasoactive pharmacotherapy: the impact of a new self-injection device.[see comment]. *Br J Urol* 1993;150(6):1829-1832.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Clinical reliability of multi-drug intracavernous vasoactive pharmacotherapy for diabetic impotence. *Acta Diabetol Lat* 1994;31(1):1-5.
- Montorsi F, Hellstrom W J, Valiquette L et al. Vardenafil provides reliable efficacy over time in men with erectile dysfunction. *Urology* 2004;64(6):1187-1195.
- Montorsi F, Perani D, Anchisi D et al. Apomorphine-induced brain modulation during sexual stimulation: a new look at central phenomena related to erectile dysfunction. *Int J Impot Res* 2003;15(3):203-209.
- Montorsi F, Salonia A, Briganti A et al. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47(5):612-621.
- Montorsi F, Verheyden B, Meuleman E et al. Long-term safety and tolerability of tadalafil in the treatment of erectile dysfunction. *Eur Urol* 2004;45(3):339-344.
- Moore R A, Derry S, McQuay H J. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. [Review] [77 refs]. *BMC Urol* 2005;5:18
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol.* 2002;26
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Morales A, Johnston B, Heaton J P et al. Testosterone supplementation for hypogonadal impotence: assessment of biochemical measures and therapeutic outcomes. *Br J Urol* 1997;157(3):849-854.
- Morales A, Johnston B, Heaton J W et al. Oral androgens in the treatment of hypogonadal impotent men.[see comment]. *Br J Urol* 1994;152(4):1115-1118.
- Morgentaler A, Barada J, Niederberger C et al. Efficacy and safety of tadalafil across ethnic groups and various risk factors in men with erectile dysfunction: Use of a novel noninferiority study design. *Br J Sex Med* 2006;3(3):492-503.
- Mulhall J P. Deciphering erectile dysfunction drug trials. [Review] [35 refs]. *Br J Urol* 2003;170(2 Pt 1):353-358.
- Mulhall J P. Sublingual apomorphine for the treatment of erectile dysfunction. [Review] [22 refs]. *Expert Opin Investig Drugs* 2002;11(2):295-302.
- Mulhall J P, Bukofzer S, Edmonds A L et al. An open-label, uncontrolled dose-optimization study of sublingual apomorphine in erectile dysfunction. *Clin Ther* 2001;23(8):1260-1271.
- Mulhall J P, Guhring P, Parker M et al. Assessment of the impact of sildenafil citrate on lower urinary tract symptoms in men with erectile dysfunction. *Br J Sex Med* 2006;3(4):662-667.
- Mulhall J P, Jahoda A E, Ahmed A et al. Analysis of the consistency of intraurethral prostaglandin E(1) (MUSE) during at-home use. *Urology* 2001;58(2):262-266.
- Mulhall J P, Jahoda A E, Cairney M et al. The causes of patient dropout from penile self-injection therapy for impotence. *Br J Urol* 1999;162(4):1291-1294.
- Mulhall J P, Jahoda A, Aviv N et al. The impact of sildenafil citrate on sexual satisfaction profiles in men with a penile prosthesis in situ. *BJU Int* 2004;93(1):97-99.

- Mulhall J P, Land S, Parker M et al. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *Br J Sex Med* 2005;2(4):532-542.
- Mulhall J P, Levine L A, Junemann K P. Erection hardness: a unifying factor for defining response in the treatment of erectile dysfunction. [Review] [37 refs]. *Urology* 2006;68(3 Suppl):17-25.
- Mulhall J, Barnas J, Aviv N et al. Sildenafil citrate response correlates with the nature and the severity of penile vascular insufficiency. *Br J Sex Med* 2005;2(1):104-108.
- Muller M J, Benkert O. Lower self-reported depression in patients with erectile dysfunction after treatment with sildenafil. *J Affect Disord* 2001;66(2-3):255-261.
- Muller M J, Ruof J, Graf-Morgenstern M et al. Quality of partnership in patients with erectile dysfunction after sildenafil treatment. *Pharmacopsychiatry* 2001;34(3):91-95.
- Murat Basar M, Tekdogan U Y, Yilmaz E et al. The efficacy of sildenafil in different etiologies of erectile dysfunction. *International Urology & Nephrology* 2001;32(3):403-407.
- Murphy A M, O'Leary M. Failure of the Ambicor inflatable penile prosthesis to deflate. *Int J Impot Res* 2005;17(3):291-292.
- Murphy J C, Srinivas S, Terris M K. Flutamide administration at 500 mg daily has similar effects on serum testosterone to 750 mg daily. *J Androl* 2004;25(4):630-634.
- Mydlo J H, Viterbo R, Crispin P. Use of combined intracorporal injection and a phosphodiesterase-5 inhibitor therapy for men with a suboptimal response to sildenafil and/or vardenafil monotherapy after radical retropubic prostatectomy. *BJU Int* 2005;95(6):843-846.
- Mydlo J H, Volpe M A, MacChia R J. Results from different patient populations using combined therapy with alprostadil and sildenafil: predictors of satisfaction. *BJU Int* 2000;86(4):469-473.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Nandipati K, Raina R, Agarwal A et al. Early combination therapy: intracavernosal injections and sildenafil following radical prostatectomy increases sexual activity and the return of natural erections. *Int J Impot Res* 2006;18(5):446-451.
- Naude J H, Le Roux P J. Topical treatment of erectile dysfunction did not show results.[comment]. *BMJ* 1998;316(7140):1318
- Nehra A, Blute M L, Barrett D M et al. Rationale for combination therapy of intraurethral prostaglandin E(1) and sildenafil in the salvage of erectile dysfunction patients desiring noninvasive therapy. *Int J Impot Res* 2002;14(Suppl 1):38-42.
- Nessel Mark A. Yohimbine and pentoxifylline in the treatment of erectile dysfunction. *Am J Psychiatry* 1994;151(3):453
- Nurnberg H G, Hensley P L. Sildenafil citrate for the management of antidepressant-associated erectile dysfunction. *Hillside J Clin Psychiatry* 2003;64Suppl-5.
- Nurnberg H G, Fava M, Gelenberg A J et al. Open-label sildenafil treatment of partial and non-responders to double-blind treatment in men with antidepressant-associated sexual dysfunction. *Int J Impot Res* 2007;19(2):167-175.
- Nurnberg H G, Gelenberg A, Hargreave T B et al. Efficacy of sildenafil citrate for the treatment of erectile dysfunction in men taking serotonin reuptake inhibitors. *Am J Psychiatry* 2001;158(11):1926-1928.
- Nurnberg H G, Lauriello J, Hensley P L et al. Sildenafil for iatrogenic serotonergic antidepressant medication-induced sexual dysfunction in 4 patients.[see comment]. *Hillside J Clin Psychiatry* 1999;60(1):33-35.
- Nurnberg H G, Seidman S N, Gelenberg A J et al. Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. *Urology* 2002;60(2 Suppl 2):58-66.
- Nurnberg H, George Hensley, Paula L et al. Sildenafil in the treatment of sexual dysfunction induced by selective serotonin reuptake inhibitors: An overview. [References]. *CNS Drugs* 2000;13(5):321-335.
- O'Sullivan J D, Hughes A J. Apomorphine-induced penile erections in Parkinson's disease. *Mov Disord* 1998;13(3):536-539.
- Ochiai A, Naya Y, Soh J et al. Efficacy of sildenafil as the first-step therapeutic tool for Japanese patients with erectile dysfunction. *Int J Impot Res* 2005;17(4):339-342.
- Ogura K, Ichioka K, Terada N et al. Role of sildenafil citrate in treatment of erectile dysfunction after radical retropubic prostatectomy. *Int J Urol*. 2004;11(3):159-163.
- Ohebshalom M, Mulhall J P. Transdermal and topical pharmacotherapy for male sexual dysfunction. *Expert Opinion on Drug Delivery* 2005;2(1):115-120.

- Ohebshalom M, Parker M, Guhring P et al. The efficacy of sildenafil citrate following radiation therapy for prostate cancer: temporal considerations. *Br J Urol* 2005;174(1):258-262.
- Opsomer R J, Wese F X, De Groote P et al. The external vacuum device in the management of erectile dysfunction. *Acta Urol Belg* 1997;65(4):13-16.
- Ormrod D, Easthope S E, Figgitt D P. Vardenafil.[erratum appears in *Drugs Aging* 2002;19(11):886]. [Review] [30 refs]. *Drugs Aging* 2002;19(3):217-227.
- Osegebe D N, Shittu O B, Aghaji A E et al. Sildenafil citrate (Viagra) for the treatment of erectile dysfunction in Nigerian men. *Int J Impot Res* 2003;15Suppl-8.
- Osterloh I H, Riley A. Clinical update on sildenafil citrate. [Review] [58 refs]. *Br J Clin Pharmacol* 2002;53(3):219-223.
- Osterloh I H, Collins M, Wicker P et al. Sildenafil citrate (VIAGRA): overall safety profile in 18 double-blind, placebo controlled, clinical trials. [Review] [0 refs]. *Int J Clin Pract* 1999;Supplement.102-105.
- Padma-Nathan H, Yeager J L. An integrated analysis of alprostadil topical cream for the treatment of erectile dysfunction in 1732 patients. *Urology* 2006;68(2):386-391.
- Padma-Nathan H, Goldstein I, Klimberg I et al. Long-term safety and efficacy of oral phentolamine mesylate (Vasomax) in men with mild to moderate erectile dysfunction. *Int J Impot Res* 2002;14(4):266-270.
- Padma-Nathan H, McMurray J G, Pullman W E et al. On-demand IC351 (Cialis) enhances erectile function in patients with erectile dysfunction. *Int J Impot Res* 2001;13(1):2-9.
- Padma-Nathan H, Montorsi F, Giuliano F et al. Vardenafil restores erectile function to normal range in men with erectile dysfunction. *Br J Sex Med* 2007;4(1):152-161.
- Pagani E, Glina S, Puech-Leao P et al. Anxiety and high plasma catecholamines do not impair phar-maco-induced erection of psychogenic erectile dysfunctional patients. *Int J Impot Res* 2003;15(4):282-286.
- Pagani E, Puech-Leao P, Glina S et al. The value of a second injection on the phar-maco-induced erection test. *Int J Impot Res* 1997;9(3):167-168.
- Pallas James, Levine Stephen B, Althof Stanley E et al. A study using Viagra in a mental health practice. [References]. *J Sex Marital Ther* 2000;26(1):41-50.
- Palumbo F, Bettocchi C, Selvaggi F P et al. Sildenafil: efficacy and safety in daily clinical experience. *Eur Urol* 2001;40(2):176-180.
- Pangkahila W I. Evaluation of transurethral application of alprostadil for erectile dysfunction in Indonesians. *Asian J Androl* 2000;2(3):233-236.
- Park K, Ku J H, Kim S W et al. Risk factors in predicting a poor response to sildenafil citrate in elderly men with erectile dysfunction. *BJU Int* 2005;95(3):366-370.
- Parkerson George R J, Willke Richard J, Hays Ron D. An international comparison of the reliability and responsiveness of the Duke Health Profile for measuring health-related quality of life of patients treated with alprostadil for erectile dysfunction. *Med Care* 1999;37(1):56-67.
- Penninga E, Jensen B A, Hansen P B et al. Anagrelide treatment in 52 patients with chronic myeloproliferative diseases. *Clinical & Laboratory Haematology* 2004;26(5):335-340.
- Perimenis P, Athanasopoulos A, Geramoutsos I et al. The incidence of pharmacologically induced priapism in the diagnostic and therapeutic management of 685 men with erectile dysfunction. *Urol Int* 2001;66(1):27-29.
- Perimenis P, Athanasopoulos A, Papatathanasopoulos P et al. Gabapentin in the management of the recurrent, refractory, idiopathic priapism. *Int J Impot Res* 2004;16(1):84-85.
- Perimenis P, Markou S, Gyftopoulos K et al. Switching from long-term treatment with self-injections to oral sildenafil in diabetic patients with severe erectile dysfunction. *Eur Urol* 2002;41(4):387-391.
- Pescatori E S, Calpista A, Artibani W et al. Self-injection devices for intracavernosal pharmacotherapy: operational classification and safety considerations. *Int J Impot Res* 1996;8(2):53-57.
- Peskircioglu L, Tekin M I, Demirag A et al. Evaluation of erectile function in renal transplant recipients. *Transplant Proc* 1998;30(3):747-749.
- Peterson C A, Bennett A H, Hellstrom W J et al. Erectile response to transurethral alprostadil, prazosin and alprostadil-prazosin combinations. *Br J Urol* 1998;159(5):1523-1527.
- Petrov V I, Vekel'yan A S, Martyushev A V et al. Impaza and Sildenafil: Comparison of Clinical Effectiveness in Patients with Erectile Dysfunction. *Bull Exp Biol Med* 2003;135-136(Suppl 1):150-151.
- Petty R, Angwin R. How real is the male menopause?. *Br J Gen Pract* 2004;248(1659):452-456.
- Pierce L J, Whittington R, Hanno P M et al. Pharmacologic erection with intracavernosal injection for men with sexual dysfunction following irradiation: a preliminary report. *Int J Radiat Oncol Biol Phys* 1991;21(5):1311-1314.

- Pohanka M, Kanovsky P, Bares M et al. The long-lasting improvement of sexual dysfunction in patients with advanced, fluctuating Parkinson's disease induced by pergolide: evidence from the results of an open, prospective, one-year trial. *Parkinsonism Relat Disord* 2005;11(8):509-512.
- Pohanka M, Kanovsky P, Bares M et al. Pergolide mesylate can improve sexual dysfunction in patients with Parkinson's disease: the results of an open, prospective, 6-month follow-up. *Eur J Neurol* 2004;11(7):483-488.
- Polak K, Wimpfing B, Berisha F et al. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. *Invest Ophthalmol Vis Sci* 2003;44(11):4872-4876.
- Pomara G, Morelli G, Montorsi F et al. Re: Montorsi F, Salonia A, Briganti A, Barbieri L, Zanni G, Surdi N, Cestari A, Montorsi P, Rigatti P. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47:612-21 (multiple letters). *Eur Urol* 2005;48(2):345-346.
- Pomara G, Morelli G, Pomara S et al. Cardiovascular parameter changes in patients with erectile dysfunction using pde-5 inhibitors: a study with sildenafil and vardenafil. *J Androl* 2004;25(4):625-629.
- Pommerville P. Drug treatments for erectile dysfunction: An update. *Geriatrics and Aging* 2004;7(6):10-16.
- Porst H. IC351 (tadalafil, Cialis): update on clinical experience. [Review] [12 refs]. *Int J Impot Res* 2002;14Suppl-64.
- Porst H. Transurethral alprostadil with MUSE (medicated urethral system for erection) vs intracavernous alprostadil--a comparative study in 103 patients with erectile dysfunction.. *Int J Impot Res* 1997;9(4):187-192.
- Porst H. Phosphodiesterase type-5 inhibitors: A critical comparative analysis. *Eau Update Series* 2004;2(2):56-63.
- Porst H, Lungimayr G, utsch-osterreichische S T E A. [Efficacy and tolerability of vardenafil within the time window of 6 hours after administration and beyond. Results of a clinical study carried out in 233 urological offices]. *MMW Fortschr Med* 2005;147(Suppl 1):27-32.
- Potempa A J, Ulbrich E, Bernard I et al. Efficacy of vardenafil in men with erectile dysfunction: a flexible-dose community practice study. *Eur Urol* 2004;46(1):73-79.
- Pradeep C, Car N, Metelko Z. Impotence in diabetic men. *Diabetol Croat* 1996;25(2):61-68.
- Price D. Sildenafil citrate (Viagra) efficacy in the treatment of erectile dysfunction in patients with common concomitant conditions. Sildenafil Study Group. *Int J Clin Pract* 1999;Supplement.102-103.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Prieto Castro R M, nglada Curado F J, Regueiro Lopez J C et al. Treatment with sildenafil citrate in renal transplant patients with erectile dysfunction. *BJU Int* 2001;88(3):241-243.
- Priyadarshi S. Oral terbutaline in the management of pharmacologically induced prolonged erection. *Int J Impot Res* 2004;16(5):424-426.
- Pryor J. Vardenafil: update on clinical experience. [Review] [10 refs]. *Int J Impot Res* 2002;14Suppl-9.
- Purvis K, Brekke I, Christiansen E. Determinants of satisfactory rigidity after intracavernosal injection with prostaglandin E1 in men with erectile failure. *Int J Impot Res* 1996;8(1):9-16.
- Radomski S B, Herschorn S, Rangaswamy S. Topical minoxidil in the treatment of male erectile dysfunction. *Br J Urol* 1994;151(5):1225-1226.
- Raffaele R, Vecchio I, Giammusso B et al. Efficacy and safety of fixed-dose oral sildenafil in the treatment of sexual dysfunction in depressed patients with idiopathic Parkinson's disease. *Eur Urol* 2002;41(4):382-386.
- Raina R, Agarwal A, Allamaneni S S et al. Sildenafil citrate and vacuum constriction device combination enhances sexual satisfaction in erectile dysfunction after radical prostatectomy. *Urology* 2005;65(2):360-364.
- Raina R, Agarwal A, Goyal K K et al. Long-term potency after iodine-125 radiotherapy for prostate cancer and role of sildenafil citrate. *Urology* 2003;62(6):1103-1108.
- Raina R, Lakin M M, Agarwal A et al. Long-term intracavernous therapy responders can potentially switch to sildenafil citrate after radical prostatectomy. *Urology* 2004;63(3):532-537.
- Raina R, Lakin M M, Agarwal A et al. Efficacy and factors associated with successful outcome of sildenafil citrate use for erectile dysfunction after radical prostatectomy. *Urology* 2004;63(5):960-966.
- Raina R, Lakin M M, Agarwal A et al. Long-term effect of sildenafil citrate on erectile dysfunction after radical prostatectomy: 3-year follow-up. *Urology* 2003;62(1):110-115.
- Raina R, Lakin M M, Thukral M et al. Long-term efficacy and compliance of intracorporeal (IC) injection for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis. *Int J Impot Res* 2003;15(5):318-322.

- Rajpurkar A, Dhabuwala C B. Comparison of satisfaction rates and erectile function in patients treated with sildenafil, intracavernous prostaglandin E1 and penile implant surgery for erectile dysfunction in urology practice. *Br J Urol* 2003;170(1):159-163.
- Rakic Z, Starcevic V, Starcevic V P et al. Testosterone treatment in men with erectile disorder and low levels of total testosterone in serum. *Arch Sex Behav* 1997;26(5):495-504.
- Ralph D J, Sleep D J, Perdok R J et al. Adverse events and patient tolerability of apomorphine SL 2 and 3 mg: A cross-study analysis of phase II and III studies. *European Urology Supplements* 2002;1(3):21-27.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Reiter W J, Schatzl G, Mark I et al. Dehydroepiandrosterone in the treatment of erectile dysfunction in patients with different organic etiologies. *Urol Res* 2001;29(4):278-281.
- Reznik I, Zemishlany Z, Kotler M et al. Sildenafil citrate for the sexual dysfunction in antidepressant-treated male patients with posttraumatic stress disorder. A preliminary pilot open-label study. *Psychotherapy & Psychosomatics* 2002;71(3):173-176.
- Richardson J D. Intracorporeal injections for the treatment of impotence. *Med J Aust* 1991;155(10):688
- Richter S, Vardi Y, Ringel A et al. Intracavernous injections: still the gold standard for treatment of erectile dysfunction in elderly men. *Int J Impot Res* 2001;13(3):172-175.
- Rizvi K, Hampson J P, Harvey J N. Do lipid-lowering drugs cause erectile dysfunction? A systematic review.[see comment]. [Review] [35 refs]. *Fam Pract* 2002;19(1):95-98.
- Roach M, Winter K, Michalski J M et al. Penile bulb dose and impotence after three-dimensional conformal radiotherapy for prostate cancer on RTOG 9406: findings from a prospective, multi-institutional, phase I/II dose-escalation study. *Int J Radiat Oncol Biol Phys* 2004;60(5):1351-1356.
- Robinson P K. An observational study of prostaglandin E-1: comparing trial and maintenance dose. *Urol Nurs* 1994;14(3):76-78.
- Rodilla F, Fuentes M D, Chuan P et al. Penile self-injection for impotence in patients after radical cystectomy. *Journal of Clinical Pharmacy & Therapeutics* 1994;19(6):359-360.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Rodrigues M, O'Grady J, Stackl W et al. Accumulation of platelets as a key mechanism of human erection. *Thromb Res* 1998;91(2):53-56.
- Rodriguez Vela L, Lledo Garcia E, Rajmil O et al. [Tadalafil vs sildenafil patient preference in Spanish men with erectile dysfunction: results from an International Multicentric Study]. *Actas Urol Esp* 2006;30(1):67-79.
- Rosas S E, Wasserstein A, Kobrin S et al. Preliminary observations of sildenafil treatment for erectile dysfunction in dialysis patients. *Am J Kidney Dis* 2001;37(1):134-137.
- Rosas-Vargas H, Coral-Vazquez R M, Tapia R et al. Glu298Asp endothelial nitric oxide synthase polymorphism is a risk factor for erectile dysfunction in the Mexican Mestizo population. *J Androl* 2004;25(5):728-732.
- Rosen R C, Shabsigh R, Kuritzky L et al. The efficacy of tadalafil in improving sexual satisfaction and overall satisfaction in men with mild, moderate, and severe erectile dysfunction: A retrospective pooled analysis of data from randomized, placebo-controlled clinical trials. *Current Medical Research & Opinion* 2005;21(11):1701-1709.
- Rosen R, Janssen E, Wiegel M et al. Psychological and interpersonal correlates in men with erectile dysfunction and their partners: a pilot study of treatment outcome with sildenafil. *J Sex Marital Ther* 2006;32(3):215-234.
- Rosenstock H A, Axelrad S D. Erectile dysfunction: on the efficacy of a phosphodiesterase inhibitor with concurrent sex therapy. *Asian J Androl* 1999;1(4):207-210.
- Rowland D L, Boedhoe H S M, Dohle G et al. Intracavernosal self-injection therapy in men with erectile dysfunction: Satisfaction and attrition in 119 patients. *Int J Impot Res* 1999;11(3):145-151.
- Rowland D L, Myers L, Culver A et al. Bupropion and sexual function: a placebo-controlled prospective study on diabetic men with erectile dysfunction. *J Clin Psychopharmacol* 1997;17(5):350-357.
- Rubio-Aurioles E, Porst H, Eardley I et al. Comparing vardenafil and sildenafil in the treatment of men with erectile dysfunction and risk factors for cardiovascular disease: a randomized, double-blind, pooled crossover study. *Br J Sex Med* 2006;3(6):1037-1049.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382

- Ruof J, Graf-Morgenstern M, Müller M J. Quality of life in patients with erection difficulties: Evaluation of a German version of the "Quality of life measure for men with erection difficulties" (QoL-Med). *Aktuel Urol* 2001;32(1):21-26.
- Saad F, Grahl A S, Aversa A et al. Effects of testosterone on erectile function: implications for the therapy of erectile dysfunction. *BJU Int* 2007;99(5):988-992.
- Saad F, Hoesl C E, Oettel M et al. Dehydroepiandrosterone treatment in the aging male - What should the urologist know?. *Eur Urol* 2005;48(5):724-733.
- Sadeghi-Nejad H, Lim H, Long K et al. Assessment of the efficacy of Viagra (sildenafil citrate) using the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS). *Urol Int* 2003;71(1):100-102.
- Sadovsky R, Althof S. Men's sexual issues. *Clinics in Family Practice* 2004;6(4 SPEC.ISS.):863-915.
- Sahu M A, Ayyaz M, Chaudhry Z. Intracavernous injections of papaverine and phentolamine for treatment of impotence. *J Coll Physicians Surg Pak* 1997;7(3):102-104.
- Saie D J, Sills E S. Hyperprolactinemia presenting with encephalomalacia-associated seizure disorder and infertility: A novel application for bromocriptine therapy in reproductive endocrinology. *Neuroendocrinol Lett* 2005;26(5):533-537.
- Salama N. Nocturnal electroimpedance volumetric assessment in diabetic men with erectile dysfunction before and after tadalafil intake. *Int J Impot Res* 2004;16(5):441-447.
- Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr.Med Res Opin.* 2003;19(4):241-262.
- Salonia Andrea, Briganti Alberto, Montorsi Piero et al. Safety and tolerability of oral erectile dysfunction treatments in the elderly. [References]. *Drugs and Aging* 2005;22(4):323-338.
- Sato Y, Horita H, Adachi H et al. Effect of oral administration of prostaglandin E1 on erectile dysfunction. *Br J Urol* 1997;80(5):772-775.
- Savoca G, Silvestre G, Belgrano E. Intracavernosal injection therapy and surgical therapy in diabetic patients with erectile dysfunction. [Review] [26 refs]. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):53-57.
- Schanz S, Hauswirth U, Ulmer A et al. Prostaglandin E(1) ethyl ester, a new agent for topical penile therapy. *Int J Impot Res* 2002;14(4):317-318.
- Schimmer A D, Ali V, Stewart A K et al. Male sexual function after autologous blood or marrow transplantation. *Biology of Blood & Marrow Transplantation* 2001;7(5):279-283.
- Schmid D M, Schurch B, Hauri D. Sildenafil in the treatment of sexual dysfunction in spinal cord-injured male patients. *Eur Urol.* 2000;38(2):184-193.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266
- Schroder F H, Whelan P, De Reijke T M et al. Metastatic prostate cancer treated by flutamide versus cyproterone acetate. Final analysis of the "European Organization for Research and Treatment of Cancer" (EORTC) Protocol 30892. *Eur Urol* 2004;45(4):457-464.
- Schulman C C, Shen W, Stohard D R et al. Integrated analysis examining first-dose success, success by dose, and maintenance of success among men taking tadalafil for erectile dysfunction. *Urology* 2004;64(4):783-788.
- Schultheiss D, Stief C G. Physiology and pathophysiology of erection: Consequences for present medical therapy of erectile dysfunction. *Andrologia* 1999;31(SUPPL. 1):59-64.
- Schultheiss D, Hiltl D M, Meschi M R et al. Pilot study of the transdermal application of testosterone gel to the penile skin for the treatment of hypogonadotropic men with erectile dysfunction. *World J Urol* 2000;18(6):431-435.
- Seftel A D. From aspiration to achievement: Assessment and noninvasive treatment of erectile dysfunction in aging men. *J Am Geriatr Soc* 2005;53(1):119-130.
- Se Graves R T, Lee J, Stevenson R et al. Tadalafil for treatment of erectile dysfunction in men on antidepressants. *J Clin Psychopharmacol* 2007;27(1):62-66.
- Seidman S N, Pesce V C, Roose S P. High-dose sildenafil citrate for selective serotonin reuptake inhibitor-associated ejaculatory delay: open clinical trial. *Hillside J Clin Psychiatry* 2003;64(6):721-725.
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Sexton W J, Benedict J F, Jarow J P. Comparison of long-term outcomes of penile prostheses and intracavernosal injection therapy.[see comment]. *Br J Urol* 1998;159(3):811-815.
- Shabbir M, Mikhailidis D M, Morgan R J. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors.[comment]. *Current Medical Research & Opinion* 2004;20(5):603-606.
- Shabsigh R. Testosterone therapy in erectile dysfunction and hypogonadism. *Br J Sex Med* 2005;2(6):785-792.

- Shabsigh R. Hypogonadism and erectile dysfunction: The role for testosterone therapy. *Int J Impot Res* 2003;15(SUPPL. 4):S9-S13.
- Shabsigh R, Burnett A L, Eardley I et al. Time from dosing to sexual intercourse attempts in men taking tadalafil in clinical trials. *BJU Int* 2005;96(6):857-863.
- Shabsigh R, Katz M, Yan G et al. Cardiovascular issues in hypogonadism and testosterone therapy. [Review] [44 refs]. *Am J Cardiol* 2005;96(12B):67M-72M.
- Shabsigh R, Padma-Nathan H, Gittleman M et al. Intracavernous alprostadil alfadex (EDEX/VIRIDAL) is effective and safe in patients with erectile dysfunction after failing sildenafil (Viagra). *Urology* 2000;55(4):477-480.
- Shamloul R. Management of honeymoon impotence. *Br J Sex Med* 2006;3(2):361-366.
- Shamloul R, Atteya A, Elnashaar A et al. Intracavernous sodium nitroprusside (SNP) versus papaverine/phentolamine in erectile dysfunction: A comparative study of short- term efficacy and side- effects. *Br J Sex Med* 2005;2(1):117-120.
- Shamloul Rany, Kamel Ihab, E-Mail Address et al. Early Treatment of Cavernositis Resulted in Erectile Function Preservation. [References]. *Br J Sex Med* 2006;3(2):320-322.
- Sharlip I D. Editorial comment. *International Braz J Urol* 2005;31(4):354-355.
- Sharlip I D. Can self-injection therapy cure impotence?. [Review] [7 refs]. *Advances in Experimental Medicine & Biology* 1997;43383-86.
- Sharma R K, Prasad N, Kapoor R et al. Treatment of erectile dysfunction with sildenafil citrate in renal transplant recipient: a cross over placebo controlled trial [abstract]. *Indian Journal of Nephrology* 2002;12(4):23-238.
- Shemtov O M, Radomski S B, Crook J. Success of sildenafil for erectile dysfunction in men treated with brachytherapy or external beam radiation for prostate cancer. *Can J Urol* 2004;11(6):2450-2455.
- Shenfeld O Z, Gofrit O N, Gdor Y et al. The role of sildenafil in the treatment of erectile dysfunction in patients with pelvic fracture urethral disruption. *Br J Urol* 2004;172(6 I):2350-2352.
- Sheu J Y, Chen K K, Lin A T et al. Long-term efficacy and safety of sildenafil for patients with erectile dysfunction. *Journal of the Chinese Medical Association: JCMSA* 2003;66(8):480-486.
- Shigemura K, Arakawa S, Kamidono S et al. Effect of sildenafil on arterial stiffness, as assessed by pulse wave velocity, in patients with erectile dysfunction. *Int J Urol* 2006;13(7):956-959.
- Shimon I, Lubina A, Gorfine M et al. Feedback inhibition of gonadotropins by testosterone in men with hypogonadotropic hypogonadism: comparison to the intact pituitary-testicular axis in primary hypogonadism. *J Androl* 2006;27(3):358-364.
- Shokeir A A, Alserafi M A, Mutabagani H. Intracavernosal versus intraurethral alprostadil: a prospective randomized study. *BJU Int* 1999;83(7):812-815.
- Siegel R L, Dubin N H, Andrade J R. Sildenafil citrate and sperm function [3] (multiple letters). *American Journal of Obstetrics & Gynecology* 2001;184(4):777-778.
- Sighinolfi M C, de Stefani S, Mofferdin A et al. Intracavernous prostaglandin E1 infusion in diabetes with associated ischemic necrosis of the glans penis. *Br J Urol* 2004;171(6 I):2380
- Silvestri A, Galetta P, Cerquetani E et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo.[see comment]. *Eur Heart J* 2003;24(21):1928-1932.
- Singh A N, Scurlock H, Catalan J. Paroxetine induced erectile dysfunction successfully treated with yohimbine in patients suffering from HIV infection. *Journal of Serotonin Research* 1995;1(4):283-285.
- Slob A K, Verhulst A C M, Gijs L et al. Intracavernous injection during diagnostic screening for erectile dysfunction: Five-year experience with over 600 patients. [References]. *Br J Sex Med* 2002;28(1):61-70.
- Smith K M, Romanelli F. Recreational use and misuse of phosphodiesterase 5 inhibitors. [Review] [56 refs]. *Journal of the American Pharmacists Association: JAPhA* 2005;45(1):63-72.
- Soh J, Naya Y, Ushijima S et al. Efficacy of sildenafil for Japanese patients with audio-visual sexual stimulation (AVSS) test by the RigiScan Plus. *Arch Androl* 2006;52(3):163-168.
- Soler J M, Previnaire J G, Denys P et al. Phosphodiesterase inhibitors in the treatment of erectile dysfunction in spinal cord-injured men. *Proc Annu Clin Spinal Cord Inj Conf* 2007;45(2):169-173.
- Sommer F, Engelmann U. Vardenafil: Bayer Yakuhin. *Curr Opin Investig Drugs* 2002;3(4):607-613.
- Sonksen J, Biering-Sorensen F. Transcutaneous nitroglycerin in the treatment of erectile dysfunction in spinal cord injured. *Paraplegia* 1992;30(8):554-557.

- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Speckens A E, Kattemolle M R, Hengeveld M W et al. A prospective long-term follow-up study of patients evaluated for erectile dysfunction: outcome and associated factors. *Int J Impot Res* 1995;7(2):101-110.
- Speel T G W, Bleumer I, Diemont W L et al. The value of sildenafil as mode of stimulation in pharmaco-penile duplex ultrasonography. *Int J Impot Res* 2001;13(4):189-191.
- Sperling H, Eisenhardt A, Virchow S et al. Sildenafil response is influenced by the G protein beta 3 subunit GNB3 C825T polymorphism: a pilot study. *Br J Urol* 2003;169(3):1048-1051.
- Stanislavov R, Nikolova V. Treatment of erectile dysfunction with pycnogenol and L-arginine. *J Sex Marital Ther* 2003;29(3):207-213.
- Steers W, Guay A T, Leriche A et al. Assessment of the efficacy and safety of Viagra (sildenafil citrate) in men with erectile dysfunction during long-term treatment. *Int J Impot Res* 2001;13(5):261-267.
- Steidle C P, McCullough A R, Kaminetsky J C et al. Early sildenafil dose optimization and personalized instruction improves the frequency, flexibility, and success of sexual intercourse in men with erectile dysfunction. *Int J Impot Res* 2007;19(2):154-160.
- Stephenson R A, Mori M, Hsieh Y C et al. Treatment of erectile dysfunction following therapy for clinically localized prostate cancer: patient reported use and outcomes from the Surveillance, Epidemiology, and End Results Prostate Cancer Outcomes Study. *Br J Urol* 2005;174(2):646-650.
- Stief C G, Holmquist F, Djamilian M et al. Preliminary results with the nitric oxide donor linsidomine chlorhydrate in the treatment of human erectile dysfunction. *Br J Urol* 1992;148(5):1437-1440.
- Stief C G, Uckert S, Jonas U. Strategies in the oral pharmacotherapy of male erectile dysfunction viewed from bench and bedside (Part II). *The Journal of Mens Health & Gender* 2005;2(3):325-332.
- Stief C G, Wetterauer U, Schaebdsau F H et al. Calcitonin-gene-related peptide: a possible role in human penile erection and its therapeutic application in impotent patients. *Br J Urol* 1991;146(4):1010-1014.
- Stief C, Padley R J, Perdok R J et al. Cross-study review of the clinical efficacy of apomorphine SL 2 and 3 mg: Pooled data from three placebo-controlled, fixed-dose crossover studies. *European Urology Supplements* 2002;1(3):12-20.
- Strahilevitz J, Rahav G, Schroers H-J et al. An outbreak of Phialemonium infective endocarditis linked to intracavernous penile injections for the treatment of impotence. *Clin Infect Dis* 2005;40(6):781-786.
- Stroberg P, Murphy A, Costigan T. Switching patients with erectile dysfunction from sildenafil citrate to tadalafil: results of a European multicenter, open-label study of patient preference. *Clin Ther* 2003;25(11):2724-2737.
- Stuckey B G A. Tadalafil phase 3 experience. *European Urology Supplements* 2002;1(8):25-30.
- Swartz D A, Todd M W. Intracavernous papaverine and glaucoma.[see comment]. *JAMA* 1990;264(5):570.
- Tam P Y, Keller T, Poppiti R et al. Hemodynamic effects of transurethral alprostadil measured by color duplex ultrasonography in men with erectile dysfunction. *Br J Urol* 1998;160(4):1321-1324.
- Tam S W, Worcel M, Wyllie M. Yohimbine: a clinical review. [Review] [152 refs]. *Pharmacol Ther* 2001;91(3):215-243.
- Tanaka T. Papaverine hydrochloride in peripheral blood and the degree of penile erection. *Br J Urol* 1990;143(6):1135-1137.
- Tariq S H, Haleem U, Omran M L et al. Erectile dysfunction: Etiology and treatment in young and old patients. *Clin Geriatr Med* 2003;19(3):539-551.
- Tas A, Ersoy A, Ersoy C et al. Efficacy of sildenafil in male dialysis patients with erectile dysfunction unresponsive to erythropoietin and/or testosterone treatments. *Int J Impot Res* 2006;18(1):61-68.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Tekdogan U, Tuncel A, Tuglu D et al. Effect of sildenafil citrate treatment on serum dehydroepiandrosterone sulfate levels in patients with erectile dysfunction. *Urology* 2006;68(3):626-630.
- Telias Isaac, Darwin Kadmon-Telias, Ana E-Mail et al. Four cases of erectile dysfunction in substance abusers treated with sildenafil. [References]. *J Addict Dis* 2002;97(11):1473-1474.
- Teloken C, Rhoden E L, Sogari P et al. Therapeutic effects of high dose yohimbine hydrochloride on organic erectile dysfunction. *Br J Urol* 1998;159(1):122-124.

- Terradas C, Levalle O, Nagelberg A et al. Sildenafil improves nocturnal penile erections in organic impotence. *Int J Impot Res* 2001;13(2):125-129.
- Tomlinson John M, Wright David, E-Mail Address et al. Impact of erectile dysfunction and its subsequent treatment with sildenafil: Qualitative study. [References]. *BMJ: British Medical Journal* 2004;328(7447):No
- Tomsak R. PDE5 inhibitors and permanent visual loss. *Int J Impot Res* 2005;17(6):547-549.
- Tosti A, Pazzaglia M, Soli M et al. Evaluation of sexual function with an international index of erectile function in subjects taking finasteride for androgenetic alopecia.[see comment]. *Arch Dermatol* 2004;140(7):857-858.
- Trinchieri A, Nicola M, Masini F et al. Prospective comprehensive assessment of sexual function after retropubic non nerve sparing radical prostatectomy for localized prostate cancer. *Arch Ital Urol Androl* 2005;77(4):219-223.
- Truss M C, Becker A J, Thon W F et al. Intracavernous calcitonin gene-related peptide plus prostaglandin E1: possible alternative to penile implants in selected patients. *Eur Urol* 1994;26(1):40-45.
- Tsai Y S, Lin J S, Lin Y M. Safety and efficacy of alprostadil sterile powder (S. Po., CAVERJECT) in diabetic patients with erectile dysfunction. *Eur Urol* 2000;38(2):177-183.
- Tsujimura A, Yamanaka M, Takahashi T et al. The clinical studies of sildenafil for the ageing male. *Int J Androl* 2002;25(1):28-33.
- Turk S, Karalezli G, Tonbul H Z et al. Erectile dysfunction and the effects of sildenafil treatment in patients on haemodialysis and continuous ambulatory peritoneal dialysis. *Nephrol.Dial.Transplant.* 2001;16(9):1818-1822.
- Turner L A, Althof S E. The clinical effectiveness of self-injection and external vacuum devices in the treatment of erectile dysfunction: a six-month comparison. *Psychiatr Med* 1992;10(2):283-293.
- Turner L A, Althof S E, Levine S B et al. Twelve-month comparison of two treatments for erectile dysfunction: self-injection versus external vacuum devices. *Urology* 1992;39(2):139-144.
- Urciuoli R, Cantisani T A, Carlini I M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Valicenti R K, Choi E, Chen C et al. Sildenafil citrate effectively reverses sexual dysfunction induced by three-dimensional conformal radiation therapy. *Urology* 2001;57(4):769-773.
- Valiquette L, Montorsi F, Hellstrom W J et al. Penetration and maintenance of erection with vardenafil: a time-from-dosing analysis. *Can J Urol* 2005;12(3):2687-2698.
- van Basten J P, Van Driel M F, Jonker-Pool G et al. Sexual functioning in testosterone-supplemented patients treated for bilateral testicular cancer. *Br J Urol* 1997;79(3):461-467.
- van Moorselaar R J, Hartung R, Emberton M et al. Alfuzosin 10 mg once daily improves sexual function in men with lower urinary tract symptoms and concomitant sexual dysfunction. *BJU Int* 2005;95(4):603-608.
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Dijk M, Skrekas T, De La et al. The association between lower urinary tract symptoms and sexual dysfunction: Fact or fiction?. *Curr Opin Urol* 2005;15(1):39-44.
- Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
- Vardi Y, Sprecher E, Gruenwald I. Logistic regression and survival analysis of 450 impotent patients treated with injection therapy: long-term dropout parameters.. *Br J Urol* 2000;163(2):467-470.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Virag R. Indications and early results of sildenafil (Viagra) in erectile dysfunction. *Urology* 1999;54(6):1073-1077.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.
- Vitezic D. A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction. [Review] [72 refs]. *Drug Saf* 2001;24(4):255-265.
- von Heyden B, Donatucci C F, Kaula N et al. Intracavernous pharmacotherapy for impotence: selection of appropriate agent and dose. [Review] [23 refs]. *Br J Urol* 1993;149(5 Pt 2):1288-1290.

- Wagner G, Montorsi F, Auerbach S et al. Sildenafil citrate (VIAGRA) improves erectile function in elderly patients with erectile dysfunction: a subgroup analysis. *J Gerontol A Biol. Sci Med Sci* 2001;56(2):M113-M119.
- Wagrell L, Schelin S, Nordling J et al. Three-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomized multicenter study. *Urology* 2004;64(4):698-702.
- Wang C J, Wu C C, Huang C H et al. A comparative study with intracavernous injection of prostaglandin E1 versus papaverine for the diagnostic assessment of erectile impotence. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1992;8(11):585-590.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Webb D J, Freestone S, Allen M J et al. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. *Am J Cardiol* 1999;83(5A):21C-28C.
- Weber D C, Bieri S, Kurtz J M et al. Prospective pilot study of sildenafil for treatment of postradiotherapy erectile dysfunction in patients with prostate cancer. *Am J Clin Oncol* 1999;17(11):3444-3449.
- Weidner W, Schroeder-Printzen I, Fischer C et al. Experience in the treatment of erectile dysfunction using the intracavernosal self-injection of papaverine: Results of a prospective study after a median follow-up of 42 months involving 135 patients and 10766 injections. *World J Urol* 1992;10(3):179-182.
- Weiss J N, Badlani G H, Ravalli R et al. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6(3):171-174.
- Weiss J N, Ravalli R, Badlani G H. Intracavernous pharmacotherapy in psychogenic impotence. *Urology* 1991;37(5):441-443.
- Wen H S, Hsieh C H, Hsu G L et al. The synergism of penile venous surgery and oral sildenafil in treating patients with erectile dysfunction.[see comment]. *Int J Androl* 2005;28(5):297-303.
- Werneke U, Crowe M. Review of patients with erectile dysfunction attending the Maudsley psychosexual clinic in 1999: The impact of sildenafil. *Sexual & Relationship Therapy* 2002;17(2):171-185.
- Werthman P, Rajfer J. MUSE therapy: preliminary clinical observations. *Urology* 1997;50(5):809-811.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Williams G. Male erectile dysfunction. *Prescribers' Journal* 2000;40(1):49-58.
- Williams G, Abbou C C, Amar E T et al. The effect of transurethral alprostadil on the quality of life of men with erectile dysfunction, and their partners. MUSE Study Group. *Br J Urol* 1998;82(6):847-854.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):
- Willke R J, Glick H A, McCarron T J et al. Quality of life effects of alprostadil therapy for erectile dysfunction. *Br J Urol* 1997;157(6):2124-2128.
- Wise Thomas N. Psychosocial side effects of sildenafil therapy for erectile dysfunction. *J Sex Marital Ther* 1999;25(2):145-150.
- Wolfson B, Pickett S, Scott N E et al. Intraurethral prostaglandin E-2 cream: a possible alternative treatment for erectile dysfunction. *Urology* 1993;42(1):73-75.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wu C C, Xue Z Y, Apichat K et al. The use of alprostadil sterile powder in a home self-injection study of Asian men with erectile dysfunction. *Clin Ther* 1996;18(2):256-264.
- Wylie Kevan R, Hallam-Jones Ruth A, Steward David et al. The combination of penoscrotal rings and PDE5i's in the treatment of erectile dysfunction - the Sheffield PDE5i and Ring Duo Technique. Two case reports. [References]. *Sexual and Relationship Therapy* 2006;21(2):209-215.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yaman O, Tokatli Z, Akand M et al. Characteristics of sildenafil erections in healthy young men. *Asian J Androl* 2005;7(4):395-398.
- Yassin A A, Saad F. Improvement of sexual function in men with late-onset hypogonadism treated with testosterone only. *Br J Sex Med* 2007;4(2):497-501.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.
- Yassin A A, Saad F, Traish A. Testosterone undecanoate restores erectile function in a subset of patients with venous leakage: a series of case reports. *Br J Sex Med* 2006;3(4):727-735.

- Yenicierioglu Y, Kefi A, Aslan G et al. Efficacy and safety of sildenafil for treating erectile dysfunction in patients on dialysis. *BJU Int* 2002;90(4):442-445.
- Zaher T F. Papaverine plus prostaglandin E1 versus prostaglandin E1 alone for intracorporeal injection therapy. *Int Urol Nephrol* 1998;30(2):193-196.
- Zargooshi J. Unconsummated marriage: clarification of aetiology; treatment with intracorporeal injection. *BJU Int* 2000;86(1):75-79.
- Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200
- Zelevsky M J, McKee A B, Lee H et al. Efficacy of oral sildenafil in patients with erectile dysfunction after radiotherapy for carcinoma of the prostate. *Urology* 1999;53(4):775-778.
- Zesiewicz T A, Helal M, Hauser R A. Sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men with Parkinson's disease. *Mov Disord* 2000;15(2):305-308.
- Zhang Y, Guan D L, Ou T W et al. Sildenafil citrate treatment for erectile dysfunction after kidney transplantation. *Transplant Proc* 2005;37(5):2100-2103.
- Ziegler D. Management of erectile dysfunction in diabetic patients. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):58-65.
- Zippe C D, Kedia A W, Kedia K et al. Treatment of erectile dysfunction after radical prostatectomy with sildenafil citrate (Viagra). *Urology* 1998;52(6):963-966.
- Zippe C D, Kedia S, Kedia A W et al. Sildenafil citrate (Viagra) after radical retropubic prostatectomy: pro. *Urology* 1999;54(4):583-586.
- Zlotta A R, Teillac P, Raynaud J P et al. Evaluation of male sexual function in patients with Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), Tamsulosin or Finasteride. *Eur Urol* 2005;48(2):269-276.
- Zorgniotti A. "On demand" oral drug for erection in impotent men'. *Br J Urol* 1992;147308
- Zorgniotti A W. Experience with buccal phentolamine mesylate for impotence. *Int J Impot Res* 1994;6(1):37-41.
- Zusman R M, Morales A, Glasser D B et al. Overall cardiovascular profile of sildenafil citrate. [Review] [33 refs]. *Am J Cardiol* 1999;83(5A):35C-44C.
- Not applicable.**
- Annual update 2004/2005 - Treatment of genitourinary disorders. *Drugs of the Future* 2005;30(9):931-934.
- Abrams J. Time course of the interaction between tadalafil and nitrates.[comment]. *J Am Coll Cardiol* 2004;43(11):2150-2151.
- Adaikan P G, Chong Y S, Chew S S L et al. Male sexual dysfunction. *Curr Obstet Gynaecol* 2000;10(1):23-28.
- Ahl J, Kinon B J, Liu-Seifert H. Sexual dysfunction associated with neuroleptic-induced hyperprolactinemia improves with reduction in prolactin levels. *Ann N Y Acad Sci* 2004;1032(pp 289-290):-290.
- Ahuja S K, Krane N K, Hellstrom W J. Penile prostheses in the management of impotence in patients with end-stage renal disease. *J La State Med Soc* 1998;150(1):32-34.
- Akbari F, Alavi M, Esteghamati A et al. Effect of renal transplantation on sperm quality and sex hormone levels. *BJU Int* 2003;92(3):281-283.
- Akkus E, Kadioglu A, Esen A et al. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. *Eur Urol* 2002;41(3):298-304.
- Alexandre B, Lemaire A, Desvaux P et al. Intracavernous injections of prostaglandin E1 for erectile dysfunction: patient satisfaction and quality of sex life on long-term treatment. *Br J Sex Med* 2007;4(2):426-431.
- Alfonso A, Rieniets K I, Vigersky R A. Incidence and clinical significance of elevated macroprolactin levels in patients with hyperprolactinemia. *Endocr Pract* 2006;12(3):275-280.
- Alivizatos G, Skolarikos A, Laguna P. Recent data upon impotence, incontinence and quality of life issues concerning radical prostatectomy. [Review] [74 refs]. *Arch Esp Urol* 2003;56(3):321-330.
- Althof S E. Quality of life and erectile dysfunction. *Urology* 2002;59(6):803-810.
- Althof S E, Corty E W, Levine S B et al. EDITS: development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. *Urology* 1999;53(4):793-799.
- Althof Stanley E, Turner Louisa A. Self-injection therapy and external vacuum devices in the treatment of erectile dysfunction: Methods and outcome. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Anderson R A, Bancroft J, Wu F C. The effects of exogenous testosterone on sexuality and mood of normal men. *Journal of Clinical Endocrinology & Metabolism* 1992;75(6):1503-1507.

- Anderson R A, Martin C W, Kung A W et al. 7Alpha-methyl-19-nortestosterone maintains sexual behavior and mood in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 1999;84(10):3556-3562.
- Anderson R A, Wallace A M, Sattar N et al. Evidence for tissue selectivity of the synthetic androgen 7 alpha-methyl-19-nortestosterone in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 2003;88(6):2784-2793.
- Andersson K-E. Pharmacology of penile erection. *Pharmacol Rev* 2001;53(3):417-450.
- Andolsek K M. Alprostadil for the treatment of erectile dysfunction. *Am Fam Physician* 1997;55(5):1902-1903.
- Andriole G, Bruchofsky N, Chung L W K et al. Dihydrotestosterone and the prostate: The scientific rationale for 5 α -reductase inhibitors in the treatment of benign prostatic hyperplasia. *Br J Urol* 2004;172(4 I):1399-1403.
- Anonymous. Tadalafil: new preparation. Slightly more convenient, but poorly assessed in organic disorders. *Prescrire Int* 2003;12(68):213-215.
- Anonymous. Tadalafil (cialis) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1172):101-102.
- Anonymous. First study of Viagra in black men demonstrates effective, well-tolerated treatment. *Urol Nurs* 2002;22(4):285-286.
- Anonymous. Study shows patients taking vardenafil consistently completed sexual intercourse. *Urol Nurs* 2001;21(6):413-414.
- Anonymous. Apomorphine (TAP holdings). 6a beta-aporphine-10,11-diol hydrochloride hemihydrate, apomorphine hydrochloride, spontane, Uprima. *Drugs in R & D* 1999;2(6):415-416.
- Anonymous. Intraurethral alprostadil for impotence. *Medical Letter on Drugs & Therapeutics* 1997;39(997):32
- Anonymous. Treatment for impotence gains FDA approval. *Am J Health Syst Pharm* 1995;52(19):2078-2079.
- Anonymous. Intracavernous injection of alprostadil for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 1995;37(958):83-84.
- Anonymous. Vardenafil works for 10 hours. *Can Pharm J* 2005;275(7360):133
- Anonymous. Treatment duration of action is important in ED. *Can Pharm J* 2004;273(7330):878
- Anonymous. Dutasteride. *Prescrire Int* 2004;13(73):183
- Anonymous. Erratum: Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo controlled, crossover study (*Indian Journal of Pharmacology* (2004) vol. 37 (5) (317)). *Indian J Pharmacol* 2004;36(6):391
- Anonymous. Partnership struck between Bayer and Schering. *Nat Rev Genet* 2004;3(10):819
- Anonymous. Erectile dysfunction drugs may reduce fertility but help depression. *Can Pharm J* 2004;272(7294):439
- Anonymous. Sildenafil appears safe and effective for some heart failure patients. *Can Pharm J* 2004;272(7290):310
- Anonymous. What to do when oral treatment fails?. *Int J Impot Res* 2003;15(SUPPL. 7):S30-S32.
- Anonymous. Oral drug treatment of erectile dysfunction. *Int J Impot Res* 2003;15(SUPPL. 7):S27-S29.
- Anonymous. Counselling and increased dose of sildenafil improves response in ED. *British Journal of Diabetes & Vascular Disease* 2003;3(6):445
- Anonymous. Improve erectile function early after prostatectomy. *Med Today* 2003;4(11):8-9.
- Anonymous. Recent FDA approval of new erectile dysfunction drug provides first challenge to sildenafil. *Geriatrics and Aging* 2003;6(8):11
- Anonymous. New PDE 5 inhibitor efficacious for erectile dysfunction in diabetics. *Cardiology Review* 2003;20(10):
- Anonymous. Inhaled apomorphine promising for erectile dysfunction treatment. *Can Pharm J* 2003;271(7261):170
- Anonymous. Transurethral alprostadil. *Prescrire Int* 2002;11(61):144
- Anonymous. IDdb News focus. *Current Drug Discovery* 2003;(pp 10-13):-13.
- Anonymous. Sildenafil effective for sexual dysfunction associated with use of antidepressants. *Can Pharm J* 2003;270(7231):41
- Anonymous. Vardenafil prolongs improved erectile function in diabetics. *Cardiology Review* 2002;19(10):38-39.
- Anonymous. Erectile dysfunction treated effectively with tadalafil. *Economics of Neuroscience* 2001;3(11):19

- Anonymous. New erectile dysfunction drug useful in diabetes. *Can Pharm J* 2001;267(7173):669
- Anonymous. Erectile dysfunction - Alprostadil. *Manuf Chem Aerosol News* 2001;72(11):21
- Anonymous. Erectile dysfunction - Vardenafil. *Manuf Chem Aerosol News* 2001;72(6):25
- Anonymous. FDA approves oral therapy for erectile dysfunction. *Am J Health Syst Pharm* 1998;55(10):981-984.
- Anonymous. Sildenafil Viagra(R) UK-92480: Treatment of erectile dysfunction phosphodiesterase V inhibitor. *Drugs of the Future* 1998;23(2):242-243.
- Anonymous. Intracavernosal alprostadil for erectile dysfunction. *Hospital Practice (Office Edition)* 1996;31(8):136-137.
- Anonymous. Intracavernous alprostadil: Effective therapy for erectile dysfunction. *Drugs & Therapy Perspectives* 1996;7(6):1-5.
- Anonymous. Heart drug with 'viagra side-effect'. *Indian J Med Sci* 1999;53(5):236
- Anonymous. What to do if Viagra won't do. *Harvard Mens Health Watch* 2005;9(10):4-8.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: intracavernous injection of prostaglandin E1. *JAMA* 1991;265(24):3321-3323.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: papaverine and phentolamine. *JAMA* 1990;264(6):752-754.
- Ansong K S, Punwaney R B. An assessment of the clinical relevance of serum testosterone level determination in the evaluation of men with low sexual drive. *Br J Urol* 1999;162(3 I):719-721.
- Ansong K S, Lewis C, Jenkins P et al. Epidemiology of erectile dysfunction: a community-based study in rural New York State. *Ann Epidemiol* 2000;10(5):293-296.
- Arafa M, Eid H, Shamloul R. Significance of phentolamine redosing during prostaglandin E1 penile color Doppler ultrasonography in diagnosis of vascular erectile dysfunction. *Int J Urol* 2007;14(5):476-477.
- Araujo A B, O'Donnell A B, Brambilla D J et al. Prevalence and incidence of androgen deficiency in middle-aged and older men: Estimates from the Massachusetts male aging study. *Journal of Clinical Endocrinology & Metabolism* 2004;89(12):5920-5926.
- Araujo Andre B, Durante Richard, Feldman Henry A et al. The relationship between depressive symptoms and male erectile dysfunction: Cross-sectional results from the Massachusetts male aging study. *Psychosom Med* 1998;60(4):458-465.
- Arnavaz A, Aurich A, Weissenborn K et al. Effect of sildenafil (Viagra) on cerebral blood flow velocity: a pilot study. *Psychiatry Res* 2003;122(3):207-209.
- Arnold R, Beer D, Bhalay G et al. 8-Aryl xanthines potent inhibitors of phosphodiesterase 5. *Bioorg Med Chem Lett* 2002;12(18):2587-2590.
- Aronson J K. Features of this month's Journal. *Br J Clin Pharmacol* 2003;55(4):327-328.
- Arslan D, Esen A A, Secil M et al. A new method for the evaluation of erectile dysfunction: sildenafil plus Doppler ultrasonography. *Br J Urol* 2001;166(1):181-184.
- Arthur R. Cardiovascular disorders and erectile dysfunction. *British Journal of Cardiology* 2002;9(3):144-145.
- Ashton A K, Jamerson B D, Weinstein W L et al. Antidepressant-related adverse effects impacting treatment compliance: Results of a patient survey. *Current Therapeutic Research, Clinical & Experimental* 2005;66(2):96-106.
- Atala A. What's new in urology. *J Am Coll Surg* 2004;199(3):446-461.
- Atikeler M K, Gecit I, Senol F A. Optimum usage of prilocaine-lidocaine cream in premature ejaculation. *Andrologia* 2002;34(6):356-359.
- Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: quetiapine-induced sexual dysfunctions. *Int J Impot Res* 2005;17(2):201-203.
- Avasthi A, Basu D, Kulhara P et al. Psychosexual dysfunction in Indian male patients: Revisited after seven years. *Arch Sex Behav* 1994;23(6):685-695.
- Aversa A, Mazzilli F, Rossi T et al. Effects of sildenafil (Viagra) administration on seminal parameters and post-ejaculatory refractory time in normal males. *Hum Reprod* 2000;15(1):131-134.
- Aydin S, Unal D, Erol H et al. Multicenter clinical evaluation of the aetiology of erectile dysfunction: a survey report. *International Urology & Nephrology* 2001;32(4):699-703.
- Ayub W, Fletcher S. End-stage renal disease and erectile dysfunction. Is there any hope?. *Nephrology Dialysis Transplantation* 2000;15(10):1525-1528.
- Bagatell C J, Heiman J R, Rivier J E et al. Effects of endogenous testosterone and estradiol on sexual behavior in normal young men. [erratum appears in *J Clin Endocrinol Metab* 1994 Jun;78(6):1520]. *Journal of Clinical Endocrinology & Metabolism* 1994;78(3):711-716.

- Baggaley M R, Hirst J F, Watson J P. Outcome of patients referred to a psychosexual clinic with erectile failure. *Sexual & Marital Therapy* 1996;11(2):123-130.
- Bai W J, Zhu J C, Jiang H et al. [A comparative study of different vasoactive drugs in the treatment of impotence]. *Chinese Journal of Urology* 1992;13(6):453-455.
- Bailey J, Evans J P, Hardy M et al. Synopsis: 2005 Annual Meeting of the American Society of Andrology. *J Androl* 2005;26(6):678-688.
- Bancroft J, Munoz M, Beard M et al. The effects of a new alpha-2 adrenoceptor antagonist on sleep and nocturnal penile tumescence in normal male volunteers and men with erectile dysfunction. *Psychosom Med* 1995;57(4):345-356.
- Baniel J, Israilov S, Segenreich E et al. Comparative evaluation of treatments for erectile dysfunction in patients with prostate cancer after radical retropubic prostatectomy. *BJU Int* 2001;88(1):58-62.
- Barnas J, Parker M, Guhring P et al. The utility of tamsulosin in the management of orgasm-associated pain: a pilot analysis.[see comment]. *Eur Urol* 2005;47(3):361-365.
- Barqawi A, O'Donnell C, Kumar R et al. Correlation between LUTS (AUA-SS) and erectile dysfunction (SHIM) in an age-matched racially diverse male population: data from the Prostate Cancer Awareness Week (PCAW). *Int J Impot Res* 2005;17(4):370-374.
- Bartlik Barbara D, Kaplan Peter, Kaplan Helen S. Psychostimulants apparently reverse sexual dysfunction secondary to selective serotonin re-uptake inhibitors. *J Sex Marital Ther* 1995;21(4):264-271.
- Bayes M, Rabasseda X, Prous J R. Gateways to Clinical Trials. *Methods & Findings in Experimental & Clinical Pharmacology* 2004;26(9):723-753.
- bdel-Khalek M, El-Hammady S, Ibrahiem el. A 4-year follow-up of a randomized prospective study comparing transurethral electrovaporization of the prostate with neodymium: YAG laser therapy for treating benign prostatic hyperplasia. *BJU Int* 2003;91(9):801-805.
- Beard S, Hunn A, Wight J. Treatments for spasticity and pain in multiple sclerosis: A systematic review. *Health Technol Assess* 2003;7(40):111p
- Beasley C M, Mitchell M I, Dmitrienko A A et al. The combined use of ibutilide as an active control with intensive electrocardiographic sampling and signal averaging as a sensitive method to assess the effects of tadalafil on the human QT interval.[see comment]. *J Am Coll Cardiol* 2005;46(4):678-687.
- Becher E, Glina S. Erectile dysfunction in Latin America and treatment with sildenafil citrate (Viagra): Introduction. *Int J Impot Res* 2002;14(SUPPL. 2):S1-S2.
- Bella A J, Brock G B. Tadalafil: A comprehensive update. *Journal of Drug Evaluation* 2004;2(8):225-246.
- Benson G S. The clinical evaluation of the patient presenting with erectile dysfunction: what is reasonable?. [Review] [27 refs]. *Semin Urol* 1990;8(2):94-99.
- Beretta G, Saltarelli O, Marzotto M et al. Transcutaneous minoxidil in the treatment of erectile dysfunctions in spinal cord injured men. *Acta Eur Fertil* 1993;24(1):27-30.
- Bestane W J, Bestane M C, Ramos N A. Prospective study of sodium nitroprusside in pharmacologically induced erection. *Braz J Urol* 2001;27(2):155-158.
- Beutel M E, Wiltink J, Hauck E W et al. Correlations between hormones, physical, and affective parameters in aging urologic outpatients. *Eur Urol* 2005;47(6):749-755.
- Bhatia M S, Malik S C. Dhat syndrome--a useful diagnostic entity in Indian culture. *Br J Psychiatry* 1991;159(Nov.):691-695.
- Bivalacqua T J, Hellstrom W J G. Potential application of gene therapy for the treatment of erectile dysfunction. *J Androl* 2001;22(2):183-190.
- Black A M, Day A G, Morales A. The reliability of clinical and biochemical assessment in symptomatic late-onset hypogonadism: Can a case be made for a 3-month therapeutic trial?. *BJU Int* 2004;94(7):1066-1070.
- Blander D S, Sanchez-Ortiz R F, Broderick G A. Sex inventories: can questionnaires replace erectile dysfunction testing?. *Urology* 1999;54(4):719-723.
- Boccon Gibod L. Is transurethral needle ablation a safe and effective treatment for lower urinary tract symptoms secondary to BPH?. *Nature Clinical Practice Urology* 2004;1(1):24-25.
- Bochinski D J, Dean R C, Lue T F. Erectile dysfunction and priapism. *Nat Clin Pract Urol* 2004;1(1):49-53.
- Bodie J A, Beeman W W, Monga M. Psychogenic erectile dysfunction. *Int J Psychiatry Med* 2003;33(3):273-293.
- Bodie J, Lewis J, Schow D et al. Laboratory evaluations of erectile dysfunction: an evidence based approach. *Br J Urol* 2003;169(6):2262-2264.
- Bodner D R, Leffler B, Frost F. The role of intracavernous injection of vasoactive medications for the restoration of erection in spinal cord injured males: a three year follow up. *Paraplegia* 1992;30(2):118-120

- Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.
- Boolell M, Allen M J, Ballard S A et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int J Impot Res* 1996;8(2):47-52.
- Boshier A, Wilton L V, Shakir S A W. Evaluation of the safety of sildenafil for male erectile dysfunction: Experience gained in general practice use in England in 1999. *BJU Int* 2004;93(6):796-801.
- Bouloux P. Testim 1% testosterone gel for the treatment of male hypogonadism. [Review] [33 refs]. *Clin Ther* 2005;27(3):286-298.
- Boydak B, Nalbantgil S, Fici F et al. A randomised comparison of the effects of nebivolol and atenolol with and without chlorthalidone on the sexual function of hypertensive men. *Clinical Drug Investigation* 2005;25(6):409-416.
- Braatvedt G D. Outcome of managing impotence in clinical practice. *N Z Med J* 1999;112(1092):272-274.
- Brake M, Loertzer H, Horsch R et al. Treatment of Peyronie's disease with local interferon-alpha 2b. *BJU Int* 2001;87(7):654-657.
- Bratus D, Hlebic G, Hajdinjak T. 16905960 of erectile dysfunction. *Croat Med J* 2007;48(1):76-80.
- Brazil M. Viagra for broken hearts?. *Nat Rev Genet* 2005;4(3):190
- Brennemann W, Kohler W, Zierz S et al. Testicular dysfunction in adrenomyeloneuropathy. *Eur J Endocrinol* 1997;137(1):34-39.
- Brennemann W, Stitz B, Van Ahlen H et al. Treatment of idiopathic erectile dysfunction in men with the opiate antagonist naltrexone--a double-blind study. *J Androl* 1993;14(6):407-410.
- Briganti A, Chun F K H, Salonia A et al. A comparative review of apomorphine formulations for erectile dysfunction: Recommendations for use in the elderly. *Drugs Aging* 2006;23(4):309-319.
- Briganti A, Salonia A, Gallina A et al. Drug insight: Oral phosphodiesterase type 5 inhibitors for erectile dysfunction. *Nature Clinical Practice Urology* 2005;2(5):239-247.
- Briganti A, Salonia A, Zanni G et al. Erectile dysfunction and radical prostatectomy: An update. *Eau Update Series* 2004;2(2):84-92.
- Brindis R G, Kloner R A. Sildenafil in patients with cardiovascular disease. [Review] [33 refs]. *Am J Cardiol* 2003;92(9A):26M-36M.
- Brixius K, Middeke M, Lichtenthal A et al. Nitric oxide, erectile dysfunction and beta-blocker treatment (MR NOED study): Benefit of nebivolol versus metoprolol in hypertensive men. *Clinical & Experimental Pharmacology & Physiology* 2007;34(4):327-331.
- Broderick G A, Allen G, McClure R D. Vacuum tumescence devices: the role of papaverine in the selection of patients. *Br J Urol* 1991;145(2):284-286.
- Brooks D P, Giuliano F. Genitourinary diseases. *Drug Discovery Today: Therapeutic Strategies* 2005;2(1):iii-iv.
- Brown J S, Wessells H, Chancellor M B et al. Urologic complications of diabetes. *Diabetes Care* 2005;28(1):177-185.
- Buchholz N P, Weuste R, Mattarelli G et al. Post-vasectomy erectile dysfunction. *J Psychosom Res* 1994;38(7):759-762.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. *Urologe* 2005;Ausg. A. 44(9):1045-1046, 1048-51.
- Buena F, Swerdloff R S, Steiner B S et al. Sexual function does not change when serum testosterone levels are pharmacologically varied within the normal male range. *Fertility & Sterility* 1993;59(5):1118-1123.
- Bukofzer S, Livesey N. Safety and tolerability of apomorphine SL (Uprima). *Int J Impot Res* 2001;13(SUPPL. 3):S40-S44.
- Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.
- Burnett A L. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: A randomized controlled trial: Editorial comment 2. *Urology* 2003;62(1):126
- Burnett A L. Vasoactive pharmacotherapy to cure erectile dysfunction: fact or fiction?. [Review] [45 refs]. *Urology* 2005;65(2):224-230.
- Burnett A L. The impact of sildenafil on molecular science and sexual health. *Eur Urol* 2004;46(1):9-14.
- Burns-Cox N, Gingell C. The andropause: fact or fiction?. [Review] [49 refs]. *Postgrad Med J* 1997;73(863):553-556.
- Buvat J. Hyperprolactinemia and sexual function in men: a short review. [Review] [26 refs]. *Int J Impot Res* 2003;15(5):373-377.

- Buvat J, Boujadoue G. Testosterone replacement therapy in the ageing man. *The Journal of Mens Health & Gender* 2005;2(4):396-399.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Campbell M. Beneficial cardiovascular effects and safety of sildenafil reported in trio of studies. *Cardiology Review* 2001;18(6):27
- Cappelleri J C, Siegel R L, Glasser D B et al. Relationship between patient self-assessment of erectile dysfunction and the sexual health inventory for men. *Clin Ther* 2001;23(10):1707-1719.
- Cara A M, Lopes-Martins R A B, Antunes E et al. The role of histamine in human penile erection. *Br J Urol* 1995;75(2):220-224.
- Carani C, Bancroft J, Granata A et al. Testosterone and erectile function, nocturnal penile tumescence and rigidity, and erectile response to visual erotic stimuli in hypogonadal and eugonadal men. *Psychoneuroendocrinology* 1992;17(6):647-654.
- Carani C, Scuteri A, Marrama P et al. The effects of testosterone administration and visual erotic stimuli on nocturnal penile tumescence in normal men. *Horm Behav* 1990;24(3):435-441.
- Cardenas D D, Ditunno J, Graziani V et al. Phase 2 trial of sustained-release fampridine in chronic spinal cord injury. *Proc Annu Clin Spinal Cord Inj Conf* 2007;45(2):158-168.
- Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.
- Carey Michael P, Wincze John P, Meisler Andrew W. Sexual dysfunction: Male erectile disorder. Barlow, David H (Ed) 1993;(1993):534
- Carosa E, Benvenga S, Trimarchi F et al. Sexual inactivity results in reversible reduction of LH bioavailability. *Int J Impot Res* 2002;14(2):93-99.
- Carson C C. PNU-83757: a new agent for the treatment of erectile dysfunction.[comment]. *Curr Urol Rep* 2002;3(6):465-466.
- Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.
- Carson C C, Hatzichristou D G, Carrier S. Erratum: Erectile response with vardenafil in sildenafil nonresponders: A multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial (*BJU International* (2004) 94 (1301-1309)). *BJU Int* 2005;96(3):466
- Carson C C, Rajfer J, Eardley I et al. The efficacy and safety of tadalafil: an update. *BJU Int* 2004;93(9):1276-1281.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Caspi A, Goldenberg M M. Sildenafil: A new drug treatment for male erectile dysfunction. *P & T* 1998;23(5):
- Cawello W, Schweer H, Dietrich B et al. Pharmacokinetics of prostaglandin E1 and its main metabolites after intracavernous injection and short-term infusion of prostaglandin E1 in patients with erectile dysfunction. *Br J Urol* 1997;158(4):1403-1407.
- Cecchi M, Sepich C A, Felipetto R et al. Vacuum constriction device and topical minoxidil for management of impotence. *Arch Esp Urol* 1995;48(10):1058-1059.
- Chaiban J T, Azar S T. Erectile dysfunction in diabetic patients. *J Med Liban* 2004;52(4):217-219.
- Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.
- Chatterjee R, Andrews H O, McGarrigle H H et al. Cavernosal arterial insufficiency is a major component of erectile dysfunction in some recipients of high-dose chemotherapy/chemoradiotherapy for haematological malignancies. *Bone Marrow Transplant* 2000;25(11):1185-1189.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Chaudhuri T K, Fink S, Burger R H et al. Nuclear penogram: Non-invasive technique to monitor and record effect of pharmacologically-induced penile erection in impotence therapy. *Urology* 1990;35(1):98
- Cheitlin M D, Hutter A M, Brindis R G et al. Use of sildenafil (Viagra) in patients with cardiovascular disease. *Circulation* 1999;99(1):168-177.
- Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.

- Chen J, Greenstein A, Kaver I et al. Use of automatic insulin injector for intracorporeal injection in erectile dysfunction. *Br J Urol* 1994;152(2):461-462.
- Chen J, Mabjeesh N J, Greenstein A. Sildenafil versus the vacuum erection device: patient preference. *Br J Urol* 2001;166(5):1779-1781.
- Chen J, Wollman Y, Chernichovsky T et al. Effect of oral administration of high-dose nitric oxide donor L-arginine in men with organic erectile dysfunction: results of a double-blind, randomized, placebo-controlled study. *BJU Int* 1999;83(3):269-273.
- Chen K-C, Minor T X, Rahman N U et al. The additive erectile recovery effect of brain-derived neurotrophic factor combined with vascular endothelial growth factor in a rat model of neurogenic impotence. *BJU Int* 2005;95(7):1077-1080.
- Chen K-K, Jiann B-P, Lin J S N et al. Erratum: Efficacy and safety of on-demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study (*Journal of Sexual Medicine* vol. 1 (2)). *Br J Sex Med* 2005;2(1):158
- Cheng J Y W, Ng E M L, Chen R Y L et al. Prevalence of erectile dysfunction in Asian populations: A meta-analysis. *Int J Impot Res* 2007;19(3):229-244.
- Chew K K. Prevalence of hypogonadism in the aging male and male erectile dysfunction in Asia-Pacific countries. *Asian J Androl* 2003;5(2):171-172.
- Chew K K, Stuckey B G. Clinical course of penile fibrosis in intracavernosal prostaglandin E1 injection therapy: a follow-up of 44 patients. *Int J Impot Res* 2003;15(2):94-98.
- Chew K K, Stuckey B G A. Use of transurethral alprostadil (MUSE) (prostaglandin E1) for glans tumescence in a patient with penile prosthesis. *Int J Impot Res* 2000;12(3):195-196.
- Chew K K, Stuckey B G A, Thompson P L. Erectile dysfunction, sildenafil and cardiovascular risk. *Med J Aust* 2000;172(6):279-283.
- Chia S. Management of premature ejaculation -- a comparison of treatment outcome in patients with and without erectile dysfunction. *Int J Androl* 2002;25(5):301-305.
- Chinegwundoh F, Anie K A. Treatments for priapism in boys and men with sickle cell disease. [Review] [16 refs]. *Cochrane Database Syst Rev* 2004;(4):CD004198
- Chiu K C, Cohan P, Martinez D et al. Adrenal insufficiency after medical therapy for prolactin and adrenocorticotropic hormone co-producing pituitary macroadenoma without hypercortisolism. *Endocr Pract* 2001;11(6):443-446.
- Chiu Y J, Reid I A. Effect of sildenafil on renin secretion in human subjects. *Experimental biology and medicine* (Maywood, NJ) 2002;227(8):620-625.
- Christ B, Brockmeier D, Hauck E W et al. Interactions of sildenafil and tacrolimus in men with erectile dysfunction after kidney transplantation. *Urology* 2001;58(4):589-593.
- Christ G J, Melman A. The application of gene therapy to the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):111-112.
- Chue P. Gabapentin treatment for premature ejaculation [3]. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 2004;49(9):644-645.
- Cimentepe E, Unsal A, Saglam R. Randomized clinical trial comparing transurethral needle ablation with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: results at 18 months. *J Endourol* 2003;17(2):103-107.
- Clark C. Erectile dysfunction and other problems. *Can Pharm J* 2004;272(7299):608-610.
- Clark R V, Hermann D J, Cunningham G R et al. Marked Suppression of Dihydrotestosterone in Men with Benign Prostatic Hyperplasia by Dutasteride, a Dual 5 α -Reductase Inhibitor. *Journal of Clinical Endocrinology & Metabolism* 2004;89(5):2179-2184.
- Claro J A, Passerotti C C, Figueiredo Neto A C et al. An alternative non-invasive treatment for Peyronie's disease. *International Braz J Urol* 2004;30(3):199-204.
- Clough J. CNS-targeted sexual dysfunction drug for men and women. *Drug Discov Today* 2002;7(9):492-494.
- Coelho O R. Tolerability and safety profile of sildenafil citrate (Viagra) in Latin American patient populations. *Int J Impot Res* 2002;14(Suppl 2):54-59.
- Coker C, Bettocchi C, Pryor J. Caverject, a new licensed prostaglandin preparation for use in erectile dysfunction. *J Androl* 1994;15(6 SUPPL.):71S
- Coleman C I, Carabino J M, Vergara C M et al. Vardenafil. *Hosp Formul* 2003;38(3):131-148.
- Collazos J, Martinez E, Mayo J et al. Sexual dysfunction in HIV-infected patients treated with highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2002;31(3):322-326.
- Colp G M, Scropo F I. Can self-directed pelvic floor exercises improve erectile function?. *Nature Clinical Practice Urology* 2005;2(3):128-129.
- Conti C R, Pepine C J, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. *Am J Cardiol* 1999;83(5A):29C-34C.

- Contreras L N, Masini A M, Danna M M et al. Glucocorticoids: their role on gonadal function and LH secretion. *Minerva Endocrinol* 1996;21(2):43-46.
- Cooper A J, Losztyn S, Russell N C et al. Medroxyprogesterone acetate, nocturnal penile tumescence, laboratory arousal, and sexual acting out in a male with schizophrenia. *Arch Sex Behav* 1990;19(4):361-372.
- Cormio L, Nisen H, Ruutu M et al. Etilefrine in the prevention of prolonged erection after diagnostic pharmacological stimulation. *Ann Chir Gynaecol* 1996;85(3):247-250.
- Corona G, Mannucci E, Fisher A D et al. Effect of hyperprolactinemia in male patients consulting for sexual dysfunction. *Br J Sex Med* 2007;4(5):1485-1493.
- Corona G, Mannucci E, Petrone L et al. ANDROTEST: a structured interview for the screening of hypogonadism in patients with sexual dysfunction. *Br J Sex Med* 2006;3(4):706-715.
- Corona G, Mannucci E, Petrone L et al. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. *Int J Impot Res* 2006;18(2):190-197.
- Corona G, Mannucci E, Schulman C et al. Psychobiologic correlates of the metabolic syndrome and associated sexual dysfunction. *Eur Urol* 2006;50(3):595-604.
- Creasey G H. Lecture 6: restoration of male sexual function following spinal cord injury. *Int J Impot Res* 2000;12 Suppl 3S54-S55.
- Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.
- Crum-Cianflone N F, Bavaro M, Hale B et al. Erectile dysfunction and hypogonadism among men with HIV. *AIDS Patient Care & Stds* 2007;21(1):9-19.
- Culha M, Mutlu N, Acar O et al. Patient-partner satisfaction with intracavernous medication supported with oral agents in selected cases of Peyronie's disease: A ten-month follow-up study. *International Urology & Nephrology* 1999;31(2):257-262.
- Curran M, Keating G. Tadalafil.[erratum appears in *Drugs*. 2003;63(23):2703]. [Review] [31 refs]. *Drugs* 2003;63(20):2203-2212.
- Curri S B, Menchini Fabris F. Evidence and results obtained with a new Trans-Epidermal Barrier (T.E.B.) drug in the medical treatment of vascular impotence. *Boll Chim Farm* 1996;135(5):316-334.
- Cyranski D. Malaysian researchers bet big on home-grown Viagra. *Nat Med* 2005;11(9):912
- Czuriga I, Riecanaky I, Bodnar J et al. Comparison of the New Cardioselective Beta-Blocker Nebivolol with Bisoprolol in Hypertension: The Nebivolol, Bisoprolol Multicenter Study (NEBIS). *Cardiovascular Drugs & Therapy* 2003;17(3):257-263.
- Dang G, Matern R, Bivalacqua T J et al. Intralesional interferon-alpha-2B injections for the treatment of Peyronie's disease. *South Med J* 2004;97(1):42-46.
- Davis B E, Weigel J W, Whitford C S. Treatment of male impotence: a new option. *Kans Med* 1990;91(12):325-326.
- Davis J M. American College of Neuropsychopharmacology - 43rd annual meeting. 12-16 December 2004, San Juan, Puerto Rico. *IDrugs* 2005;8(2):100-103.
- Davis M E, Brewster M E. Cyclodextrin-based pharmaceuticals: Past, present and future. *Nat Rev Genet* 2004;3(12):1023-1035.
- De Meyer J M, Oosterlinck W. Influence of the method of intracavernous injection on penile rigidity: a possible pharmacokinetic explanation. *Urology* 1997;49(2):248-252.
- De Tejada I. Vardenafil Duration of Action. *Eur Urol* 2006;50(5):901-902.
- De Tejada I, Garvey D S, Schroeder J D et al. Design and evaluation of nitrosylated alpha-adrenergic receptor antagonists as potential agents for the treatment of impotence. *Journal of Pharmacology & Experimental Therapeutics* 1999;290(1):121-128.
- Degirmenci B, Acar M, Albayrak R et al. Effects of sildenafil citrate (Viagra) on renal arteries: An evaluation with Doppler ultrasound. *Urol Int* 2006;77(2):170-172.
- Del Popolo G, Li Marzi V, Mondaini N et al. Time/duration effectiveness of sildenafil versus tadalafil in the treatment of erectile dysfunction in male spinal cord-injured patients. *Proc Annu Clin Spinal Cord Inj Conf* 2004;42(11):643-648.
- Delizonna L L, Wincze J P, Litz B T et al. A comparison of subjective and physiological measures of mechanically produced and erotically produced erections (or, is an erection an erection?). *J Sex Marital Ther* 2001;27(1):21-31.
- Denisov M F, Davis J M, Brecher M. Re: Prolactin levels and adverse events in patients treated with risperidone [8] (multiple letters). *J Clin Psychopharmacol* 2002;22(5):538-540.
- Derby C A, Araujo A B, Johannes C B et al. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 2000;12(4):197-204.

- Derby C A, Barbour M M, Hume A L et al. Drug therapy and prevalence of erectile dysfunction in the Massachusetts Male Aging Study cohort. *Pharmacotherapy* 2001;21(6):676-683.
- Derouet H, Nolden W, Jost W H et al. Treatment of erectile dysfunction by an external ischiocavernous muscle stimulator. *Eur Urol* 1998;34(4):355-359.
- Desouza C, Parulkar A, Lumpkin D et al. Acute and prolonged effects of sildenafil on brachial artery flow-mediated dilatation in type 2 diabetes.. *Diabetes Care* 2002;25(8):1336-1339.
- Dietzen C J, Lloyd L K. Complications of intracavernous injections and penile prostheses in spinal cord injured men. *Archives of Physical Medicine & Rehabilitation* 1992;73(7):652-655.
- Dinelli N, Salinitri G, Pomara G et al. Role of pharmacologic rehabilitation in the recovery of sexual function following radical prostatectomy. *Minerva Urol Nefrol* 2005;57(4):325-329.
- Dinsmore W W. Medical treatment of impotence with papaverine and phentolamine intracavernosal injection. *Ulster Med J* 1990;59(2):174-176.
- Dinsmore W W, Gingell C, Hackett G et al. Treating men with predominantly nonpsychogenic erectile dysfunction with intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector system: a multicentre double-blind placebo-controlled study. *BJU Int* 1999;83(3):274-279.
- Djavan B, Milani S, Fong Y K. Dutasteride: A novel dual inhibitor of 5 α -reductase for benign prostatic hyperplasia. *Expert Opin Pharmacother* 2005;6(2):311-317.
- Doggrell S A. Comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction. *Expert Opin Pharmacother* 2005;6(1):75-84.
- Donatucci C F, Lue T F. Erectile dysfunction in men under 40: etiology and treatment choice. *Int J Impot Res* 1993;5(2):97-103.
- Doumas M, Tsakiris A, Douma S et al. Beneficial effects of switching from beta-blockers to nebivolol on the erectile function of hypertensive patients. *Asian J Androl* 2006;8(2):177-182.
- Dundar S O. Visual loss associated with erectile dysfunction drugs. *Can J Ophthalmol* 2007;42(1):10-12.
- Dupont Simon. Multiple sclerosis and sexual functioning: A review. *Clin Rehabil* 1995;9(2):135-141.
- Durackova Z, Trebaticky B, Novotny V et al. Lipid metabolism and erectile function improvement by Pycnogenol, extract from the bark of *Pinus pinaster* in patients suffering from erectile dysfunction - A pilot study. *Adv Food Nutr Res* 2003;23(9):1189-1198.
- Eandi J A, Yao A P, Javidan J. Penile paraffinoma: the delayed presentation. *Int Urol Nephrol* 2007;
- Eardley I. New oral therapies for the treatment of erectile dysfunction. *Br J Urol* 1998;81(1):122-127.
- Earle C M, Keogh E J, Ker J K et al. The role of intracavernosal vasoactive agents to overcome impotence due to spinal cord injury. *Paraplegia* 1992;30(4):273-276.
- Earle C M, Stuckey B G, Ching H L et al. The incidence and management of priapism in Western Australia: a 16 year audit. *Int J Impot Res* 2003;15(4):272-276.
- Edwards G, Muirhead G J. *British Journal of Clinical Pharmacology: Introduction*. *Br J Clin Pharmacol* 2002;53(SUPPL. 1):1S-3S.
- Ekmekcioglu O, Inci M, Demirci D et al. Effects of sildenafil citrate on ejaculation latency, detumescence time, and refractory period: placebo-controlled, double-blind, crossover laboratory setting study. *Urology* 2005;65(2):347-352.
- Ekselius L, Von Knorring L. Effect on sexual function of long-term treatment with selective serotonin reuptake inhibitors in depressed patients treated in primary care. *J Clin Psychopharmacol* 2001;21(2):154-160.
- El Malik E M A. Erectile dysfunction: An update of diagnosis and management. *Qatar Medical Journal* 2000;9(2):9-17.
- El-Bahnasawy M S, El-Assmy A, Dawood A et al. Effect of the use of internal iliac artery for renal transplantation on penile vascularity and erectile function: A prospective study. *Br J Urol* 2004;172(6 I):2335-2339.
- El-Rufaie Omer E F, Bener Abdulbari, Abuzeid Mohamed S O et al. Sexual dysfunction among type II diabetic men: A controlled study. *J Psychosom Res* 1997;43(6):605-612.
- El-Sakka A I. Penile axial rigidity and Doppler ultrasonography parameters in patients with erectile dysfunction: association with type 2 diabetes. *Urology* 2003;62(3):525-531.
- Emilien G. Alprox-TD NexMed Inc. *Current Opinion in Central & Peripheral Nervous System Investigational Drugs* 2000;2(3):311-320.
- Ende A R, Lo Re V, DiNubile M J et al. Erectile dysfunction in an urban HIV-positive population. *AIDS Patient Care & Stds* 2006;20(2):75-78.

- Engelhardt P F, Daha L K, Zils T et al. Acupuncture in the treatment of psychogenic erectile dysfunction: first results of a prospective randomized placebo-controlled study. *Int J Impot Res* 2003;15(5):343-346.
- Engelson E S, Pi-Sunyer F X, Kotler D P. Effects of megestrol acetate therapy on body composition and circulating testosterone concentrations in patients with AIDS. *Int J STD AIDS* 1995;9(9):1107-1108.
- Engl T, Beecken W-D, Wolfram M et al. Uro pharmacology: Current and future strategies in the treatment of erectile dysfunction and benign prostate hyperplasia. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(10):527-533.
- English J C, King D H C, Foley J P. Penile shaft hypopigmentation: Lichen sclerosus occurring after the initiation of alprostadil intracavernous injections for erectile dysfunction. *J Am Acad Dermatol* 1998;39(5 1):801-803.
- Ensign C. First-line therapies for erectile dysfunction. [Review] [8 refs]. *JAAPA* 2001;14(10):17-20.
- Erdogru T, Kocak T, Serdaroglu P et al. Evaluation and therapeutic approaches of voiding and erectile dysfunction in neurological Behcet's syndrome. *Br J Urol* 1999;162(1):147-153.
- Ernst E. Chinese herbal medicines for consumers in the West. Focus on Alternative & Complementary Therapies 2005;10(2):94-97.
- Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol*. 1998;159(2):433-436.
- Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.
- Esposito K, Giugliano F, Martedi E et al. High proportions of erectile dysfunction in men with the metabolic syndrome. *Diabetes Care* 2005;28(5):1201-1203.
- Evans M F. Viagra! Are we ready?. *Can Fam Physician* 1998;44:2103-2105.
- Fagan Peter J, Blum Lois H. Issues in the psychotherapeutic treatment of sexual dysfunction following radical retropubic prostatectomy. Rosen, Raymond C (Ed); Leiblum, Sandra R (Ed) 1995;(1995):400
- Fagan T C, Buttler S, Marbury T et al. Cardiovascular safety of sublingual apomorphine in patients on stable doses of oral antihypertensive agents and nitrates. *Am J Cardiol* 2001;88(7):760-766.
- Faiman C. Endocrine causes of impotence. *Cleve Clin J Med* 1993;60(6):428-429.
- Fazeli-Matin S, Montague D K, Angermeier K W et al. Penile fracture after intracavernous injection therapy. *Br J Urol* 1998;159(6):2094
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.
- Fedele D, Lamonica M, Bax G. Experience with sildenafil in diabetes. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):49-52.
- Fekete F, Fabian E. [Effectiveness and adverse effects of sildenafil in erectile dysfunction]. *Orv.Hetil.* 2000;141(3):115-118.
- Feldman H A, Goldstein I, Hatzichristou D G et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *Br J Urol* 1994;151(1):54-61.
- Feldman H A, Johannes C B, Derby C A et al. Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study. *Prev Med* 2000;30(4):328-338.
- Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.
- Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.
- Finkbeiner A. Random musing about a little blue pill. *J Ark Med Soc* 1998;95(3):100-101.
- Fishbain David A. Impact of sildenafil on male erectile disorder due to psychological factors. *Can J Psychiatry* 2000;45(1):85-86.
- Fisher W A, Rosen R C, Eardley I et al. The Multinational Men's Attitudes to Life Events and Sexuality (MALES) Study Phase II: Understanding PDE5 inhibitor treatment seeking patterns, among men with erectile dysfunction. *Br J Sex Med* 2004;1(2):150-160.
- Flack J M. The effect of doxazosin on sexual function in patients with benign prostatic hyperplasia, hypertension, or both.[see comment]. [Review] [47 refs]. *Int J Clin Pract* 2002;56(7):527-530.
- Foresta C, Caretta N, Rossato M et al. Role of androgens in erectile function. *Br J Urol* 2004;171(6 Pt 1):2358-2362.

- Foulks C J, Cushner H M. Sexual dysfunction in the male dialysis patient: pathogenesis, evaluation, and therapy. [Review] [105 refs]. *Am J Kidney Dis* 1986;8(4):211-222.
- Frank T. Tadalafil (Cialis-Lilly). *Consultant Pharmacist* 2004;19(4):280-281.
- Frank T. Vardenafil (Levitra-Bayer) GSK. *Consultant Pharmacist* 2004;19(4):278-280.
- Franzen D, Metha A, Seifert N et al. Effects of beta-blockers on sexual performance in men with coronary heart disease. A prospective, randomized and double blinded study. *Int J Impot Res* 2001;13(6):348-351.
- Fraunfelder F W, Fraunfelder F T. Scientific Challenges in Postmarketing Surveillance of Ocular Adverse Drug Reactions. *Am J Ophthalmol* 2007;143(1):
- Freemantle N. Valuing the effects of sildenafil in erectile dysfunction. *Br Med J* 2000;320(7243):1156-1157.
- Freytag S O, Stricker H, Pegg J et al. Phase I Study of Replication-Competent Adenovirus-Mediated Double-Suicide Gene Therapy in Combination with Conventional-Dose Three-Dimensional Conformal Radiation Therapy for the Treatment of Newly Diagnosed, Intermediate- to High-Risk Prostate Cancer. *Cancer Res* 2003;63(21):7497-7506.
- Fu Q, Yao D-H, Jiang Y-Q. Effect of sodium nitroprusside on hemodynamics of corpus cavernosum in Chinese. *Asian J Androl* 2001;3(4):311-313.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Fulgram P F, Cochran J S, Denman J L et al. Re: Disappointing initial results with transurethral alprostadil for erectile dysfunction in a urology practice setting [5]. *Br J Urol* 1999;162(4):1390
- Gallo L, Perdoni S, Autorino R et al. Recovery of erection after pelvic urologic surgery: our experience. *Int J Impot Res* 2005;17(6):484-493.
- Gerstenbluth R E, Maniam P N, Corty E W et al. Prostate-specific antigen changes in hypogonadal men treated with testosterone replacement. *J Androl* 2002;23(6):922-926.
- Ghezzi A, Malvestiti G M, Baldini S et al. Erectile impotence in multiple sclerosis: A neurophysiological study. *J Neurol* 1995;242(3):123-126.
- Giammusso B, Gattuso U, Vanaclocha V et al. Percutaneous lumbar sympathectomy in the treatment of erectile dysfunction secondary to cavernous adrenergic hypertone: initial results of an original technique. *Arch Ital Urol Androl* 2005;77(1):5-9.
- Giampietro O, Ferdeghini M, Cerri M et al. Evaluation of the hypothalamic-pituitary-testicular interaction in diabetic males. *European J Lab Med* 1994;2(2):83-89.
- Gillies H C, Roblin D, Jackson G. Coronary and systemic hemodynamic effects of sildenafil citrate: From basic science to clinical studies in patients with cardiovascular disease. *Int J Cardiol* 2002;86(2-3):131-141.
- Ginsberg D L. Gabapentin treatment of premature ejaculation. *Primary Psychiatry* 2004;11(12):20-21.
- Ginsberg D L. Vardenafil treatment of sertraline-induced sexual dysfunction. *Primary Psychiatry* 2004;11(11):23-24.
- Ginsberg David L. Sildenafil-dihydrocodeine interaction results in prolonged erections. [References]. *Primary Psychiatry* 2003;10(2):23
- Ginzburg R, Wong Y, Fader J S. Effect of bupropion on sexual dysfunction. *Ann Pharmacother* 2005;39(12):2096-2099.
- Giuberti A, Picozzi S C, Mazza L et al. Testosterone supplementation in hypogonadal men: our personal experience. *Arch Ital Urol Androl* 2005;77(4):191-193.
- Giuliano F. Control of penile erection by the melanocortineric system: Experimental evidences and therapeutic perspectives. *J Androl* 2004;25(5):683-691.
- Giuliano F, Allard J, Rampin O et al. Pro-erectile effect of systemic apomorphine: Existence of a spinal site of action. *Br J Urol* 2002;167(1):402-406.
- Giuliano F, Hultling C, El Masry W S et al. Randomized trial of sildenafil for the treatment of erectile dysfunction in spinal cord injury. Sildenafil Study Group. *Ann Neurol*. 1999;46(1):15-21.
- Giuliano F, Pena B M, Mishra A et al. Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction. *Qual Life Res* 2001;10(4):359-369.
- Giuliano Francois, Pena Beatrice, Mishra Avnish et al. "Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction": Erratum. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 2002;11(6):613-670.
- Gladh Y M, Rahgozar M, Hammar M L et al. Prevalence of symptoms possibly related to PADAM, in a Swedish population aged 55, 65 and 75 years. *Maturitas* 2005;50(3):161-166.
- Glasser S P. Revisiting erectile dysfunction in cardiovascular patients. *Cardiology Review* 2003;20(12):42-43.

- Glasser S P. Safety of PDE 5 inhibition in patients with cardiovascular disease. *Cardiology Review* 2002;19(11):32-33.
- Glenn D R J, McClure N, Lewis S E M. The hidden impact of diabetes on male sexual dysfunction and fertility. *Hum Fertil* 2003;6(4):174-179.
- Goldenberg M M. Safety and efficacy of sildenafil citrate in the treatment of male erectile dysfunction. *Clin Ther*. 1998;20(6):1033-1048.
- Goldstein I. Oral phentolamine: an alpha-1, alpha-2 adrenergic antagonist for the treatment of erectile dysfunction. [Review] [9 refs]. *Int J Impot Res* 2000;12Suppl-80.
- Gontero P, Fontana F, Zitella A et al. A prospective evaluation of efficacy and compliance with a multistep treatment approach for erectile dysfunction in patients after non-nerve sparing radical prostatectomy. *BJU Int* 2005;95(3):359-365.
- Gore J L, Swerdloff R S, Rajfer J. Androgen deficiency in the etiology and treatment of erectile dysfunction. *Urol Clin North Am* 2005;32(4):457-468.
- Govier F E, McClure R D, Kramer-Levien D. Endocrine screening for sexual dysfunction using free testosterone determinations. *Br J Urol* 1996;156(2 Pt 1):405-408.
- Graul A, Castaner J. Phentolamine Mesilate. Treatment of erectile dysfunction. *Drugs of the Future* 1998;23(7):725-728.
- Graul A I. Latest findings on the diagnosis and treatment of erectile dysfunction. *Drug News Perspect* 1996;9(9):572-575.
- Gray P B, Singh A B, Woodhouse L J et al. Dose-dependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. *Journal of Clinical Endocrinology & Metabolism* 2005;90(7):3838-3846.
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.
- Green H J, Pakenham K I, Headley B C et al. Coping and health-related quality of life in men with prostate cancer randomly assigned to hormonal medication or close monitoring. *Psychooncology* 2002;11(5):401-414.
- Green J S A, Holden S T R, Ingram P et al. An investigation of erectile dysfunction in Gwent, Wales. *BJU Int* 2001;88(6):551-553.
- Greenstein A, Plymate S R, Katz P G. Visually stimulated erection in castrated men. *Br J Urol* 1995;153(3:Pt 1):t-2.
- Gresser U, Gleiter C H. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil--review of the literature. [Review] [92 refs]. *Eur J Med Res* 2002;7(10):435-446.
- Gross A J, Sauerwein D H, Kutzenberger J et al. Penile prostheses in paraplegic men. *Br J Urol* 1996;78(2):262-264.
- Grover J K, Vats V, Ajeeta. Sildenafil (Viagra(TM)). *Medico-Legal Update* 1998;3(1-2):67-78.
- Grugni G, Carani C, Maestroni G et al. Melatonin levels in psychogenic impotence. *Hormone & Metabolic Research* 1994;26(9):440-441.
- Grunwald J E, Jacob S S, Siu K et al. Acute effects of sildenafil citrate (Viagra) on intraocular pressure in open-angle glaucoma. *Am J Ophthalmol* 2001;132(6):872-874.
- Gryglewska B, Grodzicki T. Betaxolol in elderly patients in primary care. *New Medicine* 2003;6(4):108-111.
- Guay A T, Sabharwal P, Varma S et al. Delayed diagnosis of psychological erectile dysfunction because of the presence of macroprolactinemia. *Journal of Clinical Endocrinology & Metabolism* 1996;81(7):2512-2514.
- Guay D R P. Geriatric pharmacotherapy updates. *American Journal Geriatric Pharmacotherapy* 2004;2(1):81-87.
- Guirguis W R, Maytom M C, Orr M et al. SILDENAFIL FOR ERECTILE DYSFUNCTION - A ONE-YEAR STUDY. 151st Annual Meeting of the American Psychiatric Association 1998;Toronto, Ontario, Canada. 30th May-4th June. 1998. Issue No. 63, 1998.
- Guo Y L, Zhu J C, Pan T M et al. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction. *Chinese Journal of Urology* 2001;22(7):389-394.
- Gupta N, Sawlani K K, Tripathi A K. Appropriate use of sildenafil citrate in male erectile dysfunction.[see comment]. [Review] [52 refs]. *J Assoc Physicians India* 2001;49:889-896.
- Gupta S, Salimpour P, Saenz de et al. A possible mechanism for alteration of human erectile function by digoxin: inhibition of corpus cavernosum sodium/potassium adenosine triphosphatase activity. *Br J Urol* 1998;159(5):1529-1536.
- Hackett G I. The treatment of patients with diabetes. *Int J STD AIDS* 1996;7(Suppl 3):24-26.
- Haensel S M, Klem T M, Hop W C et al. Fluoxetine and premature ejaculation: a double-blind, crossover, placebo-controlled study. *J Clin Psychopharmacol* 1998;18(1):72-77.
- Haensel S M, Rowland D L, Kallan K T. Clomipramine and sexual function in men with premature ejaculation and controls. *Br J Urol* 1996;156(4):1310-1315.

- Hamed S, Mohamed K, El-taher A et al. The sexual and reproductive health in men with generalized epilepsy: A multidisciplinary evaluation. *Int J Impot Res* 2006;18(3):287-295.
- Hammadeh M Y, Philp T. Transurethral electrovaporization of the prostate (TUVF) is effective, safe and durable. [Review] [28 refs]. *Prostate Cancer & Prostatic Diseases* 2003;6(2):121-126.
- Hammadeh M Y, Madaan S, Hines J et al. 5-year outcome of a prospective randomized trial to compare transurethral electrovaporization of the prostate and standard transurethral resection. *Urology* 2003;61(6):1166-1171.
- Hanash K A. Comparative results of goal oriented therapy for erectile dysfunction.. *Br J Urol* 1997;157(6):2135-2138.
- Harman S M. Testosterone, Sexuality, and Erectile Function in Aging Men. *J Androl* 2003;24(6 SUPPL.):S42-S45.
- Hartmann Uwe, Langer Dieter. Combination of psychosexual therapy and intrapenile injections in the treatment of erectile dysfunctions: Rationale and predictors of outcome. *J Sex Educ Ther* 1993;19(1):1-12.
- Harwood P J, Grotz M, Eardley I et al. Erectile dysfunction after fracture of the pelvis. *Journal of Bone & Joint Surgery - British Volume* 2005;87(3):281-290.
- Haslam M T. A trial of idazoxan and yohimbine in erectile dysfunction. *Sex Marital Ther* 1992;7(3):261-266.
- Hatzichristou D G. Sildenafil citrate: lessons learned from 3 years of clinical experience. [Review] [60 refs]. *Int J Impot Res* 2002;14Suppl-52.
- Hatzichristou D G. Current treatment and future perspectives for erectile dysfunction. [Review] [85 refs]. *Int J Impot Res* 1998;10Suppl-13.
- Hatzimouratidis K, Hatzichristou D. Testosterone and erectile function: an unresolved enigma. *Eur Urol* 2007;52(1):26-28.
- Hatzimouratidis K, Hatzichristou D. Phosphodiesterase Type 5 Inhibitors: The Day After. *Eur Urol* 2007;51(1):75-89.
- Hatzimouratidis K, Hatzichristou D G. A comparative review of the options for treatment of erectile dysfunction: Which treatment for which patient?. *Drugs* 2005;65(12):1621-1650.
- Hawton Keith, Catalan Jose, Fagg Joan. Sex therapy for erectile dysfunction: Characteristics of couples, treatment outcome, and prognostic factors. *Arch Sex Behav* 1992;21(2):161-175.
- Hazell P. Review of new compounds available in Australia for the treatment of attention-deficit hyperactivity disorder. *Australasian Psychiatry* 2004;12(4):369-375.
- He X Q, Hong B F, Wang X X et al. Evaluation of efficacy and safety of oral sildenafil citrate therapy for men with erectile dysfunction. *Pharmaceutical Journal of Chinese Peoples Liberation Army* 2002;18(4):205-208.
- Heaton J. New classification system for erectile dysfunction therapies. *J Androl* 1998;19(4):399-404.
- Heaton J P. Key issues from the clinical trials of apomorphine SL. *World J Urol* 2001;19(1):25-31.
- Heaton J P W, Altwein J E. The role of apomorphine SL in the treatment of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):36-38.
- Heaton J P W, Wagner Porst, Eid Wyllie. Apomorphine: An update of clinical trial results. *Int J Impot Res* 2000;12(SUPPL. 4):S67-S73.
- Heaton J P, Dean J, Sleep D J. Sequential administration enhances the effect of apomorphine SL in men with erectile dysfunction. *Int J Impot Res* 2002;14(1):61-64.
- Hellstrom W J G, Kendirci M. Type 5 Phosphodiesterase Inhibitors: Curing Erectile Dysfunction. *Eur Urol* 2006;49(6):942-945.
- Hellstrom W J, Overstreet J W, Yu A et al. Tadalafil has no detrimental effect on human spermatogenesis or reproductive hormones.[see comment]. *Br J Urol* 2003;170(3):887-891.
- Hellstrom Wayne J G, Egan Robert A, McGee Hall T et al. "Visual field defect and intracerebral hemorrhage associated with use of vardenafil (Levitra)": Comment and Reply. [References]. *Neurology* 2006;66(2):293-294.
- Herrmann H C, Chang G, Klugherz B D et al. Hemodynamic effects of sildenafil in men with severe coronary artery disease.[see comment]. *N Engl J Med* 2000;342(22):1622-1626.
- Hirshkowitz M, Moore C A, O'Connor S et al. Androgen and sleep-related erections. *J Psychosom Res* 1997;42(6):541-546.
- Hirst J F, Watson J P. Referrals aged 60+ to an inner-city psychosexual dysfunction clinic. *Sexual & Marital Therapy* 1996;11(2):131-146.
- Hofner K, Claes H, De Reijke T M et al. Tamsulosin 0.4 mg once daily: effect on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. *Eur Urol* 1999;36(4):335-341.
- Hollander J B, Gonzalez J, Norman T. Patient satisfaction with pharmacologic erection program. *Urology* 1992;39(5):439-441.
- Holt S. Natural approaches to promote sexual function: Part 1: Viagra versus a natural approach. *Alternative & Complementary Therapies* 1999;5(4):204-208.

- Holtkamp M, Weissinger F, Meierkord H. Erectile dysfunction with topiramate. *Epilepsia* 2005;46(1):166-167.
- Hong B, Ji Y H, Hong J H et al. A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report.[see comment]. *Br J Urol* 2002;168(5):2070-2073.
- Hopps C V, Mulhall J P. Novel agents for sexual dysfunction. *BJU Int* 2003;92(6):534-538.
- Horita H, Sato Y, Adachi H et al. Effects of levodopa on nocturnal penile tumescence: a preliminary study. *J Androl* 1998;19(5):619-624.
- Howes O D, Wheeler M J, Pilowsky L S et al. Sexual function and gonadal hormones in patients taking antipsychotic treatment for schizophrenia or schizoaffective disorder. *Hillside J Clin Psychiatry* 2007;68(3):361-367.
- Howes Oliver D, Smith Shubulade, Aitchison Kathy J E. Comments on "Prolactin Levels and Erectile Function in Patients Treated With Risperidone." [References]. *J Clin Psychopharmacol* 2005;25(4):393-394.
- Huang S T, Hsieh M L. Different hemodynamic responses by color Doppler ultrasonography studies between sildenafil non-responders and responders. *Asian J Androl* 2007;9(1):129-133.
- Huang W J, Chen K K, Chang L S. Correlation between voiding and erectile function in patients with symptomatic benign prostatic hyperplasia. *Journal of the Chinese Medical Association: JCMA* 2005;68(4):178-182.
- Hubler J, Szanto A, Konyves K. Methylene blue as a means of treatment for priapism caused by intracavernous injection to combat erectile dysfunction. *International Urology & Nephrology* 2003;35(4):519-521.
- Hultling C. Partners' perceptions of the efficacy of sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Clin Pract* 1999;Supplement.102-108.
- Hummel S, Paisley S, Morgan A et al. Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: A systematic review. *Health Technol Assess* 2003;7(33):157p
- Hunter R H, Joy C B, Kennedy E et al. Risperidone versus typical antipsychotic medication for schizophrenia.[update of Cochrane Database Syst Rev. 2000;(2):CD000440; PMID: 10796543]. [Review] [105 refs]. *Cochrane Database Syst Rev* 2003;(2):CD000440
- Hyer S L, Duckworth K, Jones C. Managing erectile disorders in diabetes: The one stop andrology clinic. *Practical Diabetes International* 1998;15(8):225-226.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Israilov S, Baniel J, Shmueli J et al. Treatment program for erectile dysfunction in patients with cardiovascular diseases. *Am J Cardiol* 2004;93(6):689-693.
- Jackson G. Erectile dysfunction and cardiovascular disease.[see comment]. [Review] [46 refs]. *Int J Clin Pract* 1999;53(5):363-368.
- Jackson G. Treatment of erectile dysfunction in patients with cardiovascular disease: Guide to drug selection. *Drugs* 2004;64(14):1533-1545.
- Jackson G. Vardenafil - PDE5 inhibitor number 3. *Int J Clin Pract* 2004;58(3):229
- Jackson G. PDE5 inhibitors: Looking beyond ED. *Int J Clin Pract* 2003;57(3):159-160.
- Jackson G. Sildenafil (Viagra): New data, new confidence in treating erectile dysfunction in the cardiovascular patient. *Int J Clin Pract* 2002;56(2):75
- Jackson G. Phosphodiesterase 5 inhibition: Effects on the coronary vasculature. *Int J Clin Pract* 2001;55(3):183-188.
- Jackson G. The metabolic syndrome and erectile dysfunction: multiple vascular risk factors and hypogonadism. *Eur Urol* 2006;50(3):426-427.
- Jackson G, Montorsi P, Cheitlin M D. Cardiovascular safety of sildenafil citrate (Viagra): an updated perspective. [Review] [52 refs]. *Urology* 2006;68(3 Suppl):47-60.
- Jackson G, Sweeney M, Osterloh I H. Sildenafil citrate (Viagra(TM)): A cardiovascular overview. *British Journal of Cardiology* 1999;6(6):325-334.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- James J S. Frequent urination, leg cramps, leg weakness, erection difficulties: HIV myelopathy amino acid study. *AIDS Treat News* 2000;(344):3-4.
- Jani A B. The effectiveness of combining hormone therapy and radiotherapy in the treatment of prostate cancer. *Expert Opin Pharmacother* 2004;5(12):2469-2477.
- Jani A B, Kao J, Heimann R et al. Hormone therapy and radiotherapy for early prostate cancer: A utility-adjusted number needed to treat (NNT) analysis. *Int J Radiat Oncol Biol Phys* 2005;61(3):687-694.
- Jarow J P, Nana-Sinkam P, Sabbagh M et al. Outcome analysis of goal directed therapy for impotence. *Br J Urol* 1996;155(5):1609-1612.

- Jeong S-J, Park K, Moon J-D et al. Bicycle saddle shape affects penile blood flow. *Int J Impot Res* 2002;14(6):513-517.
- Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.
- Jordan G H. What's new in urology. *J Am Coll Surg* 2003;197(3):444-457.
- Kadioglu A, Erdogru T, Tellaloglu S. Evaluation of penile arteries in papaverine-induced erection with color Doppler ultrasonography. *Arch Esp Urol* 1995;48(6):654-658.
- Kamel H K, Morley J E. The management of erectile dysfunction. *Reproductive Medicine Review* 2001;9(1):35-47.
- Kang B J, Lee S J, Kim M D et al. A placebo-controlled, double-blind trial of Ginkgo biloba for antidepressant-induced sexual dysfunction. *Hum Psychopharmacol* 2002;17(6):279-284.
- Kaplan S A, Meehan A G, Shah A. The age related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Br J Urol* 2006;176(4 Pt 1):1524-1527.
- Karlawish J H, Casarett D. Sildenafil for diabetic men with erectile dysfunction.[comment]. *JAMA* 1999;282(10):940-941.
- Kassouf W, Carrier S. A comparison of the International Index of Erectile Function and erectile dysfunction studies.. *BJU Int* 2003;91(7):667-669.
- Kaufman J M, Hatzichristou D G, Mulhall J P et al. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *Br J Urol* 1994;151(3):612-618.
- Keijzers G B. Aviptadil (Senatek). [Review] [36 refs]. *Curr Opin Investig Drugs* 2001;2(4):545-549.
- Keles I, Aydin G, Orkun S et al. Two clinical problems in elderly men: osteoporosis and erectile dysfunction. *Arch Androl* 2005;51(3):177-184.
- Kell P. Cardiovascular safety of sildenafil. *Int J STD AIDS* 2002;13(7):439-443.
- Keoghane S R, Sullivan M E, Miller M A W. The aetiology, pathogenesis and management of priapism. *BJU Int* 2002;90(2):149-154.
- Kerfoot W W, Park H Y, Schwartz L B et al. Characterization of calcium channel blocker induced smooth muscle relaxation using a model of isolated corpus cavernosum. *Br J Urol* 1993;150(1):249-252.
- Kernohan A F, McIntyre M, Hughes D M et al. An oral yohimbine/L-arginine combination (NMI 861) for the treatment of male erectile dysfunction: a pharmacokinetic, pharmacodynamic and interaction study with intravenous nitroglycerine in healthy male subjects. *Br J Clin Pharmacol* 2005;59(1):85-93.
- Khalaf I M, Levinson I P. Erectile dysfunction in the Africa/Middle East Region: Epidemiology and experience with sildenafil citrate (Viagra). *Int J Impot Res* 2003;15(SUPPL. 1):S1-S2.
- Khan L A. Sildenafil citrate (Viagra). *JK Pract* 2001;8(1):52-53.
- Khan M A, Raistrick M, Mikhailidis D P et al. MUSE: clinical experience. *Current Medical Research & Opinion* 2002;18(2):64-67.
- Kilic S, Ergin H, Baydinc Y C. Venlafaxine extended release for the treatment of patients with premature ejaculation: a pilot, single-blind, placebo-controlled, fixed-dose crossover study on short-term administration of an antidepressant drug. *Int J Androl* 2005;28(1):47-52.
- Kilic S, Salih M, Anafarta K et al. Adenosine: a new agent in the diagnosis of impotence. *Int J Impot Res* 1994;6(4):191-198.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Kim N N. Phosphodiesterase type 5 inhibitors: A biochemical and clinical correlation survey. *Int J Impot Res* 2003;15(SUPPL. 5):S13-S19.
- Kim N N, Dhir V, Azadzo K M et al. Pilot study of the endothelin-A receptor selective antagonist BMS-193884 for the treatment of erectile dysfunction. *J Androl* 2001;23(1):76-83.
- Kim S C, Seo K K, Lee S K et al. Comparison of the synergistic effects of tamsulosin versus phentolamine on penile erection: In vitro and in vivo studies. *Urol Res* 1999;27(6):437-444.
- Kim S C, Seo K K, Park B D et al. Risk factors for an early increase in dose of vasoactive agents for intracavernous pharmacotherapy. *Urol Int* 2000;65(4):204-207.
- Kimoto Y, Sakamoto S, Fujikawa K et al. Up-titration of vardenafil dose from 10 mg to 20 mg improved erectile function in men with spinal cord injury. *Int J Urol* 2006;13(11):1428-1433.

- Kirby R S. Report from London. Prostate Cancer & Prostatic Diseases 2005;8(4):299
- Kirby R S, Andersen M, Gratzke P et al. A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. BJU Int 2001;87(3):192-200.
- Kirby R S, O'Leary M P, Carson C. Efficacy of extended-release doxazosin and doxazosin standard in patients with concomitant benign prostatic hyperplasia and sexual dysfunction.. BJU Int 2005;95(1):103-109.
- Kiriakova N, Kiriakov A, Schneider E et al. Therapeutic effect of essential phospholipids on functional sexual disorders in males. Journal of the European Academy of Dermatology & Venereology 1998;11(2):191-193.
- Kleinberg D L, Davis J M, De Coster R et al. Prolactin levels and adverse events in patients treated with risperidone.[see comment]. J Clin Psychopharmacol 1999;19(1):57-61.
- Kley H K, Stremmel W, Kley J B et al. Testosterone treatment of men with idiopathic hemochromatosis. Clin Investig 1992;70(7):566-572.
- Kloner R A. Cardiovascular risk and sildenafil. [Review] [27 refs]. Am J Cardiol 2000;86(2A):57F-61F.
- Kloner R A, Zusman R M. Cardiovascular effects of sildenafil citrate and recommendations for its use. [Review] [21 refs]. Am J Cardiol 1999;84(5B):11N-17N.
- Kloner R A, Brindis R G, Cheitlin M D et al. Roundtable discussion: Tadalafil study group. Am J Cardiol 2003;92(9 SUPPL. 1):58M-65M.
- Kloner R A, Hutter A M, Emmick J T et al. Time course of the interaction between tadalafil and nitrates.[see comment]. J Am Coll Cardiol 2003;42(10):1855-1860.
- Kloner R A, Jackson G, Emmick J T et al. Interaction between the phosphodiesterase 5 inhibitor, tadalafil and 2 alpha-blockers, doxazosin and tamsulosin in healthy normotensive men. Br J Urol 2004;172(5:Pt 1):t-40.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil in patients on common antihypertensive therapies. [Review] [5 refs]. Am J Cardiol 2003;92(9A):47M-57M.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil. [Review] [12 refs]. Am J Cardiol 2003;92(9A):37M-46M.
- Klotz T, Mathers M J, Braun M et al. Effectiveness of oral L-arginine in first-line treatment of erectile dysfunction in a controlled crossover study. Urol Int 1999;63(4):220-223.
- Knegtering R, Castelein S, Bous H et al. A Randomized Open-Label Study of the Impact of Quetiapine Versus Risperidone on Sexual Functioning. J Clin Psychopharmacol 2004;24(1):56-61.
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. Urol Int 1991;47(3):144-148.
- Knoll L D, Benson R C, Bilhartz D L et al. A randomized crossover study using yohimbine and isoxsuprine versus pentoxifylline in the management of vasculogenic impotence.. Br J Urol 1996;155(1):144-146.
- Kobayashi T, Okuno H, Nishiyama H et al. Adult-onset idiopathic hypogonadotropic hypogonadism presented with erectile and ejaculatory disorder. Int J Urol 2002;9(10):604-606.
- Kramer-Levien D J. Papaverine--the medical implant. AUA J 1987;7(4):13-Jun.
- Krause W, Mueller U, Mazur A. Measurement of steroid levels in saliva in a population-based survey of lifestyle, medical conditions, marriage, sex life and hormone status in aging men: A feasibility study. Aging Male 2002;5(4):203-215.
- Kriston L, Harms A, Berner M M. A meta-regression analysis of treatment effect modifiers in trials with flexible-dose oral sildenafil for erectile dysfunction in broad-spectrum populations. Int J Impot Res 2006;18(6):559-565.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. Lancet 1988;1(8575-6):54-59.
- Kuba R, Pohanka M, Zakopcan J et al. Sexual dysfunctions and blood hormonal profile in men with focal epilepsy. Epilepsia 2006;47(12):2135-2140.
- Kukreja R C, Ockaili R, Salloum F et al. Cardioprotection with phosphodiesterase-5 inhibition - A novel preconditioning strategy. Journal of Molecular & Cellular Cardiology 2004;36(2):165-173.
- Kunelius P, Hakkinen J, Lukkarinen O. Is high-dose yohimbine hydrochloride effective in the treatment of mixed-type impotence? A prospective, randomized, controlled double-blind crossover study. Urology 1997;49(3):441-444.
- Kupez D. Alprostadil for the treatment of erectile dysfunction. J Am Acad Nurse Pract 1996;21(5):143-145.
- Kupelian V, Shabsigh R, Travison T G et al. Is there a relationship between sex hormones and erectile dysfunction? Results from the Massachusetts Male Aging Study. Br J Urol 2006;176(6 Pt 1):2584-2588.
- Kvistborg A, Halse J, Bakke S et al. Long-term treatment of macroprolactinomas with CV 205-502. Acta Endocrinol (Copenh) 1993;128(4):301-307.

- La Pera G, Franco Giannotti C, Taggi F et al. Prevalence of sexual disorders in those young males who later become drug abusers. *J Sex Marital Ther* 2003;29(2):149-156.
- La Vignera S, Calogero A E, Cannizzaro M A et al. Erectile vascular dysfunction and analysis of the risk factors related to it. Clinical experience. *Minerva Endocrinol* 2007;32(1):17-21.
- Labbate Lawrence A. "Sex and serotonin reuptake inhibitor antidepressants": Erratum. *Psychiatr Ann* 1999;29(12):683
- Labbate Lawrence A, Croft Harry A, Oleshansky Marvin A E. Antidepressant-Related Erectile Dysfunction: Management via Avoidance, Switching Antidepressants, Antidotes, and Adaptation. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl 10):11-19.
- Labbate Lawrence A, Grimes Jamie, Hines Alan et al. Sexual dysfunction induced by serotonin reuptake antidepressants. *J Sex Marital Ther* 1998;24(1):3-12.
- Lamberg L. New drug for erectile dysfunction boon for many, 'viagravation' for some. *J Am Med Assoc* 1998;280(10):867-869.
- Larson T R. Current treatment options for benign prostatic hyperplasia and their impact on sexual function. *Urology* 2003;61(4):692-698.
- Lasaponara F, Paradiso M, Milan M G et al. Erectile dysfunction after kidney transplantation: our 22 years of experience.[see comment]. *Transplant Proc* 2004;36(3):502-504.
- Laties A, Sharlip I. Ocular safety in patients using sildenafil citrate therapy for erectile dysfunction. [Review] [81 refs]. *Br J Sex Med* 2006;3(1):12-27.
- Laties A M, Zrenner E. Viagra (sildenafil citrate) and ophthalmology. *Progress in Retinal & Eye Research* 2002;21(5):485-506.
- Laties A M, Fraunfelder F T, Flach A J et al. Ocular safety of Viagra, (sildenafil citrate). *Trans Am Ophthalmol Soc* 1999;97(pp 115-128):-128.
- Latini D M, Penson D F, Lubeck D P et al. Longitudinal differences in disease specific quality of life in men with erectile dysfunction: Results from the exploratory comprehensive evaluation of erectile dysfunction study. *Br J Urol* 2003;169(4):1437-1442.
- Laumann Edward O, West Suzanne, Glasser Dale et al. Prevalence and Correlates of Erectile Dysfunction by Race and Ethnicity Among Men Aged 40 or Older in the United States: From the Male Attitudes Regarding Sexual Health Survey. [References]. *Br J Sex Med* 2007;4(1):57-65.
- Lawless C, Cree J. Oral medications in the management of erectile dysfunction. [Review] [15 refs]. *J Am Board Fam Pract* 1998;11(4):307-314.
- Lawless C, Force R W. Sildenafil for erectile dysfunction. *J Fam Pract* 1998;47(2):97-98.
- Lawrence I G, Price D E, Howlett T A et al. Correcting impotence in the male dialysis patient: experience with testosterone replacement and vacuum tumescence therapy. *Am J Kidney Dis* 1998;31(2):313-319.
- Lea A P, Bryson H M, Balfour J A. Intracavernous alprostadil. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in erectile dysfunction. [Review] [123 refs]. *Drugs Aging* 1996;8(1):56-74.
- Lebret T, Herve J M, Gorny P et al. Efficacy and safety of a novel combination of L-arginine glutamate and yohimbine hydrochloride: a new oral therapy for erectile dysfunction. *Eur Urol* 2002;41(6):608-613.
- Lee W R. The role of androgen deprivation therapy combined with prostate brachytherapy. [Review] [31 refs]. *Urology* 2002;60(3:Suppl 1):Suppl-44.
- Lehmann K, Casella R, Blochlinger A et al. Reasons for discontinuing intracavernous injection therapy with prostaglandin E1 (alprostadil). *Urology* 1999;53(2):397-400.
- Lehmann K, John H, Kacl G et al. Variable response to intracavernous prostaglandin E1 testing for erectile dysfunction. *Urology* 1999;54(3):539-543.
- Lenze E J, Karp J F, Mulsant B H et al. Somatic symptoms in late-life anxiety: Treatment issues. *Journal of Geriatric Psychiatry & Neurology* 2005;18(2):89-96.
- Lenzi A. The role of the medical andrologist in the assisted reproduction era. *J Endocrinol Invest* 2003;26(3):268-273.
- Leslie S J, Atkins G, Oliver J J et al. No adverse hemodynamic interaction between sildenafil and red wine. *Clinical Pharmacology & Therapeutics* 2004;76(4):365-370.
- Levien T, Baker D E. Lepirudin and sildenafil citrate. *Hosp Pharm* 1998;33(12):1524-1552.
- Levine S B. A slightly different idea. *Arch Sex Behav* 2005;34(1):38-39.
- Levy M M. Benefits being missed [5]. *Can Pharm J* 2005;274(7334):109
- Lewis R L, Sadovsky R, Eardley I et al. The efficacy of tadalafil in clinical populations. *Br J Sex Med* 2005;2(4):517-531.

- Lexchin J. New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?. *Can Fam Physician* 2002;48(SEPT.):1487-1492.
- Li J Y, Li X Y, Li M et al. Decline of serum levels of free testosterone in aging healthy Chinese men. *Aging Male* 2005;8(3-4):203-206.
- Licht M R. Use of oral sildenafil (Viagra) in the treatment of erectile dysfunction. [Review] [13 refs]. *Compr Ther* 1999;25(2):90-94.
- Lim P H C, Man K L, Foo C N et al. Clinical efficacy and safety of sildenafil citrate (Viagra) in a multi-racial population in Singapore: A retrospective study of 1520 patients. *Int J Urol* 2002;9(6):308-315.
- Lim P H C, Moorthy P, Benton K G F. The clinical safety of Viagra. *Ann N Y Acad Sci* 2002;962(pp 378-388):-388.
- Limoge J P, Olins E, Henderson D et al. Minimally invasive therapies in the treatment of erectile dysfunction in anticoagulated cases: a study of satisfaction and safety. *Br J Urol* 1996;155(4):1276-1279.
- Lin C-S, Xin Z-C, Lin G et al. Phosphodiesterases as therapeutic targets. *Urology* 2003;61(4):685-691.
- Lincoln T M. Cyclic GMP and phosphodiesterase 5 inhibitor therapies: What's on the horizon. *Mol Pharmacol* 2004;66(1):11-13.
- Lindsey I. What is the incidence of sexual dysfunction in males following rectal excision for benign and malignant diseases?. *National Research Register* 2000;2000.
- Linet O I, Neff L L. Intracavernous prostaglandin E1 in erectile dysfunction. *Clin Investig* 1994;72(2):139-149.
- Linnebur S A. Pharmacotherapy update: What's new about old medications. *Annals of Long Term Care* 2004;12(9):34-44.
- Lipshultz L I. Injection therapy for erectile dysfunction. *N Engl J Med* 1996;334(14):913-914.
- Lipshultz L I, Kim E D. Treatment of erectile dysfunction in men with diabetes. *J Am Med Assoc* 1999;281(5):465-466.
- Llisterri J L, Lozano Vidal J V, Aznar Vicente J et al. Sexual dysfunction in hypertensive patients treated with losartan. *Am J Med Sci* 2001;321(5):336-341.
- Long R L, Sherman L S, Lombardi T J. A goal-oriented, cost-effective approach to the diagnosis and treatment of 24 male erectile dysfunction. [Review] [24 refs]. *J Ky Med Assoc* 1995;93(11):500-508.
- Loudon Julia B. Potential confusion between erectile dysfunction and premature ejaculation: An evaluation of men presenting with erectile difficulty at a sex therapy clinic. *Sexual & Marital Therapy* 1998;13(4):397-403.
- Lu J, SJ Fan J, Zhu J et al. The prospective and randomized control study of Viagra combined with Andriol in the treatment of ED in the aging male. *Chinese Journal of Andrology* 2003;17(3):194-196.
- Lue T F. Erectile dysfunction. *N Engl J Med* 2000;342(24):1802-1813.
- Lue T F. Impotence after radical pelvic surgery: physiology and management. [Review] [56 refs]. *Urol Int* 1991;46(3):259-265.
- Lukkarinen O, Tonttila P, Hellstrom P et al. Non-prosthetic surgery in the treatment of erectile dysfunction. A retrospective study of 45 impotent patients in the University of Oulu. *Scandinavian Journal of Urology & Nephrology* 1998;32(1):42-46.
- Lunenfeld B. Androgen therapy in the aging male. [Review] [110 refs]. *World J Urol* 2003;21(5):292-305.
- Maan Z, Arya M, Shergill I et al. Peyronie's disease: An update of the medical management. *Expert Opin Pharmacother* 2004;5(4):799-805.
- Maas R, Schwedhelm E, Albsmeier J et al. The pathophysiology of erectile dysfunction related to endothelial dysfunction and mediators of vascular function. *Vasc Med* 2002;7(3):213-225.
- Mahmud A, Hennessy M, Feely J. Effect of sildenafil on blood pressure and arterial wave reflection in treated hypertensive men. *J Hum Hypertens* 2001;15(10):707-713.
- Maier U, Koinig G. Andrological findings in young patients under long-term antidepressive therapy with clomipramine. *Psychopharmacology (Berl)* 1994;116(3):357-359.
- Mak R, De Backer G, Kornitzer M et al. Prevalence and correlates of erectile dysfunction in a population-based study in Belgium. *Eur Urol* 2002;41(2):132-138.
- Manasia P, Pomerol J, Ribe N et al. Comparison of the efficacy and safety of 90 mg versus 20 mg fluoxetine in the treatment of premature ejaculation. *Br J Urol* 2003;170(1):164-165.
- Manecke R G, Mulhall J P. Medical treatment of erectile dysfunction. [Review] [69 refs]. *Ann Med* 1999;31(6):388-398.
- Manganiello V. International Journal of Impotence Research: Editorial commentary. *Int J Impot Res* 2004;16(SUPPL. 1):S1-S3.
- Mann K, Klingler T, Noe S et al. Effects of yohimbine on sexual experiences and nocturnal penile tumescence and rigidity in erectile dysfunction. *Arch Sex Behav* 1996;25(1):1-16.

- Mann R D. Introduction - Tadalafil. *Journal of Drug Evaluation* 2004;2(8):223
- Mann R D. Executive summary sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):221-223.
- Manning M, Junemann K P, Scheepe J R et al. Long-term followup and selection criteria for penile revascularization in erectile failure.[see comment]. *Br J Urol* 1998;160(5):1680-1684.
- Marberger M, Roehrborn C G, Marks L S et al. Relationship among serum testosterone, sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. *Journal of Clinical Endocrinology & Metabolism* 2006;91(4):1323-1328.
- Margel D, Tal R, Livne P M et al. Predictors of erectile function improvement in obstructive sleep apnea patients with long-term CPAP treatment. *Int J Impot Res* 2005;17(2):186-190.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- Marquer C, Bressolle F. Moxisylyte: A review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic use in impotence. *Fundam Clin Pharmacol* 1998;12(4):377-387.
- Martin D J, Badwan K, Parker M et al. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. *Br J Urol* 2002;168(6):2483-2485.
- Martins F E, Reis J P. Visual erotic stimulation test for initial screening of psychogenic erectile dysfunction: a reliable noninvasive alternative?. *Br J Urol* 1997;157(1):134-139.
- Masand P S, Ashton A K, Gupta S et al. Sustained-release bupropion for selective serotonin reuptake inhibitor-induced sexual dysfunction: a randomized, double-blind, placebo-controlled, parallel-group study.[see comment]. *Am J Psychiatry* 2001;158(5):805-807.
- Matthew A G, Goldman A, Trachtenberg J et al. Sexual dysfunction after radical prostatectomy: Prevalence, treatments, restricted use of treatments and distress. *Br J Urol* 2005;174(6):2105-2110.
- Maytom M C, Derry F A, Dinsmore W W et al. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord*. 1999;37(2):110-116.
- McCarthy Barry W. Relapse prevention strategies and techniques with erectile dysfunction. *J Sex Marital Ther* 2001;27(1):1-8.
- McClellan K J, Goa K L. Transdermal testosterone. [Review] [17 refs]. *Drugs* 1998;55(2):253-258.
- McClure R D. Endocrine evaluation and therapy of erectile dysfunction. [Review] [77 refs]. *Urol Clin North Am* 1988;15(1):53-64.
- McConnell J D, Roehrborn C G, Bautista O M et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
- McCullough A R, Barada J H, Fawzy A et al. Achieving treatment optimization with sildenafil citrate (Viagra) in patients with erectile dysfunction. *Urology* 2002;60(2 Suppl 2):28-38.
- McKinlay J B. The worldwide prevalence and epidemiology of erectile dysfunction. [Review] [17 refs]. *Int J Impot Res* 2000;12Suppl-S11.
- McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992;9265A
- McMahon C G. Nonsurgical treatment of cavernosal venous leakage. *Urology* 1997;49(1):97-100.
- McMahon C G. Treatment of Erectile Dysfunction with Chronic Dosing of Tadalafil. *Eur Urol* 2006;50(2):215-217.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- McMahon C G, Stuckey B G A, Andersen M et al. Efficacy of sildenafil citrate (viagra) in men with premature ejaculation. *Br J Sex Med* 2005;2(3):368-375.
- Mealy N E. NBI-69733. *Drugs of the Future* 2004;29(6):642
- Mealy N E. GPI-1485. *Drugs of the Future* 2004;29(6):640
- Mealy N E. EMR-62203. *Drugs of the Future* 2004;29(6):639
- Mealy N E. Dasantafil. *Drugs of the Future* 2004;29(6):633
- Mealy N E. DA-8159. *Drugs of the Future* 2004;29(6):631

- Mealy N E. Avanafil. *Drugs of the Future* 2004;29(6):628-629.
- Mealy N E. Alprostadil cream. *Drugs of the Future* 2004;29(6):626-627.
- Mealy N E, Bayes M. PT-141. *Drugs of the Future* 2004;29(11):1177
- Mealy N E, Bayes M. ABT-724. *Drugs of the Future* 2005;30(9):935
- Mehdiyev T V. Intracavernous injection probe of vasoactive preparations in the diagnosis of erectile dysfunctions in patients with diabetes mellitus. *Azerbaijanski Meditsinski Zhurnal* 2002;(pp 17-19):-19.
- Meinhardt W, Kropman R F, Vermeij P et al. The influence of medication on erectile function. *Int J Impot Res* 1997;9(1):17-26.
- Melman A, Bar-Chama N, McCullough A et al. The first human trial for gene transfer therapy for the treatment of erectile dysfunction: preliminary results. *Eur Urol* 2005;48(2):314-318.
- Mendelson W B, Gujavarty K, Slintak C et al. Reported sexual dysfunction in obstructive sleep apnea patients. *Ann Clin Psychiatry* 1990;2(2):93-101.
- Merrick G S, Wallner K E, Butler W M. Minimizing prostate brachytherapy-related morbidity. *Urology* 2003;62(5):786-792.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Meyhoff H H, Rosenkilde P, Bodker A. Non-invasive management of impotence with transcutaneous nitroglycerin. *Br J Urol* 1992;69(1):88-90.
- Migliari R, Muscas G, Usai E. Effect of Casodex on sleep-related erections in patients with advanced prostate cancer. *Br J Urol* 1992;148(2 I):338-341.
- Mikhail N. Efficacy and safety of sildenafil in patients with congestive heart failure [7]. *Arch Intern Med* 2004;164(18):2067-2068.
- Millard R J, Stricker P D, Lynch W J et al. Risks of self-injection therapy for impotence. *Med J Aust* 1996;165(2):117-118.
- Miller D C, Wei J T, Dunn R L et al. Use of medications or devices for erectile dysfunction among long-term prostate cancer treatment survivors: potential influence of sexual motivation and/or indifference. *Urology* 2006;68(1):166-171.
- Miller N, Smolkin M E, Bissonette E et al. Undetectable prostate specific antigen at 6-12 months: a new marker for early success in hormonally treated patients after prostate brachytherapy. *Cancer* 2005;103(12):2499-2506.
- Mills R D, Sethia K K. Maximisation of the erectile response in the investigation of impotence. *Int J Impot Res* 1999;11(1):29-32.
- Mills T M, Lewis R W. The role of androgens in the erectile response: A 1999 perspective. *Mol Urol* 1999;3(2):75-80.
- Milman H A, Arnold S B, Rivera-Miranda G et al. Neurologic, psychological, and aggressive disturbances with sildenafil. *Ann Pharmacother* 2002;36(7-8):1129-1134.
- Mirone V G, Stief C G. Efficacy of apomorphine SL in erectile dysfunction.[erratum appears in *BJU Int* 2002 Jan;89(1):140]. [Review] [11 refs]. *BJU Int* 2001;88(Suppl 3):25-29.
- Mittleman M A, Glasser D B, Orazem J. Clinical trials of sildenafil citrate (Viagra) demonstrate no increase in risk of myocardial infarction and cardiovascular death compared with placebo. *Int J Clin Pract* 2003;57(7):597-600.
- Mittleman M M, Rosen R C. Evaluating clinical trial design results and analysis of drug treatments for erectile dysfunction. *Int J Impot Res* 2003;15(4):x-xiii.
- Miwa Y, Kaneda T, Yokoyama O. Correlation between the Aging Males' Symptoms Scale and sex steroids, gonadotropins, dehydroepiandrosterone sulfate, and growth hormone levels in ambulatory men. *Br J Sex Med* 2006;3(4):723-726.
- Mohr B A, Bhasin S, Link C L et al. The effect of changes in adiposity on testosterone levels in older men: longitudinal results from the Massachusetts Male Aging Study. *Eur J Endocrinol* 2006;155(3):443-452.
- Montejo A L, Llorca G, Izquierdo J A et al. Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction.[see comment]. *Hillside J Clin Psychiatry* 2001;62Suppl-21.
- Montejo-Gonzalez A L, Llorca G, Izquierdo J A et al. SSRI-induced sexual dysfunction: fluoxetine, paroxetine, sertraline, and fluvoxamine in a prospective, multicenter, and descriptive clinical study of 344 patients. *Journal of Sex and Marital Therapy* 1997;23(3):176-194.
- Montorsi F. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil: Editorial comment. *Eur Urol* 2004;45(4):508-509.
- Montorsi F, Althof S E. Partner responses to sildenafil citrate (Viagra) treatment of erectile dysfunction. *Urology* 2004;63(4):762-767.

- Montorsi F, Burnett A L. Erectile dysfunction after radical prostatectomy. *BJU Int* 2004;93(1):1-2.
- Montorsi F, Briganti A, Salonia A et al. Current and Future Strategies for Preventing and Managing Erectile Dysfunction Following Radical Prostatectomy. *Eur Urol* 2004;45(2):123-133.
- Montorsi F, Briganti A, Salonia A et al. Can Phosphodiesterase Type 5 Inhibitors Cure Erectile Dysfunction?. *Eur Urol* 2006;49(6):979-986.
- Montorsi F, Guazzoni G, Boccardi A et al. Improved minimally-invasive assessment of penile haemodynamics: the combination of colour Doppler sonography and injection-stimulation test. *Int J Impot Res* 1995;7(1):33-40.
- Montorsi F, Perani D, Anchisi D et al. Brain activation patterns during video sexual stimulation following the administration of apomorphine: results of a placebo-controlled study. *Eur Urol* 2003;43(4):405-411.
- Montorsi F, Salonia A, Briganti A et al. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47(5):612-621.
- Montorsi F, Strambi L F, Guazzoni G et al. Effect of yohimbine-trazodone on psychogenic impotence: a randomized, double-blind, placebo-controlled study. *Urology* 1994;44(5):732-736.
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol*. 2002;26
- Morales A. Men's aging and sexual disorders: An update on diagnosis and treatment. *Rev Endocr Metab Disord* 2005;6(2):85-92.
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Morales Alvaro, Condra Michael, Heaton Jeremy P et al. Impotence: Organic factors and management approach. *Sexual & Marital Therapy* 1991;6(2):97-106.
- Moreira E D, Lbo C F, Diament A et al. Incidence of erectile dysfunction in men 40 to 69 years old: results from a population-based cohort study in Brazil. *Urology* 2003;61(2):431-436.
- Moreira E D, Lisboa Lobo C F, Villa M et al. Prevalence and correlates of erectile dysfunction in Salvador, northeastern Brazil: a population-based study. *Int J Impot Res* 2002;14Suppl-9.
- Morley John E, Kaiser Fran E. Aging and sexuality. *Vellas, Bruno (Ed); Albarede, J* 1992;-L(Ed):1992-165.
- Mulhall J P. Deciphering erectile dysfunction drug trials. [Review] [35 refs]. *Br J Urol* 2003;170(2 Pt 1):353-358.
- Mulhall J P. Sublingual apomorphine for the treatment of erectile dysfunction. [Review] [22 refs]. *Expert Opin Investig Drugs* 2002;11(2):295-302.
- Mulhall J P, bdel-Moneim A, Abobakr R et al. Improving the accuracy of vascular testing in impotent men: correcting hemodynamic alterations using a vasoactive medication re-dosing schedule. *Br J Urol* 2001;166(3):923-926.
- Mulhall J P, Daller M, Traish A M et al. Intracavernosal forskolin: Role in management of vasculogenic impotence resistant to standard 3-agent pharmacotherapy. *Br J Urol* 1997;158(5):1752-1759.
- Mulhall J P, Levine L A, Junemann K P. Erection hardness: a unifying factor for defining response in the treatment of erectile dysfunction. [Review] [37 refs]. *Urology* 2006;68(3 Suppl):17-25.
- Mulligan T, Schmitt B. Testosterone for erectile failure. *J Gen Intern Med* 1993;8(9):517-521.
- Mulligan T, Frick M F, Zuraw Q C et al. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 2006;60(7):762-769.
- Muneer A, Ralph D J, Minhas S. Sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):225-246.
- Munoz M, Bancroft J, Beard M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 2. The erectile response to erotic stimuli in men with erectile dysfunction, in relation to age and in comparison with normal volunteers. *Psychopharmacology (Berl)* 1994;115(4):471-477.
- Munoz M, Bancroft J, Turner M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 1. The erectile response to erotic stimuli in volunteers. *Psychopharmacology (Berl)* 1994;115(4):463-470.
- Murphy A M, O'Leary M. Failure of the Ambicor inflatable penile prosthesis to deflate. *Int J Impot Res* 2005;17(3):291-292.
- Murphy J C, Srinivas S, Terris M K. Flutamide administration at 500 mg daily has similar effects on serum testosterone to 750 mg daily. *J Androl* 2004;25(4):630-634.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.

- Nakata M, Takashima S, Kaminou T et al. Embolotherapy for venous impotence: use of ethanol. *Journal of Vascular & Interventional Radiology* 2000;11(8):1053-1057.
- Nakonezny P A, Byerly M J, Rush A J. The relationship between serum prolactin level and sexual functioning among male outpatients with schizophrenia or schizoaffective disorder: A randomized double-blind trial of risperidone vs. quetiapine. *J Sex Marital Ther* 2007;33(3):203-216.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Nandwani R, Gourlay Y. Possible interaction between sildenafil and HIV combination therapy [1]. *Lancet* 1999;353(9155):840
- Narayan P, Trachtenberg J, Lepor H et al. A dose-response study of the effect of flutamide on benign prostatic hyperplasia: results of a multicenter study. *Urology* 1996;47(4):497-504.
- Neese Leah E, Schover Leslie R, Klein Eric A et al. Finding help for sexual problems after prostate cancer treatment: A phone survey of men's and women's perspectives. [References]. *Psychooncology* 2003;12(5):463-473.
- Nehra A, Blute M L, Barrett D M et al. Rationale for combination therapy of intraurethral prostaglandin E(1) and sildenafil in the salvage of erectile dysfunction patients desiring noninvasive therapy. *Int J Impot Res* 2002;14(Suppl 1):38-42.
- Neumeyer K, Kirkpatrick P. Tadalafil and vardenafil. *Nat Rev Genet* 2004;3(4):295-296.
- Nicolosi A, Moreira E D, Shirai M et al. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology* 2003;61(1):201-206.
- Nieschlag E, Swerdloff R, Behre H M et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *Int J Androl* 2005;28(3):125-127.
- Nurnberg H G, Hensley P L. Sildenafil citrate for the management of antidepressant-associated erectile dysfunction. *Hillside J Clin Psychiatry* 2003;64Suppl-5.
- Nurnberg H G, Gelenberg A, Hargreave T B et al. Efficacy of sildenafil citrate for the treatment of erectile dysfunction in men taking serotonin reuptake inhibitors. *Am J Psychiatry* 2001;158(11):1926-1928.
- Nurnberg H G, Seidman S N, Gelenberg A J et al. Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. *Urology* 2002;60(2 Suppl 2):58-66.
- Nurnberg H, George. Erectile Dysfunction and Comorbid Depression: Prevalence, Treatment Strategies, and Associated Medical Conditions. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl10):3-4.
- Nurnberg H, George Hensley, Paula L et al. Sildenafil in the treatment of sexual dysfunction induced by selective serotonin reuptake inhibitors: An overview. [References]. *CNS Drugs* 2000;13(5):321-335.
- O'Sullivan J D. Apomorphine as an alternative to sildenafil in Parkinson's disease. [References]. *Journal of Neurology, Neurosurgery & Psychiatry* 2002;72(5):681
- O'Sullivan J D, Hughes A J. Apomorphine-induced penile erections in Parkinson's disease. *Mov Disord* 1998;13(3):536-539.
- Oefelein M G. Time to normalization of serum testosterone after 3-month luteinizing hormone-releasing hormone agonist administered in the neoadjuvant setting: implications for dosing schedule and neoadjuvant study consideration.[see comment]. *Br J Urol* 1998;160(5):1685-1688.
- Ohebshalom M, Mulhall J P. Transdermal and topical pharmacotherapy for male sexual dysfunction. *Expert Opinion on Drug Delivery* 2005;2(1):115-120.
- Ojumu A, Dobs A S. Is Hypogonadism a Risk Factor for Sexual Dysfunction?. *J Androl* 2003;24(6 SUPPL.):S46-S51.
- Onu P E. Depot medroxyprogesterone in the management of benign prostatic hyperplasia. *Eur Urol* 1995;28(3):229-235.
- Opsomer R J, Wese F X, De Groote P et al. The external vacuum device in the management of erectile dysfunction. *Acta Urol Belg* 1997;65(4):13-16.
- Ormrod D, Easthope S E, Figgitt D P. Vardenafil.[erratum appears in *Drugs Aging* 2002;19(11):886]. [Review] [30 refs]. *Drugs Aging* 2002;19(3):217-227.
- Osterloh I H, Riley A. Clinical update on sildenafil citrate. [Review] [58 refs]. *Br J Clin Pharmacol* 2002;53(3):219-223.
- Osterloh I H, Collins M, Wicker P et al. Sildenafil citrate (VIAGRA): overall safety profile in 18 double-blind, placebo controlled, clinical trials. [Review] [0 refs]. *Int J Clin Pract* 1999;Supplement.102-105.
- Owens J. Seeking selectivity. *Nat Rev Genet* 2005;4(2):106
- Ozbek E, Yurekli M, Soyulu A et al. The role of adrenomedullin in varicocele and impotence. *BJU Int* 2000;86(6):694-698.

- Ozdel O, Oguzhanoglu A, Oguzhanoglu N K et al. A follow-up study of male sexual disorders: The neurophysiological assessments, anxiety-depression levels, and response to fluoxetine treatment [10]. *J Clin Psychopharmacol* 2004;24(4):461-463.
- Padma-Nathan H, Eardley I, Kloner R A et al. A 4-year update on the safety of sildenafil citrate (Viagra). [Review] [88 refs]. *Urology* 2002;60(2:Suppl 2):Suppl-90.
- Pagani E, Glina S, Puech-Leao P et al. Anxiety and high plasma catecholamines do not impair phar-maco-induced erection of psychogenic erectile dysfunctional patients. *Int J Impot Res* 2003;15(4):282-286.
- Paice Judith A, Penn Richard D, Ryan Will G. Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. *J Pain Symptom Manage* 1994;9(2):126-131.
- Paick J S, Yang J H, Kim S W et al. Severity of erectile dysfunction in married impotent patients: interrelationship with anthropometry, hormones, metabolic profiles and lifestyle. *Int J Urol* 2007;14(1):48-53.
- Paick J S, Yang J H, Kim S W et al. The role of prolactin levels in the sexual activity of married men with erectile dysfunction. *BJU Int* 2006;98(6):1269-1273.
- Paick S H, Meehan A, Lee M et al. The relationship among lower urinary tract symptoms, prostate specific antigen and erectile dysfunction in men with benign prostatic hyperplasia: results from the proscar long-term efficacy and safety study. *Br J Urol* 2005;173(3):903-907.
- Palha A P, Gomes F A, Martins A S et al. [Clinical, multicentric, and open study to evaluate the efficacy of and tolerance to sildenafil in patients with erectile dysfunction]. *Acta Med Port.* 2002;15(4):249-256.
- Pan C C, Lin J S N, Wong W S. Comparison of effect on erection between vacuum constriction devices and intra-cavernous injection of prostaglandin E1. *Asian J Surg* 1997;20(2):162-166.
- Papatsoris A G, Deliveliotis C, Singer C et al. Erectile dysfunction in Parkinson's disease. *Urology* 2006;67(3):447-451.
- Parazzini F, Menchini Fabris F, Bortolotti A et al. Frequency and determinants of erectile dysfunction in Italy. *Eur Urol* 2000;37(1):43-49.
- Paris G, Sponsel W E, Sandoval S S et al. Sildenafil increases ocular perfusion. *Int Ophthalmol* 2001;23(4-6):355-358.
- Parker C. The Scandinavian Prostate Cancer Group Study: The case for conservative management. *BJU Int* 2005;96(7):952-953.
- Parsons J K, Marschke P, Maples P et al. Effect of methylprednisolone on return of sexual function after nerve-sparing radical retropubic prostatectomy. *Urology* 2004;64(5):987-990.
- Patankar M. Sildenafil citrate. *J Indian Med Assoc* 2000;98(12):
- Patterson D, Kloner R, Effron M et al. The effect of tadalafil on the time to exercise-induced myocardial ischaemia in subjects with coronary artery disease. *Br J Clin Pharmacol* 2005;60(5):459-468.
- Pegge N C, Twomey A M, Vaughton K et al. The role of endothelial dysfunction in the pathophysiology of erectile dysfunction in diabetes and in determining response to treatment. *Diabet Med* 2006;23(8):873-878.
- Penninga E, Jensen B A, Hansen P B et al. Anagrelide treatment in 52 patients with chronic myeloproliferative diseases. *Clinical & Laboratory Haematology* 2004;26(5):335-340.
- Penson D F, Feng Z, Kuniyuki A et al. General quality of life 2 years following treatment for prostate cancer: what influences outcomes? Results from the prostate cancer outcomes study.[see comment]. *Am J Clin Oncol* 2003;21(6):1147-1154.
- Perez Martin A, Skinner Eila C, Meyerowitz Beth E E. Sexuality and intimacy following radical prostatectomy: Patient and partner perspectives. [References]. *Health Psychol* 2002;21(3):288-293.
- Perimenis P, Athanasopoulos A, Papatanasopoulos P et al. Gabapentin in the management of the recurrent, refractory, idiopathic priapism. *Int J Impot Res* 2004;16(1):84-85.
- Pescatori E S, Calpista A, Artibani W et al. Self-injection devices for intracavernosal pharmacotherapy: operational classification and safety considerations. *Int J Impot Res* 1996;8(2):53-57.
- Pescatori E S, Silingardi V, Galeazzi G M et al. Audiovisual sexual stimulation by virtual glasses is effective in inducing complete cavernosal smooth muscle relaxation: a pharmacocavernosometric study. *Int J Impot Res* 2000;12(2):83-88.
- Phelps J S, Jain A, Monga M. The PsychoedPlusMed approach to erectile dysfunction treatment: the impact of combining a psychoeducational intervention with sildenafil. *J Sex Marital Ther* 2004;30(5):305-314.
- Philipp M, Kohnen R, Benkert O. A comparison study of moclobemide and doxepin in major depression with special reference to effects on sexual dysfunction. *Int Clin Psychopharmacol* 1993;7(3-4):149-153.
- Philipp M, Tiller J W G, Baier D et al. Comparison of moclobemide with selective serotonin reuptake inhibitors (SSRIs) on sexual function in depressed adults. *Eur Neuropsychopharmacol* 2000;10(5):305-314.

- Phillips B G, Kato M, Pesek C A et al. Sympathetic activation by sildenafil.[see comment]. *Circulation* 2000;102(25):3068-3073.
- Pirotte B, de Tullio P, Antoine M-H et al. New insights into the development of ATP-sensitive potassium channel openers. *Expert Opinion on Therapeutic Patents* 2005;15(5):497-504.
- Pisters L L, von Eschenbach A C, Scott S M et al. The efficacy and complications of salvage cryotherapy of the prostate. *J Urol* 1997;157(3):921-925.
- Pittler M, Ernst E. Trials have shown yohimbine is effective for erectile dysfunction [14]. *Br Med J* 1998;317(7156):478
- Polak K, Wimpissinger B, Berisha F et al. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. *Invest Ophthalmol Vis Sci* 2003;44(11):4872-4876.
- Pollack Mark H, Reiter Stewart, Hammerness Paul. Genitourinary and sexual adverse effects of psychotropic medication. *Int J Psychiatry Med* 1992;22(4):305-327.
- Pomara G, Morelli G, Montorsi F et al. Re: Montorsi F, Salonia A, Briganti A, Barbieri L, Zanni G, Surdi N, Cestari A, Montorsi P, Rigatti P. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47:612-21 (multiple letters). *Eur Urol* 2005;48(2):345-346.
- Pomerantz J M. Viagra and medical necessity. *Drug Benefit Trends* 2002;14(10):33+40
- Pommerville P. Drug treatments for erectile dysfunction: An update. *Geriatrics and Aging* 2004;7(6):10-16.
- Pommerville P J. From bedside to bed. Recovery of sexual function after prostate cancer. *Can Fam Physician* 2005;51(JULY):941-943+948.
- Porst H. IC351 (tadalafil, Cialis): update on clinical experience. [Review] [12 refs]. *Int J Impot Res* 2002;14Suppl-64.
- Porst H. Phosphodiesterase type-5 inhibitors: A critical comparative analysis. *Eau Update Series* 2004;2(2):56-63.
- Porst H C. Re-dosing of prostaglandin-E1 versus prostaglandin-E1 plus phentolamine in male erectile dysfunction: a dynamic color power Doppler study. *Int J Impot Res* 2000;12(2):134-135.
- Porst H, Giuliano F, Glina S et al. Evaluation of the Efficacy and Safety of Once-a-Day Dosing of Tadalafil 5 mg and 10 mg in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial. *Eur Urol* 2006;50(2):351-359.
- Pouaha J, Martin S, Reichert-Penetrat S et al. Thalidomide and sexual dysfunction in men.[comment]. *Br J Dermatol* 2002;146(6):1112-1113.
- Power-Smith Parsley. Beneficial sexual side-effects from fluoxetine. *Br J Psychiatry Suppl* 1994;164 Feb 1994, 249-250. <http://249-250>.
- Pradeep C, Car N, Metelko Z. Impotence in diabetic men. *Diabetol Croat* 1996;25(2):61-68.
- Pratt-Ubunama M N, Nishizaka M K, Calhoun D A. Aldosterone antagonism: An emerging strategy for effective blood pressure lowering. *Curr Hypertens Rep* 2005;7(3):186-192.
- Preskorn S H. Duloxetine. *Journal of Psychiatric Practice* 2004;10(6):375-385.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Prins J, Blanker M H, Bohnen A M et al. Prevalence of erectile dysfunction: A systematic review of population-based studies. *Int J Impot Res* 2002;14(6):422-432.
- Priyadarshi S. Oral terbutaline in the management of pharmacologically induced prolonged erection. *Int J Impot Res* 2004;16(5):424-426.
- Pryor J. Vardenafil: update on clinical experience. [Review] [10 refs]. *Int J Impot Res* 2002;14Suppl-9.
- Pryor J P. Orgasmic and ejaculatory dysfunction. *Sexual & Relationship Therapy* 2002;17(1):87-95.
- Qian L X, Wu H F, Xu H et al. Multi-center Evaluation of Efficacy and Safety of Oral Mesylate Phentolamine for the Treatment of Erectile Dysfunction. *Int J Androl* 2001;7(5):302-305.
- Quinn M J, Jefferson K, Persad R. Benign prostatic hyperplasia and sexual dysfunction [3] (multiple letters). *Lancet* 2003;361(9368):1562
- Quirk J, Thornton M, Neumeyer K et al. Cardiology and vascular disorders. *Nat Rev Genet* 2004;3(7 SUPPL.):S12-S17.
- Radomski S B, Herschorn S, Rangaswamy S. Topical minoxidil in the treatment of male erectile dysfunction. *Br J Urol* 1994;151(5):1225-1226.
- Ramasubbu R. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.

- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Reffelmann T, Kloner R A. Effects of sildenafil on myocardial infarct size, microvascular function, and acute ischemic left ventricular dilation. *Cardiovasc Res* 2003;59(2):441-449.
- Reyes J A, Tan D A, Quimpo J A et al. The Philippine Male Aging Survey. *Aging Male* 2004;7(3):227-235.
- Rhoden E L, Estrada C, Levine L et al. The value of pituitary magnetic resonance imaging in men with hypogonadism.[see comment]. *Br J Urol* 2003;170(3):795-798.
- Richardson J D. Intracorporeal injections for the treatment of impotence. *Med J Aust* 1991;155(10):688
- Richter S, Vardi Y, Ringel A et al. Intracavernous injections: still the gold standard for treatment of erectile dysfunction in elderly men. *Int J Impot Res* 2001;13(3):172-175.
- Riley Alan. Oral treatments for erectile dysfunction. *Int J STD AIDS* 1996;7(Suppl 3):16-18.
- Rizvi K, Hampson J P, Harvey J N. Do lipid-lowering drugs cause erectile dysfunction? A systematic review.[see comment]. [Review] [35 refs]. *Fam Pract* 2002;19(1):95-98.
- Roach M, Winter K, Michalski J M et al. Penile bulb dose and impotence after three-dimensional conformal radiotherapy for prostate cancer on RTOG 9406: findings from a prospective, multi-institutional, phase I/II dose-escalation study. *Int J Radiat Oncol Biol Phys* 2004;60(5):1351-1356.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Roizenblatt S, Guilleminault C, Poyares D et al. A double-blind, placebo-controlled, crossover study of sildenafil in obstructive sleep apnea. *Arch Intern Med* 2006;166(16):1763-1767.
- Rojewski M T, Korper S, Schrezenmeier H. Arsenic trioxide therapy in acute promyelocytic leukemia and beyond: From bench to bedside. *Leuk Lymphoma* 2004;45(12):2387-2401.
- Rosano G M, Marazzi G, Patrizi R et al. Comparison of trimetazidine plus sildenafil to chronic nitrates in the control of myocardial ischemia during sexual activity in patients with coronary artery disease. *Am J Cardiol* 2005;95(3):327-331.
- Rosas-Vargas H, Coral-Vazquez R M, Tapia R et al. Glu298Asp endothelial nitric oxide synthase polymorphism is a risk factor for erectile dysfunction in the Mexican Mestizo population. *J Androl* 2004;25(5):728-732.
- Rose V L. Sildenafil in the treatment of erectile dysfunction. *Am Fam Physician* 1998;58(1):268
- Rosen R C, Kostis J B. Overview of phosphodiesterase 5 inhibition in erectile dysfunction. *Am J Cardiol* 2003;92(9 SUPPL. 1):9M-18M.
- Rosen R C, Lane R M, Menza M. Effects of SSRIs on sexual function: a critical review.[see comment]. [Review] [255 refs]. *J Clin Psychopharmacol* 1999;19(1):67-85.
- Rosen R C, Shabsigh R, Kuritzky L et al. The efficacy of tadalafil in improving sexual satisfaction and overall satisfaction in men with mild, moderate, and severe erectile dysfunction: A retrospective pooled analysis of data from randomized, placebo-controlled clinical trials. *Current Medical Research & Opinion* 2005;21(11):1701-1709.
- Rosen Raymond C. Erectile dysfunction: The medicalization of male sexuality. *Clin Psychol Rev* 1996;16(6):497-519.
- Rosen Raymond C, Leiblum Sandra R. Treatment of male erectile disorder: Current options and dilemmas. *Sexual & Marital Therapy* 1993;8(1):5-8.
- Rosen Raymond C, Leiblum Sandra, Risa. Erectile disorders: An overview of historical trends and clinical perspectives. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Rosenthal B D, May N R, Metro M J et al. Adjunctive use of AndroGel (testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone. *Urology* 2006;67(3):571-574.
- Rowland D L, Greenleaf W J, Dorfman L J et al. Aging and sexual function in men. *Arch Sex Behav* 1993;22(6):545-557.
- Rowland D L, Kallan K, Slob A K. Yohimbine, erectile capacity, and sexual response in men. *Arch Sex Behav* 1997;26(1):49-62.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382
- Ruof J, Graf-Morgenstern M, Mnlter M J. Quality of life in patients with erection difficulties: Evaluation of a German version of the "Quality of life measure for men with erection difficulties" (QoL-Med). *Aktuel Urol* 2001;32(1):21-26.
- Ryder R E, Close C F, Moriarty K T et al. Impotence in diabetes: aetiology, implications for treatment and preferred vacuum device. *Diabet Med* 1992;9(10):893-898.

- Saad F, Grahl A S, Aversa A et al. Effects of testosterone on erectile function: implications for the therapy of erectile dysfunction. *BJU Int* 2007;99(5):988-992.
- Saad F, Hoesl C E, Oettel M et al. Dehydroepiandrosterone treatment in the aging male - What should the urologist know?. *Eur Urol* 2005;48(5):724-733.
- Sadock Virginia A. A sexually compulsive male with erectile dysfunction treated with Viagra: Discussion. *Journal of Sex Education & Therapy* 1998;23(4):275-277.
- Safarinejad M R. Prevalence and risk factors for erectile dysfunction in a population-based study in Iran. *Int J Impot Res* 2003;15(4):246-252.
- Sairam K, Kulinskaya E, Boustead G B et al. Prevalence of undiagnosed prostate cancer in men with erectile dysfunction. *BJU Int* 2002;89(3):261-263.
- Sak S C, Eardley I. What is the relationship between benign prostatic hyperplasia and sexual function?. *Sexual & Relationship Therapy* 2004;19(4):431-443.
- Sakamoto H, Shimada M, Yoshida H. Hemodynamic evaluation of the penile arterial system in patients with erectile dysfunction using power doppler imaging. *Urology* 2002;60(3):480-484.
- Saks Bonnie R. A sexually compulsive male with erectile dysfunction treated with Viagra: Case report. *Journal of Sex Education & Therapy* 1998;23(4):271-274.
- Salonia A, Barbieri L, Chen J et al. Comparison of the effect of sildenafil and apomorphine SL on nocturnal erections in healthy volunteers: a placebo-controlled study. *Eur Urol* 2005;47(4):524-529.
- Salonia A, Maga T, Colombo R et al. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. *Br J Urol* 2002;168(6):2486-2489.
- Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr.Med Res Opin.* 2003;19(4):241-262.
- Salonia Andrea, Briganti Alberto, Montorsi Piero et al. Safety and tolerability of oral erectile dysfunction treatments in the elderly. [References]. *Drugs and Aging* 2005;22(4):323-338.
- Samarasinghe Y, Rivas-Toro H. HEART UK 18th annual medical and scientific meeting: From diabetes to mixed hyperlipidaemias. *British Journal of Cardiology* 2004;11(5):364-365.
- Sathe R S, Komisaruk B R, Ladas A K et al. Naltrexone-induced augmentation of sexual response in men. *Arch Med Res* 2001;32(3):221-226.
- Sato Y, Horita H, Adachi H et al. Effect of oral administration of prostaglandin E1 on erectile dysfunction. *Br J Urol* 1997;80(5):772-775.
- Sato Y, Suzuki N, Adachi H et al. Evaluation of the alleviative action of neurotrophin for penile pain associated with intracavernous injection of prostaglandin E1 assessed using the visual analogue scale. *Int J Impot Res* 1998;10(1):1-3.
- Savoca G, Silvestre G, Belgrano E. Intracavernosal injection therapy and surgical therapy in diabetic patients with erectile dysfunction. [Review] [26 refs]. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):53-57.
- Scalvini T, Martini P R, Obici L et al. Infertility and Hypergonadotropic Hypogonadism as First Evidence of Hereditary Apolipoprotein A-I Amyloidosis. *Br J Urol* 2007;
- Schiavi Raul C, Schanzer Harry, Sozio Giampaolo et al. Erectile function and penile blood pressure in diabetes mellitus. *J Sex Marital Ther* 1994;20(2):119-124.
- Schimmer A D, Ali V, Stewart A K et al. Male sexual function after autologous blood or marrow transplantation. *Biology of Blood & Marrow Transplantation* 2001;7(5):279-283.
- Scholz M, Strum S. Re: Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: results of a prospective, randomized trial.[comment]. *Br J Urol* 1999;161(6):1914-1915.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266
- Schrader S, Mills A, Scheperle M et al. Improvement in sexual functioning and satisfaction in nonresponders to testosterone gel: clinical effectiveness in hypogonadal, HIV-positive males. *Clin Cornerstone* 2005;7 Suppl 4S26-S31.
- Schroder F H, Whelan P, De Reijke T M et al. Metastatic prostate cancer treated by flutamide versus cyproterone acetate. Final analysis of the "European Organization for Research and Treatment of Cancer" (EORTC) Protocol 30892. *Eur Urol* 2004;45(4):457-464.
- Schultheiss D, Stief C G. Physiology and pathophysiology of erection: Consequences for present medical therapy of erectile dysfunction. *Andrologia* 1999;31(SUPPL. 1):59-64.

- Schwartz E J, Wong P, Graydon R J. Sildenafil preserves intracorporeal smooth muscle after radical retropubic prostatectomy. *Br J Urol* 2004;171(2 I):771-774.
- Seftel A. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(6):2297-2300.
- Seftel A. Effect of lifestyle changes on erectile dysfunction in obese men. A randomized controlled trial. *Br J Urol* 2005;173(2):544-545.
- Seftel A D. From aspiration to achievement: Assessment and noninvasive treatment of erectile dysfunction in aging men. *J Am Geriatr Soc* 2005;53(1):119-130.
- Seftel A D. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(4 I):1364-1366.
- Segraves R T. Pharmacological enhancement of human sexual behavior. *Journal of Sex Education & Therapy* 1991;17(4):283-289.
- Segraves R, Taylor. Two additional uses for sildenafil in psychiatric patients. [References]. *J Sex Marital Ther* 1999;25(4):265-266.
- Segraves Robert, Taylor Segraves, Kathleen Blindt et al. Sexual function in patients taking bupropion sustained release. *Hillside J Clin Psychiatry* 1995;56(8):374
- Seidman Stuart N. Exploring the relationship between depression and erectile dysfunction in aging men. *Hillside J Clin Psychiatry* 2002;63(Suppl5):5-12.
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Seyam R M, Albakry A, Ghobish A et al. Prevalence of erectile dysfunction and its correlates in Egypt: a community-based study. *Int J Impot Res* 2003;15(4):237-245.
- Shabbir M, Mikhailidis D M, Morgan R J. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors.[comment]. *Current Medical Research & Opinion* 2004;20(5):603-606.
- Shabbir M, Shah J S, Kirby R S. Cardiac failure and benign prostatic hyperplasia: Management of common comorbidities. *BJU Int* 2005;95(3):278-280.
- Shabsigh R. Testosterone therapy in erectile dysfunction. [Review] [34 refs]. *Aging Male* 2004;7(4):312-318.
- Shabsigh R. Testosterone therapy in erectile dysfunction and hypogonadism. *Br J Sex Med* 2005;2(6):785-792.
- Shabsigh R. Hypogonadism and erectile dysfunction: The role for testosterone therapy. *Int J Impot Res* 2003;15(SUPPL. 4):S9-S13.
- Shabsigh R, Katz M, Yan G et al. Cardiovascular issues in hypogonadism and testosterone therapy. [Review] [44 refs]. *Am J Cardiol* 2005;96(12B):67M-72M.
- Shakir S A W, Wilton L V, Boshier A et al. Cardiovascular events in users of sildenafil: Results from first phase of prescription event monitoring in England. *Br Med J* 2001;322(7287):651-652.
- Shamloul R. Management of honeymoon impotence. *Br J Sex Med* 2006;3(2):361-366.
- Shamloul R, El-Dakhly M, Ghanem H et al. Intracavernous chlorpromazine versus phentolamine: A double-blind clinical comparative study. *Br J Sex Med* 2004;1(3):310-313.
- Shamloul R, Ghanem H M, Salem A et al. The value of penile duplex in the prediction of intracavernous drug-induced priapism. *Int J Impot Res* 2004;16(1):78-79.
- Shamsa A, Motavalli S M, Aghdam B. Erectile function in end-stage renal disease before and after renal transplantation. *Transplant Proc* 2005;37(7):3087-3089.
- Sharlip I D. Editorial comment. *International Braz J Urol* 2005;31(4):354-355.
- Sharlip I D. Can self-injection therapy cure impotence?. [Review] [7 refs]. *Advances in Experimental Medicine & Biology* 1997;43383-86.
- Shimon I, Lubina A, Gorfine M et al. Feedback inhibition of gonadotropins by testosterone in men with hypogonadotropic hypogonadism: comparison to the intact pituitary-testicular axis in primary hypogonadism. *J Androl* 2006;27(3):358-364.
- Siegel R L, Dubin N H, Andrade J R. Sildenafil citrate and sperm function [3] (multiple letters). *American Journal of Obstetrics & Gynecology* 2001;184(4):777-778.
- Sighinolfi M C, de Stefani S, Mofferdin A et al. Intracavernous prostaglandin E1 infusion in diabetes with associated ischemic necrosis of the glans penis. *Br J Urol* 2004;171(6 I):2380
- Silvestri A, Galetta P, Cerquetani E et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo.[see comment]. *Eur Heart J* 2003;24(21):1928-1932.
- Singer Carlos, Weiner William J, Sanchez-Ramos J et al. Sexual function in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry* 1991;54(10):942

- Sipski M, Alexander C, Guo X et al. Cardiovascular effects of sildenafil in men with SCIs at and above T6. *Topics in Spinal Cord Injury Rehabilitation* 2003;8(3):26-34.
- Siraj Q H, Bomanji J, Akhtar M A et al. Quantitation of pharmacologically-induced penile erections: The value of radionuclide phallography in the objective evaluation of erectile haemodynamics. *Nucl Med Commun* 1990;11(6):445-458.
- Slob A K, Dohle G R, Incrocci L. 'Sildenafil and pharmacopenile duplex ultrasonography' by Speel et al: Inconclusive results. *Int J Impot Res* 2002;14(2):136-137.
- Slob A, Koos Steyvers, Christel L et al. Routine psychophysiological screening of 384 men with erectile dysfunction. *J Sex Marital Ther* 1998;24(4):273-279.
- Smith K J, Roberts M S. The cost-effectiveness of sildenafil. *Ann Intern Med* 2000;132(12):933-937.
- Smith K M, Romanelli F. Recreational use and misuse of phosphodiesterase 5 inhibitors. [Review] [56 refs]. *Journal of the American Pharmacists Association: JAPhA* 2005;45(1):63-72.
- Sobh M A, Abd el, Hamid I et al. Effect of erythropoietin on sexual potency in chronic haemodialysis patients. A preliminary study. *Scand J Urol Nephrol* 1992;26(2):181-185.
- Sogari P R, Teloken C, Souto C A. Atropine role in the pharmacological erection test: study of 228 patients.. *Br J Urol* 1997;158(5):1760-1763.
- Sohle G R. Re: The age-related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Eur Urol* 2007;51(5):1440
- Sohn Michael, Sikora Richard. Ginkgo biloba extract in the therapy of erectile dysfunction. *Journal of Sex Education & Therapy* 1991;17(1):53-61.
- Solursh L, Solursh D S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *International Journal of Adolescent Medicine & Health* 1994;7(2):119-124.
- Solursh Lionel P, Solursh Diane S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *Int J Adolesc Med Health* 1994;7(2):119-124.
- Sonda L P, Mazo R, Chancellor M B. The role of yohimbine for the treatment of erectile impotence. *J Sex Marital Ther* 1990;16(1):15-21.
- Sonksen J, Biering-Sorensen F. Transcutaneous nitroglycerin in the treatment of erectile dysfunction in spinal cord injured. *Paraplegia* 1992;30(8):554-557.
- Sorbera L A, Martin L, Rabasseda X et al. Vardenafil. Treatment of erectile dysfunction. Phosphodiesterase 5 inhibitor. *Drugs of the Future* 2001;26(2):141-144.
- Sparwasser C, Drescher P, Pust R A et al. Long-term results of therapy with intracavernous injections and penile venous surgery in chronic erectile dysfunction. *Scand J Urol Nephrol Suppl* 1994;157(Suppl):107-112.
- Speakman M T, Kloner R A. Viagra and cardiovascular disease. *Journal of Cardiovascular Pharmacology & Therapeutics* 1999;4(4):259-267.
- Srilatha B, Adaikan P G, Chong Y S. Relevance of oestradiol-testosterone balance in erectile dysfunction patients' prognosis. *Singapore Med J* 2007;48(2):114-118.
- Stas S N, Anastasiadis A G, Fisch H et al. Urologic aspects of andropause. *Urology* 2003;61(2):261-266.
- Steers W D. Tachyphylaxis and phosphodiesterase type 5 inhibitors.[comment]. *Br J Urol* 2002;168(1):207
- Steers W D. Viagra - After one year. *Urology* 1999;54(1):12-17.
- Steidle C, Witt M A, Matrisciano J et al. Sexual functioning and satisfaction in nonresponders to testosterone gel: Potential effectiveness of retreatment in hypogonadal males. *Clin Cornerstone* 2005;7 Suppl 4S20-S25.
- Steiger A, Holsboer F, Benkert O. Studies of nocturnal penile tumescence and sleep electroencephalogram in patients with major depression and in normal controls. *Acta Psychiatr Scand* 1993;87(5):358-363.
- Steiger Axel, Benkert O, Holsboer F. Effects of long-term treatment with the MAO-A inhibitor moclobemide on sleep EEG and nocturnal hormonal secretion in normal men. *Neuropsychobiology* 1994;30(2-3):101-105.
- Stief C G, Uckert S, Jonas U. Strategies in the oral pharmacotherapy of male erectile dysfunction viewed from bench and bedside (Part II). *The Journal of Mens Health & Gender* 2005;2(3):325-332.
- Stief C G, Uckert S, Becker A J et al. The effect of the specific phosphodiesterase (PDE) inhibitors on human and rabbit cavernous tissue in vitro and in vivo. *Br J Urol* 1998;159(4):1390-1393.
- Stief C, Padley R J, Perdok R J et al. Cross-study review of the clinical efficacy of apomorphine SL 2 and 3 mg: Pooled data from three placebo-controlled, fixed-dose crossover studies. *European Urology Supplements* 2002;1(3):12-20.

- Stolk E A, Busschbach J J, Caffa M et al. Cost utility analysis of sildenafil compared with papaverine-phentolamine injections.[see comment]. *BMJ* 2000;320(7243):1165-1168.
- Strachan M W, Teoh W L, Don-Wauchope A C et al. Clinical and radiological features of patients with macroprolactinaemia. *Clin Endocrinol (Oxf)* 2003;59(3):339-346.
- Strahilevitz J, Rahav G, Schroers H-J et al. An outbreak of Phialemonium infective endocarditis linked to intracavernous penile injections for the treatment of impotence. *Clin Infect Dis* 2005;40(6):781-786.
- Stroberg P, Murphy A, Costigan T. Switching patients with erectile dysfunction from sildenafil citrate to tadalafil: results of a European multicenter, open-label study of patient preference. *Clin Ther.* 2003;25(11):2724-2737.
- Struthers A D. Aldosterone blockade in heart failure. *J Renin Angiotensin Aldosterone Syst* 2004;5(SUPPL. 1):S23-S27.
- Stuckey B G A. Tadalafil phase 3 experience. *European Urology Supplements* 2002;1(8):25-30.
- Suetomi T, Endo F, Takeshima H et al. Evaluation of the effectiveness of sildenafil using questionnaire methods versus audio-visual sexual stimulation. *Int J Urol* 2005;12(4):369-373.
- Suzuki F, Shimizu C, Umetsu M et al. Adult-onset idiopathic hypogonadotropic hypogonadism due to isolated pituitary gonadotropin deficiency. *Adv Intern Med* 2004;43(7):571-574.
- Svartberg J, Aasebo U, Hjalmsen A et al. Testosterone treatment improves body composition and sexual function in men with COPD, in a 6-month randomized controlled trial.. *Respir Med* 2004;98(9):906-913.
- Swartz D A, Todd M W. Intracavernous papaverine and glaucoma.[see comment]. *JAMA* 1990;264(5):570
- Szucs A, Janszky J, Barsi P et al. Sleep-related painful erection is associated with neurovascular compression of basal forebrain [5]. *J Neurol* 2002;249(4):486-487.
- T'Sjoen G, Feyen E, De Kuyper P et al. Self-referred patients in an aging male clinic: much more than androgen deficiency alone. *Aging Male* 2003;6(3):157-165.
- Tam S W, Worcel M, Wyllie M. Yohimbine: a clinical review. [Review] [152 refs]. *Pharmacol Ther* 2001;91(3):215-243.
- Tarhan F, Canguven O, Kuyumcuoglu U. Intracavernous sodium nitroprusside (SNP) versus papaverine/phentolamine in erectile dysfunction: a comparative study of short-term efficacy and side-effects.[comment]. *Br J Sex Med* 2006;3(2):377
- Tarhan F, Kuyumcuoglu U, Kolsuz A et al. Effect of intracavernosal sodium nitroprusside in impotence. *Urol Int* 1996;56(4):211-214.
- Tas A, Dilek K, Gullulu M et al. Treatment of erectile dysfunction in hemodialysis patients and effects of sildenafil [abstract]. XXXVIII Congress of the European Renal Association European Dialysis & Transplant Association June 24-27 2003;2001, Vienna, Austria 131p. 2003.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Teillac P, Bono A V, Irani J et al. The role of luteinizing hormone-releasing hormone therapy in locally advanced prostate cancer and biochemical failure: Considerations for optimal use. *Clin Ther* 2005;27(3):273-285.
- Teloken P E, Smith E B, Lodowsky C et al. Defining association between sleep apnea syndrome and erectile dysfunction. *Urology* 2006;67(5):1033-1037.
- Thadani U, Smith W, Nash S et al. The effect of vardenafil, a potent and highly selective phosphodiesterase-5 inhibitor for the treatment of erectile dysfunction, on the cardiovascular response to exercise in patients with coronary artery disease. *J Am Coll Cardiol* 2002;40(11):2006-2012.
- Thaveundayil J X, Hambalek R, Ng Ying et al. Prolonged penile erections induced by hydroxyzine: Possible mechanism of action. *Neuropsychobiology* 1994;30(1):4-6.
- Thrasher J B. What's new in urology. *J Am Coll Surg* 2005;201(3):438-448.
- Tindall B, Forde S, Goldstein D et al. Sexual dysfunction in advanced HIV disease. *AIDS Care* 1994;6(1):105-107.
- Tomlinson J. Viagra and its use in cardiovascular disease.[erratum appears in *J Hum Hypertens* 2000 Apr;14(4):283]. [Review] [11 refs]. *J Hum Hypertens* 1999;13(9):593-594.
- Tomova A, Kumanov P. Are dehydroepiandrosterone sulphate and lipids associated with erectile dysfunction? [References]. *Maturitas* 2005;50(4):294-299.
- Tordjman G. NO/Pg E1: a new association in the treatment of erectile impotence. *Contracept Fertil Sex (Paris)* 1993;21, pp.509-510, 1993.
- Tosti A, Pazzaglia M, Soli M et al. Evaluation of sexual function with an international index of erectile function in subjects taking finasteride for androgenetic alopecia.[see comment]. *Arch Dermatol* 2004;140(7):857-858.

- Traish A M, Goldstein I, Kim N N. Testosterone and erectile function: from basic research to a new clinical paradigm for managing men with androgen insufficiency and erectile dysfunction. *Eur Urol* 2007;52(1):54-70.
- Trinchieri A, Nicola M, Masini F et al. Prospective comprehensive assessment of sexual function after retropublic non nerve sparing radical prostatectomy for localized prostate cancer. *Arch Ital Urol Androl* 2005;77(4):219-223.
- Truss M C, Becker A J, Djamilian M H et al. Role of the nitric oxide donor linsidomine chlorhydrate (SIN-1) in the diagnosis and treatment of erectile dysfunction. *Urology* 1994;44(4):553-556.
- Tsai S K, Hong C Y. Intracavernosal metaraminol for treatment of intraoperative penile erection. *Postgrad Med J* 1990;66(780):831-833.
- Tsujimura A, Matsumiya K, Matsuoka Y et al. Bioavailable testosterone with age and erectile dysfunction. *Br J Urol* 2003;170(6 Pt 1):2345-2347.
- Tuzgen S, Karamehmetoglu S S, Karacan I et al. Use of sildenafil in the treatment of erectile dysfunction in patients with spinal cord injury. *Neurosurgery Quarterly* 2006;16(1):40-43.
- Tzivoni D, Klein J, Hisdai D et al. The Israel Heart Society expert consensus document: The cardiac patient and sexual activity in the era of sildenafil (Viagra). *Israel Medical Association Journal*: Imaj 2000;2(1):63-65.
- Unnikrishnan A G, Rajaratnam S, Seshadri M S et al. The 'hook effect' on serum prolactin estimation in a patient with macroprolactinoma. *Neurol India* 2001;49(1):78-80.
- Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Uygun M C, Arik A I, Altug U et al. Effects of the 5 alpha-reductase inhibitor finasteride on serum levels of gonadal, adrenal, and hypophyseal hormones and its clinical significance: a prospective clinical study. *Steroids* 1998;63(4):208-213.
- Valdevenito R, Melman A. Intracavernous self-injection pharmacotherapy program: analysis of results and complications. *Int J Impot Res* 1994;6(2):81-91.
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy.[comment]. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Jonker-Pool G et al. Sexual functioning in testosterone-supplemented patients treated for bilateral testicular cancer. *Br J Urol* 1997;79(3):461-467.
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Dijk M, Skrekas T, De La et al. The association between lower urinary tract symptoms and sexual dysfunction: Fact or fiction?. *Curr Opin Urol* 2005;15(1):39-44.
- Van Moorselaar J. LUTS and Sexual Dysfunction: Implications for Management of BPH. *European Urology Supplements* 2003;2(10):13-20.
- Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
- Vatansever H S, Kayikcioglu O, Gumus B. Histopathologic effect of chronic use of sildenafil citrate on the choroid & retina in male rats. *Indian J Med Res* 2003;117(MAY):211-215.
- Verit A, Oguz H. Ophthalmic aspects of erectile dysfunction drugs [3]. *Am J Ophthalmol* 2006;141(3):598
- Vick R N, Benevides M, Patel M et al. The efficacy, safety and tolerability of intracavernous PNU-83757 for the treatment of erectile dysfunction.. *Br J Urol* 2002;167(6):2618-2623.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Vickers M A, Wright E A. Erectile dysfunction in the patient with diabetes mellitus. *Am J Manag Care* 2004;10(1 SUPPL.):S3-S11.
- Vidal J, Curcoll L, Roig T et al. Intracavernous pharmacotherapy for management of erectile dysfunction in multiple sclerosis patients. *Rev Neurol* 1995;23(120):269-271.
- Vinik A I, Maser R E, Mitchell B D et al. Diabetic autonomic neuropathy. [Review] [192 refs]. *Diabetes Care* 2003;26(5):1553-1579.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.

- Vitezic D. A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction. [Review] [72 refs]. *Drug Saf* 2001;24(4):255-265.
- Vlachopoulos C, Hirata K, O'Rourke M F. Effect of sildenafil on arterial stiffness and wave reflection. *Vasc Med* 2003;8(4):243-248.
- Vogt H J, Brandl P, Kockott G et al. Double-blind, placebo-controlled safety and efficacy trial with yohimbine hydrochloride in the treatment of nonorganic erectile dysfunction. *Int J Impot Res* 1997;9(3):155-161.
- Wagner G, Mulhall J. Pathophysiology and diagnosis of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):3-10.
- Wagner G, Rabkin J, Rabkin R. Effects of testosterone replacement therapy on sexual interest, function, and behavior in HIV+ men. *J Sex Res* 1997;34(1):27-33.
- Wagner Gorm, Kaplan Helen, Singer. The new injection treatment for impotence: Medical and psychological aspects. *Refuat Hapeh Vehashinayim* 1993;x, 210 pp. Philadelphia, PA, US210
- Wagrell L, Schelin S, Nordling J et al. Three-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomized multicenter study. *Urology* 2004;64(4):698-702.
- Wald M, Seftel A D, Ross L S et al. Computational models for detection of erectile dysfunction. *Br J Urol* 2005;173(1):167-170.
- Waldbaum R S. The safety of PDE5 inhibitors in ED treatment: Putting cardiovascular concerns to rest. *Cardiology Review* 2005;22(9):23-24.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Wang Z, Liu B C, Chen B et al. Randomized controlled study on erectile dysfunction treated by trazodone. *Chinese Journal of Andrology* 2002;16(3):236-238.
- Ware J, Catesby Rose F, Vincent McBrayer et al. The acute effects of nefazodone, trazodone and buspirone on sleep and sleep-related penile tumescence in normal subjects. *Sleep: Journal of Sleep Research & Sleep Medicine* 1994;17(6):544-550.
- Watanabe T, Chancellor M B, Rivas D A et al. Epidemiology of current treatment for sexual dysfunction in spinal cord injured men in the USA model spinal cord injury centers. *J Spinal Cord Med* 1996;19(3):186-189.
- Webb D J, Freestone S, Allen M J et al. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. *Am J Cardiol* 1999;83(5A):21C-28C.
- Webb D J, Muirhead G J, Wulff M et al. Sildenafil citrate potentiates the hypotensive effects of nitric oxide donor drugs in male patients with stable angina. *J Am Coll Cardiol* 2000;36(1):25-31.
- Wegner H E H, Knispel H H, Meier T et al. Nitric oxide donor, linsidomine chlorhydrate (SIN-1), in the diagnosis and treatment of erectile dysfunction: Critical appraisal and review of the literature. *International Urology & Nephrology* 1995;27(5):621-628.
- Weinhardt L S, Carey M P. Prevalence of erectile disorder among men with diabetes mellitus: Comprehensive review, methodological critique, and suggestions for future research. *J Sex Res* 1996;33(3):205-214.
- Weinsaft J W, Hickey K, Bokhari S et al. Effects of tadalafil on myocardial blood flow in patients with coronary artery disease. *Coron Artery Dis* 2006;17(6):493-499.
- Weiske W-H. Invasive diagnosis and therapy - Are they still reasonable in the age of sildenafil?. *Andrologia* 1999;31(SUPPL. 1):95-97.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Wessells H, Fuciarelli K, Hansen J et al. Synthetic melanotropic peptide initiates erections in men with psychogenic erectile dysfunction: double-blind, placebo controlled crossover study. *Br J Urol* 1998;160(2):389-393.
- Wessells H, Gralnek D, Dorr R et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000;56(4):641-646.
- Wheatley D. Triple-blind, placebo-controlled trial of Ginkgo biloba in sexual dysfunction due to antidepressant drugs. *Hum Psychopharmacol* 2004;19(8):545-548.
- Wilke D R, Parker C, Andonowski A et al. Testosterone and erectile function recovery after radiotherapy and long-term androgen deprivation with luteinizing hormone-releasing hormone agonists. *BJU Int* 2006;97(5):963-968.
- Williams G. Male erectile dysfunction. *Prescribers' Journal* 2000;40(1):49-58.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):

- Wilt T J, Fink H A. Is antidepressant plus sildenafil a recipe for priapism?. *Postgrad Med* 2004;116(6):11-12.
- Witt Deborah K. Yohimbine for erectile dysfunction. *J Fam Pract* 1998;46(4):282-283.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wyllie M G. The hunt for pink Viagra. *BJU Int* 2005;95(1):181-182.
- Wyllie M G. Let's hope for more in 2004. *BJU Int* 2004;93(1):175-176.
- Wyllie M G. The Second International Consultation on Erectile Dysfunction: Highlights from the pharmaceutical industry. *BJU Int* 2003;92(6):645-646.
- Wyllie M G. The genesis of a phytopharmaceutical industry (Mark II). *BJU Int* 2003;91(7):721-722.
- Yajima T, Yajima Y, Koppiker N et al. No clinically important effects on intraocular pressure after short-term administration of sildenafil citrate (Viagra). *Am J Ophthalmol* 2000;129(5):675-676.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yaman O, Tokatli Z, Akand M et al. Characteristics of sildenafil erections in healthy young men. *Asian J Androl* 2005;7(4):395-398.
- Yamanaka M, Shirai M, Shiina H et al. Vascular endothelial growth factor restores erectile function through inhibition of apoptosis in diabetic rat penile crura. *Br J Urol* 2005;173(1):318-323.
- Yan J Y, Yang W Z. A comparative effects of Sildenafil and Yohimbine for the treatment of erectile dysfunction. *Chinese Journal of Andrology* 2000;14(2):103-105.
- Yarkony G M. Enhancement of sexual function and fertility in spinal cord-injured males. [Review] [40 refs]. *Am J Phys Med Rehabil* 1990;69(2):81-87.
- Yassin A A, Saad F. Treatment of sexual dysfunction of hypogonadal patients with long-acting testosterone undecanoate (Nebido). [Review] [25 refs]. *World J Urol* 2006;24(6):639-644.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.
- Yasumoto R, Nishisaka N, Sakakura T et al. Ethanol embolization for impotent patients with venous leakage: A new technique and initial results. *Minimally Invasive Therapy & Allied Technologies: Mitat* 1996;5(6):564-566.
- Yeager J, Beihn R M. Retention and migration of alprostadil cream applied topically to the glans meatus for erectile dysfunction. *Int J Impot Res* 2005;17(1):91-95.
- Youssef A F, Fort F L, Ronsen B et al. Evaluation of apomorphine HCl effects on reproductive endpoints: Studies in male rats and dogs. *J Toxicol Sci* 1999;51(2):273-279.
- Zaslau S, Nicolis C, Galea G et al. A simplified pharmacologic erection program for patients with spinal cord injury. *J Spinal Cord Med* 1999;22(4):303-307.
- Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200
- Zhao L. Clinical observation on the therapeutic effects of heavy moxibustion plus point-injection in treatment of impotence. *J Tradit Chin Med* 2004;24(2):126-127.
- Zhigang Long, Xiaowei Liu, Shengbo Lu. Therapy of impotence with traditional Chinese medicine. *Journal of Sex Education & Therapy* 1994;20(2):140-143.
- Ziegler D. Management of erectile dysfunction in diabetic patients. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):58-65.
- Zini Dante, Carani Cesare, Baldini Augusto et al. Sexual behavior of men with isolated hypogonadotropic hypogonadism or prepubertal anterior panhypopituitarism. *Horm Behav* 1990;24(2):174-185.
- Zlotta A R, Teillac P, Raynaud J P et al. Evaluation of male sexual function in patients with Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), Tamsulosin or Finasteride. *Eur Urol* 2005;48(2):269-276.
- Zusman R M. Cardiovascular data on sildenafil citrate: introduction.[erratum appears in *Am J Cardiol* 1999 Jul 15;84(2):244]. *Am J Cardiol* 1999;83(5A):1C-2C.
- Zusman R M, Morales A, Glasser D B et al. Overall cardiovascular profile of sildenafil citrate. [Review] [33 refs]. *Am J Cardiol* 1999;83(5A):35C-44C.
- Zusman R M, Prisant L M, Brown M J. Effect of sildenafil citrate on blood pressure and heart rate in men with erectile dysfunction taking concomitant antihypertensive medication. Sildenafil Study Group. *J Hypertens* 2000;18(12):1865-1869.

Observational injection study with < 6 months followup in duration.

- Bancroft J, Smith G, Munoz M et al. Erectile response to visual erotic stimuli before and after intracavernosal papaverine, and its relationship to nocturnal penile tumescence and psychometric assessment. *Br J Urol* 1991;68(6):629-638.
- Beretta G, Marzotto M, Zanollo A et al. Office treatment: intracavernous injections of prostaglandin E1 (PG E1) and improvement of spontaneous erections. *Acta Eur Fertil* 1991;22(4):221-223.
- Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.
- Brown S L, Haas C A, Koehler M et al. Hepatotoxicity related to intracavernous pharmacotherapy with papaverine. *Urology* 1998;52(5):844-847.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Chun S S, Fenemore J, Heaton J P et al. Enhancement of erectile responses to vasoactive drugs by a variable amplitude oscillation device. *Int J Impot Res* 1996;8(4):221-225.
- Dinsmore W W, Alderdice D K. Vasoactive intestinal polypeptide and phentolamine mesylate administered by autoinjector in the treatment of patients with erectile dysfunction resistant to other intracavernosal agents. *Br J Urol* 1998;81(3):437-440.
- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Goonawardena S A, de Silva W A, Ketheeswaran T. Pharmacologically induced penile erections in the assessment and treatment of erectile impotence: a preliminary study of 100 patients. *Ceylon Med J* 1997;42(2):72-74.
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.
- Kadioglu A, Erdogru T, Tellaloglu S. Combined intracavernous injection of papaverine and stimulation (CIS) test. *J Androl* 1994;15 Suppl50S-53S.
- Katlowitz N M, Albano G J, Morales P et al. Potentiation of drug-induced erection with audiovisual sexual stimulation. *Urology* 1993;41(5):431-434.
- Katlowitz N, Albano G J, Patsias G et al. Effect of multidose intracorporeal injection and audiovisual sexual stimulation in vasculogenic impotence. *Urology* 1993;42(6):695-697.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Mansi M K, Alkhubair W K, Huraib S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *Br J Urol* 1998;159(6):1927-1930.
- McMahon C G. A pilot study of the role of intracavernous injection of vasoactive intestinal peptide (VIP) and phentolamine mesylate in the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(4):233-236.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Mirone V, Imbimbo C, Fabrizio F et al. Ketanserin plus prostaglandin E1 (PGE-1) as intracavernosal therapy for patients with erectile dysfunction unresponsive to PGE-1 alone. *Br J Urol* 1996;77(5):736-739.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Pagani E, Puech-Leao P, Glina S et al. The value of a second injection on the pharmaco-induced erection test. *Int J Impot Res* 1997;9(3):167-168.

Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.

Rodilla F, Fuentes M D, Chuan P et al. Penile self-injection for impotence in patients after radical cystectomy. *Journal of Clinical Pharmacy & Therapeutics* 1994;19(6):359-360.

Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.

Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266

Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.

Stief C G, Holmquist F, Djamilian M et al. Preliminary results with the nitric oxide donor linsidomine chlorhydrate in the treatment of human erectile dysfunction. *Br J Urol* 1992;148(5):1437-1440.

Stief C G, Wetterauer U, Schaebdsau F H et al. Calcitonin-gene-related peptide: a possible role in human penile erection and its therapeutic application in impotent patients. *Br J Urol* 1991;146(4):1010-1014.

Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.

Weiss J N, Ravalli R, Badlani G H. Intracavernous pharmacotherapy in psychogenic impotence. *Urology* 1991;37(5):441-443.

Observational injection study > or = to 6 months in duration.

al-Juburi A Z, O'Donnell P D. Follow up outcome of intracavernous papaverine. *J Ark Med Soc* 1990;86(10):383-385.

Armstrong D K, Convery A G, Dinsmore W W. Reasons for patient drop-out from an intracavernous auto-injection programme for erectile dysfunction. *Br J Urol* 1994;74(1):99-101.

Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.

Chen J, Godschalk M F, Katz P G et al. Incidence of penile pain after injection of a new formulation of prostaglandin E1.[see comment]. *Br J Urol* 1995;154(1):77-79.

Chen J, Godschalk M F, Katz P G et al. Combining intracavernous injection and external vacuum as treatment for erectile dysfunction.[see comment]. *Br J Urol* 1995;153(5):1476-1477.

Cooper A J. Evaluation of I-C papaverine in patients with psychogenic and organic impotence. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1991;36(8):574-578.

Dhabuwala C B, Kerkar P, Bhutwala A et al. Intracavernous papaverine in the management of psychogenic impotence. *Arch Androl* 1990;24(2):185-191.

Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.

Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.

Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.

Godschalk M, Gheorghiu D, Chen J et al. Long-term efficacy of a new formulation of prostaglandin E1 as treatment for erectile failure.. *Br J Urol* 1996;155(3):915-917.

Govier F E, McClure R D, Weissman R M et al. Experience with triple-drug therapy in a pharmacological erection program.[see comment]. *Br J Urol* 1993;150(6):1822-1824.

Incrocci L, Hop W C, Slob A K. Visual erotic and vibrotactile stimulation and intracavernous injection in screening men with erectile dysfunction: a 3 year experience with 406 cases. *Int J Impot Res* 1996;8(4):227-232.

Irwin M B, Kata E J. High attrition rate with intracavernous injection of prostaglandin E1 for impotency. *Urology* 1994;43(1):84-87.

Jiann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.

Kattan S A. The acceptance of satisfaction of Saudi males to vasoactive autoinjection intracavernous therapy, external negative pressure device and penile prosthesis in the treatment of erectile dysfunction. *Ann Saudi Med* 2002;22(3-4):149-152.

- Knispel H H, Huland H. Influence of cause on choice of therapy in 174 patients with erectile dysfunction. *Br J Urol* 1992;147(5):1274-1276.
- Lim P H, Ng F C. Erectile dysfunction in Singapore men: presentation, diagnosis, treatment and results. *Ann Acad Med Singapore* 1992;21(2):248-253.
- Lottman P E, Hendriks J C, Vrugink P A et al. The impact of marital satisfaction and psychological counselling on the outcome of ICI-treatment in men with ED. *Int J Impot Res* 1998;10(2):83-87.
- Lundberg L, Olsson J-O, Kihl B. Long-term experience of self-injection therapy with prostaglandin E1 for erectile dysfunction. *Scand J Urol Nephrol* 1996;30(5):395-397.
- Maniam P, Seftel A D, Corty E W et al. Nocturnal penile tumescence activity unchanged after long-term intracavernous injection therapy. *Br J Urol* 2001;165(3):830-832.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993;42(5):554-558.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Four-drug intracavernous therapy for impotence due to corporeal veno-occlusive dysfunction. *Br J Urol* 1993;149(5 Pt 2):1291-1295.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Intracavernous vasoactive pharmacotherapy: the impact of a new self-injection device.[see comment]. *Br J Urol* 1993;150(6):1829-1832.
- Mulhall J P, Jahoda A E, Cairney M et al. The causes of patient dropout from penile self-injection therapy for impotence. *Br J Urol* 1999;162(4):1291-1294.
- Mulhall J P, Land S, Parker M et al. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *Br J Sex Med* 2005;2(4):532-542.
- Perimenis P, Athanasopoulos A, Geramoutsos I et al. The incidence of pharmacologically induced priapism in the diagnostic and therapeutic management of 685 men with erectile dysfunction. *Urol Int* 2001;66(1):27-29.
- Rowland D L, Boedhoe H S M, Dohle G et al. Intracavernosal self-injection therapy in men with erectile dysfunction: Satisfaction and attrition in 119 patients. *Int J Impot Res* 1999;11(3):145-151.
- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Speckens A E, Kattemolle M R, Hengeveld M W et al. A prospective long-term follow-up study of patients evaluated for erectile dysfunction: outcome and associated factors. *Int J Impot Res* 1995;7(2):101-110.
- Tariq S H, Haleem U, Omran M L et al. Erectile dysfunction: Etiology and treatment in young and old patients. *Clin Geriatr Med* 2003;19(3):539-551.
- Turner L A, Althof S E. The clinical effectiveness of self-injection and external vacuum devices in the treatment of erectile dysfunction: a six-month comparison. *Psychiatr Med* 1992;10(2):283-293.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Weidner W, Schroeder-Printzen I, Fischer C et al. Experience in the treatment of erectile dysfunction using the intracavernosal self-injection of papaverine: Results of a prospective study after a median follow-up of 42 months involving 135 patients and 10766 injections. *World J Urol* 1992;10(3):179-182.
- Weiss J N, Badlani G H, Ravalli R et al. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6(3):171-174.
- Not relevant by study design.**
- Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.
- Anderson D C, Seifert C F. Topical nitrate treatment of impotence. [Review] [17 refs]. *Ann Pharmacother* 1993;27(10):1203-1205.
- Anonymous. Sildenafil for erectile dysfunction. *Drug Ther.Bull* 1998;36(11):81-84.
- Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.
- Anonymous. Vasoactive intestinal peptide/phentolamine. *Invicorp, vasopotin. Drugs in R & D* 1999;2(6):436-438.
- Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;
- Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329

- Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.
- Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.
- Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.
- Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.
- Chiang H-S, Kao Y H, Sheu M T. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995;24(5):767-769.
- Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.
- Derry F, Hultling C, Seftel A D et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. *Urology* 2002;60(2 Suppl 2):49-57.
- Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol.* 1998;159(2):433-436.
- Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.
- Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.
- Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.
- Hellstrom W J. Vardenafil: a new approach to the treatment of erectile dysfunction. [Review] [37 refs]. *Curr Urol Rep* 2003;4(6):479-487.
- Holmes S. Tadalafil: a new treatment for erectile dysfunction. *BJU Int* 2003;91(6):466-468.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- Keating G M, Scott L J. Vardenafil: a review of its use in erectile dysfunction. *Drugs* 2003;63(23):2673-2703.
- Keating G M, Scott L J. Spotlight on vardenafil in erectile dysfunction. *Drugs Aging* 2004;21(2):135-140.
- Kloner R A. Cardiovascular effects of the 3 phosphodiesterase-5 inhibitors approved for the treatment of erectile dysfunction. [Review] [57 refs]. *Circulation* 2004;110(19):3149-3155.
- Langtry H D, Markham A. Sildenafil: a review of its use in erectile dysfunction. *Drugs* 1999;57(6):967-989.
- Lewis R W. Intraurethral and topical agents. *Med Actual* 2000;36(2-3):113-119.
- Licht M R, Schover L R. Sildenafil (Viagra) for treating male erectile dysfunction. *Cleve Clin J Med* 1998;65(6):
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.
- McMahon C G. Topiglan: MacroChem. *Curr Opin Investig Drugs* 2002;3(4):602-606.
- Mikhail N. Does Testosterone Have a Role in Erectile Function?. *Am J Med* 2006;119:373-382.
- Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *Br J Sex Med* 2005;2(5):658-667.
- Moore R A, Derry S, McQuay H J. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. [Review] [77 refs]. *BMC Urol* 2005;5:18
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol.* 2002;2:6
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.

Padma-Nathan H, Eardley I, Kloner R A et al. A 4-year update on the safety of sildenafil citrate (Viagra). [Review] [88 refs]. *Urology* 2002;60(2:Suppl 2):Suppl-90.

Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.

Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382

Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.

Sommer F, Engelmann U. Vardenafil: Bayer Yakuhin. *Curr Opin Investig Drugs* 2002;3(4):607-613.

Sternbach Harvey. Age-associated testosterone decline in men: Clinical issues for psychiatry. *Am J Psychiatry* 1998;155(10):1310-1318.

Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect. Disord.* 2005;88(3):241-254.

Tomsak R. PDE5 inhibitors and permanent visual loss. *Int J Impot Res* 2005;17(6):547-549.

Tran D, Howes L G. Cardiovascular safety of sildenafil. *Drug Saf* 2003;26(7):453-460.

Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784

Not an original study, or population of interest, intervention of interest, or outcome of interest.

Abdallah H M. Comparison of Alprostadil (Caverject) and a combination of vasoactive drugs as local injections for the treatment of erectile dysfunction. *Int Urol Nephrol* 1998;30(5):617-620.

Abrams J. Time course of the interaction between tadalafil and nitrates. [comment]. *J Am Coll Cardiol* 2004;43(11):2150-2151.

Adaikan P G, Chong Y S, Chew S S L et al. Male sexual dysfunction. *Curr Obstet Gynaecol* 2000;10(1):23-28.

Adams M A, Perdok R J, Padley R J et al. Safety and tolerability of apomorphine SL in men with cardiovascular disorders. *European Urology Supplements* 2002;1(3):28-32.

Agelink M W, Schmitz T, Rembrink K et al. Cardiovascular effects of sildenafil citrate (Viagra): a naturalistic cross-over study. *Eur J Med Res* 2001;6(11):459-464.

Ahuja S K, Krane N K, Hellstrom W J. Penile prostheses in the management of impotence in patients with end-stage renal disease. *J La State Med Soc* 1998;150(1):32-34.

Aizenberg Dov, Gur Shay, Zemishlany Zvi et al. Mianserin, a 5-HT-sub(2a/2c) and alpha -sub-2 antagonist, in the treatment of sexual dysfunction induced by serotonin reuptake inhibitors. *Clin Neuropharmacol* 1997;20(3):210-214.

Aizenberg Dov, Weizman Abraham, Barak Yoram et al. Sildenafil for selective serotonin reuptake inhibitor-induced erectile dysfunction in elderly male depressed patients. [References]. *J Sex Marital Ther* 2003;29(4):297-303.

al-Juburi A Z, O'Donnell P D. Follow up outcome of intracavernous papaverine. *J Ark Med Soc* 1990;86(10):383-385.

Alivizatos G, Skolarikos A, Laguna P. Recent data upon impotence, incontinence and quality of life issues concerning radical prostatectomy. [Review] [74 refs]. *Arch Esp Urol* 2003;56(3):321-330.

Allan C A, McLachlan R I. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol (Oxf)* 2004;60(6):653-670.

Althof S E, Cappelleri J C, Shpilsky A et al. Treatment responsiveness of the Self-Esteem And Relationship questionnaire in erectile dysfunction. *Urology* 2003;61(5):888-892.

Althof S E, O' Leary M P, Cappelleri J C et al. Self-esteem, confidence, and relationships in men treated with sildenafil citrate for erectile dysfunction: results of two double-blind, placebo-controlled trials. *J Gen Intern Med* 2006;21(10):1069-1074.

Altwein J E, Keuler F U. Oral treatment of erectile dysfunction with apomorphine SL. [Review] [34 refs]. *Urol Int* 2001;67(4):257-263.

Anderson D C, Seifert C F. Topical nitrate treatment of impotence. [Review] [17 refs]. *Ann Pharmacother* 1993;27(10):1203-1205.

Anderson R A, Bancroft J, Wu F C. The effects of exogenous testosterone on sexuality and mood of normal men. *Journal of Clinical Endocrinology & Metabolism* 1992;75(6):1503-1507.

Andersson K-E. Pharmacology of penile erection. *Pharmacol Rev* 2001;53(3):417-450.

Anonymous. Sildenafil and erectile dysfunction: new preparation. *Helpful. Prescrire.Int* 1998;7(38):163-165.

- Anonymous. Sublingual apomorphine: new preparation. In erectile disorders: a narrow therapeutic margin. *Prescrire.Int* 2002;11(59):76-79.
- Anonymous. Vardenafil (levitra) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1166):77-78.
- Anonymous. Viagra: a blueprint for safety and reliability. *Johns Hopkins Medical Letter, Health After 50* 2002;14(10):4-5.
- Anonymous. Vasoactive intestinal peptide/phentolamine. *Invicorp, vasopotin. Drugs in R & D* 1999;2(6):436-438.
- Anonymous. Treatment for impotence gains FDA approval. *Am J Health Syst Pharm* 1995;52(19):2078-2079.
- Anonymous. L-arginine. *Altern Med Rev* 2005;10(2):139-147.
- Anonymous. Use of sildenafil for ED classes II and III. *S Afr Med J* 2005;95(1):38
- Anonymous. Patient preference of ED drugs studied. *British Journal of Diabetes & Vascular Disease* 2003;3(6):444
- Anonymous. New drug for erectile dysfunction. *Can Pharm J* 2002;268(7200):756
- Anonymous. Vardenafil improves erectile function in men with diabetes. *Can Pharm J* 2001;267(7155):
- Anonymous. Alprostadil for erectile impotence. *Drug & Therapeutics Bulletin* 1995;33(8):61-62.
- Anonymous. What to do if Viagra won't do. *Harvard Mens Health Watch* 2005;9(10):4-8.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: intracavernous injection of prostaglandin E1. *JAMA* 1991;265(24):3321-3323.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: papaverine and phentolamine. *JAMA* 1990;264(6):752-754.
- Aranda P, Ruilope L M, Calvo C et al. Erectile dysfunction in essential arterial hypertension and effects of sildenafil: results of a Spanish national study. *Am J Hypertens* 2004;17(2):139-145.
- Ardicoglu A, Kocakoc E, Tuygun U O et al. Effectiveness of vardenafil versus papaverine in penile Doppler ultrasonography. *Urol Int* 2005;75(1):75-79.
- Ardicoglu A, Kocakoc E, Yuzgec V et al. Hemodynamic effects of sildenafil citrate (Viagra) on segmental branches of bilateral renal arteries. *International Urology & Nephrology* 2005;37(4):785-789.
- Armstrong D K, Convery A G, Dinsmore W W. Reasons for patient drop-out from an intracavernous auto-injection programme for erectile dysfunction. *Br J Urol* 1994;74(1):99-101.
- Armstrong D K, Convery A, Dinsmore W W. Prostaglandin E1 in the medical management of erectile dysfunction in a genito-urinary medicine clinic. *Ulster Med J* 1994;63(1):18-22.
- Arver S, Dobs A S, Meikle A W et al. Improvement of sexual function in testosterone deficient men treated for 1 year with a permeation enhanced testosterone transdermal system. *Br J Urol* 1996;155(5):1604-1608.
- Ashok S, Sigman M. Bioavailable testosterone should be used for the determination of androgen levels in infertile men. *Br J Urol* 2007;177(4):1443-1446.
- Ashton Adam, Keller. Yohimbine in the treatment of male erectile dysfunction. *Am J Psychiatry* 1994;151(9):1397
- Assalian Pierre. Sildenafil for St. John wort-induced sexual dysfunction. [References]. *J Sex Marital Ther* 2000;26(4):357-358.
- Atmaca M, Kuloglu M, Tezcan E. Sildenafil use in patients with olanzapine-induced erectile dysfunction. *Int J Impot Res* 2002;14(6):547-549.
- Aukst-Margetic B, Margetic B. An open-label series using loratadine for the treatment of sexual dysfunction associated with selective serotonin reuptake inhibitors. *Prog Neuropsychopharmacol Biol Psychiatry* 2005;29(5):754-756.
- Aversa A, Bonifacio V, Moretti C et al. Re-dosing of prostaglandin-E1 versus prostaglandin-E1 plus phentolamine in male erectile dysfunction: a dynamic color power Doppler study. *Int J Impot Res* 2000;12(1):33-40.
- Aviv A, Shelef A, Weizman A. An open-label trial of sildenafil addition in risperidone-treated male schizophrenia patients with erectile dysfunction. *Hillside J Clin Psychiatry* 2004;65(1):97-103.
- Ayub W, Fletcher S. End-stage renal disease and erectile dysfunction. Is there any hope?. *Nephrology Dialysis Transplantation* 2000;15(10):1525-1528.
- Bacar M M, Batislam E, Altinok D et al. Sildenafil citrate for penile hemodynamic determination: an alternative to intracavernosal agents in Doppler ultrasound evaluation of erectile dysfunction. *Urology* 2001;57(4):623-626.
- Bach Amy K, Barlow David H, Wincze John P E. The enhancing effects of manualized treatment for erectile dysfunction among men using sildenafil: A preliminary investigation. [References]. *Behav Ther* 2004;35(1):55-73.

- Bai W J, Zhu J C, Jiang H et al. [A comparative study of different vasoactive drugs in the treatment of impotence]. *Chinese Journal of Urology* 1992;13(6):453-455.
- Bain J. Andropause. Testosterone replacement therapy for aging men. [Review] [55 refs]. *Can Fam Physician* 2001;47:91-97.
- Balon Richard. Sildenafil and sexual dysfunction associated with antidepressants. [References]. *J Sex Marital Ther* 1999;25(4):259-264.
- Balon Richard. Fluvoxamine-induced erectile dysfunction responding to sildenafil. *J Sex Marital Ther* 1998;24(4):313-317.
- Bancroft J, Gutierrez P. Erectile dysfunction in men with and without diabetes mellitus: a comparative study.[see comment]. *Diabet Med* 1996;13(1):84-89.
- Bancroft J, Smith G, Munoz M et al. Erectile response to visual erotic stimuli before and after intracavernosal papaverine, and its relationship to nocturnal penile tumescence and psychometric assessment. *Br J Urol* 1991;68(6):629-638.
- Baniel J, Israilov S, Engelstein D et al. Three-year outcome of a progressive treatment program for erectile dysfunction with intracavernous injections of vasoactive drugs. *Urology* 2000;56(4):647-652.
- Barrou B, Cuzin B, Malavaud B et al. Early experience with sildenafil for the treatment of erectile dysfunction in renal transplant recipients. *Nephrol.Dial.Transplant.* 2003;18(2):411-417.
- Beal K, Mears J G. Short report: Penile lymphoma following local injections for erectile dysfunction. *Leuk Lymphoma* 2001;42(1-2):247-249.
- Becher E. Topical alprostadil cream for the treatment of erectile dysfunction. [Review] [46 refs]. *Expert Opin Pharmacother* 2004;5(3):623-632.
- Behrend L, Vibe-Petersen J, Perrild H. Sildenafil in the treatment of erectile dysfunction in men with diabetes: demand, efficacy and patient satisfaction. *Int J Impot Res* 2005;17(3):264-269.
- Bell D S H, Cutter G R, Hayne V B et al. Factors predicting efficacy of phentolamine-papaverine intracorporeal injection for treatment of erectile dysfunction in diabetic male. *Urology* 1992;40(1):36-40.
- Benatov R, Reznik I, Zemishlany Z. Sildenafil citrate (Viagra) treatment of sexual dysfunction in a schizophrenic patient. [References]. *Eur Psychiatry* 1999;14(6):353-355.
- Benchekroun A, Faik M, Benjelloun S et al. A baseline-controlled, open-label, flexible dose-escalation study to assess the safety and efficacy of sildenafil citrate (Viagra) in patients with erectile dysfunction. *Int J Impot Res* 2003;15(Suppl 1):19-24.
- Benevides M D, Carson C C. Intraurethral application of alprostadil in patients with failed inflatable penile prosthesis. *Br J Urol* 2000;163(3):785-787.
- Beretta G, Marzotto M, Zanollo A et al. Office treatment: intracavernous injections of prostaglandin E1 (PG E1) and improvement of spontaneous erections. *Acta Eur Fertil* 1991;22(4):221-223.
- Berner M M, Kriston L, Harms A. Efficacy of PDE-5-inhibitors for erectile dysfunction. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. *Int J Impot Res* 2005;
- Billington C J, Shafer R B, Morley J E. Effects of opioid blockade with nalmeferene in older impotent men. *Life Sci* 1990;47(9):799-805.
- Bird T D, Lipe H P, Crabtree L D. Impotence associated with the Charcot-Marie-Tooth syndrome. *Eur Neurol* 1994;34(3):155-157.
- Bischoff E. Vardenafil preclinical trial data: Potency, pharmacodynamics, pharmacokinetics, and adverse events. *Int J Impot Res* 2004;16(SUPPL. 1):S34-S37.
- Black A M, Day A G, Morales A. The reliability of clinical and biochemical assessment in symptomatic late-onset hypogonadism: Can a case be made for a 3-month therapeutic trial?. *BJU Int* 2004;94(7):1066-1070.
- Blanker M H, Thomas S, Bohnen A M. Systematic review of Viagra RCTs. *Br J Gen Pract* 2002;52(477):329
- Blonde L. Sildenafil citrate for erectile dysfunction in men with diabetes and cardiovascular risk factors: a retrospective analysis of pooled data from placebo-controlled trials. *Curr Med Res Opin* 2006;22(11):2111-2120.
- Bocchi E A, Guimaraes G, Mocelin A et al. Sildenafil effects on exercise, neurohormonal activation, and erectile dysfunction in congestive heart failure: a double-blind, placebo-controlled, randomized study followed by a prospective treatment for erectile dysfunction. *Circulation* 2002;106(9):1097-1103.
- Bodansky H J E. Successful tadalafil treatment for erectile dysfunction associated with Charcot-Marie-Tooth syndrome. [References]. *Sexual and Relationship Therapy* 2006;21(1):87-89.
- Bolona E R, Uruga M V, Haddad R M et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clin Proc* 2007;82(1):20-28.

- Bouloux P. Testim 1% testosterone gel for the treatment of male hypogonadism. [Review] [33 refs]. *Clin Ther* 2005;27(3):286-298.
- Boyarsky B K, Haque W, Rouleau M R et al. Sexual functioning in depressed outpatients taking mirtazapine. *Depression & Anxiety* 1999;9(4):175-179.
- Braatvedt G D. Outcome of managing impotence in clinical practice. *N Z Med J* 1999;112(1092):272-274.
- Brazil M. Viagra for broken hearts?. *Nat Rev Genet* 2005;4(3):190
- Briganti A, Salonia A, Gallina A et al. Drug insight: Oral phosphodiesterase type 5 inhibitors for erectile dysfunction. *Nature Clinical Practice Urology* 2005;2(5):239-247.
- Brignardello E, Manti R, Papotti M et al. Ectopic secretion of LH by an endocrine pancreatic tumor. *J Endocrinol Invest* 2004;27(4):361-365.
- Brindis R G, Kloner R A. Sildenafil in patients with cardiovascular disease. [Review] [33 refs]. *Am J Cardiol* 2003;92(9A):26M-36M.
- Brisson T E, Broderick G A, Thiel D D et al. Vardenafil rescue rates of sildenafil nonresponders: objective assessment of 327 patients with erectile dysfunction. *Urology* 2006;68(2):397-401.
- Brock G B, McMahon C G, Chen K K et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. *Br J Urol* 2002;168(4 Pt 1):1332-1336.
- Brock G, Chan J, Carrier S et al. The treatment of erectile dysfunction study: focus on treatment satisfaction of patients and partners. *BJU Int* 2007;99(2):376-382.
- Brown S L, Haas C A, Koehler M et al. Hepatotoxicity related to intracavernous pharmacotherapy with papaverine. *Urology* 1998;52(5):844-847.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. *Urologe* 2005;Ausg. A. 44(9):1045-1046, 1048-51.
- Burge M R, Lanzi R A, Skarda S T et al. Idiopathic hypogonadotropic hypogonadism in a male runner is reversed by clomiphene citrate. *Fertility & Sterility* 1997;67(4):783-785.
- Burls A, Gold L, Clark W. Systematic review of randomised controlled trials of sildenafil (Viagra) in the treatment of male erectile dysfunction. *Br J Gen.Pract.* 2001;51(473):1004-1012.
- Burnett A L. Vasoactive pharmacotherapy to cure erectile dysfunction: fact or fiction?. [Review] [45 refs]. *Urology* 2005;65(2):224-230.
- Burns-Cox N, Gingell C. The andropause: fact or fiction?. [Review] [49 refs]. *Postgrad Med J* 1997;73(863):553-556.
- Buvat J. Hyperprolactinemia and sexual function in men: a short review. [Review] [26 refs]. *Int J Impot Res* 2003;15(5):373-377.
- Buvat J, Montorsi F. Safety and tolerability of apomorphine SL in patients with erectile dysfunction. *BJU Int* 2001;88(3):30-35.
- Buvat J, Lemaire A, Ratajczyk J. Acceptance, efficacy and preference of Sildenafil in patients on long term auto-intracavernosal therapy: a study with follow-up at one year. *Int J Impot Res* 2002;14(6):483-486.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Cappelleri J C, Althof S E, Siegel R L et al. Association between the Erectile Dysfunction Inventory of Treatment Satisfaction and the Self-Esteem and Relationship Questionnaire following treatment with sildenafil citrate for men with erectile dysfunction. *Value Health* 2005;8(Suppl 1):54-60.
- Cappelleri J C, Bell S S, Althof S E et al. Comparison between sildenafil-treated subjects with erectile dysfunction and control subjects on the Self-Esteem And Relationship questionnaire. *Br J Sex Med* 2006;3(2):274-282.
- Carani C, Granata A R, Bancroft J et al. The effects of testosterone replacement on nocturnal penile tumescence and rigidity and erectile response to visual erotic stimuli in hypogonadal men. *Psychoneuroendocrinology* 1995;20(7):743-753.
- Carani C, Zini D, Baldini A et al. Effects of androgen treatment in impotent men with normal and low levels of free testosterone. *Arch Sex Behav* 1990;19(3):223-234.
- Caretta N, Palego P, Ferlin A et al. Resumption of spontaneous erections in selected patients affected by erectile dysfunction and various degrees of carotid wall alteration: Role of tadalafil. *Eur Urol* 2005;48(2):326-332.
- Carey F, Quah S P, Dinsmore W. Postal survey to determine how many patients continued to seek treatment with sildenafil following sildenafil trials. *Int J STD AIDS* 2003;14(7):501-502.
- Carey M P, Johnson B T. Effectiveness of yohimbine in the treatment of erectile disorder: four meta-analytic integrations. *Arch Sex Behav* 1996;25(4):341-360.

- Carosa E, Martini P, Brandetti F et al. Type V phosphodiesterase inhibitor treatments for erectile dysfunction increase testosterone levels. *Clin Endocrinol (Oxf)* 2004;61(3):382-386.
- Carson C C, Burnett A L, Levine L A et al. The efficacy of sildenafil citrate (Viagra) in clinical populations: an update. *Urology* 2002;60(2 Suppl 2):12-27.
- Carson C C, Rajfer J, Eardley I et al. The efficacy and safety of tadalafil: an update. *BJU Int* 2004;93(9):1276-1281.
- Caruso S, Intelisano G, Farina M et al. Efficacy and safety of daily intake of apomorphine SL in men affected by erectile dysfunction and mild hyperprolactinemia: a prospective, open-label, pilot study. *Urology* 2003;62(5):922-927.
- Casella R, Deckart A, Bachmann A et al. The patient's self-evaluation better predicts the degree of erectile dysfunction than the response to intracavernous alprostadil testing. *Urol Int* 2004;72(3):216-220.
- Chaiban J T, Azar S T. Erectile dysfunction in diabetic patients. *J Med Liban* 2004;52(4):217-219.
- Chatterjee R, Kottaridis P D, McGarrigle H H et al. Management of erectile dysfunction by combination therapy with testosterone and sildenafil in recipients of high-dose therapy for haematological malignancies. *Bone Marrow Transplant* 2002;29(7):607-610.
- Cheitlin M D, Hutter A M, Brindis R G et al. Use of sildenafil (Viagra) in patients with cardiovascular disease. *Circulation* 1999;99(1):168-177.
- Chen J K, Hwang T I, Yang C R. Comparison of effects following the intracorporeal injection of papaverine and prostaglandin E1. *Br J Urol* 1992;69(4):404-407.
- Chen J, Godschalk M F, Katz P G et al. Incidence of penile pain after injection of a new formulation of prostaglandin E1.[see comment]. *Br J Urol* 1995;154(1):77-79.
- Chen J, Godschalk M F, Katz P G et al. Combining intracavernous injection and external vacuum as treatment for erectile dysfunction.[see comment]. *Br J Urol* 1995;153(5):1476-1477.
- Chen J, Godschalk M, Katz P G et al. The lowest effective dose of prostaglandin E1 as treatment for erectile dysfunction.. *Br J Urol* 1995;153(1):80-81.
- Chen J, Mabeesh N J, Greenstein A et al. Clinical efficacy of sildenafil in patients on chronic dialysis. *Br J Urol* 2001;165(3):819-821.
- Chen J, Sofer M, Kaver I et al. Concomitant use of sildenafil and a vacuum entrapment device for the treatment of erectile dysfunction. *Br J Urol* 2004;171(1):292-295.
- Chen K-K, Jiann B-P, Lin J S N et al. Erratum: Efficacy and safety of on- demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double- blind, parallel, placebo-controlled clinical study (*Journal of Sexual Medicine* vol. 1 (2)). *Br J Sex Med* 2005;2(1):158
- Cheng E. Real-life safety and efficacy of vardenafil in the treatment of erectile dysfunction-results from 30,010 U.S. patients. *Br J Sex Med* 2007;4(2):432-439.
- Chew K K. Prevalence of hypogonadism in the aging male and male erectile dysfunction in Asia-Pacific countries. *Asian J Androl* 2003;5(2):171-172.
- Chew K K, Stuckey B G A. Use of transurethral alprostadil (MUSE) (prostaglandin E1) for glans tumescence in a patient with penile prosthesis. *Int J Impot Res* 2000;12(3):195-196.
- Chew K K, Stuckey B G A, Thompson P L. Erectile dysfunction, sildenafil and cardiovascular risk. *Med J Aust* 2000;172(6):279-283.
- Chia S. Management of premature ejaculation -- a comparison of treatment outcome in patients with and without erectile dysfunction. *Int J Androl* 2002;25(5):301-305.
- Chia S J, Ramesh K, Earnest A. Clinical application of prognostic factors for patients with organic causes of erectile dysfunction on 100 mg of sildenafil citrate. *Int J Urol* 2004;11(12):1104-1109.
- Chiang H S, Wen T C, Liang J F. Titration study of MUSE (Medicated Urethral System for Erection) in erectile dysfunction. *J Formos Med Assoc* 2000;99(12):926-930.
- Chiang H-S, Kao Y H, Sheu M T. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995;24(5):767-769.
- Chiang P-H, Tsai E-M, Chiang C-P. The role of trazodone in the treatment of erectile dysfunction. Kao-Hsiung i Hsueh Ko Hsueh Tsa Chih [Kaohsiung Journal of Medical Sciences] 1994;10(6):287-294.
- Chinegwundoh F, Anie K A. Treatments for priapism in boys and men with sickle cell disease. [Review] [16 refs]. *Cochrane Database Syst Rev* 2004;(4):CD004198
- Choi H K, Adimoelja A, Kim S C et al. A dose-response study of alprostadil sterile powder (S.Po.) (Caverject) for the treatment of erectile dysfunction in Korean and Indonesian men. *Int J Impot Res* 1997;9(1):47-51.

- Christ B, Brockmeier D, Hauck E W et al. Investigation on interaction between tacrolimus and sildenafil in kidney-transplanted patients with erectile dysfunction. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(3):149-156.
- Christ G J, Melman A. The application of gene therapy to the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):111-112.
- Chun S S, Fenemore J, Heaton J P et al. Enhancement of erectile responses to vasoactive drugs by a variable amplitude oscillation device. *Int J Impot Res* 1996;8(4):221-225.
- Clark C. Erectile dysfunction and other problems. *Can Pharm J* 2004;272(7299):608-610.
- Claro J A, Ximenes S F, Nardoza A et al. Effect of sildenafil in cavernous arteries of patients with erectile dysfunction. *International Braz J Urol* 2003;29(4):320-326.
- Cohen J S. Comparison of FDA reports of patient deaths associated with sildenafil and with injectable alprostadil. *Ann Pharmacother* 2001;35(3):285-288.
- Conti C R, Pepine C J, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. *Am J Cardiol* 1999;83(5A):29C-34C.
- Cooper A J. Evaluation of I-C papaverine in patients with psychogenic and organic impotence. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 1991;36(8):574-578.
- Copel L, Katz R, Blachar A et al. Clinical and duplex US assessment of effects of sildenafil on cavernosal arteries of the penis: Comparison with intracavernosal injection of vasoactive agents - Initial experience. *Radiology* 2005;237(3):986-991.
- Corona G, Mannucci E, Fisher A D et al. Effect of hyperprolactinemia in male patients consulting for sexual dysfunction. *Br J Sex Med* 2007;4(5):1485-1493.
- Corona G, Mannucci E, Schulman C et al. Psychobiologic correlates of the metabolic syndrome and associated sexual dysfunction. *Eur Urol* 2006;50(3):595-604.
- Costabile R A, Spevak M, Fishman I J et al. Efficacy and safety of transurethral alprostadil in patients with erectile dysfunction following radical prostatectomy. *Br J Urol* 1998;160(4):1325-1328.
- Crowe S M, Streetman D S. Vardenafil treatment for erectile dysfunction. [Review] [43 refs]. *Ann Pharmacother* 2004;38(1):77-85.
- Curran M, Keating G. Tadalafil.[erratum appears in *Drugs*. 2003;63(23):2703]. [Review] [31 refs]. *Drugs* 2003;63(20):2203-2212.
- Dachille G, Pagliarulo V, Ludovico G M et al. Sexual dysfunction in patients under dialytic treatment. *Minerva Urol Nefrol* 2006;58(2):195-200.
- Davis B E, Weigel J W, Whitford C S. Treatment of male impotence: a new option. *Kans Med* 1990;91(12):325-326.
- De Rose A F, Giglio M, Traverso P et al. Combined oral therapy with sildenafil and doxazosin for the treatment of non-organic erectile dysfunction refractory to sildenafil monotherapy. *Int J Impot Res* 2002;14(1):50-53.
- De Meyer J M, Thibo P, Hatzichriston D G. The effect of re-dosing of vasodilators on the intracavernosal pressure and on the penile rigidity. *Eur Urol* 1998;33(3):293-297.
- De Siati M, Saugo M, Franzolin N. The start of pharmacological activity after sublingual administration of sildenafil citrate in 30 patients affected by erectile dysfunction. *Arch Ital Urol Androl* 2003;75(1):18-20.
- Decter R M, Furness P D, Nguyen T A et al. Reproductive understanding, sexual functioning and testosterone levels in men with spina bifida. *Br J Urol* 1997;157(4):1466-1468.
- Derby C A, Araujo A B, Johannes C B et al. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 2000;12(4):197-204.
- Derry F, Hultling C, Seftel A D et al. Efficacy and safety of sildenafil citrate (Viagra) in men with erectile dysfunction and spinal cord injury: a review. *Urology* 2002;60(2 Suppl 2):49-57.
- Dhabuwala C B, Kerkar P, Bhutwala A et al. Intracavernous papaverine in the management of psychogenic impotence. *Arch Androl* 1990;24(2):185-191.
- Dinsmore W W. Medical treatment of impotence with papaverine and phentolamine intracavernosal injection. *Ulster Med J* 1990;59(2):174-176.
- Dinsmore W W, Alderdice D K. Vasoactive intestinal polypeptide and phentolamine mesylate administered by autoinjector in the treatment of patients with erectile dysfunction resistant to other intracavernosal agents. *Br J Urol* 1998;81(3):437-440.
- Dizon M N, Vesely D L. Gonadotropin-secreting pituitary tumor associated with hypersecretion of testosterone and hypogonadism after hypophysectomy. *Endocr Pract* 2002;8(3):225-231.

- Doggrell S A. Comparison of clinical trials with sildenafil, vardenafil and tadalafil in erectile dysfunction. *Expert Opin Pharmacother* 2005;6(1):75-84.
- Donatucci C F, Lue T F. Erectile dysfunction in men under 40: etiology and treatment choice. *Int J Impot Res* 1993;5(2):97-103.
- Donatucci C, Eardley I, Buvat J et al. Vardenafil improves erectile function in men with erectile dysfunction irrespective of disease severity and disease classification. *Br J Sex Med* 2004;1(3):301-309.
- Dundar S O, Dayanir Y, Topalolu A et al. Effect of sildenafil on ocular hemodynamics in 3 months regular use. *Int J Impot Res* 2006;18(3):282-286.
- Dundar S O, Topalolu A, Dundar M et al. Effects of sildenafil on blue-on-yellow and white-on-white Humphrey perimetry in 3 months regular use. *Arb Paul Ehrlich Inst Georg Speyer Haus Ferdinand Blum Inst Frankf A M* 2006;20(7):810-813.
- Dunn A. Sildenafil: A new therapy for erectile dysfunction. *Conn Med* 1998;62(7):413-416.
- Dusing R. Effect of the angiotensin II antagonist valsartan on sexual function in hypertensive men. *Blood Pressure Supplement* 2003;229-34.
- Eardley I. New oral therapies for the treatment of erectile dysfunction. *Br J Urol* 1998;81(1):122-127.
- El Malik E M A. Erectile dysfunction: An update of diagnosis and management. *Qatar Medical Journal* 2000;9(2):9-17.
- El-Sakka A I. Efficacy of sildenafil citrate in treatment of erectile dysfunction: effect of type 2 diabetes. *Eur Urol* 2004;46(4):503-509.
- El-Sakka A I. Efficacy of sildenafil citrate in treatment of erectile dysfunction: impact of associated premature ejaculation and low desire. *Urology* 2006;68(3):642-647.
- El-Sakka A I, Hassoba H M, Elbakry A M et al. Prostatic specific antigen in patients with hypogonadism: Effect of testosterone replacement. *Br J Sex Med* 2005;2(2):235-240.
- Elhanbly S, Schoor R, Elmogy M et al. What nonresponse to intracavernous injection really indicates: a determination by quantitative analysis. *Br J Urol* 2002;167(1):192-196.
- Engel J D, McVary K T. Transurethral alprostadil as therapy for patients who withdrew from or failed prior intracavernous injection therapy. *Urology* 1998;51(5):687-692.
- Engelhardt P F, Daha L K, Zils T et al. Acupuncture in the treatment of psychogenic erectile dysfunction: first results of a prospective randomized placebo-controlled study. *Int J Impot Res* 2003;15(5):343-346.
- Engelhardt P F, Plas E, Hubner W A et al. Comparison of intraurethral liposomal and intracavernosal prostaglandin-E1 in the management of erectile dysfunction. *Br J Urol* 1998;81(3):441-444.
- Engl T, Beecken W-D, Wolfram M et al. Uro pharmacology: Current and future strategies in the treatment of erectile dysfunction and benign prostate hyperplasia. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(10):527-533.
- English J C, King D H C, Foley J P. Penile shaft hypopigmentation: Lichen sclerosus occurring after the initiation of alprostadil intracavernous injections for erectile dysfunction. *J Am Acad Dermatol* 1998;39(5 D):801-803.
- Erbagci A, Yagci F, Sarica K et al. Evaluation and therapeutic regulation of erectile dysfunction with visual stimulation test. An objective approach by using sildenafil citrate test. *Urol.Int* 2002;69(1):21-26.
- Erdogru T, Usta M F, Ceken K et al. Is sildenafil citrate an alternative agent in the evaluation of penile vascular system with color Doppler ultrasound?. *Urol Int* 2002;68(4):255-260.
- Ernst E, Pittler M H. Yohimbine for erectile dysfunction: a systematic review and meta-analysis of randomized clinical trials. *J Urol.* 1998;159(2):433-436.
- Escobar-Jimenez F. [Efficacy and safety of sildenafil in men with type 2 diabetes mellitus and erectile dysfunction]. *Med Clin (Barc)* 2002;119(4):121-124.
- Espinoza R, Melchor J L, Gracida C. Sildenafil (Viagra) in kidney transplant recipients with erectile dysfunction. *Transplant Proc* 2002;34(1):408-409.
- Fagelman E, Fagelman A, Shabsigh R. Efficacy, safety, and use of sildenafil in urologic practice. *Urology* 2001;57(6):1141-1144.
- Fava M, Rankin M A, Alpert J E et al. An open trial of oral sildenafil in antidepressant-induced sexual dysfunction. *Psychotherapy & Psychosomatics* 1998;67(6):328-331.
- Fazeli-Matin S, Montague D K, Angermeier K W et al. Penile fracture after intracavernous injection therapy. *Br J Urol* 1998;159(6):2094
- Fedele D, Coscelli C, Cucinotta D et al. Management of erectile dysfunction in diabetic subjects: results from a survey of 400 diabetes centres in Italy. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2001;14(5):277-282.

- Fein R L. Classification of sexual dysfunction for management of intracavernous medication-induced erections.[see comment]. *Br J Urol* 1990;143(2):298-301.
- Feldman R, Meuleman E J, Steers W. Sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: analysis of two flexible dose-escalation studies. Sildenafil Study Group. *Int J Clin Pract* 1999;102(Suppl Jun.):100-102.
- Fink H A, Mac Donald R, Rutks I R et al. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. *Arch Intern Med* 2002;162(12):1349-1360.
- Fink H A, MacDonald R, Rutks I R et al. Trazodone for erectile dysfunction: a systematic review and meta-analysis. *BJU Int* 2003;92(4):441-446.
- Fishbain David A. Impact of sildenafil on male erectile disorder due to psychological factors. *Can J Psychiatry* 2000;45(1):85-86.
- Flack J M. The effect of doxazosin on sexual function in patients with benign prostatic hyperplasia, hypertension, or both.[see comment]. [Review] [47 refs]. *Int J Clin Pract* 2002;56(7):527-530.
- Fonseca V, Seftel A, Denne J et al. Impact of diabetes mellitus on the severity of erectile dysfunction and response to treatment: analysis of data from tadalafil clinical trials. *Diabetologia* 2004;47(11):1914-1923.
- Foresta C, Caretta N, Lana A et al. Relationship Between Vascular Damage Degrees and Endothelial Progenitor Cells in Patients with Erectile Dysfunction: Effect of Vardenafil Administration and PDE5 Expression in the Bone Marrow. *Eur Urol* 2007;51(5):1411-1419.
- Foresta C, Ferlin A, De Toni L et al. Circulating endothelial progenitor cells and endothelial function after chronic Tadalafil treatment in subjects with erectile dysfunction. *Int J Impot Res* 2006;18(5):484-488.
- Foulks C J, Cushner H M. Sexual dysfunction in the male dialysis patient: pathogenesis, evaluation, and therapy. [Review] [105 refs]. *Am J Kidney Dis* 1986;8(4):211-222.
- Fox K M, Thadani U, Ma P T et al. Sildenafil citrate does not reduce exercise tolerance in men with erectile dysfunction and chronic stable angina. *Eur Heart J* 2003;24(24):2206-2212.
- Freitas D, Athanazio R, Almeida D et al. Sildenafil improves quality of life in men with heart failure and erectile dysfunction. *Int J Impot Res* 2006;18(2):210-212.
- Fugl-Meyer A R, Lodnert G, Branholm I B et al. On life satisfaction in male erectile dysfunction. *Int J Impot Res* 1997;9(3):141-148.
- Fugl-Meyer K S, Stothard D, Belger M et al. The effect of tadalafil on psychosocial outcomes in Swedish men with erectile distress: a multicentre, non-randomised, open-label clinical study. *Int J Clin Pract* 2006;60(11):1386-1393.
- Fujisawa M, Sawada K. Clinical efficacy and safety of sildenafil in elderly patients with erectile dysfunction. *Arch Androl* 2004;50(4):255-260.
- Fulgham P F, Cochran J S, Denman J L et al. Disappointing initial results with transurethral alprostadil for erectile dysfunction in a urology practice setting.. *Br J Urol* 1998;160(6 Pt 1):2041-2046.
- Gana T E, Quizanos L F, Castell R et al. A dose-response study of alprostadil in patients with erectile dysfunction. *Curr Ther Res Clin Exp* 1996;57(9):700-710.
- Garcia-Bravo A M, Suarez-Hernandez D, Ruiz-Fernandez M A et al. Determination of changes in blood pressure during administration of sildenafil (Viagra) in patients with spinal cord injury and erectile dysfunction. *Proc Annu Clin Spinal Cord Inj Conf* 2006;44(5):301-308.
- Ghanem H, Sherif T, bdEl-Gawad T et al. Short term use of intracavernous vasoactive drugs in the treatment of persistent psychogenic erectile dysfunction. *Int J Impot Res* 1998;10(4):211-214.
- Gheorghiu S, Godschalk M, Gentili A et al. Quality of life in patients using self-administered intracavernous injections of prostaglandin E1 for erectile dysfunction. *Br J Urol* 1996;156(1):80-81.
- Giammusso B, Morgia G, Spampinato A et al. Improved pallesthetic sensitivity of pudendal nerve in impotent diabetic patients treated with acetyl-L-carnitine. *Acta Urologica Italica* 1996;10(3):185-187.
- Gil A, Martinez E, Oyaguez I et al. Erectile dysfunction in a primary care setting: results of an observational, no-control-group, prospective study with sildenafil under routine conditions of use. *Int J Impot Res* 2001;13(6):338-347.
- Gilbert H W, Gingell J C. The results of an intracorporeal papaverine clinic. *Sex Marital Ther* 1991;6(1):49-56.
- Gilbert H W, Gillatt D A, Desai K M et al. Intracorporeal papaverine injection in androgen deprived men. *J R Soc Med* 1990;83(3):161
- Gilbert R N, Graham C W, Regan J B. Double-blind-cross-over trial of testosterone enanthate in impotent men with low or low-normal serum testosterone levels. *Br J Urol* 1992;147264
- Gillies H C, Roblin D, Jackson G. Coronary and systemic hemodynamic effects of sildenafil citrate: From basic science to clinical studies in patients with cardiovascular disease. *Int J Cardiol* 2002;86(2-3):131-141.

- Gingell C, Buvat J, Jardin A et al. Sildenafil citrate (VIAGRA(TM)), an oral treatment for erectile function: 1-year, open-label, extension studies. *Int J Clin Pract* 1999;(pp 30-31):-31.
- Ginsberg D L. Vardenafil treatment of sertraline-induced sexual dysfunction. *Primary Psychiatry* 2004;11(11):23-24.
- Ginsberg David L. Sildenafil-dihydrocodeine interaction results in prolonged erections. [References]. *Primary Psychiatry* 2003;10(2):23
- Ginzburg R, Wong Y, Fader J S. Effect of bupropion on sexual dysfunction. *Ann Pharmacother* 2005;39(12):2096-2099.
- Giuliano F, Donatucci C, Montorsi F et al. Vardenafil is effective and well-tolerated for treating erectile dysfunction in a broad population of men, irrespective of age. *BJU Int* 2005;95(1):110-116.
- Giuliano F, Montorsi F, Mirone V et al. Switching from intracavernous prostaglandin E1 injections to oral sildenafil citrate in patients with erectile dysfunction: results of a multicenter European study. The Sildenafil Multicenter Study Group. *Br J Urol* 2000;164(3:Pt 1):t-11.
- Giuliano F, Pena B M, Mishra A et al. Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction. *Qual Life Res* 2001;10(4):359-369.
- Giuliano F, Rubio-Aurioles E, Kennelly M et al. Efficacy and safety of vardenafil in men with erectile dysfunction caused by spinal cord injury. *Neurology* 2006;66(2):210-216.
- Glenn D R J, McClure N, Lewis S E M. The hidden impact of diabetes on male sexual dysfunction and fertility. *Hum Fertil* 2003;6(4):174-179.
- Glina S, Sotomayor M, Gatchalian E et al. Timing of dose relative to sexual intercourse attempt in previous sildenafil citrate users treated with tadalafil. *Br J Sex Med* 2006;3(2):309-319.
- Godschalk M F, Chen J, Katz P G et al. Prostaglandin E1 as treatment for erectile failure in elderly men. *J Am Geriatr Soc* 1994;42(12):1263-1265.
- Godschalk M, Gheorghiu D, Chen J et al. Long-term efficacy of a new formulation of prostaglandin E1 as treatment for erectile failure.. *Br J Urol* 1996;155(3):915-917.
- Gogtay N J, Bichile S K, Pinto C J et al. Erectile dysfunction and sildenafil citrate.[comment]. *J Assoc Physicians India* 2001;49:871-872.
- Goldenberg M M. Safety and efficacy of sildenafil citrate in the treatment of male erectile dysfunction. *Clin Ther*. 1998;20(6):1033-1048.
- Goldstein I. Oral phentolamine: an alpha-1, alpha-2 adrenergic antagonist for the treatment of erectile dysfunction. [Review] [9 refs]. *Int J Impot Res* 2000;12Suppl-80.
- Goldstein I. A 36-week, open label, non-comparative study to assess the long-term safety of sildenafil citrate (VIAGRA) in patients with erectile dysfunction. *Int J Clin Pract* 1999;Supplement.102-109.
- Goldstein I, Auerbach S, Padma-Nathan H et al. Axial penile rigidity as primary efficacy outcome during multi-institutional in-office dose titration clinical trials with alprostadil alfadex in patients with erectile dysfunction. Alprostadil Alfadex Study Group. *Int J Impot Res* 2000;12(4):205-211.
- Goldstein I, Kim E, Steers W D et al. Efficacy and safety of tadalafil in men with erectile dysfunction with a high prevalence of comorbid conditions: results from MOMENTUS: multiple observations in men with erectile dysfunction in National Tadalafil Study in the US. *Br J Sex Med* 2007;4(1):166-175.
- Gomery P, Bullock A, McGettigan J et al. Tadalafil is efficacious in Black American and Hispanic men with erectile dysfunction: results from multiple observations in men with erectile dysfunction in national tadalafil study in the US (MOMENTUS). *Int J Impot Res* 2007;19(1):76-83.
- Goonawardena S A, de Silva W A, Ketheeswaran T. Pharmacologically induced penile erections in the assessment and treatment of erectile impotence: a preliminary study of 100 patients. *Ceylon Med J* 1997;42(2):72-74.
- Gore J L, Swerdloff R S, Rajfer J. Androgen deficiency in the etiology and treatment of erectile dysfunction. *Urol Clin North Am* 2005;32(4):457-468.
- Govier F E, McClure R D, Weissman R M et al. Experience with triple-drug therapy in a pharmacological erection program.[see comment]. *Br J Urol* 1993;150(6):1822-1824.
- Greco E A, Pili M, Bruzziches R et al. Testosterone:estradiol ratio changes associated with long-term tadalafil administration: a pilot study. *Br J Sex Med* 2006;3(4):716-722.
- Greco E, Polonio-Balbi P. Penile rigidity in erectile dysfunction treated with alprostadil. *Lancet* 1997;350(9092):1682
- Greco E, Balbi P P, Virag R. Self intra-cavernous injections as a successful treatment in pure neurogenic impotence. *Riv Neurol* 1991;61(1):35-38.

- Green B G, Martin S. Clinical assessment of sildenafil in the treatment of neurogenic male sexual dysfunction: After the hype. *NeuroRehabilitation* 2000;15(2):101-105.
- Greenstein A, Mabjeesh N J, Sofer M et al. Does sildenafil combined with testosterone gel improve erectile dysfunction in hypogonadal men in whom testosterone supplement therapy alone failed?[see comment]. *Br J Urol* 2005;173(2):530-532.
- Gresser U, Gleiter C H. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil--review of the literature. [Review] [92 refs]. *Eur J Med Res* 2002;7(10):435-446.
- Gross A J, Sauerwein D H, Kutzenberger J et al. Penile prostheses in paraplegic men. *Br J Urol* 1996;78(2):262-264.
- Grossman E B, Swan S K, Muirhead G J et al. The pharmacokinetics and hemodynamics of sildenafil citrate in male hemodialysis patients. *Kidney Int* 2004;66(1):367-374.
- Grover J K, Vats V, Ajeeta. Sildenafil (Viagra(TM)). *Medico-Legal Update* 1998;3(1-2):67-78.
- Guay A T, Perez J B, Jacobson J et al. Efficacy and safety of sildenafil citrate for treatment of erectile dysfunction in a population with associated organic risk factors.[erratum appears in *J Androl* 2002 Jan-Feb;23(1):113]. *J Androl* 2001;22(5):793-797.
- Guay A T, Perez J B, Velasquez E et al. Clinical experience with intraurethral alprostadil (MUSE) in the treatment of men with erectile dysfunction. A retrospective study. Medicated urethral system for erection. *Eur Urol* 2000;38(6):671-676.
- Guay A T, Spark R F, Jacobson J et al. Yohimbine treatment of organic erectile dysfunction in a dose-escalation trial. *Int J Impot Res* 2002;14(1):25-31.
- Gupta N, Sawlani K K, Tripathi A K. Appropriate use of sildenafil citrate in male erectile dysfunction.[see comment]. [Review] [52 refs]. *J Assoc Physicians India* 2001;49:889-896.
- Gupta Sanjay, Masand Prakash, Ashton Adam K et al. Phenelzine-induced sexual dysfunction treated with sildenafil. *J Sex Marital Ther* 1999;25(2):131-135.
- Gutierrez P, Hernandez P, Mas M. Combining programmed intracavernous PGE1 injections and sildenafil on demand to salvage sildenafil nonresponders.. *Int J Impot Res* 2005;17(4):354-358.
- Hammadeh M Y, Madaan S, Hines J et al. 5-year outcome of a prospective randomized trial to compare transurethral electrovaporization of the prostate and standard transurethral resection. *Urology* 2003;61(6):1166-1171.
- Harding L M, Adeniyi A, Everson R et al. Comparison of a needle-free high-pressure injection system with needle-tipped injection of intracavernosal alprostadil for erectile dysfunction. *Int J Impot Res* 2002;14(6):498-501.
- Harrold L R, Gurwitz J H, Field T S et al. The diffusion of a novel therapy into clinical practice: the case of sildenafil.[see comment]. *Arch Intern Med* 2000;160(22):3401-3405.
- Harwood P J, Grotz M, Eardley I et al. Erectile dysfunction after fracture of the pelvis. *Journal of Bone & Joint Surgery - British Volume* 2005;87(3):281-290.
- Hatzichristou D G. Sildenafil citrate: lessons learned from 3 years of clinical experience. [Review] [60 refs]. *Int J Impot Res* 2002;14(Suppl-52).
- Hatzichristou D G. Current treatment and future perspectives for erectile dysfunction. [Review] [85 refs]. *Int J Impot Res* 1998;10(Suppl-13).
- Hatzichristou D G, Apostolidis A, Tzortzis V et al. Sildenafil versus intracavernous injection therapy: efficacy and preference in patients on intracavernous injection for more than 1 year. *Br J Urol* 2000;164(4):1197-1200.
- Hatzichristou D, Vardi Y, Papp G et al. Effect of tadalafil on sexual timing behavior patterns in men with erectile dysfunction: integrated analysis of randomized, placebo controlled trials. *Br J Urol* 2005;174(4 Pt 1):1356-1359.
- Hatzimouratidis K, Hatzichristou D. Phosphodiesterase Type 5 Inhibitors: The Day After. *Eur Urol* 2007;51(1):75-89.
- Hatzimouratidis K, Hatzichristou D G. A comparative review of the options for treatment of erectile dysfunction: Which treatment for which patient?. *Drugs* 2005;65(12):1621-1650.
- Hauck E W, Altinkilic B M, Schroeder-Printzen I et al. Prostaglandin E1 long-term self-injection programme for treatment of erectile dysfunction--a follow-up of at least 5 years. *Andrologia* 1999;31(Suppl):Suppl-103.
- He X Q, Hong B F, Wang X X et al. Evaluation of efficacy and safety of oral sildenafil citrate therapy for men with erectile dysfunction. *Pharmaceutical Journal of Chinese Peoples Liberation Army* 2002;18(4):205-208.
- Heaton J P. Key issues from the clinical trials of apomorphine SL. *World J Urol* 2001;19(1):25-31.
- Heaton J P W, Wagner Porst, Eid Wyllie. Apomorphine: An update of clinical trial results. *Int J Impot Res* 2000;12(SUPPL. 4):S67-S73.
- Heaton J P, Lording D, Liu S N et al. Intracavernosal alprostadil is effective for the treatment of erectile dysfunction in diabetic men. *Int J Impot Res* 2001;13(6):317-321.

- Heaton J P, Morales A, Adams M A et al. Recovery of erectile function by the oral administration of apomorphine. *Urology* 1995;45(2):200-206.
- Hellstrom W J. Vardenafil: a new approach to the treatment of erectile dysfunction. [Review] [37 refs]. *Curr Urol Rep* 2003;4(6):479-487.
- Hirsch I H, Schanne F J, Carsello J et al. Sequential penile ultrasound monitoring of patients treated with chronic intracavernous prostaglandin E1. *Urology* 1995;45(6):1037-1041.
- Hirsch I H, Smith R L, Chancellor M B et al. Use of intracavernous injection of prostaglandin E1 for neuropathic erectile dysfunction. *Paraplegia* 1994;32(10):661-664.
- Hollander J B, Gonzalez J, Norman T. Patient satisfaction with pharmacologic erection program. *Urology* 1992;39(5):439-441.
- Holmes S. Tadalafil: a new treatment for erectile dysfunction. *BJU Int* 2003;91(6):466-468.
- Hong E K, Lepor H, McCullough A R. Time dependent patient satisfaction with sildenafil for erectile dysfunction (ED) after nerve-sparing radical retropubic prostatectomy (RRP). *Int J Impot Res* 1999;11(SUPPL. 1):S15-S22.
- Hong J H, Ahn T Y. Oral testosterone replacement in Korean patients with PADAM. *Aging Male* 2002;5(1):52-56.
- Hookes J. Asian Federation of Medicinal Chemistry (AFMC) - Fifth International Medicinal Chemistry Symposium: 14-17 October 2003, Kyoto, Japan. *IDrugs* 2003;6(11):1013-1015.
- Huang S T, Hsieh M L. Different hemodynamic responses by color Doppler ultrasonography studies between sildenafil non-responders and responders. *Asian J Androl* 2007;9(1):129-133.
- Hubler J, Szanto A, Konyves K. Methylene blue as a means of treatment for priapism caused by intracavernous injection to combat erectile dysfunction. *International Urology & Nephrology* 2003;35(4):519-521.
- Hwang T I, Chen H E, Tsai T F et al. Combined use of androgen and sildenafil for hypogonadal patients unresponsive to sildenafil alone. *Int J Impot Res* 2006;18(4):400-404.
- Incrocchi L, Hop W C, Slob A K. Visual erotic and vibrotactile stimulation and intracavernous injection in screening men with erectile dysfunction: a 3 year experience with 406 cases. *Int J Impot Res* 1996;8(4):227-232.
- Irwin M B, Kata E J. High attrition rate with intracavernous injection of prostaglandin E1 for impotency. *Urology* 1994;43(1):84-87.
- Isidori A M, Giannetta E, Gianfrilli D et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clin Endocrinol (Oxf.)* 2005;63(4):381-394.
- Ismail M, Abbott L, Hirsch I H. Experience with intracavernous PGE-1 in the treatment of erectile dysfunction: dose considerations and efficacy. *Int J Impot Res* 1997;9(1):39-42.
- Israilov S, Niv E, Livne P M et al. Intracavernous injections for erectile dysfunction in patients with cardiovascular diseases and failure or contraindications for sildenafil citrate. *Int J Impot Res* 2002;14(1):38-43.
- Israilov S, Shmueli J, Niv E et al. Evaluation of a progressive treatment program for erectile dysfunction in patients with diabetes mellitus. *Int J Impot Res* 2005;17(5):431-436.
- Jackson G. Sildenafil (Viagra): New data, new confidence in treating erectile dysfunction in the cardiovascular patient. *Int J Clin Pract* 2002;56(2):75
- Jackson G, Keltai M, Csanady M et al. Hemodynamic effects of sildenafil citrate and isosorbide mononitrate in men with coronary artery disease and erectile dysfunction. *Br J Sex Med* 2005;2(3):407-414.
- Jackson G, Kloner R A, Costigan T M et al. Update on clinical trials of tadalafil demonstrates no increased risk of cardiovascular adverse events. *Br J Sex Med* 2004;1(2):161-167.
- Jackson G, Montorsi P, Cheitlin M D. Cardiovascular safety of sildenafil citrate (Viagra): an updated perspective. [Review] [52 refs]. *Urology* 2006;68(3 Suppl):47-60.
- Jacobsen F M. Fluoxetine-induced sexual dysfunction and an open trial of yohimbine.[see comment]. *Hillside J Clin Psychiatry* 1992;53(4):119-122.
- Jain P, Rademaker A W, McVary K T. Testosterone supplementation for erectile dysfunction: results of a meta-analysis. *Br J Urol* 2000;164(2):371-375.
- Jarow J P, Burnett A L, Geringer A M. Clinical efficacy of sildenafil citrate based on etiology and response to prior treatment.[see comment]. *Br J Urol* 1999;162(3:Pt 1):t-5.
- Giann B P, Yu C C, Su C C et al. Rechallenge prior sildenafil nonresponders. *Int J Impot Res* 2004;16(1):64-68.
- Giann B P, Yu C C, Tsai J Y et al. What to learn about sildenafil in the treatment of erectile dysfunction from 3-year clinical experience. *Int J Impot Res* 2003;15(6):412-417.
- Giann B-P, Yu C-C, Su C-C. Impact of introduction of sildenafil on other treatment modalities for erectile dysfunction: A study of nationwide and local hospital sales. *Int J Impot Res* 2004;16(6):527-530.

- John H, Lehmann K, Hauri D. Intraurethral prostaglandin improves quality of vacuum erection therapy. *Eur Urol* 1996;29(2):224-226.
- Juergense P H, Botev R, Wuerth D et al. Erectile dysfunction in chronic peritoneal dialysis patients: incidence and treatment with sildenafil. *Perit Dial Int* 2001;21(4):355-359.
- Kadioglu A, Erdogru T, Tellaloglu S. Combined intracavernous injection of papaverine and stimulation (CIS) test. *J Androl* 1994;15 Suppl50S-53S.
- Kaplan B, Ben-Rafael Z, Peled Y et al. Oral sildenafil may reverse secondary ejaculatory dysfunction during infertility treatment. *Fertility & Sterility* 1999;72(6):1144-1145.
- Kaplan Helen S. The combined use of sex therapy and intrapenile injections in the treatment of impotence. *J Sex Marital Ther* 1990;16(4):195-207.
- Kaplan S A, Reis R B, Kohn I J et al. Combination therapy using oral alpha-blockers and intracavernosal injection in men with erectile dysfunction. *Urology* 1998;52(5):739-743.
- Karabulut A, Peskircioglu L, Ozkardes H et al. Objective penile vascular response to intraurethral prostaglandin E2 (dinoprostone). *Urol Int* 2001;67(2):160-162.
- Kassouf W, Carrier S. A comparison of the International Index of Erectile Function and erectile dysfunction studies.. *BJU Int* 2003;91(7):667-669.
- Katlowitz N M, Albano G J, Morales P et al. Potentiation of drug-induced erection with audiovisual sexual stimulation. *Urology* 1993;41(5):431-434.
- Katlowitz N, Albano G J, Patsias G et al. Effect of multidose intracorporeal injection and audiovisual sexual stimulation in vasculogenic impotence. *Urology* 1993;42(6):695-697.
- Kattan S A. The acceptance of satisfaction of Saudi males to vasoactive autoinjection intracavernous therapy, external negative pressure device and penile prosthesis in the treatment of erectile dysfunction. *Ann Saudi Med* 2002;22(3-4):149-152.
- Kaufman J M, Hatzichristou D G, Mulhall J P et al. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *Br J Urol* 1994;151(3):612-618.
- Keating G M, Scott L J. Vardenafil: a review of its use in erectile dysfunction. *Drugs* 2003;63(23):2673-2703.
- Keating G M, Scott L J. Spotlight on vardenafil in erectile dysfunction. *Drugs Aging* 2004;21(2):135-140.
- Kedia S, Zippe C D, Agarwal A et al. Treatment of erectile dysfunction with sildenafil citrate (Viagra) after radiation therapy for prostate cancer. *Urology* 1999;54(2):308-312.
- Kendirci M, Bivalacqua T J, Hellstrom W J. Vardenafil: a novel type 5 phosphodiesterase inhibitor for the treatment of erectile dysfunction. *Expert Opin Pharmacother* 2004;5(4):923-932.
- Khan M A, Raistrick M, Mikhailidis D P et al. MUSE: clinical experience. *Current Medical Research & Opinion* 2002;18(2):64-67.
- Khan M M, Khwaja M. Open label study of intracavernous injection of alpostadil alphadex in the treatment of erectile dysfunction. *J Postgrad Med Inst* 2005;19(1):52-57.
- Kim E D, McVary K T. Topical prostaglandin-E1 for the treatment of erectile dysfunction.. *Br J Urol* 1995;153(6):1828-1830.
- Kim E D, el-Rashidy R, McVary K T. Papaverine topical gel for treatment of erectile dysfunction. *Br J Urol* 1995;153(2):361-365.
- Kim J M, Joh Y D, Huh J D et al. Doppler sonography of the penile cavernosal artery: comparison of intraurethral instillation and intracorporeal injection of prostaglandin E1. *J Clin Ultrasound* 2001;29(5):273-278.
- Kim N N, Christianson D W, Traish A M. Role of arginase in the male and female sexual arousal response. *Br J Nutr* 2004;134(10 SUPPL.):2873S-2879S.
- Kim S C, Ahn T Y, Choi H K et al. Multicenter study of the treatment of erectile dysfunction with transurethral alprostadil (MUSE) in Korea. *Int J Impot Res* 2000;12(2):97-101.
- Kim S C, Chang I H, Jeon H J. Preference for oral sildenafil or intracavernosal injection in patients with erectile dysfunction already using intracavernosal injection for > 1 year. *BJU Int* 2003;92(3):277-280.
- Kim S C, Lee S W, Seo K K. Characteristics of pain following intracavernous injection of prostaglandin E1. *J Korean Med Sci* 1997;12(4):327-331.
- Kloner R A. Cardiovascular risk and sildenafil. [Review] [27 refs]. *Am J Cardiol* 2000;86(2A):57F-61F.
- Kloner R A, Zusman R M. Cardiovascular effects of sildenafil citrate and recommendations for its use. [Review] [21 refs]. *Am J Cardiol* 1999;84(5B):11N-17N.
- Kloner R A, Brown M, Prisant L M et al. Effect of sildenafil in patients with erectile dysfunction taking antihypertensive therapy. Sildenafil Study Group. *Am J Hypertens* 2001;14(1):70-73.
- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil in patients on common antihypertensive therapies. [Review] [5 refs]. *Am J Cardiol* 2003;92(9A):47M-57M.

- Kloner R A, Mitchell M, Emmick J T. Cardiovascular effects of tadalafil. [Review] [12 refs]. *Am J Cardiol* 2003;92(9A):37M-46M.
- Kloner R A, Sadovsky R, Johnson E G et al. Efficacy of tadalafil in the treatment of erectile dysfunction in hypertensive men on concomitant thiazide diuretic therapy. *Int J Impot Res* 2005;17(5):450-454.
- Kloner R A, Sadovsky R, Johnson E G et al. Efficacy of tadalafil in the treatment of erectile dysfunction in hypertensive men on concomitant thiazide diuretic therapy. *Br J Urol* 2006;175(4):1450
- Knispel H H. Penile venous surgery in impotence: results in highly selected cases. *Urol Int* 1991;47(3):144-148.
- Knispel H H, Huland H. Influence of cause on choice of therapy in 174 patients with erectile dysfunction. *Br J Urol* 1992;147(5):1274-1276.
- Koksai M, Ozdemir H, Kargi S et al. The effects of sildenafil on ocular blood flow. *Acta Ophthalmol Scand* 2005;83(3):355-359.
- Kongkanand A, Opanuraks J, Tantiwongse K et al. Evaluating dose regimens of apomorphine, an open-label study. *Int J Impot Res* 2003;15(Suppl 2):10-12.
- Kongkanand A, Ratana-Olarn K, Wuddhikarn S et al. Evaluation of transurethral alprostadil for safety and efficacy in men with erectile dysfunction. *J Med Assoc Thai* 2002;85(2):223-228.
- Kramer-Levien D J. Papaverine--the medical implant. *AUAA J* 1987;7(4):13-Jun.
- Kriston L, Harms A, Berner M M. A meta-regression analysis of treatment effect modifiers in trials with flexible-dose oral sildenafil for erectile dysfunction in broad-spectrum populations. *Int J Impot Res* 2006;18(6):559-565.
- Kromann-Andersen B. Intracavernosal pharmacotherapy with injection pen. *Lancet* 1988;1(8575-6):54-59.
- Kuba R, Pohanka M, Zakopcan J et al. Sexual dysfunctions and blood hormonal profile in men with focal epilepsy. *Epilepsia* 2006;47(12):2135-2140.
- Kunelius P, Lukkarinen O. Intracavernous self-injection of prostaglandin E1 in the treatment of erectile dysfunction. *Int J Impot Res* 1999;11(1):21-24.
- Kuzmarov I W, Ross D, Skamene A et al. A sexual tune-up program as an adjunct to intracavernous pharmacotherapy. *Can J Hum Sex* 1993;2(4):239-241.
- Labbate Lawrence A, Grimes Jamie B, Hines Alan et al. Bupropion treatment of serotonin reuptake antidepressant-associated sexual dysfunction. *Ann Clin Psychiatry* 1997;9(4):241-245.
- Lakin M M, Montague D K, VanderBrug Medendorp S et al. Intracavernous injection therapy: Analysis of results and complications. *Br J Urol* 1990;143(6):1138-1141.
- Lal S, Kiely M E, Thavundayil J X et al. Effect of bromocriptine in patients with apomorphine-responsive erectile impotence: an open study. *J Psychiatry Neurosci* 1991;16(5):262-266.
- Lance R, Albo M, Costabile R A et al. Oral trazodone as empirical therapy for erectile dysfunction: a retrospective review. *Urology* 1995;46(1):117-120.
- Lane B Z, Ausmundson S J, Butler R S et al. Use of a visual analog scale to assess pain of injection with intracavernous injection therapy. *Br J Sex Med* 2005;2(3):428-431.
- Laties A, Sharlip I. Ocular safety in patients using sildenafil citrate therapy for erectile dysfunction. [Review] [81 refs]. *Br J Sex Med* 2006;3(1):12-27.
- Laties A M, Zrenner E. Viagra (sildenafil citrate) and ophthalmology. *Progress in Retinal & Eye Research* 2002;21(5):485-506.
- Laties A M, Fraunfelder F T, Flach A J et al. Ocular safety of Viagra, (sildenafil citrate). *Trans Am Ophthalmol Soc* 1999;97(pp 115-128):-128.
- Lawless C, Cree J. Oral medications in the management of erectile dysfunction. [Review] [15 refs]. *J Am Board Fam Pract* 1998;11(4):307-314.
- Lawless C, Force R W. Sildenafil for erectile dysfunction. *J Fam Pract* 1998;47(2):97-98.
- Lawrence I G, Price D E, Howlett T A et al. Correcting impotence in the male dialysis patient: experience with testosterone replacement and vacuum tumescence therapy. *Am J Kidney Dis* 1998;31(2):313-319.
- Le Bon O, Lion K, Verbanck P et al. Fluparoxan in male erectile disorder: A case report. *Yakubutsu Seishin Kodo* 1995;9(1):67-68.
- Lea A P, Bryson H M, Balfour J A. Intracavernous alprostadil. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in erectile dysfunction. [Review] [123 refs]. *Drugs Aging* 1996;8(1):56-74.
- Lee J, Pommerville P, Brock G et al. Physician-rated patient preference and patient- and partner-rated preference for tadalafil or sildenafil citrate: results from the Canadian 'Treatment of Erectile Dysfunction' observational study. *BJU Int* 2006;98(3):623-629.

- Lee W R. The role of androgen deprivation therapy combined with prostate brachytherapy. [Review] [31 refs]. *Urology* 2002;60(3:Suppl 1):Suppl-44.
- Levine L A, Latchamsetty K C. Treatment of erectile dysfunction in patients with Peyronie's disease using sildenafil citrate. *Int J Impot Res* 2002;14(6):478-482.
- Levitt E E, Mulcahy J J. The effect of intracavernosal injection of papaverine hydrochloride on orgasm latency. *Br J Sex Med* 1995;21(1):39-42.
- Lewis R L, Sadovsky R, Eardley I et al. The efficacy of tadalafil in clinical populations. *Br J Sex Med* 2005;2(4):517-531.
- Lewis R W. Intraurethral and topical agents. *Med Actual* 2000;36(2-3):113-119.
- Li M K, Lim P H, Wong M Y et al. Transurethral alprostadil for the treatment of erectile dysfunction: results of a multicentre trial. *Ann Acad Med Singapore* 2000;29(6):727-731.
- Lim P H, Ng F C. Erectile dysfunction in Singapore men: presentation, diagnosis, treatment and results. *Ann Acad Med Singapore* 1992;21(2):248-253.
- Lim P H C, Man K L, Foo C N et al. Clinical efficacy and safety of sildenafil citrate (Viagra) in a multi-racial population in Singapore: A retrospective study of 1520 patients. *Int J Urol* 2002;9(6):308-315.
- Liu L C, Wu C C, Liu L H et al. Comparison of the effects of papaverine versus prostaglandin E1 on penile blood flow by color duplex sonography. *Eur Urol* 1991;19(1):49-53.
- Livi U, Faggian G, Sorbara C et al. Use of prostaglandin E1 in the treatment of sexual impotence after heart transplantation: initial clinical experience. *Journal of Heart & Lung Transplantation* 1993;12(3):484-486.
- Lombardo T, Giammusso B, Frontini V et al. Thalassaemic men affected by erectile dysfunction treated with transurethral alprostadil: case report. *Hum Reprod* 2000;15(11):2375-2378.
- Long R L, Sherman L S, Lombardi T J. A goal-oriented, cost-effective approach to the diagnosis and treatment of 24 male erectile dysfunction. [Review] [24 refs]. *J Ky Med Assoc* 1995;93(11):500-508.
- Lottman P E, Hendriks J C, Vrugink P A et al. The impact of marital satisfaction and psychological counselling on the outcome of ICI-treatment in men with ED. *Int J Impot Res* 1998;10(2):83-87.
- Lowentritt B H, Scardino P T, Miles B J et al. Sildenafil citrate after radical retropubic prostatectomy. *Br J Urol* 1999;162(5):1614-1617.
- Lowy M, Collins S, Bloch M et al. Quality of erection questionnaire correlates: change in erection quality with erectile function, hardness, and psychosocial measures in men treated with sildenafil for erectile dysfunction. *Br J Sex Med* 2007;4(1):83-92.
- Lue T F. Impotence after radical pelvic surgery: physiology and management. [Review] [56 refs]. *Urol Int* 1991;46(3):259-265.
- Lukkarinen O, Tonttila P, Hellstrom P et al. Non-prosthetic surgery in the treatment of erectile dysfunction. A retrospective study of 45 impotent patients in the University of Oulu. *Scandinavian Journal of Urology & Nephrology* 1998;32(1):42-46.
- Lundberg L, Olsson J-O, Kihl B. Long-term experience of self-injection therapy with prostaglandin E1 for erectile dysfunction. *Scand J Urol Nephrol* 1996;30(5):395-397.
- Lunenfeld B. Androgen therapy in the aging male. [Review] [110 refs]. *World J Urol* 2003;21(5):292-305.
- Magoha G A. Sildenafil (Viagra) in the treatment of male erectile dysfunction in Nairobi. *East Afr Med J* 2000;77(2):76-79.
- Manecke R G, Mulhall J P. Medical treatment of erectile dysfunction. [Review] [69 refs]. *Ann Med* 1999;31(6):388-398.
- Maniam P, Seftel A D, Carty E W et al. Nocturnal penile tumescence activity unchanged after long-term intracavernous injection therapy. *Br J Urol* 2001;165(3):830-832.
- Mansi M K, Alkhdair W K, Huraib S. Treatment of erectile dysfunction after kidney transplantation with intracavernosal self-injection of prostaglandin E1. *Br J Urol* 1998;159(6):1927-1930.
- Marberger M, Roehrborn C G, Marks L S et al. Relationship among serum testosterone, sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. *Journal of Clinical Endocrinology & Metabolism* 2006;91(4):1323-1328.
- Mark S D, Keane T E, Vandemark R M et al. Impotence following pelvic fracture urethral injury: incidence, aetiology and management. *Br J Urol* 1995;75(1):62-64.
- Markou S, Perimenis P, Gyftopoulos K et al. Vardenafil (Levitra) for erectile dysfunction: a systematic review and meta-analysis of clinical trial reports. *Int J Impot Res* 2004;16(6):470-478.

- Marks L S, Duda C, Dorey F J et al. Treatment of erectile dysfunction with sildenafil.[see comment]. *Urology* 1999;53(1):19-24.
- Marshall G A, Breza J, Lue T F. Improved hemodynamic response after long-term intracavernous injection for impotence. *Urology* 1994;43(6):844-848.
- Martin-Morales A, Haro J M, Beardsworth A et al. Therapeutic effectiveness and patient satisfaction after 6 months of treatment with tadalafil, sildenafil, and vardenafil: results from the erectile dysfunction observational study (EDOS). *Eur Urol* 2007;51(2):541-550.
- Martin-Morales A, Moncada Iribarren I, Cruz Navarro N et al. [Efficacy and safety of two dosing regimens with Tadalafil in Spanish men with erectile dysfunction: results from the SURE study in 14 European countries]. *Actas Urol Esp* 2006;30(8):791-800.
- Martinez R, Puigvert A, Pomerol J M et al. Clinical experience with apomorphine hydrochloride: the first 107 patients. *Br J Urol* 2003;170(6:Pt 1):t-5.
- Martinez-Jabaloyas J M, Gil-Salom M, Villamon-Fort R et al. Prognostic factors for response to sildenafil in patients with erectile dysfunction. *Eur Urol* 2001;40(6):641-647.
- Martinez-Pineiro L, Cortes R, Cuervo E et al. Prospective comparative study with intracavernous sodium nitroprusside and prostaglandin E1 in patients with erectile dysfunction. *Eur Urol* 1998;34(4):350-354.
- Matthew A G, Goldman A, Trachtenberg J et al. Sexual dysfunction after radical prostatectomy: Prevalence, treatments, restricted use of treatments and distress. *Br J Urol* 2005;174(6):2105-2110.
- Maytom M C, Derry F A, Dinsmore W W et al. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord*. 1999;37(2):110-116.
- McClure R D. Endocrine evaluation and therapy of erectile dysfunction. [Review] [77 refs]. *Urol Clin North Am* 1988;15(1):53-64.
- McClure R D, Oses R, Ernest M L. Hypogonadal impotence treated by transdermal testosterone. *Urology* 1991;37(3):224-228.
- McConnell J D, Roehrborn C G, Bautista O M et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
- McCullough A R, Barada J H, Fawzy A et al. Achieving treatment optimization with sildenafil citrate (Viagra) in patients with erectile dysfunction. *Urology* 2002;60(2 Suppl 2):28-38.
- McCullough A R, Carson C C, Hatzichristou D. A prospective study of the beneficial effects of dose optimization and customized instructions on patient satisfaction with sildenafil citrate (Viagra) for erectile dysfunction. *Urology* 2006;68(3 Suppl):38-46.
- McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992;9:265A
- McMahon C. Efficacy and safety of daily tadalafil in men with erectile dysfunction previously unresponsive to on-demand tadalafil. *Br J Sex Med* 2004;1(3):292-300.
- McMahon C G. High dose sildenafil citrate as a salvage therapy for severe erectile dysfunction. *Int J Impot Res* 2002;14(6):533-538.
- McMahon C G. An attempt to standardize the pharmacological diagnostic screening of vasculogenic impotence with prostaglandin E1. *Int J Impot Res* 1995;7(2):83-90.
- McMahon C G. Topiglan: MacroChem. *Curr Opin Investig Drugs* 2002;3(4):602-606.
- McMahon C G. A pilot study of the role of intracavernous injection of vasoactive intestinal peptide (VIP) and phentolamine mesylate in the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(4):233-236.
- McMahon C G. Priapism associated with concurrent use of phosphodiesterase inhibitor drugs and intracavernous injection therapy. *Int J Impot Res* 2003;15(5):383-384.
- McMahon C G, Samali R, Johnson H. Efficacy, safety and patient acceptance of sildenafil citrate as treatment for erectile dysfunction. *Br J Urol* 2000;164(4):1192-1196.
- McMahon C G, Samali R, Johnson H. Treatment of intracorporeal injection nonresponse with sildenafil alone or in combination with triple agent intracorporeal injection therapy. *Br J Urol* 1997;162(6):1992-1997.
- McMahon C, Lording D, Stuckey B et al. Vardenafil improved erectile function in a "real-life" broad population study of men with moderate to severe erectile dysfunction in Australia and New Zealand. *Br J Sex Med* 2006;3(5):892-900.
- McVary K T, Polepalle S, Riggi S et al. Topical prostaglandin E1 SEPA gel for the treatment of erectile dysfunction.. *Br J Urol* 1999;162(3 Pt 1):732

- Mealy N E. Alprostadil cream. *Drugs of the Future* 2004;29(6):626-627.
- Mealy N E, Bayes M. PT-141. *Drugs of the Future* 2004;29(11):1177
- Mehdiyev T V. Intracavernous injection probe of vasoactive preparations in the diagnosis of erectile dysfunctions in patients with diabetes mellitus. *Azerbaijanski Meditsinskii Zhurnal* 2002;(pp 17-19):-19.
- Meinhardt W, de la, Fuente R B et al. Prostaglandin E1 with phentolamine for the treatment of erectile dysfunction. *Int J Impot Res* 1996;8(1):5-7.
- Meinhardt W, Nijeholt A A, Kropman R F et al. Comparison of a mixture of papaverine, phentolamine and prostaglandin E1 with other intracavernous injections. *Eur Urol* 1994;26(4):319-321.
- Mellinger B C, Fried J J, Darracott Vaughan. Papaverine-induced penile blood flow acceleration in impotent men measured by duplex scanning. *Br J Urol* 1990;144(4):897-899.
- Merrick G S, Butler W M, Lief J H et al. Efficacy of sildenafil citrate in prostate brachytherapy patients with erectile dysfunction. *Urology* 1999;53(6):1112-1116.
- Metawea B, El-Nashar A R, Gad-Allah A et al. Intracavernous papaverine/phentolamine-induced priapism can be accurately predicted with color Doppler ultrasonography. *Urology* 2005;66(4):858-860.
- Meyhoff H H, Rosenkilde P, Bodker A. Non-invasive management of impotence with transcutaneous nitroglycerin. *Br J Urol* 1992;69(1):88-90.
- Mikhail N. Does Testosterone Have a Role in Erectile Function?. *Am J Med* 2006;119:373-382.
- Millard R J, Stricker P D, Lynch W J et al. Risks of self-injection therapy for impotence. *Med J Aust* 1996;165(2):117-118.
- Miller N, Smolkin M E, Bissonette E et al. Undetectable prostate specific antigen at 6-12 months: a new marker for early success in hormonally treated patients after prostate brachytherapy. *Cancer* 2005;103(12):2499-2506.
- Mills T M, Lewis R W. The role of androgens in the erectile response: A 1999 perspective. *Mol Urol* 1999;3(2):75-80.
- Mirone V G, Stief C G. Efficacy of apomorphine SL in erectile dysfunction.[erratum appears in *BJU Int* 2002 Jan;89(1):140]. [Review] [11 refs]. *BJU Int* 2001;88(Suppl 3):25-29.
- Mirone V, Imbimbo C, Fabrizio F et al. Ketanserin plus prostaglandin E1 (PGE-1) as intracavernosal therapy for patients with erectile dysfunction unresponsive to PGE-1 alone. *Br J Urol* 1996;77(5):736-739.
- Mirone V, Palmieri A, Cucinotta D et al. Flexible-dose vardenafil in a community-based population of men affected by erectile dysfunction: a 12-week open-label, multicenter trial. *Br J Sex Med* 2005;2(6):842-847.
- Mittleman M A, Glasser D B, Orazem J. Clinical trials of sildenafil citrate (Viagra) demonstrate no increase in risk of myocardial infarction and cardiovascular death compared with placebo. *Int J Clin Pract* 2003;57(7):597-600.
- Mittleman M A, Maclure M, Glasser D B. Evaluation of acute risk for myocardial infarction in men treated with sildenafil citrate. *Am J Cardiol* 2005;96(3):443-446.
- Moemen M N, Hamed H A, Kamel I I et al. Clinical and sonographic assessment of the side effects of intracavernous injection of vasoactive substances. *Int J Impot Res* 2004;16(2):143-145.
- Moncada I, Jara J, Subira D et al. Efficacy of sildenafil citrate at 12 hours after dosing: re-exploring the therapeutic window. *Eur Urol* 2004;46(3):357-360.
- Montorsi F, Althof S E. Partner responses to sildenafil citrate (Viagra) treatment of erectile dysfunction. *Urology* 2004;63(4):762-767.
- Montorsi F, McCullough A. Efficacy of sildenafil citrate in men with erectile dysfunction following radical prostatectomy: A systematic review of clinical data. *Br J Sex Med* 2005;2(5):658-667.
- Montorsi F, Althof S E, Sweeney M et al. Treatment satisfaction in patients with erectile dysfunction switching from prostaglandin E(1) intracavernosal injection therapy to oral sildenafil citrate. *Int J Impot Res* 2003;15(6):444-449.
- Montorsi F, Briganti A, Salonia A et al. Can Phosphodiesterase Type 5 Inhibitors Cure Erectile Dysfunction?. *Eur Urol* 2006;49(6):979-986.
- Montorsi F, Guazzoni G, Barbieri L et al. The effect of intracorporeal injection plus genital and audiovisual sexual stimulation versus second injection on penile color Doppler sonography parameters. *Br J Urol* 1996;155(2):536-540.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993;42(5):554-558.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Four-drug intracavernous therapy for impotence due to corporeal veno-occlusive dysfunction. *Br J Urol* 1993;149(5 Pt 2):1291-1295.

- Montorsi F, Guazzoni G, Bergamaschi F et al. Intracavernous vasoactive pharmacotherapy: the impact of a new self-injection device.[see comment]. *Br J Urol* 1993;150(6):1829-1832.
- Montorsi F, Guazzoni G, Bergamaschi F et al. Clinical reliability of multi-drug intracavernous vasoactive pharmacotherapy for diabetic impotence. *Acta Diabetol Lat* 1994;31(1):1-5.
- Montorsi F, Hellstrom W J, Valiquette L et al. Vardenafil provides reliable efficacy over time in men with erectile dysfunction. *Urology* 2004;64(6):1187-1195.
- Montorsi F, Perani D, Anchisi D et al. Apomorphine-induced brain modulation during sexual stimulation: a new look at central phenomena related to erectile dysfunction. *Int J Impot Res* 2003;15(3):203-209.
- Montorsi F, Salonia A, Briganti A et al. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47(5):612-621.
- Montorsi F, Verheyden B, Meuleman E et al. Long-term safety and tolerability of tadalafil in the treatment of erectile dysfunction. *Eur Urol* 2004;45(3):339-344.
- Moore R A, Derry S, McQuay H J. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. [Review] [77 refs]. *BMC Urol* 2005;518
- Moore R A, Edwards J E, McQuay H J. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. *BMC Urol*. 2002;26
- Morales A, Gingell C, Collins M et al. Clinical safety of oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):69-73.
- Morales A, Johnston B, Heaton J P et al. Testosterone supplementation for hypogonadal impotence: assessment of biochemical measures and therapeutic outcomes. *Br J Urol* 1997;157(3):849-854.
- Morales A, Johnston B, Heaton J W et al. Oral androgens in the treatment of hypogonadal impotent men.[see comment]. *Br J Urol* 1994;152(4):1115-1118.
- Morgentaler A, Barada J, Niederberger C et al. Efficacy and safety of tadalafil across ethnic groups and various risk factors in men with erectile dysfunction: Use of a novel noninferiority study design. *Br J Sex Med* 2006;3(3):492-503.
- Mulhall J P. Deciphering erectile dysfunction drug trials. [Review] [35 refs]. *Br J Urol* 2003;170(2 Pt 1):353-358.
- Mulhall J P. Sublingual apomorphine for the treatment of erectile dysfunction. [Review] [22 refs]. *Expert Opin Investig Drugs* 2002;11(2):295-302.
- Mulhall J P, Bukofzer S, Edmonds A L et al. An open-label, uncontrolled dose-optimization study of sublingual apomorphine in erectile dysfunction. *Clin Ther* 2001;23(8):1260-1271.
- Mulhall J P, Guhring P, Parker M et al. Assessment of the impact of sildenafil citrate on lower urinary tract symptoms in men with erectile dysfunction. *Br J Sex Med* 2006;3(4):662-667.
- Mulhall J P, Jahoda A E, Ahmed A et al. Analysis of the consistency of intraurethral prostaglandin E(1) (MUSE) during at-home use. *Urology* 2001;58(2):262-266.
- Mulhall J P, Jahoda A E, Cairney M et al. The causes of patient dropout from penile self-injection therapy for impotence. *Br J Urol* 1999;162(4):1291-1294.
- Mulhall J P, Jahoda A, Aviv N et al. The impact of sildenafil citrate on sexual satisfaction profiles in men with a penile prosthesis in situ. *BJU Int* 2004;93(1):97-99.
- Mulhall J P, Land S, Parker M et al. The use of an erectogenic pharmacotherapy regimen following radical prostatectomy improves recovery of spontaneous erectile function. *Br J Sex Med* 2005;2(4):532-542.
- Mulhall J P, Levine L A, Junemann K P. Erection hardness: a unifying factor for defining response in the treatment of erectile dysfunction. [Review] [37 refs]. *Urology* 2006;68(3 Suppl):17-25.
- Mulhall J, Barnas J, Aviv N et al. Sildenafil citrate response correlates with the nature and the severity of penile vascular insufficiency. *Br J Sex Med* 2005;2(1):104-108.
- Muller M J, Benkert O. Lower self-reported depression in patients with erectile dysfunction after treatment with sildenafil. *J Affect Disord* 2001;66(2-3):255-261.
- Muller M J, Ruof J, Graf-Morgenstern M et al. Quality of partnership in patients with erectile dysfunction after sildenafil treatment. *Pharmacopsychiatry* 2001;34(3):91-95.
- Murat Basar M, Tekdogan U Y, Yilmaz E et al. The efficacy of sildenafil in different etiologies of erectile dysfunction. *International Urology & Nephrology* 2001;32(3):403-407.
- Murphy A M, O'Leary M. Failure of the Ambicor inflatable penile prosthesis to deflate. *Int J Impot Res* 2005;17(3):291-292.

- Murphy J C, Srinivas S, Terris M K. Flutamide administration at 500 mg daily has similar effects on serum testosterone to 750 mg daily. *J Androl* 2004;25(4):630-634.
- Mydlo J H, Viterbo R, Crispin P. Use of combined intracorporal injection and a phosphodiesterase-5 inhibitor therapy for men with a suboptimal response to sildenafil and/or vardenafil monotherapy after radical retropubic prostatectomy. *BJU Int* 2005;95(6):843-846.
- Mydlo J H, Volpe M A, MacChia R J. Results from different patient populations using combined therapy with alprostadil and sildenafil: predictors of satisfaction. *BJU Int* 2000;86(4):469-473.
- Nagai A, Kusumi N, Tsuboi H et al. Intracavernous injection of prostaglandin E1 is effective in patients with erectile dysfunction not responding to phosphodiesterase 5 inhibitors. *Acta Med Okayama* 2005;59(6):279-280.
- Nalesnik J G, Jones L, Kraus S R. Group B streptococcal septicemia following intracavernous injection therapy for erectile dysfunction in diabetes. *Br J Urol* 2004;172(1):151-152.
- Nandipati K, Raina R, Agarwal A et al. Early combination therapy: intracavernosal injections and sildenafil following radical prostatectomy increases sexual activity and the return of natural erections. *Int J Impot Res* 2006;18(5):446-451.
- Naude J H, Le Roux P J. Topical treatment of erectile dysfunction did not show results.[comment]. *BMJ* 1998;316(7140):1318
- Nehra A, Blute M L, Barrett D M et al. Rationale for combination therapy of intraurethral prostaglandin E(1) and sildenafil in the salvage of erectile dysfunction patients desiring noninvasive therapy. *Int J Impot Res* 2002;14(Suppl 1):38-42.
- Nessel Mark A. Yohimbine and pentoxifylline in the treatment of erectile dysfunction. *Am J Psychiatry* 1994;151(3):453
- Nurnberg H G, Hensley P L. Sildenafil citrate for the management of antidepressant-associated erectile dysfunction. *Hillside J Clin Psychiatry* 2003;64Suppl-5.
- Nurnberg H G, Fava M, Gelenberg A J et al. Open-label sildenafil treatment of partial and non-responders to double-blind treatment in men with antidepressant-associated sexual dysfunction. *Int J Impot Res* 2007;19(2):167-175.
- Nurnberg H G, Gelenberg A, Hargreave T B et al. Efficacy of sildenafil citrate for the treatment of erectile dysfunction in men taking serotonin reuptake inhibitors. *Am J Psychiatry* 2001;158(11):1926-1928.
- Nurnberg H G, Lauriello J, Hensley P L et al. Sildenafil for iatrogenic serotonergic antidepressant medication-induced sexual dysfunction in 4 patients.[see comment]. *Hillside J Clin Psychiatry* 1999;60(1):33-35.
- Nurnberg H G, Seidman S N, Gelenberg A J et al. Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. *Urology* 2002;60(2 Suppl 2):58-66.
- Nurnberg H, George Hensley, Paula L et al. Sildenafil in the treatment of sexual dysfunction induced by selective serotonin reuptake inhibitors: An overview. [References]. *CNS Drugs* 2000;13(5):321-335.
- O'Sullivan J D, Hughes A J. Apomorphine-induced penile erections in Parkinson's disease. *Mov Disord* 1998;13(3):536-539.
- Ochiai A, Naya Y, Soh J et al. Efficacy of sildenafil as the first-step therapeutic tool for Japanese patients with erectile dysfunction. *Int J Impot Res* 2005;17(4):339-342.
- Ogura K, Ichioka K, Terada N et al. Role of sildenafil citrate in treatment of erectile dysfunction after radical retropubic prostatectomy. *Int J Urol*. 2004;11(3):159-163.
- Ohebshalom M, Mulhall J P. Transdermal and topical pharmacotherapy for male sexual dysfunction. *Expert Opinion on Drug Delivery* 2005;2(1):115-120.
- Ohebshalom M, Parker M, Guhring P et al. The efficacy of sildenafil citrate following radiation therapy for prostate cancer: temporal considerations. *Br J Urol* 2005;174(1):258-262.
- Opsomer R J, Wese F X, De Groote P et al. The external vacuum device in the management of erectile dysfunction. *Acta Urol Belg* 1997;65(4):13-16.
- Ormrod D, Easthope S E, Figgitt D P. Vardenafil.[erratum appears in *Drugs Aging* 2002;19(11):886]. [Review] [30 refs]. *Drugs Aging* 2002;19(3):217-227.
- Osegebe D N, Shittu O B, Aghaji A E et al. Sildenafil citrate (Viagra) for the treatment of erectile dysfunction in Nigerian men. *Int J Impot Res* 2003;15Suppl-8.
- Osterloh I H, Riley A. Clinical update on sildenafil citrate. [Review] [58 refs]. *Br J Clin Pharmacol* 2002;53(3):219-223.
- Osterloh I H, Collins M, Wicker P et al. Sildenafil citrate (VIAGRA): overall safety profile in 18 double-blind, placebo controlled, clinical trials. [Review] [0 refs]. *Int J Clin Pract* 1999;Supplement.102-105.
- Padma-Nathan H, Yeager J L. An integrated analysis of alprostadil topical cream for the treatment of erectile dysfunction in 1732 patients. *Urology* 2006;68(2):386-391.

- Padma-Nathan H, Goldstein I, Klimberg I et al. Long-term safety and efficacy of oral phentolamine mesylate (Vasomax) in men with mild to moderate erectile dysfunction. *Int J Impot Res* 2002;14(4):266-270.
- Padma-Nathan H, McMurray J G, Pullman W E et al. On-demand IC351 (Cialis) enhances erectile function in patients with erectile dysfunction. *Int J Impot Res* 2001;13(1):2-9.
- Padma-Nathan H, Montorsi F, Giuliano F et al. Vardenafil restores erectile function to normal range in men with erectile dysfunction. *Br J Sex Med* 2007;4(1):152-161.
- Pagani E, Glina S, Puech-Leao P et al. Anxiety and high plasma catecholamines do not impair pharmaco-induced erection of psychogenic erectile dysfunctional patients. *Int J Impot Res* 2003;15(4):282-286.
- Pagani E, Puech-Leao P, Glina S et al. The value of a second injection on the pharmaco-induced erection test. *Int J Impot Res* 1997;9(3):167-168.
- Pallas James, Levine Stephen B, Althof Stanley E et al. A study using Viagra in a mental health practice. [References]. *J Sex Marital Ther* 2000;26(1):41-50.
- Palumbo F, Bettocchi C, Selvaggi F P et al. Sildenafil: efficacy and safety in daily clinical experience. *Eur Urol* 2001;40(2):176-180.
- Pangkahila W I. Evaluation of transurethral application of alprostadil for erectile dysfunction in Indonesians. *Asian J Androl* 2000;2(3):233-236.
- Park K, Ku J H, Kim S W et al. Risk factors in predicting a poor response to sildenafil citrate in elderly men with erectile dysfunction. *BJU Int* 2005;95(3):366-370.
- Parkerson George R J, Willke Richard J, Hays Ron D. An international comparison of the reliability and responsiveness of the Duke Health Profile for measuring health-related quality of life of patients treated with alprostadil for erectile dysfunction. *Med Care* 1999;37(1):56-67.
- Penninga E, Jensen B A, Hansen P B et al. Anagrelide treatment in 52 patients with chronic myeloproliferative diseases. *Clinical & Laboratory Haematology* 2004;26(5):335-340.
- Perimenis P, Athanasopoulos A, Geramoutsos I et al. The incidence of pharmacologically induced priapism in the diagnostic and therapeutic management of 685 men with erectile dysfunction. *Urol Int* 2001;66(1):27-29.
- Perimenis P, Athanasopoulos A, Papathanasopoulos P et al. Gabapentin in the management of the recurrent, refractory, idiopathic priapism. *Int J Impot Res* 2004;16(1):84-85.
- Perimenis P, Markou S, Gyftopoulos K et al. Switching from long-term treatment with self-injections to oral sildenafil in diabetic patients with severe erectile dysfunction. *Eur Urol* 2002;41(4):387-391.
- Pescatori E S, Calpista A, Artibani W et al. Self-injection devices for intracavernosal pharmacotherapy: operational classification and safety considerations. *Int J Impot Res* 1996;8(2):53-57.
- Peskircioglu L, Tekin M I, Demirag A et al. Evaluation of erectile function in renal transplant recipients. *Transplant Proc* 1998;30(3):747-749.
- Peterson C A, Bennett A H, Hellstrom W J et al. Erectile response to transurethral alprostadil, prazosin and alprostadil-prazosin combinations. *Br J Urol* 1998;159(5):1523-1527.
- Petrov V I, Vekel'yan A S, Martyushev A V et al. Impaza and Sildenafil: Comparison of Clinical Effectiveness in Patients with Erectile Dysfunction. *Bull Exp Biol Med* 2003;135-136(Suppl 1):150-151.
- Petty R, Angwin R. How real is the male menopause?. *Br J Gen Pract* 2004;248(1659):452-456.
- Pierce L J, Whittington R, Hanno P M et al. Pharmacologic erection with intracavernosal injection for men with sexual dysfunction following irradiation: a preliminary report. *Int J Radiat Oncol Biol Phys* 1991;21(5):1311-1314.
- Pohanka M, Kanovsky P, Bares M et al. The long-lasting improvement of sexual dysfunction in patients with advanced, fluctuating Parkinson's disease induced by pergolide: evidence from the results of an open, prospective, one-year trial. *Parkinsonism Relat Disord* 2005;11(8):509-512.
- Pohanka M, Kanovsky P, Bares M et al. Pergolide mesylate can improve sexual dysfunction in patients with Parkinson's disease: the results of an open, prospective, 6-month follow-up. *Eur J Neurol* 2004;11(7):483-488.
- Polak K, Wimpissinger B, Berisha F et al. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. *Invest Ophthalmol Vis Sci* 2003;44(11):4872-4876.
- Pomara G, Morelli G, Montorsi F et al. Re: Montorsi F, Salonia A, Briganti A, Barbieri L, Zanni G, Surdi N, Cestari A, Montorsi P, Rigatti P. Vardenafil for the treatment of erectile dysfunction: A critical review of the literature based on personal clinical experience. *Eur Urol* 2005;47:612-21 (multiple letters). *Eur Urol* 2005;48(2):345-346.
- Pomara G, Morelli G, Pomara S et al. Cardiovascular parameter changes in patients with erectile dysfunction using pde-5 inhibitors: a study with sildenafil and vardenafil. *J Androl* 2004;25(4):625-629.

- Pommerville P. Drug treatments for erectile dysfunction: An update. *Geriatrics and Aging* 2004;7(6):10-16.
- Porst H. IC351 (tadalafil, Cialis): update on clinical experience. [Review] [12 refs]. *Int J Impot Res* 2002;14Suppl-64.
- Porst H. Transurethral alprostadil with MUSE (medicated urethral system for erection) vs intracavernous alprostadil--a comparative study in 103 patients with erectile dysfunction.. *Int J Impot Res* 1997;9(4):187-192.
- Porst H. Phosphodiesterase type-5 inhibitors: A critical comparative analysis. *Eau Update Series* 2004;2(2):56-63.
- Porst H, Lungimayr G, utsch-osterreichische S T E A. [Efficacy and tolerability of vardenafil within the time window of 6 hours after administration and beyond. Results of a clinical study carried out in 233 urological offices]. *MMW Fortschr Med* 2005;147(Suppl 1):27-32.
- Potempa A J, Ulbrich E, Bernard I et al. Efficacy of vardenafil in men with erectile dysfunction: a flexible-dose community practice study. *Eur Urol* 2004;46(1):73-79.
- Pradeep C, Car N, Metelko Z. Impotence in diabetic men. *Diabetol Croat* 1996;25(2):61-68.
- Price D. Sildenafil citrate (Viagra) efficacy in the treatment of erectile dysfunction in patients with common concomitant conditions. Sildenafil Study Group. *Int J Clin Pract* 1999;Supplement.102-103.
- Price D E, Cooksey G, Jehu D et al. The management of impotence in diabetic men by vacuum tumescence therapy. *Diabet Med* 1991;8(10):964-967.
- Prieto Castro R M, nglada Curado F J, Regueiro Lopez J C et al. Treatment with sildenafil citrate in renal transplant patients with erectile dysfunction. *BJU Int* 2001;88(3):241-243.
- Priyadarshi S. Oral terbutaline in the management of pharmacologically induced prolonged erection. *Int J Impot Res* 2004;16(5):424-426.
- Pryor J. Vardenafil: update on clinical experience. [Review] [10 refs]. *Int J Impot Res* 2002;14Suppl-9.
- Purvis K, Brekke I, Christiansen E. Determinants of satisfactory rigidity after intracavernosal injection with prostaglandin E1 in men with erectile failure. *Int J Impot Res* 1996;8(1):9-16.
- Radomski S B, Herschorn S, Rangaswamy S. Topical minoxidil in the treatment of male erectile dysfunction. *Br J Urol* 1994;151(5):1225-1226.
- Raffaele R, Vecchio I, Giammusso B et al. Efficacy and safety of fixed-dose oral sildenafil in the treatment of sexual dysfunction in depressed patients with idiopathic Parkinson's disease. *Eur Urol* 2002;41(4):382-386.
- Raina R, Agarwal A, Allamaneni S S et al. Sildenafil citrate and vacuum constriction device combination enhances sexual satisfaction in erectile dysfunction after radical prostatectomy. *Urology* 2005;65(2):360-364.
- Raina R, Agarwal A, Goyal K K et al. Long-term potency after iodine-125 radiotherapy for prostate cancer and role of sildenafil citrate. *Urology* 2003;62(6):1103-1108.
- Raina R, Lakin M M, Agarwal A et al. Long-term intracavernous therapy responders can potentially switch to sildenafil citrate after radical prostatectomy. *Urology* 2004;63(3):532-537.
- Raina R, Lakin M M, Agarwal A et al. Efficacy and factors associated with successful outcome of sildenafil citrate use for erectile dysfunction after radical prostatectomy. *Urology* 2004;63(5):960-966.
- Raina R, Lakin M M, Agarwal A et al. Long-term effect of sildenafil citrate on erectile dysfunction after radical prostatectomy: 3-year follow-up. *Urology* 2003;62(1):110-115.
- Raina R, Lakin M M, Thukral M et al. Long-term efficacy and compliance of intracorporeal (IC) injection for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis. *Int J Impot Res* 2003;15(5):318-322.
- Rajpurkar A, Dhabuwala C B. Comparison of satisfaction rates and erectile function in patients treated with sildenafil, intracavernous prostaglandin E1 and penile implant surgery for erectile dysfunction in urology practice. *Br J Urol* 2003;170(1):159-163.
- Rakic Z, Starcevic V, Starcevic V P et al. Testosterone treatment in men with erectile disorder and low levels of total testosterone in serum. *Arch Sex Behav* 1997;26(5):495-504.
- Ralph D J, Sleep D J, Perdok R J et al. Adverse events and patient tolerability of apomorphine SL 2 and 3 mg: A cross-study analysis of phase II and III studies. *European Urology Supplements* 2002;1(3):21-27.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Rashid A. The efficacy and safety of PDE5 inhibitors. [Review] [30 refs]. *Clin Cornerstone* 2005;7(1):47-56.
- Reiter W J, Schatzl G, Mark I et al. Dehydroepiandrosterone in the treatment of erectile dysfunction in patients with different organic etiologies. *Urol Res* 2001;29(4):278-281.

- Reznik I, Zemishlany Z, Kotler M et al. Sildenafil citrate for the sexual dysfunction in antidepressant-treated male patients with posttraumatic stress disorder. A preliminary pilot open-label study. *Psychotherapy & Psychosomatics* 2002;71(3):173-176.
- Richardson J D. Intracorporeal injections for the treatment of impotence. *Med J Aust* 1991;155(10):688
- Richter S, Vardi Y, Ringel A et al. Intracavernous injections: still the gold standard for treatment of erectile dysfunction in elderly men. *Int J Impot Res* 2001;13(3):172-175.
- Rizvi K, Hampson J P, Harvey J N. Do lipid-lowering drugs cause erectile dysfunction? A systematic review.[see comment]. [Review] [35 refs]. *Fam Pract* 2002;19(1):95-98.
- Roach M, Winter K, Michalski J M et al. Penile bulb dose and impotence after three-dimensional conformal radiotherapy for prostate cancer on RTOG 9406: findings from a prospective, multi-institutional, phase I/II dose-escalation study. *Int J Radiat Oncol Biol Phys* 2004;60(5):1351-1356.
- Robinson P K. An observational study of prostaglandin E-1: comparing trial and maintenance dose. *Urol Nurs* 1994;14(3):76-78.
- Rodilla F, Fuentes M D, Chuan P et al. Penile self-injection for impotence in patients after radical cystectomy. *Journal of Clinical Pharmacy & Therapeutics* 1994;19(6):359-360.
- Rodrigues M, Granegger S, O'Grady J et al. Accumulation of platelets as a key mechanism of human erection. A scintigraphic study in patients with erectile dysfunction receiving intracavernous injection of PGE1, papaverine/phentolamine. *Advances in Experimental Medicine & Biology* 1997;43379-82.
- Rodrigues M, O'Grady J, Stackl W et al. Accumulation of platelets as a key mechanism of human erection. *Thromb Res* 1998;91(2):53-56.
- Rodriguez Vela L, Lledo Garcia E, Rajmil O et al. [Tadalafil vs sildenafil patient preference in Spanish men with erectile dysfunction: results from an International Multicentric Study]. *Actas Urol Esp* 2006;30(1):67-79.
- Rosas S E, Wasserstein A, Kobrin S et al. Preliminary observations of sildenafil treatment for erectile dysfunction in dialysis patients. *Am J Kidney Dis* 2001;37(1):134-137.
- Rosas-Vargas H, Coral-Vazquez R M, Tapia R et al. Glu298Asp endothelial nitric oxide synthase polymorphism is a risk factor for erectile dysfunction in the Mexican Mestizo population. *J Androl* 2004;25(5):728-732.
- Rosen R C, Shabsigh R, Kuritzky L et al. The efficacy of tadalafil in improving sexual satisfaction and overall satisfaction in men with mild, moderate, and severe erectile dysfunction: A retrospective pooled analysis of data from randomized, placebo-controlled clinical trials. *Current Medical Research & Opinion* 2005;21(11):1701-1709.
- Rosen R, Janssen E, Wiegel M et al. Psychological and interpersonal correlates in men with erectile dysfunction and their partners: a pilot study of treatment outcome with sildenafil. *J Sex Marital Ther* 2006;32(3):215-234.
- Rosenstock H A, Axelrad S D. Erectile dysfunction: on the efficacy of a phosphodiesterase inhibitor with concurrent sex therapy. *Asian J Androl* 1999;1(4):207-210.
- Rowland D L, Boedhoe H S M, Dohle G et al. Intracavernosal self-injection therapy in men with erectile dysfunction: Satisfaction and attrition in 119 patients. *Int J Impot Res* 1999;11(3):145-151.
- Rowland D L, Myers L, Culver A et al. Bupropion and sexual function: a placebo-controlled prospective study on diabetic men with erectile dysfunction. *J Clin Psychopharmacol* 1997;17(5):350-357.
- Rubio-Aurioles E, Porst H, Eardley I et al. Comparing vardenafil and sildenafil in the treatment of men with erectile dysfunction and risk factors for cardiovascular disease: a randomized, double-blind, pooled crossover study. *Br J Sex Med* 2006;3(6):1037-1049.
- Rudkin L, Taylor M J, Hawton K. Strategies for managing sexual dysfunction induced by antidepressant medication. [Review] [61 refs]. *Cochrane Database Syst Rev* 2004;(4):CD003382
- Ruof J, Graf-Morgenstern M, Moller M J. Quality of life in patients with erection difficulties: Evaluation of a German version of the "Quality of life measure for men with erection difficulties" (QoL-Med). *Aktuel Urol* 2001;32(1):21-26.
- Saad F, Grahl A S, Aversa A et al. Effects of testosterone on erectile function: implications for the therapy of erectile dysfunction. *BJU Int* 2007;99(5):988-992.
- Saad F, Hoesl C E, Oettel M et al. Dehydroepiandrosterone treatment in the aging male - What should the urologist know?. *Eur Urol* 2005;48(5):724-733.
- Sadeghi-Nejad H, Lim H, Long K et al. Assessment of the efficacy of Viagra (sildenafil citrate) using the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS). *Urol Int* 2003;71(1):100-102.
- Sadovsky R, Althof S. Men's sexual issues. *Clinics in Family Practice* 2004;6(4 SPEC.ISS.):863-915.
- Sahu M A, Ayyaz M, Chaudhry Z. Intracavernous injections of papaverine and phentolamine for treatment of impotence. *J Coll Physicians Surg Pak* 1997;7(3):102-104.

- Saie D J, Sills E S. Hyperprolactinemia presenting with encephalomalacia-associated seizure disorder and infertility: A novel application for bromocriptine therapy in reproductive endocrinology. *Neuroendocrinol Lett* 2005;26(5):533-537.
- Salama N. Nocturnal electrobioimpedance volumetric assessment in diabetic men with erectile dysfunction before and after tadalafil intake. *Int J Impot Res* 2004;16(5):441-447.
- Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr.Med Res Opin.* 2003;19(4):241-262.
- Salonia Andrea, Briganti Alberto, Montorsi Piero et al. Safety and tolerability of oral erectile dysfunction treatments in the elderly. [References]. *Drugs and Aging* 2005;22(4):323-338.
- Sato Y, Horita H, Adachi H et al. Effect of oral administration of prostaglandin E1 on erectile dysfunction. *Br J Urol* 1997;80(5):772-775.
- Savoca G, Silvestre G, Belgrano E. Intracavernosal injection therapy and surgical therapy in diabetic patients with erectile dysfunction. [Review] [26 refs]. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):53-57.
- Schanz S, Hauswirth U, Ulmer A et al. Prostaglandin E(1) ethyl ester, a new agent for topical penile therapy. *Int J Impot Res* 2002;14(4):317-318.
- Schimmer A D, Ali V, Stewart A K et al. Male sexual function after autologous blood or marrow transplantation. *Biology of Blood & Marrow Transplantation* 2001;7(5):279-283.
- Schmid D M, Schurch B, Hauri D. Sildenafil in the treatment of sexual dysfunction in spinal cord-injured male patients. *Eur Urol.* 2000;38(2):184-193.
- Schouman M, Lacroix P, Amer M. Suppression of prostaglandin E1-induced pain by dilution of the drug with lidocaine before intracavernous injection. *Br J Urol* 1992;148(4):1266
- Schroder F H, Whelan P, De Reijke T M et al. Metastatic prostate cancer treated by flutamide versus cyproterone acetate. Final analysis of the "European Organization for Research and Treatment of Cancer" (EORTC) Protocol 30892. *Eur Urol* 2004;45(4):457-464.
- Schulman C C, Shen W, Stothard D R et al. Integrated analysis examining first-dose success, success by dose, and maintenance of success among men taking tadalafil for erectile dysfunction. *Urology* 2004;64(4):783-788.
- Schultheiss D, Stief C G. Physiology and pathophysiology of erection: Consequences for present medical therapy of erectile dysfunction. *Andrologia* 1999;31(SUPPL. 1):59-64.
- Schultheiss D, Hiltl D M, Meschi M R et al. Pilot study of the transdermal application of testosterone gel to the penile skin for the treatment of hypogonadotropic men with erectile dysfunction. *World J Urol* 2000;18(6):431-435.
- Seftel A D. From aspiration to achievement: Assessment and noninvasive treatment of erectile dysfunction in aging men. *J Am Geriatr Soc* 2005;53(1):119-130.
- Se Graves R T, Lee J, Stevenson R et al. Tadalafil for treatment of erectile dysfunction in men on antidepressants. *J Clin Psychopharmacol* 2007;27(1):62-66.
- Seidman S N, Pesce V C, Roose S P. High-dose sildenafil citrate for selective serotonin reuptake inhibitor-associated ejaculatory delay: open clinical trial. *Hillside J Clin Psychiatry* 2003;64(6):721-725.
- Setter S M, Iltz J L, Fincham J E et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. [Review] [75 refs]. *Ann Pharmacother* 2005;39(7-8):1286-1295.
- Sexton W J, Benedict J F, Jarow J P. Comparison of long-term outcomes of penile prostheses and intracavernosal injection therapy.[see comment]. *Br J Urol* 1998;159(3):811-815.
- Shabbir M, Mikhailidis D M, Morgan R J. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors.[comment]. *Current Medical Research & Opinion* 2004;20(5):603-606.
- Shabsigh R. Testosterone therapy in erectile dysfunction and hypogonadism. *Br J Sex Med* 2005;2(6):785-792.
- Shabsigh R. Hypogonadism and erectile dysfunction: The role for testosterone therapy. *Int J Impot Res* 2003;15(SUPPL. 4):S9-S13.
- Shabsigh R, Burnett A L, Eardley I et al. Time from dosing to sexual intercourse attempts in men taking tadalafil in clinical trials. *BJU Int* 2005;96(6):857-863.
- Shabsigh R, Katz M, Yan G et al. Cardiovascular issues in hypogonadism and testosterone therapy. [Review] [44 refs]. *Am J Cardiol* 2005;96(12B):67M-72M.
- Shabsigh R, Padma-Nathan H, Gittleman M et al. Intracavernous alprostadil alfadex (EDEX/VIRIDAL) is effective and safe in patients with erectile dysfunction after failing sildenafil (Viagra). *Urology* 2000;55(4):477-480.
- Shamloul R. Management of honeymoon impotence. *Br J Sex Med* 2006;3(2):361-366.
- Shamloul R, Atteya A, Elnashaar A et al. Intracavernous sodium nitroprusside (SNP) versus papaverine/phentolamine in erectile dysfunction: A comparative study of short- term efficacy and side-effects. *Br J Sex Med* 2005;2(1):117-120.

- Shamloul Rany, Kamel Ihab, E-Mail Address et al. Early Treatment of Cavernosis Resulted in Erectile Function Preservation. [References]. *Br J Sex Med* 2006;3(2):320-322.
- Sharlip I D. Editorial comment. *International Braz J Urol* 2005;31(4):354-355.
- Sharlip I D. Can self-injection therapy cure impotence?. [Review] [7 refs]. *Advances in Experimental Medicine & Biology* 1997;43383-86.
- Sharma R K, Prasad N, Kapoor R et al. Treatment of erectile dysfunction with sildenafil citrate in renal transplant recipient: a cross over placebo controlled trial [abstract]. *Indian Journal of Nephrology* 2002;12(4):23-238.
- Shemtov O M, Radomski S B, Crook J. Success of sildenafil for erectile dysfunction in men treated with brachytherapy or external beam radiation for prostate cancer. *Can J Urol* 2004;11(6):2450-2455.
- Shenfeld O Z, Gofrit O N, Gdor Y et al. The role of sildenafil in the treatment of erectile dysfunction in patients with pelvic fracture urethral disruption. *Br J Urol* 2004;172(6 I):2350-2352.
- Sheu J Y, Chen K K, Lin A T et al. Long-term efficacy and safety of sildenafil for patients with erectile dysfunction. *Journal of the Chinese Medical Association: JCMA* 2003;66(8):480-486.
- Shigemura K, Arakawa S, Kamidono S et al. Effect of sildenafil on arterial stiffness, as assessed by pulse wave velocity, in patients with erectile dysfunction. *Int J Urol* 2006;13(7):956-959.
- Shimon I, Lubina A, Gorfine M et al. Feedback inhibition of gonadotropins by testosterone in men with hypogonadotropic hypogonadism: comparison to the intact pituitary-testicular axis in primary hypogonadism. *J Androl* 2006;27(3):358-364.
- Shokeir A A, Alserafi M A, Mutabagani H. Intracavernosal versus intraurethral alprostadil: a prospective randomized study. *BJU Int* 1999;83(7):812-815.
- Siegel R L, Dubin N H, Andrade J R. Sildenafil citrate and sperm function [3] (multiple letters). *American Journal of Obstetrics & Gynecology* 2001;184(4):777-778.
- Sighinolfi M C, de Stefani S, Mofferdin A et al. Intracavernous prostaglandin E1 infusion in diabetes with associated ischemic necrosis of the glans penis. *Br J Urol* 2004;171(6 I):2380
- Silvestri A, Galetta P, Cerquetani E et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo.[see comment]. *Eur Heart J* 2003;24(21):1928-1932.
- Singh A N, Scurlock H, Catalan J. Paroxetine induced erectile dysfunction successfully treated with yohimbine in patients suffering from HIV infection. *Journal of Serotonin Research* 1995;1(4):283-285.
- Slob A K, Verhulst A C M, Gijs L et al. Intracavernous injection during diagnostic screening for erectile dysfunction: Five-year experience with over 600 patients. [References]. *Br J Sex Med* 2002;28(1):61-70.
- Smith K M, Romanelli F. Recreational use and misuse of phosphodiesterase 5 inhibitors. [Review] [56 refs]. *Journal of the American Pharmacists Association: JAPhA* 2005;45(1):63-72.
- Soh J, Naya Y, Ushijima S et al. Efficacy of sildenafil for Japanese patients with audio-visual sexual stimulation (AVSS) test by the RigiScan Plus. *Arch Androl* 2006;52(3):163-168.
- Soler J M, Previnaire J G, Denys P et al. Phosphodiesterase inhibitors in the treatment of erectile dysfunction in spinal cord-injured men. *Proc Annu Clin Spinal Cord Inj Conf* 2007;45(2):169-173.
- Sommer F, Engelmann U. Vardenafil: Bayer Yakuhin. *Curr Opin Investig Drugs* 2002;3(4):607-613.
- Sonksen J, Biering-Sorensen F. Transcutaneous nitroglycerin in the treatment of erectile dysfunction in spinal cord injured. *Paraplegia* 1992;30(8):554-557.
- Sparwasser C, Treiber U, Bahren W et al. Postoperative erectile dysfunction; evaluation and treatment with intracavernous vasoactive injections. *Progress in Clinical & Biological Research* 1991;370349-354.
- Speckens A E, Kattemolle M R, Hengeveld M W et al. A prospective long-term follow-up study of patients evaluated for erectile dysfunction: outcome and associated factors. *Int J Impot Res* 1995;7(2):101-110.
- Speel T G W, Bleumer I, Diemont W L et al. The value of sildenafil as mode of stimulation in pharmaco-penile duplex ultrasonography. *Int J Impot Res* 2001;13(4):189-191.
- Sperling H, Eisenhardt A, Virchow S et al. Sildenafil response is influenced by the G protein beta 3 subunit GNB3 C825T polymorphism: a pilot study. *Br J Urol* 2003;169(3):1048-1051.
- Stanislavov R, Nikolova V. Treatment of erectile dysfunction with pycnogenol and L-arginine. *J Sex Marital Ther* 2003;29(3):207-213.
- Steers W, Guay A T, Leriche A et al. Assessment of the efficacy and safety of Viagra (sildenafil citrate) in men with erectile dysfunction during long-term treatment. *Int J Impot Res* 2001;13(5):261-267.

- Steidle C P, McCullough A R, Kaminetsky J C et al. Early sildenafil dose optimization and personalized instruction improves the frequency, flexibility, and success of sexual intercourse in men with erectile dysfunction. *Int J Impot Res* 2007;19(2):154-160.
- Stephenson R A, Mori M, Hsieh Y C et al. Treatment of erectile dysfunction following therapy for clinically localized prostate cancer: patient reported use and outcomes from the Surveillance, Epidemiology, and End Results Prostate Cancer Outcomes Study. *Br J Urol* 2005;174(2):646-650.
- Stief C G, Holmquist F, Djamilian M et al. Preliminary results with the nitric oxide donor linsidomine chlorhydrate in the treatment of human erectile dysfunction. *Br J Urol* 1992;148(5):1437-1440.
- Stief C G, Uckert S, Jonas U. Strategies in the oral pharmacotherapy of male erectile dysfunction viewed from bench and bedside (Part II). *The Journal of Mens Health & Gender* 2005;2(3):325-332.
- Stief C G, Wetterauer U, Schaebdsau F H et al. Calcitonin-gene-related peptide: a possible role in human penile erection and its therapeutic application in impotent patients. *Br J Urol* 1991;146(4):1010-1014.
- Stief C, Padley R J, Perdok R J et al. Cross-study review of the clinical efficacy of apomorphine SL 2 and 3 mg: Pooled data from three placebo-controlled, fixed-dose crossover studies. *European Urology Supplements* 2002;1(3):12-20.
- Strahilevitz J, Rahav G, Schroers H-J et al. An outbreak of Phialemonium infective endocarditis linked to intracavernous penile injections for the treatment of impotence. *Clin Infect Dis* 2005;40(6):781-786.
- Stroberg P, Murphy A, Costigan T. Switching patients with erectile dysfunction from sildenafil citrate to tadalafil: results of a European multicenter, open-label study of patient preference. *Clin Ther.* 2003;25(11):2724-2737.
- Stuckey B G A. Tadalafil phase 3 experience. *European Urology Supplements* 2002;1(8):25-30.
- Swartz D A, Todd M W. Intracavernous papaverine and glaucoma.[see comment]. *JAMA* 1990;264(5):570
- Tam P Y, Keller T, Poppiti R et al. Hemodynamic effects of transurethral alprostadil measured by color duplex ultrasonography in men with erectile dysfunction. *Br J Urol* 1998;160(4):1321-1324.
- Tam S W, Worcel M, Wyllie M. Yohimbine: a clinical review. [Review] [152 refs]. *Pharmacol Ther* 2001;91(3):215-243.
- Tanaka T. Papaverine hydrochloride in peripheral blood and the degree of penile erection. *Br J Urol* 1990;143(6):1135-1137.
- Tariq S H, Haleem U, Omran M L et al. Erectile dysfunction: Etiology and treatment in young and old patients. *Clin Geriatr Med* 2003;19(3):539-551.
- Tas A, Ersoy A, Ersoy C et al. Efficacy of sildenafil in male dialysis patients with erectile dysfunction unresponsive to erythropoietin and/or testosterone treatments. *Int J Impot Res* 2006;18(1):61-68.
- Taylor M J, Rudkin L, Hawton K. Strategies for managing antidepressant-induced sexual dysfunction: Systematic review of randomised controlled trials. *J Affect.Disord.* 2005;88(3):241-254.
- Tekdogan U, Tuncel A, Tuğlu D et al. Effect of sildenafil citrate treatment on serum dehydroepiandrosterone sulfate levels in patients with erectile dysfunction. *Urology* 2006;68(3):626-630.
- Telias Isaac, Darwin Kadmon-Telias, Ana E-Mail et al. Four cases of erectile dysfunction in substance abusers treated with sildenafil. [References]. *J Addict Dis* 2002;97(11):1473-1474.
- Teloken C, Rhoden E L, Sogari P et al. Therapeutic effects of high dose yohimbine hydrochloride on organic erectile dysfunction. *Br J Urol* 1998;159(1):122-124.
- Terradas C, Levalle O, Nagelberg A et al. Sildenafil improves nocturnal penile erections in organic impotence. *Int J Impot Res* 2001;13(2):125-129.
- Tomlinson John M, Wright David, E-Mail Address et al. Impact of erectile dysfunction and its subsequent treatment with sildenafil: Qualitative study. [References]. *BMJ: British Medical Journal* 2004;328(7447):No
- Tomsak R. PDE5 inhibitors and permanent visual loss. *Int J Impot Res* 2005;17(6):547-549.
- Tosti A, Pazzaglia M, Soli M et al. Evaluation of sexual function with an international index of erectile function in subjects taking finasteride for androgenetic alopecia.[see comment]. *Arch Dermatol* 2004;140(7):857-858.
- Trinchieri A, Nicola M, Masini F et al. Prospective comprehensive assessment of sexual function after retropubic non nerve sparing radical prostatectomy for localized prostate cancer. *Arch Ital Urol Androl* 2005;77(4):219-223.
- Truss M C, Becker A J, Thon W F et al. Intracavernous calcitonin gene-related peptide plus prostaglandin E1: possible alternative to penile implants in selected patients. *Eur Urol* 1994;26(1):40-45.
- Tsai Y S, Lin J S, Lin Y M. Safety and efficacy of alprostadil sterile powder (S. Po., CAVERJECT) in diabetic patients with erectile dysfunction. *Eur Urol* 2000;38(2):177-183.

- Tsujimura A, Yamanaka M, Takahashi T et al. The clinical studies of sildenafil for the ageing male. *Int J Androl* 2002;25(1):28-33.
- Turk S, Karalezli G, Tonbul H Z et al. Erectile dysfunction and the effects of sildenafil treatment in patients on haemodialysis and continuous ambulatory peritoneal dialysis. *Nephrol.Dial.Transplant.* 2001;16(9):1818-1822.
- Turner L A, Althof S E. The clinical effectiveness of self-injection and external vacuum devices in the treatment of erectile dysfunction: a six-month comparison. *Psychiatr Med* 1992;10(2):283-293.
- Turner L A, Althof S E, Levine S B et al. Twelve-month comparison of two treatments for erectile dysfunction: self-injection versus external vacuum devices. *Urology* 1992;39(2):139-144.
- Urciuoli R, Cantisani T A, Carlini M et al. Prostaglandin E1 for treatment of erectile dysfunction. *Cochrane Database Syst Rev* 2004;(2):CD001784
- Valicenti R K, Choi E, Chen C et al. Sildenafil citrate effectively reverses sexual dysfunction induced by three-dimensional conformal radiation therapy. *Urology* 2001;57(4):769-773.
- Valiquette L, Montorsi F, Hellstrom W J et al. Penetration and maintenance of erection with vardenafil: a time-from-dosing analysis. *Can J Urol* 2005;12(3):2687-2698.
- van Basten J P, Van Driel M F, Jonker-Pool G et al. Sexual functioning in testosterone-supplemented patients treated for bilateral testicular cancer. *Br J Urol* 1997;79(3):461-467.
- van Moorselaar R J, Hartung R, Emberton M et al. Alfuzosin 10 mg once daily improves sexual function in men with lower urinary tract symptoms and concomitant sexual dysfunction. *BJU Int* 2005;95(4):603-608.
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Dijk M, Skrekas T, De La et al. The association between lower urinary tract symptoms and sexual dysfunction: Fact or fiction?. *Curr Opin Urol* 2005;15(1):39-44.
- Vardi M, Nini A. Phosphodiesterase inhibitors for erectile dysfunction in patients with diabetes mellitus. [Review] [49 refs]. *Cochrane Database Syst Rev* 2007;(1):CD002187
- Vardi Y, Sprecher E, Gruenwald I. Logistic regression and survival analysis of 450 impotent patients treated with injection therapy: long-term dropout parameters.. *Br J Urol* 2000;163(2):467-470.
- Vickers M A, De Nobrega A M, Dluhy R G. Diagnosis and treatment of psychogenic erectile dysfunction in a urological setting: Outcomes of 18 consecutive patients. *Br J Urol* 1993;149(5 SUPPL.):1258-1261.
- Virag R. Indications and early results of sildenafil (Viagra) in erectile dysfunction. *Urology* 1999;54(6):1073-1077.
- Virag R. Intracavernous injection of papaverine for erectile failure. 1982. *Br J Urol* 2002;167(2 Pt 2):1196
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.
- Vitezic D. A risk-benefit assessment of sildenafil in the treatment of erectile dysfunction. [Review] [72 refs]. *Drug Saf* 2001;24(4):255-265.
- von Heyden B, Donatucci C F, Kaula N et al. Intracavernous pharmacotherapy for impotence: selection of appropriate agent and dose. [Review] [23 refs]. *Br J Urol* 1993;149(5 Pt 2):1288-1290.
- Wagner G, Montorsi F, Auerbach S et al. Sildenafil citrate (VIAGRA) improves erectile function in elderly patients with erectile dysfunction: a subgroup analysis. *J Gerontol A Biol.Sci Med Sci* 2001;56(2):M113-M119.
- Wagrell L, Schelin S, Nordling J et al. Three-year follow-up of feedback microwave thermotherapy versus TURP for clinical BPH: a prospective randomized multicenter study. *Urology* 2004;64(4):698-702.
- Wang C J, Wu C C, Huang C H et al. A comparative study with intracavernous injection of prostaglandin E1 versus papaverine for the diagnostic assessment of erectile impotence. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1992;8(11):585-590.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Webb D J, Freestone S, Allen M J et al. Sildenafil citrate and blood-pressure-lowering drugs: results of drug interaction studies with an organic nitrate and a calcium antagonist. *Am J Cardiol* 1999;83(5A):21C-28C.
- Weber D C, Bieri S, Kurtz J M et al. Prospective pilot study of sildenafil for treatment of postradiotherapy erectile dysfunction in patients with prostate cancer. *Am J Clin Oncol* 1999;17(11):3444-3449.
- Weidner W, Schroeder-Printzen I, Fischer C et al. Experience in the treatment of erectile dysfunction using the intracavernosal self-injection of papaverine: Results of a prospective study after a median follow-up of 42 months involving 135 patients and 10766 injections. *World J Urol* 1992;10(3):179-182.

- Weiss J N, Badlani G H, Ravalli R et al. Reasons for high drop-out rate with self-injection therapy for impotence. *Int J Impot Res* 1994;6(3):171-174.
- Weiss J N, Ravalli R, Badlani G H. Intracavernous pharmacotherapy in psychogenic impotence. *Urology* 1991;37(5):441-443.
- Wen H S, Hsieh C H, Hsu G L et al. The synergism of penile venous surgery and oral sildenafil in treating patients with erectile dysfunction.[see comment]. *Int J Androl* 2005;28(5):297-303.
- Werneke U, Crowe M. Review of patients with erectile dysfunction attending the Maudsley psychosexual clinic in 1999: The impact of sildenafil. *Sexual & Relationship Therapy* 2002;17(2):171-185.
- Werthman P, Rajfer J. MUSE therapy: preliminary clinical observations. *Urology* 1997;50(5):809-811.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Williams G. Male erectile dysfunction. *Prescribers' Journal* 2000;40(1):49-58.
- Williams G, Abbou C C, Amar E T et al. The effect of transurethral alprostadil on the quality of life of men with erectile dysfunction, and their partners. MUSE Study Group. *Br J Urol* 1998;82(6):847-854.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):
- Willke R J, Glick H A, McCarron T J et al. Quality of life effects of alprostadil therapy for erectile dysfunction. *Br J Urol* 1997;157(6):2124-2128.
- Wise Thomas N. Psychosocial side effects of sildenafil therapy for erectile dysfunction. *J Sex Marital Ther* 1999;25(2):145-150.
- Wolfson B, Pickett S, Scott N E et al. Intraurethral prostaglandin E-2 cream: a possible alternative treatment for erectile dysfunction. *Urology* 1993;42(1):73-75.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wu C C, Xue Z Y, Apichat K et al. The use of alprostadil sterile powder in a home self-injection study of Asian men with erectile dysfunction. *Clin Ther* 1996;18(2):256-264.
- Wylie Kevan R, Hallam-Jones Ruth A, Steward David et al. The combination of penoscrotal rings and PDE5i's in the treatment of erectile dysfunction - the Sheffield PDE5i and Ring Duo Technique. Two case reports. [References]. *Sexual and Relationship Therapy* 2006;21(2):209-215.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yaman O, Tokatli Z, Akand M et al. Characteristics of sildenafil erections in healthy young men. *Asian J Androl* 2005;7(4):395-398.
- Yassin A A, Saad F. Improvement of sexual function in men with late-onset hypogonadism treated with testosterone only. *Br J Sex Med* 2007;4(2):497-501.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.
- Yassin A A, Saad F, Traish A. Testosterone undecanoate restores erectile function in a subset of patients with venous leakage: a series of case reports. *Br J Sex Med* 2006;3(4):727-735.
- Yenicierioglu Y, Kefi A, Aslan G et al. Efficacy and safety of sildenafil for treating erectile dysfunction in patients on dialysis. *BJU Int* 2002;90(4):442-445.
- Zaher T F. Papaverine plus prostaglandin E1 versus prostaglandin E1 alone for intracorporeal injection therapy. *Int Urol Nephrol* 1998;30(2):193-196.
- Zargooshi J. Unconsummated marriage: clarification of aetiology; treatment with intracorporeal injection. *BJU Int* 2000;86(1):75-79.
- Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200
- Zelevsky M J, McKee A B, Lee H et al. Efficacy of oral sildenafil in patients with erectile dysfunction after radiotherapy for carcinoma of the prostate. *Urology* 1999;53(4):775-778.
- Zesiewicz T A, Helal M, Hauser R A. Sildenafil citrate (Viagra) for the treatment of erectile dysfunction in men with Parkinson's disease. *Mov Disord* 2000;15(2):305-308.
- Zhang Y, Guan D L, Ou T W et al. Sildenafil citrate treatment for erectile dysfunction after kidney transplantation. *Transplant Proc* 2005;37(5):2100-2103.
- Ziegler D. Management of erectile dysfunction in diabetic patients. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):58-65.

- Zippe C D, Kedia A W, Kedia K et al. Treatment of erectile dysfunction after radical prostatectomy with sildenafil citrate (Viagra). *Urology* 1998;52(6):963-966.
- Zippe C D, Kedia S, Kedia A W et al. Sildenafil citrate (Viagra) after radical retropubic prostatectomy: pro. *Urology* 1999;54(4):583-586.
- Zlotta A R, Teillac P, Raynaud J P et al. Evaluation of male sexual function in patients with Lower Urinary Tract Symptoms (LUTS) associated with Benign Prostatic Hyperplasia (BPH) treated with a phytotherapeutic agent (Permixon), Tamsulosin or Finasteride. *Eur Urol* 2005;48(2):269-276.
- Zorgniotti A. "On demand" oral drug for erection in impotent men'. *Br J Urol* 1992;147308
- Zorgniotti A W. Experience with buccal phentolamine mesylate for impotence. *Int J Impot Res* 1994;6(1):37-41.
- Zusman R M, Morales A, Glasser D B et al. Overall cardiovascular profile of sildenafil citrate. [Review] [33 refs]. *Am J Cardiol* 1999;83(5A):35C-44C.
- Not applicable.**
- Annual update 2004/2005 - Treatment of genitourinary disorders. *Drugs of the Future* 2005;30(9):931-934.
- Abrams J. Time course of the interaction between tadalafil and nitrates.[comment]. *J Am Coll Cardiol* 2004;43(11):2150-2151.
- Adaikan P G, Chong Y S, Chew S S L et al. Male sexual dysfunction. *Curr Obstet Gynaecol* 2000;10(1):23-28.
- Ahl J, Kinon B J, Liu-Seifert H. Sexual dysfunction associated with neuroleptic-induced hyperprolactinemia improves with reduction in prolactin levels. *Ann N Y Acad Sci* 2004;1032(pp 289-290):-290.
- Ahuja S K, Krane N K, Hellstrom W J. Penile prostheses in the management of impotence in patients with end-stage renal disease. *J La State Med Soc* 1998;150(1):32-34.
- Akbari F, Alavi M, Esteghamati A et al. Effect of renal transplantation on sperm quality and sex hormone levels. *BJU Int* 2003;92(3):281-283.
- Akkus E, Kadioglu A, Esen A et al. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. *Eur Urol* 2002;41(3):298-304.
- Alexandre B, Lemaire A, Desvaux P et al. Intracavernous injections of prostaglandin E1 for erectile dysfunction: patient satisfaction and quality of sex life on long-term treatment. *Br J Sex Med* 2007;4(2):426-431.
- Alfonso A, Rieniets K I, Vigersky R A. Incidence and clinical significance of elevated macroprolactin levels in patients with hyperprolactinemia. *Endocr Pract* 2006;12(3):275-280.
- Alivizatos G, Skolarikos A, Laguna P. Recent data upon impotence, incontinence and quality of life issues concerning radical prostatectomy. [Review] [74 refs]. *Arch Esp Urol* 2003;56(3):321-330.
- Althof S E. Quality of life and erectile dysfunction. *Urology* 2002;59(6):803-810.
- Althof S E, Corty E W, Levine S B et al. EDITS: development of questionnaires for evaluating satisfaction with treatments for erectile dysfunction. *Urology* 1999;53(4):793-799.
- Althof Stanley E, Turner Louisa A. Self-injection therapy and external vacuum devices in the treatment of erectile dysfunction: Methods and outcome. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Anderson R A, Bancroft J, Wu F C. The effects of exogenous testosterone on sexuality and mood of normal men. *Journal of Clinical Endocrinology & Metabolism* 1992;75(6):1503-1507.
- Anderson R A, Martin C W, Kung A W et al. 7Alpha-methyl-19-nortestosterone maintains sexual behavior and mood in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 1999;84(10):3556-3562.
- Anderson R A, Wallace A M, Sattar N et al. Evidence for tissue selectivity of the synthetic androgen 7 alpha-methyl-19-nortestosterone in hypogonadal men. *Journal of Clinical Endocrinology & Metabolism* 2003;88(6):2784-2793.
- Andersson K-E. Pharmacology of penile erection. *Pharmacol Rev* 2001;53(3):417-450.
- Andolsek K M. Alprostadil for the treatment of erectile dysfunction. *Am Fam Physician* 1997;55(5):1902-1903.
- Andriole G, Bruchofsky N, Chung L W K et al. Dihydrotestosterone and the prostate: The scientific rationale for 5 α -reductase inhibitors in the treatment of benign prostatic hyperplasia. *Br J Urol* 2004;172(4 I):1399-1403.
- Anonymous. Tadalafil: new preparation. Slightly more convenient, but poorly assessed in organic disorders. *Prescrire Int* 2003;12(68):213-215.
- Anonymous. Tadalafil (cialis) for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 2003;45(1172):101-102.
- Anonymous. First study of Viagra in black men demonstrates effective, well-tolerated treatment. *Urol Nurs* 2002;22(4):285-286.

- Anonymous. Study shows patients taking vardenafil consistently completed sexual intercourse. *Urol Nurs* 2001;21(6):413-414.
- Anonymous. Apomorphine (TAP holdings). 6a beta-aporphine-10,11-diol hydrochloride hemihydrate, apomorphine hydrochloride, spontane, Uprima. *Drugs in R & D* 1999;2(6):415-416.
- Anonymous. Intraurethral alprostadil for impotence. *Medical Letter on Drugs & Therapeutics* 1997;39(997):32
- Anonymous. Treatment for impotence gains FDA approval. *Am J Health Syst Pharm* 1995;52(19):2078-2079.
- Anonymous. Intracavernous injection of alprostadil for erectile dysfunction. *Medical Letter on Drugs & Therapeutics* 1995;37(958):83-84.
- Anonymous. Vardenafil works for 10 hours. *Can Pharm J* 2005;275(7360):133
- Anonymous. Treatment duration of action is important in ED. *Can Pharm J* 2004;273(7330):878
- Anonymous. Dutasteride. *Prescrire Int* 2004;13(73):183
- Anonymous. Erratum: Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo controlled, crossover study (*Indian Journal of Pharmacology* (2004) vol. 37 (5) (317)). *Indian J Pharmacol* 2004;36(6):391
- Anonymous. Partnership struck between Bayer and Schering. *Nat Rev Genet* 2004;3(10):819
- Anonymous. Erectile dysfunction drugs may reduce fertility but help depression. *Can Pharm J* 2004;272(7294):439
- Anonymous. Sildenafil appears safe and effective for some heart failure patients. *Can Pharm J* 2004;272(7290):310
- Anonymous. What to do when oral treatment fails?. *Int J Impot Res* 2003;15(SUPPL. 7):S30-S32.
- Anonymous. Oral drug treatment of erectile dysfunction. *Int J Impot Res* 2003;15(SUPPL. 7):S27-S29.
- Anonymous. Counselling and increased dose of sildenafil improves response in ED. *British Journal of Diabetes & Vascular Disease* 2003;3(6):445
- Anonymous. Improve erectile function early after prostatectomy. *Med Today* 2003;4(11):8-9.
- Anonymous. Recent FDA approval of new erectile dysfunction drug provides first challenge to sildenafil. *Geriatrics and Aging* 2003;6(8):11
- Anonymous. New PDE 5 inhibitor efficacious for erectile dysfunction in diabetics. *Cardiology Review* 2003;20(10):
- Anonymous. Inhaled apomorphine promising for erectile dysfunction treatment. *Can Pharm J* 2003;271(7261):170
- Anonymous. Transurethral alprostadil. *Prescrire Int* 2002;11(61):144
- Anonymous. IDdb News focus. *Current Drug Discovery* 2003;(pp 10-13):-13.
- Anonymous. Sildenafil effective for sexual dysfunction associated with use of antidepressants. *Can Pharm J* 2003;270(7231):41
- Anonymous. Vardenafil prolongs improved erectile function in diabetics. *Cardiology Review* 2002;19(10):38-39.
- Anonymous. Erectile dysfunction treated effectively with tadalafil. *Economics of Neuroscience* 2001;3(11):19
- Anonymous. New erectile dysfunction drug useful in diabetes. *Can Pharm J* 2001;267(7173):669
- Anonymous. Erectile dysfunction - Alprostadil. *Manuf Chem Aerosol News* 2001;72(11):21
- Anonymous. Erectile dysfunction - Vardenafil. *Manuf Chem Aerosol News* 2001;72(6):25
- Anonymous. FDA approves oral therapy for erectile dysfunction. *Am J Health Syst Pharm* 1998;55(10):981-984.
- Anonymous. Sildenafil Viagra(R) UK-92480: Treatment of erectile dysfunction phosphodiesterase V inhibitor. *Drugs of the Future* 1998;23(2):242-243.
- Anonymous. Intracavernosal alprostadil for erectile dysfunction. *Hospital Practice (Office Edition)* 1996;31(8):136-137.
- Anonymous. Intracavernous alprostadil: Effective therapy for erectile dysfunction. *Drugs & Therapy Perspectives* 1996;7(6):1-5.
- Anonymous. Heart drug with 'viagra side-effect'. *Indian J Med Sci* 1999;53(5):236
- Anonymous. What to do if Viagra won't do. *Harvard Mens Health Watch* 2005;9(10):4-8.
- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: intracavernous injection of prostaglandin E1. *JAMA* 1991;265(24):3321-3323.

- Anonymous. Diagnostic and therapeutic technology assessment. Vasoactive intracavernous pharmacotherapy for impotence: papaverine and phentolamine. *JAMA* 1990;264(6):752-754.
- Ansong K S, Punwaney R B. An assessment of the clinical relevance of serum testosterone level determination in the evaluation of men with low sexual drive. *Br J Urol* 1999;162(3 I):719-721.
- Ansong K S, Lewis C, Jenkins P et al. Epidemiology of erectile dysfunction: a community-based study in rural New York State. *Ann Epidemiol* 2000;10(5):293-296.
- Arafa M, Eid H, Shamloul R. Significance of phentolamine redosing during prostaglandin E1 penile color Doppler ultrasonography in diagnosis of vascular erectile dysfunction. *Int J Urol* 2007;14(5):476-477.
- Araujo A B, O'Donnell A B, Brambilla D J et al. Prevalence and incidence of androgen deficiency in middle-aged and older men: Estimates from the Massachusetts male aging study. *Journal of Clinical Endocrinology & Metabolism* 2004;89(12):5920-5926.
- Araujo Andre B, Durante Richard, Feldman Henry A et al. The relationship between depressive symptoms and male erectile dysfunction: Cross-sectional results from the Massachusetts male aging study. *Psychosom Med* 1998;60(4):458-465.
- Arnavaz A, Aurich A, Weissenborn K et al. Effect of sildenafil (Viagra) on cerebral blood flow velocity: a pilot study. *Psychiatry Res* 2003;122(3):207-209.
- Arnold R, Beer D, Bhalay G et al. 8-Aryl xanthines potent inhibitors of phosphodiesterase 5. *Bioorg Med Chem Lett* 2002;12(18):2587-2590.
- Aronson J K. Features of this month's Journal. *Br J Clin Pharmacol* 2003;55(4):327-328.
- Arslan D, Esen A A, Secil M et al. A new method for the evaluation of erectile dysfunction: sildenafil plus Doppler ultrasonography. *Br J Urol* 2001;166(1):181-184.
- Arthur R. Cardiovascular disorders and erectile dysfunction. *British Journal of Cardiology* 2002;9(3):144-145.
- Ashton A K, Jamerson B D, Weinstein W L et al. Antidepressant-related adverse effects impacting treatment compliance: Results of a patient survey. *Current Therapeutic Research, Clinical & Experimental* 2005;66(2):96-106.
- Atala A. What's new in urology. *J Am Coll Surg* 2004;199(3):446-461.
- Atikeler M K, Gecit I, Senol F A. Optimum usage of prilocaine-lidocaine cream in premature ejaculation. *Andrologia* 2002;34(6):356-359.
- Atmaca M, Kuloglu M, Tezcan E. A new atypical antipsychotic: quetiapine-induced sexual dysfunctions. *Int J Impot Res* 2005;17(2):201-203.
- Avasthi A, Basu D, Kulhara P et al. Psychosexual dysfunction in Indian male patients: Revisited after seven years. *Arch Sex Behav* 1994;23(6):685-695.
- Aversa A, Mazzilli F, Rossi T et al. Effects of sildenafil (Viagra) administration on seminal parameters and post-ejaculatory refractory time in normal males. *Hum Reprod* 2000;15(1):131-134.
- Aydin S, Unal D, Erol H et al. Multicenter clinical evaluation of the aetiology of erectile dysfunction: a survey report. *International Urology & Nephrology* 2001;32(4):699-703.
- Ayub W, Fletcher S. End-stage renal disease and erectile dysfunction. Is there any hope?. *Nephrology Dialysis Transplantation* 2000;15(10):1525-1528.
- Bagatell C J, Heiman J R, Rivier J E et al. Effects of endogenous testosterone and estradiol on sexual behavior in normal young men.[erratum appears in *J Clin Endocrinol Metab* 1994 Jun;78(6):1520]. *Journal of Clinical Endocrinology & Metabolism* 1994;78(3):711-716.
- Baggaley M R, Hirst J F, Watson J P. Outcome of patients referred to a psychosexual clinic with erectile failure. *Sexual & Marital Therapy* 1996;11(2):123-130.
- Bai W J, Zhu J C, Jiang H et al. [A comparative study of different vasoactive drugs in the treatment of impotence]. *Chinese Journal of Urology* 1992;13(6):453-455.
- Bailey J, Evans J P, Hardy M et al. Synopsis: 2005 Annual Meeting of the American Society of Andrology. *J Androl* 2005;26(6):678-688.
- Bancroft J, Munoz M, Beard M et al. The effects of a new alpha-2 adrenoceptor antagonist on sleep and nocturnal penile tumescence in normal male volunteers and men with erectile dysfunction. *Psychosom Med* 1995;57(4):345-356.
- Baniel J, Israilov S, Segenreich E et al. Comparative evaluation of treatments for erectile dysfunction in patients with prostate cancer after radical retropubic prostatectomy. *BJU Int* 2001;88(1):58-62.
- Barnas J, Parker M, Guhring P et al. The utility of tamsulosin in the management of orgasm-associated pain: a pilot analysis.[see comment]. *Eur Urol* 2005;47(3):361-365.
- Barqawi A, O'Donnell C, Kumar R et al. Correlation between LUTS (AUA-SS) and erectile dysfunction (SHIM) in an age-matched racially diverse male population: data from the Prostate Cancer Awareness Week (PCAW). *Int J Impot Res* 2005;17(4):370-374.

- Bartlik Barbara D, Kaplan Peter, Kaplan Helen S. Psychostimulants apparently reverse sexual dysfunction secondary to selective serotonin re-uptake inhibitors. *J Sex Marital Ther* 1995;21(4):264-271.
- Bayes M, Rabasseda X, Prous J R. Gateways to Clinical Trials. *Methods & Findings in Experimental & Clinical Pharmacology* 2004;26(9):723-753.
- bdel-Khalek M, El-Hammady S, Ibrahim el. A 4-year follow-up of a randomized prospective study comparing transurethral electrovaporization of the prostate with neodymium: YAG laser therapy for treating benign prostatic hyperplasia. *BJU Int* 2003;91(9):801-805.
- Beard S, Hunn A, Wight J. Treatments for spasticity and pain in multiple sclerosis: A systematic review. *Health Technol Assess* 2003;7(40):111p
- Beasley C M, Mitchell M I, Dmitrienko A A et al. The combined use of ibutilide as an active control with intensive electrocardiographic sampling and signal averaging as a sensitive method to assess the effects of tadalafil on the human QT interval.[see comment]. *J Am Coll Cardiol* 2005;46(4):678-687.
- Becher E, Glina S. Erectile dysfunction in Latin America and treatment with sildenafil citrate (Viagra): Introduction. *Int J Impot Res* 2002;14(SUPPL. 2):S1-S2.
- Bella A J, Brock G B. Tadalafil: A comprehensive update. *Journal of Drug Evaluation* 2004;2(8):225-246.
- Benson G S. The clinical evaluation of the patient presenting with erectile dysfunction: what is reasonable?. [Review] [27 refs]. *Semin Urol* 1990;8(2):94-99.
- Beretta G, Saltarelli O, Marzotto M et al. Transcutaneous minoxidil in the treatment of erectile dysfunctions in spinal cord injured men. *Acta Eur Fertil* 1993;24(1):27-30.
- Bestane W J, Bestane M C, Ramos N A. Prospective study of sodium nitroprusside in pharmacologically induced erection. *Braz J Urol* 2001;27(2):155-158.
- Beutel M E, Wiltink J, Hauck E W et al. Correlations between hormones, physical, and affective parameters in aging urologic outpatients. *Eur Urol* 2005;47(6):749-755.
- Bhatia M S, Malik S C. Dhat syndrome--a useful diagnostic entity in Indian culture. *Br J Psychiatry* 1991;159(Nov.):691-695.
- Bivalacqua T J, Hellstrom W J G. Potential application of gene therapy for the treatment of erectile dysfunction. *J Androl* 2001;22(2):183-190.
- Black A M, Day A G, Morales A. The reliability of clinical and biochemical assessment in symptomatic late-onset hypogonadism: Can a case be made for a 3-month therapeutic trial?. *BJU Int* 2004;94(7):1066-1070.
- Blander D S, Sanchez-Ortiz R F, Broderick G A. Sex inventories: can questionnaires replace erectile dysfunction testing?. *Urology* 1999;54(4):719-723.
- Boccon Gibod L. Is transurethral needle ablation a safe and effective treatment for lower urinary tract symptoms secondary to BPH?. *Nature Clinical Practice Urology* 2004;1(1):24-25.
- Bochinski D J, Dean R C, Lue T F. Erectile dysfunction and priapism. *Nat Clin Pract Urol* 2004;1(1):49-53.
- Bodie J A, Beeman W W, Monga M. Psychogenic erectile dysfunction. *Int J Psychiatry Med* 2003;33(3):273-293.
- Bodie J, Lewis J, Schow D et al. Laboratory evaluations of erectile dysfunction: an evidence based approach. *Br J Urol* 2003;169(6):2262-2264.
- Bodner D R, Leffler B, Frost F. The role of intracavernous injection of vasoactive medications for the restoration of erection in spinal cord injured males: a three year follow up. *Paraplegia* 1992;30(2):118-120.
- Boolell M, Allen M J, Ballard S A et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int J Impot Res* 1996;8(2):47-52.
- Boshier A, Wilton L V, Shakir S A W. Evaluation of the safety of sildenafil for male erectile dysfunction: Experience gained in general practice use in England in 1999. *BJU Int* 2004;93(6):796-801.
- Boydak B, Nalbantgil S, Fici F et al. A randomised comparison of the effects of nebivolol and atenolol with and without chlorthalidone on the sexual function of hypertensive men. *Clinical Drug Investigation* 2005;25(6):409-416.
- Brake M, Loertzer H, Horsch R et al. Treatment of Peyronie's disease with local interferon-alpha 2b. *BJU Int* 2001;87(7):654-657.
- Bratus D, Hlebic G, Hajdinjak T. 16905960 of erectile dysfunction. *Croat Med J* 2007;48(1):76-80.
- Brennemann W, Kohler W, Zierz S et al. Testicular dysfunction in adrenomyeloneuropathy. *Eur J Endocrinol* 1997;137(1):34-39.
- Brennemann W, Stitz B, Van Ahlen H et al. Treatment of idiopathic erectile dysfunction in men with the opiate antagonist naltrexone--a double-blind study. *J Androl* 1993;14(6):407-410.

- Briganti A, Chun F K H, Salonia A et al. A comparative review of apomorphine formulations for erectile dysfunction: Recommendations for use in the elderly. *Drugs Aging* 2006;23(4):309-319.
- Briganti A, Salonia A, Zanni G et al. Erectile dysfunction and radical prostatectomy: An update. *Eau Update Series* 2004;2(2):84-92.
- Brixius K, Middeke M, Lichtenthal A et al. Nitric oxide, erectile dysfunction and beta-blocker treatment (MR NOED study): Benefit of nebivolol versus metoprolol in hypertensive men. *Clinical & Experimental Pharmacology & Physiology* 2007;34(4):327-331.
- Broderick G A, Allen G, McClure R D. Vacuum tumescence devices: the role of papaverine in the selection of patients. *Br J Urol* 1991;145(2):284-286.
- Brooks D P, Giuliano F. Genitourinary diseases. *Drug Discovery Today: Therapeutic Strategies* 2005;2(1):iii-iv.
- Brown J S, Wessells H, Chancellor M B et al. Urologic complications of diabetes. *Diabetes Care* 2005;28(1):177-185.
- Buchholz N P, Weuste R, Mattarelli G et al. Post-vasectomy erectile dysfunction. *J Psychosom Res* 1994;38(7):759-762.
- Buddeberg C, Bucher T, Hornung R. [Erectile dysfunction in men in their second half of life]. *Urologe* 2005;Ausg. A. 44(9):1045-1046, 1048-51.
- Buena F, Swerdloff R S, Steiner B S et al. Sexual function does not change when serum testosterone levels are pharmacologically varied within the normal male range. *Fertility & Sterility* 1993;59(5):1118-1123.
- Bukofzer S, Livesey N. Safety and tolerability of apomorphine SL (Uprima). *Int J Impot Res* 2001;13(SUPPL. 3):S40-S44.
- Burnett A L. Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: A randomized controlled trial: Editorial comment 2. *Urology* 2003;62(1):126
- Burnett A L. Vasoactive pharmacotherapy to cure erectile dysfunction: fact or fiction?. [Review] [45 refs]. *Urology* 2005;65(2):224-230.
- Burnett A L. The impact of sildenafil on molecular science and sexual health. *Eur Urol* 2004;46(1):9-14.
- Burns-Cox N, Gingell C. The andropause: fact or fiction?. [Review] [49 refs]. *Postgrad Med J* 1997;73(863):553-556.
- Buvat J, Boujadoue G. Testosterone replacement therapy in the ageing man. *The Journal of Mens Health & Gender* 2005;2(4):396-399.
- Calof O M, Singh A B, Lee M L et al. Adverse events associated with testosterone replacement in middle-aged and older men: A meta-analysis of randomized, placebo-controlled trials. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2005;60(11):1451-1457.
- Campbell M. Beneficial cardiovascular effects and safety of sildenafil reported in trio of studies. *Cardiology Review* 2001;18(6):27
- Cappelleri J C, Siegel R L, Glasser D B et al. Relationship between patient self-assessment of erectile dysfunction and the sexual health inventory for men. *Clin Ther* 2001;23(10):1707-1719.
- Cara A M, Lopes-Martins R A B, Antunes E et al. The role of histamine in human penile erection. *Br J Urol* 1995;75(2):220-224.
- Carani C, Bancroft J, Granata A et al. Testosterone and erectile function, nocturnal penile tumescence and rigidity, and erectile response to visual erotic stimuli in hypogonadal and eugonadal men. *Psychoneuroendocrinology* 1992;17(6):647-654.
- Carani C, Scuteri A, Marrama P et al. The effects of testosterone administration and visual erotic stimuli on nocturnal penile tumescence in normal men. *Horm Behav* 1990;24(3):435-441.
- Cardenas D D, Ditunno J, Graziani V et al. Phase 2 trial of sustained-release fampridine in chronic spinal cord injury. *Proc Annu Clin Spinal Cord Inj Conf* 2007;45(2):158-168.
- Carey Michael P, Wincze John P, Meisler Andrew W. Sexual dysfunction: Male erectile disorder. Barlow, David H (Ed) 1993;(1993):534
- Carosa E, Benvenega S, Trimarchi F et al. Sexual inactivity results in reversible reduction of LH bioavailability. *Int J Impot Res* 2002;14(2):93-99.
- Carson C C. PNU-83757: a new agent for the treatment of erectile dysfunction.[comment]. *Curr Urol Rep* 2002;3(6):465-466.
- Carson C C. Re: Long-term efficacy of sildenafil and tachyphylaxis effect.[comment]. *Br J Urol* 2002;168(1):205
- Carson C C, Hatzichristou D G, Carrier S. Erratum: Erectile response with vardenafil in sildenafil nonresponders: A multicentre, double-blind, 12-week, flexible-dose, placebo-controlled erectile dysfunction clinical trial (BJU International (2004) 94 (1301-1309)). *BJU Int* 2005;96(3):466
- Caspi A, Goldenberg M M. Sildenafil: A new drug treatment for male erectile dysfunction. *P & T* 1998;23(5):

- Cawello W, Schweer H, Dietrich B et al. Pharmacokinetics of prostaglandin E1 and its main metabolites after intracavernous injection and short-term infusion of prostaglandin E1 in patients with erectile dysfunction. *Br J Urol* 1997;158(4):1403-1407.
- Cecchi M, Sepich C A, Felipetto R et al. Vacuum constriction device and topical minoxidil for management of impotence. *Arch Esp Urol* 1995;48(10):1058-1059.
- Chaiban J T, Azar S T. Erectile dysfunction in diabetic patients. *J Med Liban* 2004;52(4):217-219.
- Chang D W, Wood C G, Kroll S S et al. Cavernous nerve reconstruction to preserve erectile function following non-nerve-sparing radical retropubic prostatectomy: a prospective study. *Keisei Geka* 2003;111(3):1174-1181.
- Chatterjee R, Andrews H O, McGarrigle H H et al. Cavernosal arterial insufficiency is a major component of erectile dysfunction in some recipients of high-dose chemotherapy/chemoradiotherapy for haematological malignancies. *Bone Marrow Transplant* 2000;25(11):1185-1189.
- Chaudhuri T K, Fink S, Burger R H et al. Nuclear penogram: Non-invasive technique to monitor and record effect of pharmacologically-induced penile erection in impotence therapy. *Urology* 1990;35(1):98
- Chen C T, Valicenti R K, Lu J et al. Does hormonal therapy influence sexual function in men receiving 3D conformal radiation therapy for prostate cancer?. *Int J Radiat Oncol Biol Phys* 2001;50(3):591-595.
- Chen J, Greenstein A, Kaver I et al. Use of automatic insulin injector for intracorporeal injection in erectile dysfunction. *Br J Urol* 1994;152(2):461-462.
- Chen J, Mabjeesh N J, Greenstein A. Sildenafil versus the vacuum erection device: patient preference. *Br J Urol* 2001;166(5):1779-1781.
- Chen J, Wollman Y, Chernichovsky T et al. Effect of oral administration of high-dose nitric oxide donor L-arginine in men with organic erectile dysfunction: results of a double-blind, randomized, placebo-controlled study. *BJU Int* 1999;83(3):269-273.
- Chen K-C, Minor T X, Rahman N U et al. The additive erectile recovery effect of brain-derived neurotrophic factor combined with vascular endothelial growth factor in a rat model of neurogenic impotence. *BJU Int* 2005;95(7):1077-1080.
- Chen K-K, Jiann B-P, Lin J S N et al. Erratum: Efficacy and safety of on-demand oral tadalafil in the treatment of men with erectile dysfunction in Taiwan: A randomized, double-blind, parallel, placebo-controlled clinical study (*Journal of Sexual Medicine* vol. 1 (2)). *Br J Sex Med* 2005;2(1):158
- Cheng J Y W, Ng E M L, Chen R Y L et al. Prevalence of erectile dysfunction in Asian populations: A meta-analysis. *Int J Impot Res* 2007;19(3):229-244.
- Chew K K, Stuckey B G. Clinical course of penile fibrosis in intracavernosal prostaglandin E1 injection therapy: a follow-up of 44 patients. *Int J Impot Res* 2003;15(2):94-98.
- Chew K K, Stuckey B G A, Thompson P L. Erectile dysfunction, sildenafil and cardiovascular risk. *Med J Aust* 2000;172(6):279-283.
- Chia S. Management of premature ejaculation -- a comparison of treatment outcome in patients with and without erectile dysfunction. *Int J Androl* 2002;25(5):301-305.
- Chinegwundoh F, Anie K A. Treatments for priapism in boys and men with sickle cell disease. [Review] [16 refs]. *Cochrane Database Syst Rev* 2004;(4):CD004198
- Chiu K C, Cohan P, Martinez D et al. Adrenal insufficiency after medical therapy for prolactin and adrenocorticotrophic hormone co-producing pituitary macroadenoma without hypercortisolism. *Endocr Pract* 2001;11(6):443-446.
- Chiu Y J, Reid I A. Effect of sildenafil on renin secretion in human subjects. *Experimental biology and medicine (Maywood, NJ)* 2002;227(8):620-625.
- Christ B, Brockmeier D, Hauck E W et al. Interactions of sildenafil and tacrolimus in men with erectile dysfunction after kidney transplantation. *Urology* 2001;58(4):589-593.
- Christ G J, Melman A. The application of gene therapy to the treatment of erectile dysfunction. *Int J Impot Res* 1998;10(2):111-112.
- Chue P. Gabapentin treatment for premature ejaculation [3]. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 2004;49(9):644-645.
- Cimentepe E, Unsal A, Saglam R. Randomized clinical trial comparing transurethral needle ablation with transurethral resection of the prostate for the treatment of benign prostatic hyperplasia: results at 18 months. *J Endourol* 2003;17(2):103-107.
- Clark C. Erectile dysfunction and other problems. *Can Pharm J* 2004;272(7299):608-610.
- Clark R V, Hermann D J, Cunningham G R et al. Marked Suppression of Dihydrotestosterone in Men with Benign Prostatic Hyperplasia by Dutasteride, a Dual 5 α -Reductase Inhibitor. *Journal of Clinical Endocrinology & Metabolism* 2004;89(5):2179-2184.
- Claro J A, Passerotti C C, Figueiredo Neto A C et al. An alternative non-invasive treatment for Peyronie's disease. *International Braz J Urol* 2004;30(3):199-204.

- Clough J. CNS-targeted sexual dysfunction drug for men and women. *Drug Discov Today* 2002;7(9):492-494.
- Coelho O R. Tolerability and safety profile of sildenafil citrate (Viagra) in Latin American patient populations. *Int J Impot Res* 2002;14(Suppl 2):54-59.
- Coker C, Bettocchi C, Pryor J. Caverject, a new licensed prostaglandin preparation for use in erectile dysfunction. *J Androl* 1994;15(6 SUPPL.):71S
- Coleman C I, Carabino J M, Vergara C M et al. Vardenafil. *Hosp Formul* 2003;38(3):131-148.
- Collazos J, Martinez E, Mayo J et al. Sexual dysfunction in HIV-infected patients treated with highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes: JAIDS* 2002;31(3):322-326.
- Colp G M, Scropo F I. Can self-directed pelvic floor exercises improve erectile function?. *Nature Clinical Practice Urology* 2005;2(3):128-129.
- Conti C R, Pepine C J, Sweeney M. Efficacy and safety of sildenafil citrate in the treatment of erectile dysfunction in patients with ischemic heart disease. *Am J Cardiol* 1999;83(5A):29C-34C.
- Contreras L N, Masini A M, Danna M M et al. Glucocorticoids: their role on gonadal function and LH secretion. *Minerva Endocrinol* 1996;21(2):43-46.
- Cooper A J, Losztyn S, Russell N C et al. Medroxyprogesterone acetate, nocturnal penile tumescence, laboratory arousal, and sexual acting out in a male with schizophrenia. *Arch Sex Behav* 1990;19(4):361-372.
- Cormio L, Nisen H, Ruutu M et al. Etilefrine in the prevention of prolonged erection after diagnostic pharmacological stimulation. *Ann Chir Gynaecol* 1996;85(3):247-250.
- Corona G, Mannucci E, Petrone L et al. ANDROTEST: a structured interview for the screening of hypogonadism in patients with sexual dysfunction. *Br J Sex Med* 2006;3(4):706-715.
- Corona G, Mannucci E, Petrone L et al. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. *Int J Impot Res* 2006;18(2):190-197.
- Corona G, Mannucci E, Schulman C et al. Psychobiologic correlates of the metabolic syndrome and associated sexual dysfunction. *Eur Urol* 2006;50(3):595-604.
- Creasey G H. Lecture 6: restoration of male sexual function following spinal cord injury. *Int J Impot Res* 2000;12 Suppl 3S54-S55.
- Crum-Cianflone N F, Bavaro M, Hale B et al. Erectile dysfunction and hypogonadism among men with HIV. *AIDS Patient Care & Stds* 2007;21(1):9-19.
- Culha M, Mutlu N, Acar O et al. Patient-partner satisfaction with intracavernous medication supported with oral agents in selected cases of Peyronie's disease: A ten-month follow-up study. *International Urology & Nephrology* 1999;31(2):257-262.
- Curri S B, Menchini Fabris F. Evidence and results obtained with a new Trans-Epidermal Barrier (T.E.B.) drug in the medical treatment of vascular impotence. *Boll Chim Farm* 1996;135(5):316-334.
- Cyranoski D. Malaysian researchers bet big on home-grown Viagra. *Nat Med* 2005;11(9):912
- Czuriga I, Rieicansky I, Bodnar J et al. Comparison of the New Cardioselective Beta-Blocker Nebivolol with Bisoprolol in Hypertension: The Nebivolol, Bisoprolol Multicenter Study (NEBIS). *Cardiovascular Drugs & Therapy* 2003;17(3):257-263.
- Dang G, Matern R, Bivalacqua T J et al. Intralesional interferon-alpha-2B injections for the treatment of Peyronie's disease. *South Med J* 2004;97(1):42-46.
- Davis B E, Weigel J W, Whitford C S. Treatment of male impotence: a new option. *Kans Med* 1990;91(12):325-326.
- Davis J M. American College of Neuropsychopharmacology - 43rd annual meeting. 12-16 December 2004, San Juan, Puerto Rico. *IDrugs* 2005;8(2):100-103.
- Davis M E, Brewster M E. Cyclodextrin-based pharmaceuticals: Past, present and future. *Nat Rev Genet* 2004;3(12):1023-1035.
- De Meyer J M, Oosterlinck W. Influence of the method of intracavernous injection on penile rigidity: a possible pharmacokinetic explanation. *Urology* 1997;49(2):248-252.
- De Rosa M, Zarrilli S, Vitale G et al. Six months of treatment with cabergoline restores sexual potency in hyperprolactinemic males: an open longitudinal study monitoring nocturnal penile tumescence. *Journal of Clinical Endocrinology & Metabolism* 2004;89(2):621-625.
- De Tejada I. Vardenafil Duration of Action. *Eur Urol* 2006;50(5):901-902.
- De Tejada I, Garvey D S, Schroeder J D et al. Design and evaluation of nitrosylated alpha-adrenergic receptor antagonists as potential agents for the treatment of impotence. *Journal of Pharmacology & Experimental Therapeutics* 1999;290(1):121-128.
- Degirmenci B, Acar M, Albayrak R et al. Effects of sildenafil citrate (Viagra) on renal arteries: An evaluation with Doppler ultrasound. *Urol Int* 2006;77(2):170-172.

- Del Popolo G, Li Marzi V, Mondaini N et al. Time/duration effectiveness of sildenafil versus tadalafil in the treatment of erectile dysfunction in male spinal cord-injured patients. *Proc Annu Clin Spinal Cord Inj Conf* 2004;42(11):643-648.
- Delizonna L L, Wincze J P, Litz B T et al. A comparison of subjective and physiological measures of mechanically produced and erotically produced erections (or, is an erection an erection?). *J Sex Marital Ther* 2001;27(1):21-31.
- Denisov M F, Davis J M, Brecher M. Re: Prolactin levels and adverse events in patients treated with risperidone [8] (multiple letters). *J Clin Psychopharmacol* 2002;22(5):538-540.
- Derby C A, Araujo A B, Johannes C B et al. Measurement of erectile dysfunction in population-based studies: the use of a single question self-assessment in the Massachusetts Male Aging Study. *Int J Impot Res* 2000;12(4):197-204.
- Derby C A, Barbour M M, Hume A L et al. Drug therapy and prevalence of erectile dysfunction in the Massachusetts Male Aging Study cohort. *Pharmacotherapy* 2001;21(6):676-683.
- Derouet H, Nolden W, Jost W H et al. Treatment of erectile dysfunction by an external ischiocavernous muscle stimulator. *Eur Urol* 1998;34(4):355-359.
- Desouza C, Parulkar A, Lumpkin D et al. Acute and prolonged effects of sildenafil on brachial artery flow-mediated dilatation in type 2 diabetes.. *Diabetes Care* 2002;25(8):1336-1339.
- Dietzen C J, Lloyd L K. Complications of intracavernous injections and penile prostheses in spinal cord injured men. *Archives of Physical Medicine & Rehabilitation* 1992;73(7):652-655.
- Dinelli N, Salintri G, Pomara G et al. Role of pharmacologic rehabilitation in the recovery of sexual function following radical prostatectomy. *Minerva Urol Nefrol* 2005;57(4):325-329.
- Dinsmore W W, Gingell C, Hackett G et al. Treating men with predominantly nonpsychogenic erectile dysfunction with intracavernosal vasoactive intestinal polypeptide and phentolamine mesylate in a novel auto-injector system: a multicentre double-blind placebo-controlled study. *BJU Int* 1999;83(3):274-279.
- Djavan B, Milani S, Fong Y K. Dutasteride: A novel dual inhibitor of 5 α -reductase for benign prostatic hyperplasia. *Expert Opin Pharmacother* 2005;6(2):311-317.
- Donatucci C F, Lue T F. Erectile dysfunction in men under 40: etiology and treatment choice. *Int J Impot Res* 1993;5(2):97-103.
- Doumas M, Tsakiris A, Douma S et al. Beneficial effects of switching from beta-blockers to nebivolol on the erectile function of hypertensive patients. *Asian J Androl* 2006;8(2):177-182.
- Dundar S O. Visual loss associated with erectile dysfunction drugs. *Can J Ophthalmol* 2007;42(1):10-12.
- Dupont Simon. Multiple sclerosis and sexual functioning: A review. *Clin Rehabil* 1995;9(2):135-141.
- Durackova Z, Trebaticky B, Novotny V et al. Lipid metabolism and erectile function improvement by Pycnogenol, extract from the bark of Pinus pinaster in patients suffering from erectile dysfunction - A pilot study. *Adv Food Nutr Res* 2003;23(9):1189-1198.
- Eandi J A, Yao A P, Javidan J. Penile paraffinoma: the delayed presentation. *Int Urol Nephrol* 2007;
- Eardley I. New oral therapies for the treatment of erectile dysfunction. *Br J Urol* 1998;81(1):122-127.
- Earle C M, Keogh E J, Ker J K et al. The role of intracavernosal vasoactive agents to overcome impotence due to spinal cord injury. *Paraplegia* 1992;30(4):273-276.
- Earle C M, Stuckey B G, Ching H L et al. The incidence and management of priapism in Western Australia: a 16 year audit. *Int J Impot Res* 2003;15(4):272-276.
- Edwards G, Muirhead G J. British Journal of Clinical Pharmacology: Introduction. *Br J Clin Pharmacol* 2002;53(SUPPL. 1):1S-3S.
- Ekmekcioglu O, Inci M, Demirci D et al. Effects of sildenafil citrate on ejaculation latency, detumescence time, and refractory period: placebo-controlled, double-blind, crossover laboratory setting study. *Urology* 2005;65(2):347-352.
- Ekselius L, Von Knorring L. Effect on sexual function of long-term treatment with selective serotonin reuptake inhibitors in depressed patients treated in primary care. *J Clin Psychopharmacol* 2001;21(2):154-160.
- El-Bahnasawy M S, El-Assmy A, Dawood A et al. Effect of the use of internal iliac artery for renal transplantation on penile vascularity and erectile function: A prospective study. *Br J Urol* 2004;172(6 I):2335-2339.
- El-Rufaie Omer E F, Bener Abdulbari, Abuzeid Mohamed S O et al. Sexual dysfunction among type II diabetic men: A controlled study. *J Psychosom Res* 1997;43(6):605-612.
- El-Sakka A I. Penile axial rigidity and Doppler ultrasonography parameters in patients with erectile dysfunction: association with type 2 diabetes. *Urology* 2003;62(3):525-531.

- Emilien G. Alprox-TD NexMed Inc. *Current Opinion in Central & Peripheral Nervous System Investigational Drugs* 2000;2(3):311-320.
- Ende A R, Lo Re V, DiNubile M J et al. Erectile dysfunction in an urban HIV-positive population. *AIDS Patient Care & Stds* 2006;20(2):75-78.
- Engelson E S, Pi-Sunyer F X, Kotler D P. Effects of megestrol acetate therapy on body composition and circulating testosterone concentrations in patients with AIDS. *Int J STD AIDS* 1995;9(9):1107-1108.
- Engl T, Beecken W-D, Wolfram M et al. Uro pharmacology: Current and future strategies in the treatment of erectile dysfunction and benign prostate hyperplasia. *International Journal of Clinical Pharmacology & Therapeutics* 2004;42(10):527-533.
- Ensign C. First-line therapies for erectile dysfunction. [Review] [8 refs]. *JAAPA* 2001;14(10):17-20.
- Erdogru T, Kocak T, Serdaroglu P et al. Evaluation and therapeutic approaches of voiding and erectile dysfunction in neurological Behcet's syndrome. *Br J Urol* 1999;162(1):147-153.
- Ernst E. Chinese herbal medicines for consumers in the West. *Focus on Alternative & Complementary Therapies* 2005;10(2):94-97.
- Esposito K, Giugliano F, Martedi E et al. High proportions of erectile dysfunction in men with the metabolic syndrome. *Diabetes Care* 2005;28(5):1201-1203.
- Evans M F. Viagra! Are we ready?. *Can Fam Physician* 1998;44:2103-2105.
- Fagan Peter J, Blum Lois H. Issues in the psychotherapeutic treatment of sexual dysfunction following radical retropubic prostatectomy. Rosen, Raymond C (Ed); Leiblum, Sandra R (Ed) 1995;(1995):400
- Fagan T C, Buttler S, Marbury T et al. Cardiovascular safety of sublingual apomorphine in patients on stable doses of oral antihypertensive agents and nitrates. *Am J Cardiol* 2001;88(7):760-766.
- Faiman C. Endocrine causes of impotence. *Cleve Clin J Med* 1993;60(6):428-429.
- Fedele D, Lamonica M, Bax G. Experience with sildenafil in diabetes. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):49-52.
- Fekete F, Fabian E. [Effectiveness and adverse effects of sildenafil in erectile dysfunction]. *Orv.Hetil.* 2000;141(3):115-118.
- Feldman H A, Goldstein I, Hatzichristou D G et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *Br J Urol* 1994;151(1):54-61.
- Feldman H A, Johannes C B, Derby C A et al. Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study. *Prev Med* 2000;30(4):328-338.
- Finkbeiner A. Random musing about a little blue pill. *J Ark Med Soc* 1998;95(3):100-101.
- Fisher W A, Rosen R C, Eardley I et al. The Multinational Men's Attitudes to Life Events and Sexuality (MALES) Study Phase II: Understanding PDE5 inhibitor treatment seeking patterns, among men with erectile dysfunction. *Br J Sex Med* 2004;1(2):150-160.
- Flack J M. The effect of doxazosin on sexual function in patients with benign prostatic hyperplasia, hypertension, or both.[see comment]. [Review] [47 refs]. *Int J Clin Pract* 2002;56(7):527-530.
- Foresta C, Caretta N, Rossato M et al. Role of androgens in erectile function. *Br J Urol* 2004;171(6 Pt 1):2358-2362.
- Frank T. Tadalafil (Cialis-Lilly). *Consultant Pharmacist* 2004;19(4):280-281.
- Frank T. Vardenafil (Levitra-Bayer) GSK. *Consultant Pharmacist* 2004;19(4):278-280.
- Franzen D, Metha A, Seifert N et al. Effects of beta-blockers on sexual performance in men with coronary heart disease. A prospective, randomized and double blinded study. *Int J Impot Res* 2001;13(6):348-351.
- Fraunfelder F W, Fraunfelder F T. Scientific Challenges in Postmarketing Surveillance of Ocular Adverse Drug Reactions. *Am J Ophthalmol* 2007;143(1):
- Freemantle N. Valuing the effects of sildenafil in erectile dysfunction. *Br Med J* 2000;320(7243):1156-1157.
- Freytag S O, Stricker H, Pegg J et al. Phase I Study of Replication-Competent Adenovirus-Mediated Double-Suicide Gene Therapy in Combination with Conventional-Dose Three-Dimensional Conformal Radiation Therapy for the Treatment of Newly Diagnosed, Intermediate- to High-Risk Prostate Cancer. *Cancer Res* 2003;63(21):7497-7506.
- Fu Q, Yao D-H, Jiang Y-Q. Effect of sodium nitroprusside on hemodynamics of corpus cavernosum in Chinese. *Asian J Androl* 2001;3(4):311-313.
- Fulgram P F, Cochran J S, Denman J L et al. Re: Disappointing initial results with transurethral alprostadil for erectile dysfunction in a urology practice setting [5]. *Br J Urol* 1999;162(4):1390

- Gallo L, Perdona S, Autorino R et al. Recovery of erection after pelvic urologic surgery: our experience. *Int J Impot Res* 2005;17(6):484-493.
- Gerstenbluth R E, Maniam P N, Corty E W et al. Prostate-specific antigen changes in hypogonadal men treated with testosterone replacement. *J Androl* 2002;23(6):922-926.
- Ghezzi A, Malvestiti G M, Baldini S et al. Erectile impotence in multiple sclerosis: A neurophysiological study. *J Neurol* 1995;242(3):123-126.
- Giammusso B, Gattuso U, Vanaclocha V et al. Percutaneous lumbar sympathectomy in the treatment of erectile dysfunction secondary to cavernous adrenergic hypertone: initial results of an original technique. *Arch Ital Urol Androl* 2005;77(1):5-9.
- Giampietro O, Ferdeghini M, Cerri M et al. Evaluation of the hypothalamic-pituitary-testicular interaction in diabetic males. *European J Lab Med* 1994;2(2):83-89.
- Ginsberg D L. Gabapentin treatment of premature ejaculation. *Primary Psychiatry* 2004;11(12):20-21.
- Ginsberg D L. Vardenafil treatment of sertraline-induced sexual dysfunction. *Primary Psychiatry* 2004;11(11):23-24.
- Giuberti A, Picozzi S C, Mazza L et al. Testosterone supplementation in hypogonadal men: our personal experience. *Arch Ital Urol Androl* 2005;77(4):191-193.
- Giuliano F. Control of penile erection by the melanocortineric system: Experimental evidences and therapeutic perspectives. *J Androl* 2004;25(5):683-691.
- Giuliano F, Allard J, Rampin O et al. Pro-erectile effect of systemic apomorphine: Existence of a spinal site of action. *Br J Urol* 2002;167(1):402-406.
- Giuliano F, Hultling C, El Masry W S et al. Randomized trial of sildenafil for the treatment of erectile dysfunction in spinal cord injury. Sildenafil Study Group. *Ann Neurol*. 1999;46(1):15-21.
- Giuliano Francois, Pena Beatrice, Mishra Avnish et al. "Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction": Erratum. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 2002;11(6):613-670.
- Gladh Y M, Rahgozar M, Hammar M L et al. Prevalence of symptoms possibly related to PADAM, in a Swedish population aged 55, 65 and 75 years. *Maturitas* 2005;50(3):161-166.
- Glasser S P. Revisiting erectile dysfunction in cardiovascular patients. *Cardiology Review* 2003;20(12):42-43.
- Glasser S P. Safety of PDE 5 inhibition in patients with cardiovascular disease. *Cardiology Review* 2002;19(11):32-33.
- Glenn D R J, McClure N, Lewis S E M. The hidden impact of diabetes on male sexual dysfunction and fertility. *Hum Fertil* 2003;6(4):174-179.
- Gontero P, Fontana F, Zitella A et al. A prospective evaluation of efficacy and compliance with a multistep treatment approach for erectile dysfunction in patients after non-nerve sparing radical prostatectomy. *BJU Int* 2005;95(3):359-365.
- Govier F E, McClure R D, Kramer-Levien D. Endocrine screening for sexual dysfunction using free testosterone determinations. *Br J Urol* 1996;156(2 Pt 1):405-408.
- Graul A, Castaner J. Phentolamine Mesilate. Treatment of erectile dysfunction. *Drugs of the Future* 1998;23(7):725-728.
- Graul A I. Latest findings on the diagnosis and treatment of erectile dysfunction. *Drug News Perspect* 1996;9(9):572-575.
- Gray P B, Singh A B, Woodhouse L J et al. Dose-dependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. *Journal of Clinical Endocrinology & Metabolism* 2005;90(7):3838-3846.
- Green H J, Pakenham K I, Headley B C et al. Coping and health-related quality of life in men with prostate cancer randomly assigned to hormonal medication or close monitoring. *Psychooncology* 2002;11(5):401-414.
- Green J S A, Holden S T R, Ingram P et al. An investigation of erectile dysfunction in Gwent, Wales. *BJU Int* 2001;88(6):551-553.
- Greenstein A, Plymate S R, Katz P G. Visually stimulated erection in castrated men. *Br J Urol* 1995;153(3:Pt 1):t-2.
- Gresser U, Gleiter C H. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil--review of the literature. [Review] [92 refs]. *Eur J Med Res* 2002;7(10):435-446.
- Gross A J, Sauerwein D H, Kutzenberger J et al. Penile prostheses in paraplegic men. *Br J Urol* 1996;78(2):262-264.
- Grugni G, Carani C, Maestroni G et al. Melatonin levels in psychogenic impotence. *Hormone & Metabolic Research* 1994;26(9):440-441.
- Grunwald J E, Jacob S S, Siu K et al. Acute effects of sildenafil citrate (Viagra) on intraocular pressure in open-angle glaucoma. *Am J Ophthalmol* 2001;132(6):872-874.

- Gryglewska B, Grodzicki T. Betaxolol in elderly patients in primary care. *New Medicine* 2003;6(4):108-111.
- Guay A T, Sabharwal P, Varma S et al. Delayed diagnosis of psychological erectile dysfunction because of the presence of macroprolactinemia. *Journal of Clinical Endocrinology & Metabolism* 1996;81(7):2512-2514.
- Guay D R P. Geriatric pharmacotherapy updates. *American Journal Geriatric Pharmacotherapy* 2004;2(1):81-87.
- Guirguis W R, Maytom M C, Orr M et al. SILDENAFIL FOR ERECTILE DYSFUNCTION - A ONE-YEAR STUDY. 151st Annual Meeting of the American Psychiatric Association 1998;Toronto, Ontario, Canada. 30th May-4th June. 1998. Issue No. 63, 1998.
- Guo Y L, Zhu J C, Pan T M et al. Efficacy and safety of oral sildenafil in the treatment of erectile dysfunction. *Chinese Journal of Urology* 2001;22(7):389-394.
- Gupta S, Salimpour P, Saenz de et al. A possible mechanism for alteration of human erectile function by digoxin: inhibition of corpus cavernosum sodium/potassium adenosine triphosphatase activity. *Br J Urol* 1998;159(5):1529-1536.
- Hackett G I. The treatment of patients with diabetes. *Int J STD AIDS* 1996;7(Suppl 3):24-26.
- Haensel S M, Klem T M, Hop W C et al. Fluoxetine and premature ejaculation: a double-blind, crossover, placebo-controlled study. *J Clin Psychopharmacol* 1998;18(1):72-77.
- Haensel S M, Rowland D L, Kallan K T. Clomipramine and sexual function in men with premature ejaculation and controls. *Br J Urol* 1996;156(4):1310-1315.
- Hamed S, Mohamed K, El-taher A et al. The sexual and reproductive health in men with generalized epilepsy: A multidisciplinary evaluation. *Int J Impot Res* 2006;18(3):287-295.
- Hammadeh M Y, Philp T. Transurethral electrovaporization of the prostate (TUVP) is effective, safe and durable. [Review] [28 refs]. *Prostate Cancer & Prostatic Diseases* 2003;6(2):121-126.
- Hanash K A. Comparative results of goal oriented therapy for erectile dysfunction.. *Br J Urol* 1997;157(6):2135-2138.
- Harman S M. Testosterone, Sexuality, and Erectile Function in Aging Men. *J Androl* 2003;24(6 SUPPL.):S42-S45.
- Hartmann Uwe, Langer Dieter. Combination of psychosexual therapy and intrapenile injections in the treatment of erectile dysfunctions: Rationale and predictors of outcome. *J Sex Educ Ther* 1993;19(1):1-12.
- Harwood P J, Grotz M, Eardley I et al. Erectile dysfunction after fracture of the pelvis. *Journal of Bone & Joint Surgery - British Volume* 2005;87(3):281-290.
- Haslam M T. A trial of idazoxan and yohimbine in erectile dysfunction. *Sex Marital Ther* 1992;7(3):261-266.
- Hatzimouratidis K, Hatzichristou D. Testosterone and erectile function: an unresolved enigma. *Eur Urol* 2007;52(1):26-28.
- Hawton Keith, Catalan Jose, Fagg Joan. Sex therapy for erectile dysfunction: Characteristics of couples, treatment outcome, and prognostic factors. *Arch Sex Behav* 1992;21(2):161-175.
- Hazell P. Review of new compounds available in Australia for the treatment of attention-deficit hyperactivity disorder. *Australasian Psychiatry* 2004;12(4):369-375.
- Heaton J. New classification system for erectile dysfunction therapies. *J Androl* 1998;19(4):399-404.
- Heaton J P W, Altwein J E. The role of apomorphine SL in the treatment of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):36-38.
- Heaton J P, Dean J, Sleep D J. Sequential administration enhances the effect of apomorphine SL in men with erectile dysfunction. *Int J Impot Res* 2002;14(1):61-64.
- Hellstrom W J G, Kendirci M. Type 5 Phosphodiesterase Inhibitors: Curing Erectile Dysfunction. *Eur Urol* 2006;49(6):942-945.
- Hellstrom W J, Overstreet J W, Yu A et al. Tadalafil has no detrimental effect on human spermatogenesis or reproductive hormones.[see comment]. *Br J Urol* 2003;170(3):887-891.
- Hellstrom Wayne J G, Egan Robert A, McGee Hall T et al. "Visual field defect and intracerebral hemorrhage associated with use of vardenafil (Levitra)": Comment and Reply. [References]. *Neurology* 2006;66(2):293-294.
- Herrmann H C, Chang G, Klugherz B D et al. Hemodynamic effects of sildenafil in men with severe coronary artery disease.[see comment]. *N Engl J Med* 2000;342(22):1622-1626.
- Hirshkowitz M, Moore C A, O'Connor S et al. Androgen and sleep-related erections. *J Psychosom Res* 1997;42(6):541-546.
- Hirst J F, Watson J P. Referrals aged 60+ to an inner-city psychosexual dysfunction clinic. *Sexual & Marital Therapy* 1996;11(2):131-146.

- Hofner K, Claes H, De Reijke T M et al. Tamsulosin 0.4 mg once daily: effect on sexual function in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. *Eur Urol* 1999;36(4):335-341.
- Holt S. Natural approaches to promote sexual function: Part 1: Viagra versus a natural approach. *Alternative & Complementary Therapies* 1999;5(4):204-208.
- Holtkamp M, Weissinger F, Meierkord H. Erectile dysfunction with topiramate. *Epilepsia* 2005;46(1):166-167.
- Hong B, Ji Y H, Hong J H et al. A double-blind crossover study evaluating the efficacy of korean red ginseng in patients with erectile dysfunction: a preliminary report.[see comment]. *Br J Urol* 2002;168(5):2070-2073.
- Hopps C V, Mulhall J P. Novel agents for sexual dysfunction. *BJU Int* 2003;92(6):534-538.
- Horita H, Sato Y, Adachi H et al. Effects of levodopa on nocturnal penile tumescence: a preliminary study. *J Androl* 1998;19(5):619-624.
- Howes O D, Wheeler M J, Pilowsky L S et al. Sexual function and gonadal hormones in patients taking antipsychotic treatment for schizophrenia or schizoaffective disorder. *Hillside J Clin Psychiatry* 2007;68(3):361-367.
- Howes Oliver D, Smith Shubulade, Aitchison Kathy J E. Comments on "Prolactin Levels and Erectile Function in Patients Treated With Risperidone." [References]. *J Clin Psychopharmacol* 2005;25(4):393-394.
- Huang S T, Hsieh M L. Different hemodynamic responses by color Doppler ultrasonography studies between sildenafil non-responders and responders. *Asian J Androl* 2007;9(1):129-133.
- Huang W J, Chen K K, Chang L S. Correlation between voiding and erectile function in patients with symptomatic benign prostatic hyperplasia. *Journal of the Chinese Medical Association: JCMA* 2005;68(4):178-182.
- Hultling C. Partners' perceptions of the efficacy of sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction. *Int J Clin Pract* 1999;Supplement.102-108.
- Hummel S, Paisley S, Morgan A et al. Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: A systematic review. *Health Technol Assess* 2003;7(33):157p
- Hunter R H, Joy C B, Kennedy E et al. Risperidone versus typical antipsychotic medication for schizophrenia.[update of Cochrane Database Syst Rev. 2000;(2):CD000440; PMID: 10796543]. [Review] [105 refs]. *Cochrane Database Syst Rev* 2003;(2):CD000440
- Hyer S L, Duckworth K, Jones C. Managing erectile disorders in diabetes: The one stop andrology clinic. *Practical Diabetes International* 1998;15(8):225-226.
- Israilov S, Baniel J, Shmueli J et al. Treatment program for erectile dysfunction in patients with cardiovascular diseases. *Am J Cardiol* 2004;93(6):689-693.
- Jackson G. Erectile dysfunction and cardiovascular disease.[see comment]. [Review] [46 refs]. *Int J Clin Pract* 1999;53(5):363-368.
- Jackson G. Treatment of erectile dysfunction in patients with cardiovascular disease: Guide to drug selection. *Drugs* 2004;64(14):1533-1545.
- Jackson G. Vardenafil - PDE5 inhibitor number 3. *Int J Clin Pract* 2004;58(3):229
- Jackson G. PDE5 inhibitors: Looking beyond ED. *Int J Clin Pract* 2003;57(3):159-160.
- Jackson G. Sildenafil (Viagra): New data, new confidence in treating erectile dysfunction in the cardiovascular patient. *Int J Clin Pract* 2002;56(2):75
- Jackson G. Phosphodiesterase 5 inhibition: Effects on the coronary vasculature. *Int J Clin Pract* 2001;55(3):183-188.
- Jackson G. The metabolic syndrome and erectile dysfunction: multiple vascular risk factors and hypogonadism. *Eur Urol* 2006;50(3):426-427.
- Jackson G, Sweeney M, Osterloh I H. Sildenafil citrate (Viagra(TM)): A cardiovascular overview. *British Journal of Cardiology* 1999;6(6):325-334.
- James J S. Frequent urination, leg cramps, leg weakness, erection difficulties: HIV myelopathy amino acid study. *AIDS Treat News* 2000;(344):3-4.
- Jani A B. The effectiveness of combining hormone therapy and radiotherapy in the treatment of prostate cancer. *Expert Opin Pharmacother* 2004;5(12):2469-2477.
- Jani A B, Kao J, Heimann R et al. Hormone therapy and radiotherapy for early prostate cancer: A utility-adjusted number needed to treat (NNT) analysis. *Int J Radiat Oncol Biol Phys* 2005;61(3):687-694.
- Jarow J P, Nana-Sinkam P, Sabbagh M et al. Outcome analysis of goal directed therapy for impotence. *Br J Urol* 1996;155(5):1609-1612.
- Jeong S-J, Park K, Moon J-D et al. Bicycle saddle shape affects penile blood flow. *Int J Impot Res* 2002;14(6):513-517.
- Jordan G H. What's new in urology. *J Am Coll Surg* 2003;197(3):444-457.

- Kadioglu A, Erdogru T, Tellaloglu S. Evaluation of penile arteries in papaverine-induced erection with color Doppler ultrasonography. *Arch Esp Urol* 1995;48(6):654-658.
- Kamel H K, Morley J E. The management of erectile dysfunction. *Reproductive Medicine Review* 2001;9(1):35-47.
- Kang B J, Lee S J, Kim M D et al. A placebo-controlled, double-blind trial of Ginkgo biloba for antidepressant-induced sexual dysfunction. *Hum Psychopharmacol* 2002;17(6):279-284.
- Kaplan S A, Meehan A G, Shah A. The age related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Br J Urol* 2006;176(4 Pt 1):1524-1527.
- Karlawish J H, Casarett D. Sildenafil for diabetic men with erectile dysfunction.[comment]. *JAMA* 1999;282(10):940-941.
- Kaufman J M, Hatzichristou D G, Mulhall J P et al. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *Br J Urol* 1994;151(3):612-618.
- Keijzers G B. Aviptadil (Senatek). [Review] [36 refs]. *Curr Opin Investig Drugs* 2001;2(4):545-549.
- Keles I, Aydin G, Orkun S et al. Two clinical problems in elderly men: osteoporosis and erectile dysfunction. *Arch Androl* 2005;51(3):177-184.
- Kell P. Cardiovascular safety of sildenafil. *Int J STD AIDS* 2002;13(7):439-443.
- Keoghane S R, Sullivan M E, Miller M A W. The aetiology, pathogenesis and management of priapism. *BJU Int* 2002;90(2):149-154.
- Kerfoot W W, Park H Y, Schwartz L B et al. Characterization of calcium channel blocker induced smooth muscle relaxation using a model of isolated corpus cavernosum. *Br J Urol* 1993;150(1):249-252.
- Kernohan A F, McIntyre M, Hughes D M et al. An oral yohimbine/L-arginine combination (NMI 861) for the treatment of male erectile dysfunction: a pharmacokinetic, pharmacodynamic and interaction study with intravenous nitroglycerine in healthy male subjects. *Br J Clin Pharmacol* 2005;59(1):85-93.
- Khalaf I M, Levinson I P. Erectile dysfunction in the Africa/Middle East Region: Epidemiology and experience with sildenafil citrate (Viagra). *Int J Impot Res* 2003;15(SUPPL. 1):S1-S2.
- Khan L A. Sildenafil citrate (Viagra). *JK Pract* 2001;8(1):52-53.
- Kilic S, Ergin H, Baydinc Y C. Venlafaxine extended release for the treatment of patients with premature ejaculation: a pilot, single-blind, placebo-controlled, fixed-dose crossover study on short-term administration of an antidepressant drug. *Int J Androl* 2005;28(1):47-52.
- Kilic S, Salih M, Anafarta K et al. Adenosine: a new agent in the diagnosis of impotence. *Int J Impot Res* 1994;6(4):191-198.
- Kim N N. Phosphodiesterase type 5 inhibitors: A biochemical and clinical correlation survey. *Int J Impot Res* 2003;15(SUPPL. 5):S13-S19.
- Kim N N, Dhir V, Azadzo K M et al. Pilot study of the endothelin-A receptor selective antagonist BMS-193884 for the treatment of erectile dysfunction. *J Androl* 2001;23(1):76-83.
- Kim S C, Seo K K, Lee S K et al. Comparison of the synergistic effects of tamsulosin versus phentolamine on penile erection: In vitro and in vivo studies. *Urol Res* 1999;27(6):437-444.
- Kim S C, Seo K K, Park B D et al. Risk factors for an early increase in dose of vasoactive agents for intracavernous pharmacotherapy. *Urol Int* 2000;65(4):204-207.
- Kimoto Y, Sakamoto S, Fujikawa K et al. Up-titration of vardenafil dose from 10 mg to 20 mg improved erectile function in men with spinal cord injury. *Int J Urol* 2006;13(11):1428-1433.
- Kirby R S. Report from London. *Prostate Cancer & Prostatic Diseases* 2005;8(4):299
- Kirby R S, Andersen M, Gratzke P et al. A combined analysis of double-blind trials of the efficacy and tolerability of doxazosin-gastrointestinal therapeutic system, doxazosin standard and placebo in patients with benign prostatic hyperplasia. *BJU Int* 2001;87(3):192-200.
- Kirby R S, O'Leary M P, Carson C. Efficacy of extended-release doxazosin and doxazosin standard in patients with concomitant benign prostatic hyperplasia and sexual dysfunction.. *BJU Int* 2005;95(1):103-109.
- Kiriakova N, Kiriakov A, Schneider E et al. Therapeutic effect of essential phospholipids on functional sexual disorders in males. *Journal of the European Academy of Dermatology & Venereology* 1998;11(2):191-193.
- Kleinberg D L, Davis J M, De Coster R et al. Prolactin levels and adverse events in patients treated with risperidone.[see comment]. *J Clin Psychopharmacol* 1999;19(1):57-61.
- Kley H K, Stremmel W, Kley J B et al. Testosterone treatment of men with idiopathic hemochromatosis. *Clin Investig* 1992;70(7):566-572.
- Kloner R A, Brindis R G, Cheitlin M D et al. Roundtable discussion: Tadalafil study group. *Am J Cardiol* 2003;92(9 SUPPL. 1):58M-65M.

- Kloner R A, Hutter A M, Emmick J T et al. Time course of the interaction between tadalafil and nitrates.[see comment]. *J Am Coll Cardiol* 2003;42(10):1855-1860.
- Kloner R A, Jackson G, Emmick J T et al. Interaction between the phosphodiesterase 5 inhibitor, tadalafil and 2 alpha-blockers, doxazosin and tamsulosin in healthy normotensive men. *Br J Urol* 2004;172(5:Pt 1):t-40.
- Klotz T, Mathers M J, Braun M et al. Effectiveness of oral L-arginine in first-line treatment of erectile dysfunction in a controlled crossover study. *Urol Int* 1999;63(4):220-223.
- Knegtering R, Castelein S, Bous H et al. A Randomized Open-Label Study of the Impact of Quetiapine Versus Risperidone on Sexual Functioning. *J Clin Psychopharmacol* 2004;24(1):56-61.
- Knoll L D, Benson R C, Bilhartz D L et al. A randomized crossover study using yohimbine and isoxsuprine versus pentoxifylline in the management of vasculogenic impotence.. *Br J Urol* 1996;155(1):144-146.
- Kobayashi T, Okuno H, Nishiyama H et al. Adult-onset idiopathic hypogonadotropic hypogonadism presented with erectile and ejaculatory disorder. *Int J Urol* 2002;9(10):604-606.
- Kramer-Levien D J. Papaverine--the medical implant. *AUAA J* 1987;7(4):13-Jun.
- Krause W, Mueller U, Mazur A. Measurement of steroid levels in saliva in a population-based survey of lifestyle, medical conditions, marriage, sex life and hormone status in aging men: A feasibility study. *Aging Male* 2002;5(4):203-215.
- Kuba R, Pohanka M, Zakopcan J et al. Sexual dysfunctions and blood hormonal profile in men with focal epilepsy. *Epilepsia* 2006;47(12):2135-2140.
- Kukreja R C, Ockaili R, Salloum F et al. Cardioprotection with phosphodiesterase-5 inhibition - A novel preconditioning strategy. *Journal of Molecular & Cellular Cardiology* 2004;36(2):165-173.
- Kunelius P, Hakkinen J, Lukkarinen O. Is high-dose yohimbine hydrochloride effective in the treatment of mixed-type impotence? A prospective, randomized, controlled double-blind crossover study. *Urology* 1997;49(3):441-444.
- Kupez D. Alprostadil for the treatment of erectile dysfunction. *J Am Acad Nurse Pract* 1996;21(5):143-145.
- Kupelian V, Shabsigh R, Travison T G et al. Is there a relationship between sex hormones and erectile dysfunction? Results from the Massachusetts Male Aging Study. *Br J Urol* 2006;176(6 Pt 1):2584-2588.
- Kvistborg A, Halse J, Bakke S et al. Long-term treatment of macroprolactinomas with CV 205-502. *Acta Endocrinol (Copenh)* 1993;128(4):301-307.
- La Pera G, Franco Giannotti C, Taggi F et al. Prevalence of sexual disorders in those young males who later become drug abusers. *J Sex Marital Ther* 2003;29(2):149-156.
- La Vignera S, Calogero A E, Cannizzaro M A et al. Erectile vascular dysfunction and analysis of the risk factors related to it. Clinical experience. *Minerva Endocrinol* 2007;32(1):17-21.
- Labbate Lawrence A. "Sex and serotonin reuptake inhibitor antidepressants": Erratum. *Psychiatr Ann* 1999;29(12):683
- Labbate Lawrence A, Croft Harry A, Oleshansky Marvin A E. Antidepressant-Related Erectile Dysfunction: Management via Avoidance, Switching Antidepressants, Antidotes, and Adaptation. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl 10):11-19.
- Labbate Lawrence A, Grimes Jamie, Hines Alan et al. Sexual dysfunction induced by serotonin reuptake antidepressants. *J Sex Marital Ther* 1998;24(1):3-12.
- Lamberg L. New drug for erectile dysfunction boon for many, 'viagravation' for some. *J Am Med Assoc* 1998;280(10):867-869.
- Larson T R. Current treatment options for benign prostatic hyperplasia and their impact on sexual function. *Urology* 2003;61(4):692-698.
- Lasaponara F, Paradiso M, Milan M G et al. Erectile dysfunction after kidney transplantation: our 22 years of experience.[see comment]. *Transplant Proc* 2004;36(3):502-504.
- Latini D M, Penson D F, Lubeck D P et al. Longitudinal differences in disease specific quality of life in men with erectile dysfunction: Results from the exploratory comprehensive evaluation of erectile dysfunction study. *Br J Urol* 2003;169(4):1437-1442.
- Laumann Edward O, West Suzanne, Glasser Dale et al. Prevalence and Correlates of Erectile Dysfunction by Race and Ethnicity Among Men Aged 40 or Older in the United States: From the Male Attitudes Regarding Sexual Health Survey. [References]. *Br J Sex Med* 2007;4(1):57-65.
- Lawless C, Cree J. Oral medications in the management of erectile dysfunction. [Review] [15 refs]. *J Am Board Fam Pract* 1998;11(4):307-314.
- Lawrence I G, Price D E, Howlett T A et al. Correcting impotence in the male dialysis patient: experience with testosterone replacement and vacuum tumescence therapy. *Am J Kidney Dis* 1998;31(2):313-319.

- Lebret T, Herve J M, Gorny P et al. Efficacy and safety of a novel combination of L-arginine glutamate and yohimbine hydrochloride: a new oral therapy for erectile dysfunction. *Eur Urol* 2002;41(6):608-613.
- Lee W R. The role of androgen deprivation therapy combined with prostate brachytherapy. [Review] [31 refs]. *Urology* 2002;60(3:Suppl 1):Suppl-44.
- Lehmann K, Casella R, Blochlinger A et al. Reasons for discontinuing intracavernous injection therapy with prostaglandin E1 (alprostadil). *Urology* 1999;53(2):397-400.
- Lehmann K, John H, Kacl G et al. Variable response to intracavernous prostaglandin E1 testing for erectile dysfunction. *Urology* 1999;54(3):539-543.
- Lenze E J, Karp J F, Mulsant B H et al. Somatic symptoms in late-life anxiety: Treatment issues. *Journal of Geriatric Psychiatry & Neurology* 2005;18(2):89-96.
- Lenzi A. The role of the medical andrologist in the assisted reproduction era. *J Endocrinol Invest* 2003;26(3):268-273.
- Leslie S J, Atkins G, Oliver J J et al. No adverse hemodynamic interaction between sildenafil and red wine. *Clinical Pharmacology & Therapeutics* 2004;76(4):365-370.
- Levien T, Baker D E. Lepirudin and sildenafil citrate. *Hosp Pharm* 1998;33(12):1524-1552.
- Levine S B. A slightly different idea. *Arch Sex Behav* 2005;34(1):38-39.
- Levy M M. Benefits being missed [5]. *Can Pharm J* 2005;274(7334):109
- Lexchin J. New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?. *Can Fam Physician* 2002;48(SEPT.):1487-1492.
- Li J Y, Li X Y, Li M et al. Decline of serum levels of free testosterone in aging healthy Chinese men. *Aging Male* 2005;8(3-4):203-206.
- Licht M R. Use of oral sildenafil (Viagra) in the treatment of erectile dysfunction. [Review] [13 refs]. *Compr Ther* 1999;25(2):90-94.
- Lim P H C, Moorthy P, Benton K G F. The clinical safety of Viagra. *Ann N Y Acad Sci* 2002;962(pp 378-388):-388.
- Limoge J P, Olins E, Henderson D et al. Minimally invasive therapies in the treatment of erectile dysfunction in anticoagulated cases: a study of satisfaction and safety. *Br J Urol* 1996;155(4):1276-1279.
- Lin C-S, Xin Z-C, Lin G et al. Phosphodiesterases as therapeutic targets. *Urology* 2003;61(4):685-691.
- Lincoln T M. Cyclic GMP and phosphodiesterase 5 inhibitor therapies: What's on the horizon. *Mol Pharmacol* 2004;66(1):11-13.
- Lindsey I. What is the incidence of sexual dysfunction in males following rectal excision for benign and malignant diseases?. *National Research Register* 2000;2000.
- Linnet O I, Neff L L. Intracavernous prostaglandin E1 in erectile dysfunction. *Clin Investig* 1994;72(2):139-149.
- Linnebur S A. Pharmacotherapy update: What's new about old medications. *Annals of Long Term Care* 2004;12(9):34-44.
- Lipshultz L I. Injection therapy for erectile dysfunction. *N Engl J Med* 1996;334(14):913-914.
- Lipshultz L I, Kim E D. Treatment of erectile dysfunction in men with diabetes. *J Am Med Assoc* 1999;281(5):465-466.
- Llisterri J L, Lozano Vidal J V, Aznar Vicente J et al. Sexual dysfunction in hypertensive patients treated with losartan. *Am J Med Sci* 2001;321(5):336-341.
- Long R L, Sherman L S, Lombardi T J. A goal-oriented, cost-effective approach to the diagnosis and treatment of 24 male erectile dysfunction. [Review] [24 refs]. *J Ky Med Assoc* 1995;93(11):500-508.
- Loudon Julia B. Potential confusion between erectile dysfunction and premature ejaculation: An evaluation of men presenting with erectile difficulty at a sex therapy clinic. *Sexual & Marital Therapy* 1998;13(4):397-403.
- Lu J, SJ Fan J, Zhu J et al. The prospective and randomized control study of Viagra combined with Andriol in the treatment of ED in the aging male. *Chinese Journal of Andrology* 2003;17(3):194-196.
- Lue T F. Erectile dysfunction. *N Engl J Med* 2000;342(24):1802-1813.
- Lue T F. Impotence after radical pelvic surgery: physiology and management. [Review] [56 refs]. *Urol Int* 1991;46(3):259-265.
- Lukkarinen O, Tonttila P, Hellstrom P et al. Non-prosthetic surgery in the treatment of erectile dysfunction. A retrospective study of 45 impotent patients in the University of Oulu. *Scandinavian Journal of Urology & Nephrology* 1998;32(1):42-46.
- Lunenfeld B, Saad F, Hoesl C E. ISA, ISSAM and EAU recommendations for the investigation, treatment and monitoring of late-onset hypogonadism in males: Scientific background and rationale. *Aging Male* 2005;8(2):59-74.

- Maan Z, Arya M, Shergill I et al. Peyronie's disease: An update of the medical management. *Expert Opin Pharmacother* 2004;5(4):799-805.
- Maas R, Schwedhelm E, Albsmeier J et al. The pathophysiology of erectile dysfunction related to endothelial dysfunction and mediators of vascular function. *Vasc Med* 2002;7(3):213-225.
- Mahmud A, Hennessy M, Feely J. Effect of sildenafil on blood pressure and arterial wave reflection in treated hypertensive men. *J Hum Hypertens* 2001;15(10):707-713.
- Maier U, Koinig G. Andrological findings in young patients under long-term antidepressive therapy with clomipramine. *Psychopharmacology (Berl)* 1994;116(3):357-359.
- Mak R, De Backer G, Kornitzer M et al. Prevalence and correlates of erectile dysfunction in a population-based study in Belgium. *Eur Urol* 2002;41(2):132-138.
- Manasia P, Pomerol J, Ribe N et al. Comparison of the efficacy and safety of 90 mg versus 20 mg fluoxetine in the treatment of premature ejaculation. *Br J Urol* 2003;170(1):164-165.
- Manganiello V. International Journal of Impotence Research: Editorial commentary. *Int J Impot Res* 2004;16(SUPPL. 1):S1-S3.
- Mann K, Klingler T, Noe S et al. Effects of yohimbine on sexual experiences and nocturnal penile tumescence and rigidity in erectile dysfunction. *Arch Sex Behav* 1996;25(1):1-16.
- Mann R D. Introduction - Tadalafil. *Journal of Drug Evaluation* 2004;2(8):223
- Mann R D. Executive summary sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):221-223.
- Manning M, Junemann K P, Scheepe J R et al. Long-term followup and selection criteria for penile revascularization in erectile failure.[see comment]. *Br J Urol* 1998;160(5):1680-1684.
- Marberger M, Roehrborn C G, Marks L S et al. Relationship among serum testosterone, sexual function, and response to treatment in men receiving dutasteride for benign prostatic hyperplasia. *Journal of Clinical Endocrinology & Metabolism* 2006;91(4):1323-1328.
- Margel D, Tal R, Livne P M et al. Predictors of erectile function improvement in obstructive sleep apnea patients with long-term CPAP treatment. *Int J Impot Res* 2005;17(2):186-190.
- Marquer C, Bressolle F. Moxisylyte: A review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic use in impotence. *Fundam Clin Pharmacol* 1998;12(4):377-387.
- Martin D J, Badwan K, Parker M et al. Transdermal application of verapamil gel to the penile shaft fails to infiltrate the tunica albuginea. *Br J Urol* 2002;168(6):2483-2485.
- Martins F E, Reis J P. Visual erotic stimulation test for initial screening of psychogenic erectile dysfunction: a reliable noninvasive alternative?. *Br J Urol* 1997;157(1):134-139.
- Masand P S, Ashton A K, Gupta S et al. Sustained-release bupropion for selective serotonin reuptake inhibitor-induced sexual dysfunction: a randomized, double-blind, placebo-controlled, parallel-group study.[see comment]. *Am J Psychiatry* 2001;158(5):805-807.
- Maytom M C, Derry F A, Dinsmore W W et al. A two-part pilot study of sildenafil (VIAGRA) in men with erectile dysfunction caused by spinal cord injury. *Spinal Cord*. 1999;37(2):110-116.
- McCarthy Barry W. Relapse prevention strategies and techniques with erectile dysfunction. *J Sex Marital Ther* 2001;27(1):1-8.
- McClellan K J, Goa K L. Transdermal testosterone. [Review] [17 refs]. *Drugs* 1998;55(2):253-258.
- McConnell J D, Roehrborn C G, Bautista O M et al. The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003;349(25):2387-2398.
- McCullough A R, Barada J H, Fawzy A et al. Achieving treatment optimization with sildenafil citrate (Viagra) in patients with erectile dysfunction. *Urology* 2002;60(2 Suppl 2):28-38.
- McKinlay J B. The worldwide prevalence and epidemiology of erectile dysfunction. [Review] [17 refs]. *Int J Impot Res* 2000;12Suppl-S11.
- McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992;9:265A
- McMahon C G. Nonsurgical treatment of cavernosal venous leakage. *Urology* 1997;49(1):97-100.
- McMahon C G. Treatment of Erectile Dysfunction with Chronic Dosing of Tadalafil. *Eur Urol* 2006;50(2):215-217.
- McMahon C G, Stuckey B G A, Andersen M et al. Efficacy of sildenafil citrate (viagra) in men with premature ejaculation. *Br J Sex Med* 2005;2(3):368-375.
- Mealy N E. NBI-69733. *Drugs of the Future* 2004;29(6):642

- Mealy N E. GPI-1485. *Drugs of the Future* 2004;29(6):640
- Mealy N E. EMR-62203. *Drugs of the Future* 2004;29(6):639
- Mealy N E. Dasantafil. *Drugs of the Future* 2004;29(6):633
- Mealy N E. DA-8159. *Drugs of the Future* 2004;29(6):631
- Mealy N E. Avanafil. *Drugs of the Future* 2004;29(6):628-629.
- Mealy N E, Bayes M. PT-141. *Drugs of the Future* 2004;29(11):1177
- Mealy N E, Bayes M. ABT-724. *Drugs of the Future* 2005;30(9):935
- Mehdiyev T V. Intracavernous injection probe of vasoactive preparations in the diagnosis of erectile dysfunctions in patients with diabetes mellitus. *Azerbaijdzhanskii Meditsinskii Zhurnal* 2002;(pp 17-19):-19.
- Meinhardt W, Kropman R F, Vermeij P et al. The influence of medication on erectile function. *Int J Impot Res* 1997;9(1):17-26.
- Melman A, Bar-Chama N, McCullough A et al. The first human trial for gene transfer therapy for the treatment of erectile dysfunction: preliminary results. *Eur Urol* 2005;48(2):314-318.
- Mendelson W B, Gujavarty K, Slintak C et al. Reported sexual dysfunction in obstructive sleep apnea patients. *Ann Clin Psychiatry* 1990;2(2):93-101.
- Merrick G S, Wallner K E, Butler W M. Minimizing prostate brachytherapy-related morbidity. *Urology* 2003;62(5):786-792.
- Meyhoff H H, Rosenkilde P, Bodker A. Non-invasive management of impotence with transcutaneous nitroglycerin. *Br J Urol* 1992;69(1):88-90.
- Migliari R, Muscas G, Usai E. Effect of Casodex on sleep-related erections in patients with advanced prostate cancer. *Br J Urol* 1992;148(2 I):338-341.
- Mikhail N. Efficacy and safety of sildenafil in patients with congestive heart failure [7]. *Arch Intern Med* 2004;164(18):2067-2068.
- Millard R J, Stricker P D, Lynch W J et al. Risks of self-injection therapy for impotence. *Med J Aust* 1996;165(2):117-118.
- Miller D C, Wei J T, Dunn R L et al. Use of medications or devices for erectile dysfunction among long-term prostate cancer treatment survivors: potential influence of sexual motivation and/or indifference. *Urology* 2006;68(1):166-171.
- Miller N, Smolkin M E, Bissonette E et al. Undetectable prostate specific antigen at 6-12 months: a new marker for early success in hormonally treated patients after prostate brachytherapy. *Cancer* 2005;103(12):2499-2506.
- Mills R D, Sethia K K. Maximisation of the erectile response in the investigation of impotence. *Int J Impot Res* 1999;11(1):29-32.
- Milman H A, Arnold S B, Rivera-Miranda G et al. Neurologic, psychological, and aggressive disturbances with sildenafil. *Ann Pharmacother* 2002;36(7-8):1129-1134.
- Mittleman M M, Rosen R C. Evaluating clinical trial design results and analysis of drug treatments for erectile dysfunction. *Int J Impot Res* 2003;15(4):x-xiii.
- Miwa Y, Kaneda T, Yokoyama O. Correlation between the Aging Males' Symptoms Scale and sex steroids, gonadotropins, dehydroepiandrosterone sulfate, and growth hormone levels in ambulatory men. *Br J Sex Med* 2006;3(4):723-726.
- Mohr B A, Bhasin S, Link C L et al. The effect of changes in adiposity on testosterone levels in older men: longitudinal results from the Massachusetts Male Aging Study. *Eur J Endocrinol* 2006;155(3):443-452.
- Montejo A L, Llorca G, Izquierdo J A et al. Incidence of sexual dysfunction associated with antidepressant agents: a prospective multicenter study of 1022 outpatients. Spanish Working Group for the Study of Psychotropic-Related Sexual Dysfunction.[see comment]. *Hillside J Clin Psychiatry* 2001;62Suppl-21.
- Montejo-Gonzalez A L, Llorca G, Izquierdo J A et al. SSRI-induced sexual dysfunction: fluoxetine, paroxetine, sertraline, and fluvoxamine in a prospective, multicenter, and descriptive clinical study of 344 patients. *Journal of Sex and Marital Therapy* 1997;23(3):176-194.
- Montorsi F. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil: Editorial comment. *Eur Urol* 2004;45(4):508-509.
- Montorsi F, Burnett A L. Erectile dysfunction after radical prostatectomy. *BJU Int* 2004;93(1):1-2.
- Montorsi F, Briganti A, Salonia A et al. Current and Future Strategies for Preventing and Managing Erectile Dysfunction Following Radical Prostatectomy. *Eur Urol* 2004;45(2):123-133.
- Montorsi F, Guazzoni G, Boccardi A et al. Improved minimally-invasive assessment of penile haemodynamics: the combination of colour Doppler sonography and injection-stimulation test. *Int J Impot Res* 1995;7(1):33-40.
- Montorsi F, Perani D, Anchisi D et al. Brain activation patterns during video sexual stimulation following the administration of apomorphine: results of a placebo-controlled study. *Eur Urol* 2003;43(4):405-411.

- Montorsi F, Strambi L F, Guazzoni G et al. Effect of yohimbine-trazodone on psychogenic impotence: a randomized, double-blind, placebo-controlled study. *Urology* 1994;44(5):732-736.
- Morales A. Men's aging and sexual disorders: An update on diagnosis and treatment. *Rev Endocr Metab Disord* 2005;6(2):85-92.
- Morales Alvaro, Condra Michael, Heaton Jeremy P et al. Impotence: Organic factors and management approach. *Sexual & Marital Therapy* 1991;6(2):97-106.
- Moreira E D, Lbo C F, Diament A et al. Incidence of erectile dysfunction in men 40 to 69 years old: results from a population-based cohort study in Brazil. *Urology* 2003;61(2):431-436.
- Moreira E D, Lisboa Lobo C F, Villa M et al. Prevalence and correlates of erectile dysfunction in Salvador, northeastern Brazil: a population-based study. *Int J Impot Res* 2002;14Suppl-9.
- Morley John E, Kaiser Fran E. Aging and sexuality. Vellas, Bruno (Ed); Albareda, J 1992;-L(Ed):1992-165.
- Mulhall J P, bdel-Moneim A, Abobakr R et al. Improving the accuracy of vascular testing in impotent men: correcting hemodynamic alterations using a vasoactive medication re-dosing schedule. *Br J Urol* 2001;166(3):923-926.
- Mulhall J P, Daller M, Traish A M et al. Intracavernosal forskolin: Role in management of vasculogenic impotence resistant to standard 3-agent pharmacotherapy. *Br J Urol* 1997;158(5):1752-1759.
- Mulhall J P, Valenzuela R, Aviv N et al. Effect of testosterone supplementation on sexual function in hypogonadal men with erectile dysfunction. *Urology* 2004;63(2):348-352.
- Mulligan T, Schmitt B. Testosterone for erectile failure. *J Gen Intern Med* 1993;8(9):517-521.
- Mulligan T, Frick M F, Zuraw Q C et al. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 2006;60(7):762-769.
- Muneer A, Ralph D J, Minhas S. Sildenafil citrate (Viagra). *Journal of Drug Evaluation* 2003;1(7):225-246.
- Munoz M, Bancroft J, Beard M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 2. The erectile response to erotic stimuli in men with erectile dysfunction, in relation to age and in comparison with normal volunteers. *Psychopharmacology (Berl)* 1994;115(4):471-477.
- Munoz M, Bancroft J, Turner M. Evaluating the effects of an alpha-2 adrenoceptor antagonist on erectile function in the human male. 1. The erectile response to erotic stimuli in volunteers. *Psychopharmacology (Berl)* 1994;115(4):463-470.
- Murphy A M, O'Leary M. Failure of the Ambicor inflatable penile prosthesis to deflate. *Int J Impot Res* 2005;17(3):291-292.
- Murphy J C, Srinivas S, Terris M K. Flutamide administration at 500 mg daily has similar effects on serum testosterone to 750 mg daily. *J Androl* 2004;25(4):630-634.
- Nakata M, Takashima S, Kaminou T et al. Embolotherapy for venous impotence: use of ethanol. *Journal of Vascular & Interventional Radiology* 2000;11(8):1053-1057.
- Nakonezny P A, Byerly M J, Rush A J. The relationship between serum prolactin level and sexual functioning among male outpatients with schizophrenia or schizoaffective disorder: A randomized double-blind trial of risperidone vs. quetiapine. *J Sex Marital Ther* 2007;33(3):203-216.
- Nandwani R, Gourlay Y. Possible interaction between sildenafil and HIV combination therapy [1]. *Lancet* 1999;353(9155):840
- Narayan P, Trachtenberg J, Lepor H et al. A dose-response study of the effect of flutamide on benign prostatic hyperplasia: results of a multicenter study. *Urology* 1996;47(4):497-504.
- Neese Leah E, Schover Leslie R, Klein Eric A et al. Finding help for sexual problems after prostate cancer treatment: A phone survey of men's and women's perspectives. [References]. *Psychooncology* 2003;12(5):463-473.
- Neumeyer K, Kirkpatrick P. Tadalafil and vardenafil. *Nat Rev Genet* 2004;3(4):295-296.
- Nicolosi A, Moreira E D, Shirai M et al. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology* 2003;61(1):201-206.
- Nieschlag E, Swerdloff R, Behre H M et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU recommendations. *Int J Androl* 2005;28(3):125-127.
- Nurnberg H G, Seidman S N, Gelenberg A J et al. Depression, antidepressant therapies, and erectile dysfunction: clinical trials of sildenafil citrate (Viagra) in treated and untreated patients with depression. *Urology* 2002;60(2 Suppl 2):58-66.
- Nurnberg H, George. Erectile Dysfunction and Comorbid Depression: Prevalence, Treatment Strategies, and Associated Medical Conditions. [References]. *Hillside J Clin Psychiatry* 2003;64(Suppl10):3-4.

- O'Sullivan J D. Apomorphine as an alternative to sildenafil in Parkinson's disease. [References]. *Journal of Neurology, Neurosurgery & Psychiatry* 2002;72(5):681
- Oefelein M G. Time to normalization of serum testosterone after 3-month luteinizing hormone-releasing hormone agonist administered in the neoadjuvant setting: implications for dosing schedule and neoadjuvant study consideration.[see comment]. *Br J Urol* 1998;160(5):1685-1688.
- Ojumu A, Dobs A S. Is Hypogonadism a Risk Factor for Sexual Dysfunction?. *J Androl* 2003;24(6 SUPPL.):S46-S51.
- Onu P E. Depot medroxyprogesterone in the management of benign prostatic hyperplasia. *Eur Urol* 1995;28(3):229-235.
- Opsomer R J, Wese F X, De Groote P et al. The external vacuum device in the management of erectile dysfunction. *Acta Urol Belg* 1997;65(4):13-16.
- Osterloh I H, Riley A. Clinical update on sildenafil citrate. [Review] [58 refs]. *Br J Clin Pharmacol* 2002;53(3):219-223.
- Owens J. Seeking selectivity. *Nat Rev Genet* 2005;4(2):106
- Ozbek E, Yurekli M, Soylu A et al. The role of adrenomedullin in varicocele and impotence. *BJU Int* 2000;86(6):694-698.
- Ozdel O, Oguzhanoglu A, Oguzhanoglu N K et al. A follow-up study of male sexual disorders: The neurophysiological assessments, anxiety-depression levels, and response to fluoxetine treatment [10]. *J Clin Psychopharmacol* 2004;24(4):461-463.
- Paice Judith A, Penn Richard D, Ryan Will G. Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. *J Pain Symptom Manage* 1994;9(2):126-131.
- Paick J S, Yang J H, Kim S W et al. Severity of erectile dysfunction in married impotent patients: interrelationship with anthropometry, hormones, metabolic profiles and lifestyle. *Int J Urol* 2007;14(1):48-53.
- Paick J S, Yang J H, Kim S W et al. The role of prolactin levels in the sexual activity of married men with erectile dysfunction. *BJU Int* 2006;98(6):1269-1273.
- Paick S H, Meehan A, Lee M et al. The relationship among lower urinary tract symptoms, prostate specific antigen and erectile dysfunction in men with benign prostatic hyperplasia: results from the proscar long-term efficacy and safety study. *Br J Urol* 2005;173(3):903-907.
- Palha A P, Gomes F A, Martins A S et al. [Clinical, multicentric, and open study to evaluate the efficacy of and tolerance to sildenafil in patients with erectile dysfunction]. *Acta Med Port.* 2002;15(4):249-256.
- Pan C C, Lin J S N, Wong W S. Comparison of effect on erection between vacuum constriction devices and intracavernous injection of prostaglandin E1. *Asian J Surg* 1997;20(2):162-166.
- Papatsoris A G, Deliveliotis C, Singer C et al. Erectile dysfunction in Parkinson's disease. *Urology* 2006;67(3):447-451.
- Parazzini F, Menchini Fabris F, Bortolotti A et al. Frequency and determinants of erectile dysfunction in Italy. *Eur Urol* 2000;37(1):43-49.
- Paris G, Sponsel W E, Sandoval S S et al. Sildenafil increases ocular perfusion. *Int Ophthalmol* 2001;23(4-6):355-358.
- Parker C. The Scandinavian Prostate Cancer Group Study: The case for conservative management. *BJU Int* 2005;96(7):952-953.
- Parsons J K, Marschke P, Maples P et al. Effect of methylprednisolone on return of sexual function after nerve-sparing radical retropubic prostatectomy. *Urology* 2004;64(5):987-990.
- Patankar M. Sildenafil citrate. *J Indian Med Assoc* 2000;98(12):
- Patterson D, Kloner R, Effron M et al. The effect of tadalafil on the time to exercise-induced myocardial ischaemia in subjects with coronary artery disease. *Br J Clin Pharmacol* 2005;60(5):459-468.
- Pegge N C, Twomey A M, Vaughton K et al. The role of endothelial dysfunction in the pathophysiology of erectile dysfunction in diabetes and in determining response to treatment. *Diabet Med* 2006;23(8):873-878.
- Penson D F, Feng Z, Kuniyuki A et al. General quality of life 2 years following treatment for prostate cancer: what influences outcomes? Results from the prostate cancer outcomes study.[see comment]. *Am J Clin Oncol* 2003;21(6):1147-1154.
- Perez Martin A, Skinner Eila C, Meyerowitz Beth E E. Sexuality and intimacy following radical prostatectomy: Patient and partner perspectives. [References]. *Health Psychol* 2002;21(3):288-293.
- Perimenis P, Athanasopoulos A, Papathanasopoulos P et al. Gabapentin in the management of the recurrent, refractory, idiopathic priapism. *Int J Impot Res* 2004;16(1):84-85.
- Pescatori E S, Calpista A, Artibani W et al. Self-injection devices for intracavernosal pharmacotherapy: operational classification and safety considerations. *Int J Impot Res* 1996;8(2):53-57.
- Pescatori E S, Silingardi V, Galeazzi G M et al. Audiovisual sexual stimulation by virtual glasses is effective in inducing complete cavernosal smooth muscle relaxation: a pharmacocavernosometric study. *Int J Impot Res* 2000;12(2):83-88.

- Phelps J S, Jain A, Monga M. The PsychoedPlusMed approach to erectile dysfunction treatment: the impact of combining a psychoeducational intervention with sildenafil. *J Sex Marital Ther* 2004;30(5):305-314.
- Philipp M, Kohnen R, Benkert O. A comparison study of moclobemide and doxepin in major depression with special reference to effects on sexual dysfunction. *Int Clin Psychopharmacol* 1993;7(3-4):149-153.
- Philipp M, Tiller J W G, Baier D et al. Comparison of moclobemide with selective serotonin reuptake inhibitors (SSRIs) on sexual function in depressed adults. *Eur Neuropsychopharmacol* 2000;10(5):305-314.
- Phillips B G, Kato M, Pesek C A et al. Sympathetic activation by sildenafil.[see comment]. *Circulation* 2000;102(25):3068-3073.
- Pirotte B, de Tullio P, Antoine M-H et al. New insights into the development of ATP-sensitive potassium channel openers. *Expert Opinion on Therapeutic Patents* 2005;15(5):497-504.
- Pisters L L, von Eschenbach A C, Scott S M et al. The efficacy and complications of salvage cryotherapy of the prostate. *J Urol* 1997;157(3):921-925.
- Pittler M, Ernst E. Trials have shown yohimbine is effective for erectile dysfunction [14]. *Br Med J* 1998;317(7156):478
- Polak K, Wimpfing B, Berisha F et al. Effects of sildenafil on retinal blood flow and flicker-induced retinal vasodilatation in healthy subjects. *Invest Ophthalmol Vis Sci* 2003;44(11):4872-4876.
- Pollack Mark H, Reiter Stewart, Hammerness Paul. Genitourinary and sexual adverse effects of psychotropic medication. *Int J Psychiatry Med* 1992;22(4):305-327.
- Pomerantz J M. Viagra and medical necessity. *Drug Benefit Trends* 2002;14(10):33+40
- Pommerville P J. From bedside to bed. Recovery of sexual function after prostate cancer. *Can Fam Physician* 2005;51(JULY):941-943+948.
- Porst H C. Re-dosing of prostaglandin-E1 versus prostaglandin-E1 plus phentolamine in male erectile dysfunction: a dynamic color power Doppler study. *Int J Impot Res* 2000;12(2):134-135.
- Porst H, Giuliano F, Glina S et al. Evaluation of the Efficacy and Safety of Once-a-Day Dosing of Tadalafil 5 mg and 10 mg in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial. *Eur Urol* 2006;50(2):351-359.
- Pouaha J, Martin S, Reichert-Penetrat S et al. Thalidomide and sexual dysfunction in men.[comment]. *Br J Dermatol* 2002;146(6):1112-1113.
- Power-Smith Parsley. Beneficial sexual side-effects from fluoxetine. *Br J Psychiatry Suppl* 1994;164 Feb 1994, 249-250. [http249-250](http://249-250).
- Pratt-Ubunama M N, Nishizaka M K, Calhoun D A. Aldosterone antagonism: An emerging strategy for effective blood pressure lowering. *Curr Hypertens Rep* 2005;7(3):186-192.
- Preskorn S H. Duloxetine. *Journal of Psychiatric Practice* 2004;10(6):375-385.
- Prins J, Blanker M H, Bohnen A M et al. Prevalence of erectile dysfunction: A systematic review of population-based studies. *Int J Impot Res* 2002;14(6):422-432.
- Pryor J. Vardenafil: update on clinical experience. [Review] [10 refs]. *Int J Impot Res* 2002;14Suppl-9.
- Pryor J P. Orgasmic and ejaculatory dysfunction. *Sexual & Relationship Therapy* 2002;17(1):87-95.
- Qian L X, Wu H F, Xu H et al. Multi-center Evaluation of Efficacy and Safety of Oral Mesylate Phentolamine for the Treatment of Erectile Dysfunction. *Int J Androl* 2001;7(5):302-305.
- Quinn M J, Jefferson K, Persad R. Benign prostatic hyperplasia and sexual dysfunction [3] (multiple letters). *Lancet* 2003;361(9368):1562
- Quirk J, Thornton M, Neumeier K et al. Cardiology and vascular disorders. *Nat Rev Genet* 2004;3(7 SUPPL.):S12-S17.
- Ramasubbu R. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Ramasubbu Rajamannar. Switching to moclobemide to reverse fluoxetine-induced sexual dysfunction in patients with depression. *J Psychiatry Neurosci* 1999;24(1):45-50.
- Reffellmann T, Kloner R A. Effects of sildenafil on myocardial infarct size, microvascular function, and acute ischemic left ventricular dilation. *Cardiovasc Res* 2003;59(2):441-449.
- Reyes J A, Tan D A, Quimpo J A et al. The Philippine Male Aging Survey. *Aging Male* 2004;7(3):227-235.
- Rhoden E L, Estrada C, Levine L et al. The value of pituitary magnetic resonance imaging in men with hypogonadism.[see comment]. *Br J Urol* 2003;170(3):795-798.
- Richardson J D. Intracorporeal injections for the treatment of impotence. *Med J Aust* 1991;155(10):688

- Riley Alan. Oral treatments for erectile dysfunction. *Int J STD AIDS* 1996;7(Suppl 3):16-18.
- Riley Alan J, Riley Elizabeth J. Psychological and behavioural aspects of intracavernosal injection therapy for erectile disorder. *Sexual & Marital Therapy* 1998;13(3):273-284.
- Rizvi K, Hampson J P, Harvey J N. Do lipid-lowering drugs cause erectile dysfunction? A systematic review.[see comment]. [Review] [35 refs]. *Fam Pract* 2002;19(1):95-98.
- Roizenblatt S, Guilleminault C, Poyares D et al. A double-blind, placebo-controlled, crossover study of sildenafil in obstructive sleep apnea. *Arch Intern Med* 2006;166(16):1763-1767.
- Rojewski M T, Korper S, Schrezenmeier H. Arsenic trioxide therapy in acute promyelocytic leukemia and beyond: From bench to bedside. *Leuk Lymphoma* 2004;45(12):2387-2401.
- Rosano G M, Marazzi G, Patrizi R et al. Comparison of trimetazidine plus sildenafil to chronic nitrates in the control of myocardial ischemia during sexual activity in patients with coronary artery disease. *Am J Cardiol* 2005;95(3):327-331.
- Rose V L. Sildenafil in the treatment of erectile dysfunction. *Am Fam Physician* 1998;58(1):268
- Rosen R C, Kostis J B. Overview of phosphodiesterase 5 inhibition in erectile dysfunction. *Am J Cardiol* 2003;92(9 SUPPL. 1):9M-18M.
- Rosen R C, Lane R M, Menza M. Effects of SSRIs on sexual function: a critical review.[see comment]. [Review] [255 refs]. *J Clin Psychopharmacol* 1999;19(1):67-85.
- Rosen Raymond C. Erectile dysfunction: The medicalization of male sexuality. *Clin Psychol Rev* 1996;16(6):497-519.
- Rosen Raymond C, Leiblum Sandra R. Treatment of male erectile disorder: Current options and dilemmas. *Sexual & Marital Therapy* 1993;8(1):5-8.
- Rosen Raymond C, Leiblum Sandra, Risa. Erectile disorders: An overview of historical trends and clinical perspectives. Rosen, Raymond C (Ed); Leiblum, Sandra Risa (Ed) 1992;(1992):378
- Rosenthal B D, May N R, Metro M J et al. Adjunctive use of AndroGel (testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone. *Urology* 2006;67(3):571-574.
- Rowland D L, Greenleaf W J, Dorfman L J et al. Aging and sexual function in men. *Arch Sex Behav* 1993;22(6):545-557.
- Rowland D L, Kallan K, Slob A K. Yohimbine, erectile capacity, and sexual response in men. *Arch Sex Behav* 1997;26(1):49-62.
- Ruof J, Graf-Morgenstern M, Muller M J. Quality of life in patients with erection difficulties: Evaluation of a German version of the "Quality of life measure for men with erection difficulties" (QoL-Med). *Aktuel Urol* 2001;32(1):21-26.
- Ryder R E, Close C F, Moriarty K T et al. Impotence in diabetes: aetiology, implications for treatment and preferred vacuum device. *Diabet Med* 1992;9(10):893-898.
- Sadock Virginia A. A sexually compulsive male with erectile dysfunction treated with Viagra: Discussion. *Journal of Sex Education & Therapy* 1998;23(4):275-277.
- Safarinejad M R. Prevalence and risk factors for erectile dysfunction in a population-based study in Iran. *Int J Impot Res* 2003;15(4):246-252.
- Sairam K, Kulinskaya E, Boustead G B et al. Prevalence of undiagnosed prostate cancer in men with erectile dysfunction. *BJU Int* 2002;89(3):261-263.
- Sak S C, Eardley I. What is the relationship between benign prostatic hyperplasia and sexual function?. *Sexual & Relationship Therapy* 2004;19(4):431-443.
- Sakamoto H, Shimada M, Yoshida H. Hemodynamic evaluation of the penile arterial system in patients with erectile dysfunction using power doppler imaging. *Urology* 2002;60(3):480-484.
- Saks Bonnie R. A sexually compulsive male with erectile dysfunction treated with Viagra: Case report. *Journal of Sex Education & Therapy* 1998;23(4):271-274.
- Salonia A, Barbieri L, Chen J et al. Comparison of the effect of sildenafil and apomorphine SL on nocturnal erections in healthy volunteers: a placebo-controlled study. *Eur Urol* 2005;47(4):524-529.
- Salonia A, Maga T, Colombo R et al. A prospective study comparing paroxetine alone versus paroxetine plus sildenafil in patients with premature ejaculation. *Br J Urol* 2002;168(6):2486-2489.
- Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr.Med Res Opin.* 2003;19(4):241-262.
- Samarasinghe Y, Rivas-Toro H. HEART UK 18th annual medical and scientific meeting: From diabetes to mixed hyperlipidaemias. *British Journal of Cardiology* 2004;11(5):364-365.
- Sathe R S, Komisaruk B R, Ladas A K et al. Naltrexone-induced augmentation of sexual response in men. *Arch Med Res* 2001;32(3):221-226.

- Sato Y, Suzuki N, Adachi H et al. Evaluation of the alleviative action of neurotrophin for penile pain associated with intracavernous injection of prostaglandin E1 assessed using the visual analogue scale. *Int J Impot Res* 1998;10(1):1-3.
- Savoca G, Silvestre G, Belgrano E. Intracavernosal injection therapy and surgical therapy in diabetic patients with erectile dysfunction. [Review] [26 refs]. *Diabetes, Nutrition & Metabolism - Clinical & Experimental* 2002;15(1):53-57.
- Scalvini T, Martini P R, Obici L et al. Infertility and Hypergonadotropic Hypogonadism as First Evidence of Hereditary Apolipoprotein A-I Amyloidosis. *Br J Urol* 2007;
- Schiavi Raul C, Schanzer Harry, Sozio Giampaolo et al. Erectile function and penile blood pressure in diabetes mellitus. *J Sex Marital Ther* 1994;20(2):119-124.
- Scholz M, Strum S. Re: Recovery of spontaneous erectile function after nerve-sparing radical retropubic prostatectomy with and without early intracavernous injections of alprostadil: results of a prospective, randomized trial.[comment]. *Br J Urol* 1999;161(6):1914-1915.
- Schrader S, Mills A, Schepeler M et al. Improvement in sexual functioning and satisfaction in nonresponders to testosterone gel: clinical effectiveness in hypogonadal, HIV-positive males. *Clin Cornerstone* 2005;7 Suppl 4S26-S31.
- Schroder F H, Whelan P, De Reijke T M et al. Metastatic prostate cancer treated by flutamide versus cyproterone acetate. Final analysis of the "European Organization for Research and Treatment of Cancer" (EORTC) Protocol 30892. *Eur Urol* 2004;45(4):457-464.
- Schultheiss D, Stief C G. Physiology and pathophysiology of erection: Consequences for present medical therapy of erectile dysfunction. *Andrologia* 1999;31(SUPPL. 1):59-64.
- Schwartz E J, Wong P, Graydon R J. Sildenafil preserves intracorporeal smooth muscle after radical retropubic prostatectomy. *Br J Urol* 2004;171(2 I):771-774.
- Seftel A. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(6):2297-2300.
- Seftel A. Effect of lifestyle changes on erectile dysfunction in obese men. A randomized controlled trial. *Br J Urol* 2005;173(2):544-545.
- Seftel A D. Male and female sexual function and dysfunction; andrology. *Br J Urol* 2005;174(4 I):1364-1366.
- Segraves R T. Pharmacological enhancement of human sexual behavior. *Journal of Sex Education & Therapy* 1991;17(4):283-289.
- Segraves R, Taylor. Two additional uses for sildenafil in psychiatric patients. [References]. *J Sex Marital Ther* 1999;25(4):265-266.
- Segraves Robert, Taylor Segraves, Kathleen Blindt et al. Sexual function in patients taking bupropion sustained release. *Hillside J Clin Psychiatry* 1995;56(8):374
- Seidman Stuart N. Exploring the relationship between depression and erectile dysfunction in aging men. *Hillside J Clin Psychiatry* 2002;63(Suppl5):5-12.
- Seyam R M, Albakry A, Ghobish A et al. Prevalence of erectile dysfunction and its correlates in Egypt: a community-based study. *Int J Impot Res* 2003;15(4):237-245.
- Shabbir M, Mikhailidis D M, Morgan R J. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors.[comment]. *Current Medical Research & Opinion* 2004;20(5):603-606.
- Shabbir M, Shah J S, Kirby R S. Cardiac failure and benign prostatic hyperplasia: Management of common comorbidities. *BJU Int* 2005;95(3):278-280.
- Shabsigh R. Testosterone therapy in erectile dysfunction. [Review] [34 refs]. *Aging Male* 2004;7(4):312-318.
- Shabsigh R. Hypogonadism and erectile dysfunction: The role for testosterone therapy. *Int J Impot Res* 2003;15(SUPPL. 4):S9-S13.
- Shakir S A W, Wilton L V, Boshier A et al. Cardiovascular events in users of sildenafil: Results from first phase of prescription event monitoring in England. *Br Med J* 2001;322(7287):651-652.
- Shamloul R, El-Dakhly M, Ghanem H et al. Intracavernous chlorpromazine versus phentolamine: A double-blind clinical comparative study. *Br J Sex Med* 2004;1(3):310-313.
- Shamloul R, Ghanem H M, Salem A et al. The value of penile duplex in the prediction of intracavernous drug-induced priapism. *Int J Impot Res* 2004;16(1):78-79.
- Shamsa A, Motavalli S M, Aghdam B. Erectile function in end-stage renal disease before and after renal transplantation. *Transplant Proc* 2005;37(7):3087-3089.
- Sharlip I D. Editorial comment. *International Braz J Urol* 2005;31(4):354-355.
- Sighinolfi M C, de Stefani S, Mofferdin A et al. Intracavernous prostaglandin E1 infusion in diabetes with associated ischemic necrosis of the glans penis. *Br J Urol* 2004;171(6 I):2380

- Silvestri A, Galetta P, Cerquetani E et al. Report of erectile dysfunction after therapy with beta-blockers is related to patient knowledge of side effects and is reversed by placebo.[see comment]. *Eur Heart J* 2003;24(21):1928-1932.
- Singer Carlos, Weiner William J, Sanchez-Ramos J et al. Sexual function in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry* 1991;54(10):942
- Sipski M, Alexander C, Guo X et al. Cardiovascular effects of sildenafil in men with SCIs at and above T6. *Topics in Spinal Cord Injury Rehabilitation* 2003;8(3):26-34.
- Siraj Q H, Bomanji J, Akhtar M A et al. Quantitation of pharmacologically-induced penile erections: The value of radionuclide phallography in the objective evaluation of erectile haemodynamics. *Nucl Med Commun* 1990;11(6):445-458.
- Slob A K, Dohle G R, Incrocchi L. 'Sildenafil and pharmacopentile duplex ultrasonography' by Speel et al: Inconclusive results. *Int J Impot Res* 2002;14(2):136-137.
- Slob A, Koos Steyvers, Christel L et al. Routine psychophysiological screening of 384 men with erectile dysfunction. *J Sex Marital Ther* 1998;24(4):273-279.
- Smith K J, Roberts M S. The cost-effectiveness of sildenafil. *Ann Intern Med* 2000;132(12):933-937.
- Sobh M A, Abd el, Hamid I et al. Effect of erythropoietin on sexual potency in chronic haemodialysis patients. A preliminary study. *Scand J Urol Nephrol* 1992;26(2):181-185.
- Sogari P R, Teloken C, Souto C A. Atropine role in the pharmacological erection test: study of 228 patients.. *Br J Urol* 1997;158(5):1760-1763.
- Sohle G R. Re: The age-related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men?. *Eur Urol* 2007;51(5):1440
- Sohn Michael, Sikora Richard. Ginkgo biloba extract in the therapy of erectile dysfunction. *Journal of Sex Education & Therapy* 1991;17(1):53-61.
- Solursh L, Solursh D S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *International Journal of Adolescent Medicine & Health* 1994;7(2):119-124.
- Solursh Lionel P, Solursh Diane S. Male erectile disorders in Vietnam combat veterans with chronic post-traumatic stress disorder. *Int J Adolesc Med Health* 1994;7(2):119-124.
- Sonda L P, Mazo R, Chancellor M B. The role of yohimbine for the treatment of erectile impotence. *J Sex Marital Ther* 1990;16(1):15-21.
- Sonksen J, Biering-Sorensen F. Transcutaneous nitroglycerin in the treatment of erectile dysfunction in spinal cord injured. *Paraplegia* 1992;30(8):554-557.
- Sorbera L A, Martin L, Rabasseda X et al. Vardenafil. Treatment of erectile dysfunction. Phosphodiesterase 5 inhibitor. *Drugs of the Future* 2001;26(2):141-144.
- Sparwasser C, Drescher P, Pust R A et al. Long-term results of therapy with intracavernous injections and penile venous surgery in chronic erectile dysfunction. *Scand J Urol Nephrol Suppl* 1994;157(Suppl):107-112.
- Speakman M T, Kloner R A. Viagra and cardiovascular disease. *Journal of Cardiovascular Pharmacology & Therapeutics* 1999;4(4):259-267.
- Srilatha B, Adaikan P G, Chong Y S. Relevance of oestradiol-testosterone balance in erectile dysfunction patients' prognosis. *Singapore Med J* 2007;48(2):114-118.
- Stas S N, Anastasiadis A G, Fisch H et al. Urologic aspects of andropause. *Urology* 2003;61(2):261-266.
- Steers W D. Tachyphylaxis and phosphodiesterase type 5 inhibitors.[comment]. *Br J Urol* 2002;168(1):207
- Steers W D. Viagra - After one year. *Urology* 1999;54(1):12-17.
- Steidle C, Witt M A, Matrisciano J et al. Sexual functioning and satisfaction in nonresponders to testosterone gel: Potential effectiveness of retreatment in hypogonadal males. *Clin Cornerstone* 2005;7 Suppl 4S20-S25.
- Steiger A, Holsboer F, Benkert O. Studies of nocturnal penile tumescence and sleep electroencephalogram in patients with major depression and in normal controls. *Acta Psychiatr Scand* 1993;87(5):358-363.
- Steiger Axel, Benkert O, Holsboer F. Effects of long-term treatment with the MAO-A inhibitor moclobemide on sleep EEG and nocturnal hormonal secretion in normal men. *Neuropsychobiology* 1994;30(2-3):101-105.
- Stief C G, Uckert S, Becker A J et al. The effect of the specific phosphodiesterase (PDE) inhibitors on human and rabbit cavernous tissue in vitro and in vivo. *Br J Urol* 1998;159(4):1390-1393.
- Stolk E A, Busschbach J J, Caffa M et al. Cost utility analysis of sildenafil compared with papaverine-phentolamine injections.[see comment]. *BMJ* 2000;320(7243):1165-1168.

- Strachan M W, Teoh W L, Don-Wauchope A C et al. Clinical and radiological features of patients with macroprolactinaemia. *Clin Endocrinol (Oxf)* 2003;59(3):339-346.
- Struthers A D. Aldosterone blockade in heart failure. *J Renin Angiotensin Aldosterone Syst* 2004;5(SUPPL. 1):S23-S27.
- Suetomi T, Endo F, Takeshima H et al. Evaluation of the effectiveness of sildenafil using questionnaire methods versus audio-visual sexual stimulation. *Int J Urol* 2005;12(4):369-373.
- Suzuki F, Shimizu C, Umetsu M et al. Adult-onset idiopathic hypogonadotropic hypogonadism due to isolated pituitary gonadotropin deficiency. *Adv Intern Med* 2004;43(7):571-574.
- Svartberg J, Aasebo U, Hjalmsen A et al. Testosterone treatment improves body composition and sexual function in men with COPD, in a 6-month randomized controlled trial. *Respir Med* 2004;98(9):906-913.
- Swartz D A, Todd M W. Intracavernous papaverine and glaucoma.[see comment]. *JAMA* 1990;264(5):570
- Szucs A, Janszky J, Barsi P et al. Sleep-related painful erection is associated with neurovascular compression of basal forebrain [5]. *J Neurol* 2002;249(4):486-487.
- T'Sjoen G, Feyen E, De Kuyper P et al. Self-referred patients in an aging male clinic: much more than androgen deficiency alone. *Aging Male* 2003;6(3):157-165.
- Tarhan F, Canguven O, Kuyumcuoglu U. Intracavernous sodium nitroprusside (SNP) versus papaverine/phentolamine in erectile dysfunction: a comparative study of short-term efficacy and side-effects.[comment]. *Br J Sex Med* 2006;3(2):377
- Tarhan F, Kuyumcuoglu U, Kolsuz A et al. Effect of intracavernosal sodium nitroprusside in impotence. *Urol Int* 1996;56(4):211-214.
- Tas A, Dilek K, Gullulu M et al. Treatment of erectile dysfunction in hemodialysis patients and effects of sildenafil [abstract]. XXXVIII Congress of the European Renal Association European Dialysis & Transplant Association June 24-27 2003;2001, Vienna, Austria 131p. 2003.
- Teillac P, Bono A V, Irani J et al. The role of luteinizing hormone-releasing hormone therapy in locally advanced prostate cancer and biochemical failure: Considerations for optimal use. *Clin Ther* 2005;27(3):273-285.
- Teloken P E, Smith E B, Lodowsky C et al. Defining association between sleep apnea syndrome and erectile dysfunction. *Urology* 2006;67(5):1033-1037.
- Thadani U, Smith W, Nash S et al. The effect of vardenafil, a potent and highly selective phosphodiesterase-5 inhibitor for the treatment of erectile dysfunction, on the cardiovascular response to exercise in patients with coronary artery disease. *J Am Coll Cardiol* 2002;40(11):2006-2012.
- Thaveundayil J X, Hambalek R, Ng Ying et al. Prolonged penile erections induced by hydroxyzine: Possible mechanism of action. *Neuropsychobiology* 1994;30(1):4-6.
- Thrasher J B. What's new in urology. *J Am Coll Surg* 2005;201(3):438-448.
- Tindall B, Forde S, Goldstein D et al. Sexual dysfunction in advanced HIV disease. *AIDS Care* 1994;6(1):105-107.
- Tomlinson J. Viagra and its use in cardiovascular disease.[erratum appears in *J Hum Hypertens* 2000 Apr;14(4):283]. [Review] [11 refs]. *J Hum Hypertens* 1999;13(9):593-594.
- Tomova A, Kumanov P. Are dehydroepiandrosterone sulphate and lipids associated with erectile dysfunction? [References]. *Maturitas* 2005;50(4):294-299.
- Tordjman G. NO/Pg E1: a new association in the treatment of erectile impotence. *Contracept Fertil Sex (Paris)* 1993;21, pp.509-510, 1993.
- Traish A M, Goldstein I, Kim N N. Testosterone and erecile function: from basic research to a new clinical paradigm for managing men with androgen insufficiency and erectile dysfunction. *Eur Urol* 2007;52(1):54-70.
- Trinchieri A, Nicola M, Masini F et al. Prospective comprehensive assessment of sexual function after retropubic non nerve sparing radical prostatectomy for localized prostate cancer. *Arch Ital Urol Androl* 2005;77(4):219-223.
- Truss M C, Becker A J, Djamilian M H et al. Role of the nitric oxide donor linsidomine chlorhydrate (SIN-1) in the diagnosis and treatment of erectile dysfunction. *Urology* 1994;44(4):553-556.
- Tsai S K, Hong C Y. Intracavernosal metaraminol for treatment of intraoperative penile erection. *Postgrad Med J* 1990;66(780):831-833.
- Tsujimura A, Matsumiya K, Matsuoka Y et al. Bioavailable testosterone with age and erectile dysfunction. *Br J Urol* 2003;170(6 Pt 1):2345-2347.
- Tuzgen S, Karamehmetoglu S S, Karacan I et al. Use of sildenafil in the treatment of erectile dysfunction in patients with spinal cord injury. *Neurosurgery Quarterly* 2006;16(1):40-43.
- Tzivoni D, Klein J, Hisdai D et al. The Israel Heart Society expert consensus document: The cardiac patient and sexual activity in the era of sildenafil (Viagra). *Israel Medical Association Journal: Imaj* 2000;2(1):63-65.

- Unnikrishnan A G, Rajaratnam S, Seshadri M S et al. The 'hook effect' on serum prolactin estimation in a patient with macroprolactinoma. *Neurol India* 2001;49(1):78-80.
- Uygun M C, Arik A I, Altug U et al. Effects of the 5 alpha-reductase inhibitor finasteride on serum levels of gonadal, adrenal, and hypophyseal hormones and its clinical significance: a prospective clinical study. *Steroids* 1998;63(4):208-213.
- Valdevenito R, Melman A. Intracavernous self-injection pharmacotherapy program: analysis of results and complications. *Int J Impot Res* 1994;6(2):81-91.
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy.[comment]. *Lancet* 2000;356(9224):169
- van Basten J P, Van Driel M F, Hoekstra H J et al. Erectile dysfunction with chemotherapy. *Lancet* 2000;356(9224):169
- Van Ahlen H, Peskar B A, Sticht G et al. Pharmacokinetics of vasoactive substances administered into the human corpus cavernosum. *Br J Urol* 1994;151(5):1227-1230.
- Van Moorselaar J. LUTS and Sexual Dysfunction: Implications for Management of BPH. *European Urology Supplements* 2003;2(10):13-20.
- Vatansever H S, Kayikcioglu O, Gumus B. Histopathologic effect of chronic use of sildenafil citrate on the choroid & retina in male rats. *Indian J Med Res* 2003;117(MAY):211-215.
- Verit A, Oguz H. Ophthalmic aspects of erectile dysfunction drugs [3]. *Am J Ophthalmol* 2006;141(3):598
- Vick R N, Benevides M, Patel M et al. The efficacy, safety and tolerability of intracavernous PNU-83757 for the treatment of erectile dysfunction.. *Br J Urol* 2002;167(6):2618-2623.
- Vickers M A, Wright E A. Erectile dysfunction in the patient with diabetes mellitus. *Am J Manag Care* 2004;10(1 SUPPL.):S3-S11.
- Vidal J, Curcoll L, Roig T et al. Intracavernous pharmacotherapy for management of erectile dysfunction in multiple sclerosis patients. *Rev Neurol* 1995;23(120):269-271.
- Vinik A I, Maser R E, Mitchell B D et al. Diabetic autonomic neuropathy. [Review] [192 refs]. *Diabetes Care* 2003;26(5):1553-1579.
- Virag R, Floresco J, Richard C. Impairment of shear-stress-mediated vasodilation of cavernous arteries in erectile dysfunction. *Int J Impot Res* 2004;16(1):39-42.
- Vlachopoulos C, Hirata K, O'Rourke M F. Effect of sildenafil on arterial stiffness and wave reflection. *Vasc Med* 2003;8(4):243-248.
- Vogt H J, Brandl P, Kockott G et al. Double-blind, placebo-controlled safety and efficacy trial with yohimbine hydrochloride in the treatment of nonorganic erectile dysfunction. *Int J Impot Res* 1997;9(3):155-161.
- Wagner G, Mulhall J. Pathophysiology and diagnosis of male erectile dysfunction. *BJU International - Supplement* 2001;88(3):3-10.
- Wagner G, Rabkin J, Rabkin R. Effects of testosterone replacement therapy on sexual interest, function, and behavior in HIV+ men. *J Sex Res* 1997;34(1):27-33.
- Wagner Gorm, Kaplan Helen, Singer. The new injection treatment for impotence: Medical and psychological aspects. *Refuat Hapeh Vehashinayim* 1993;x, 210 pp. Philadelphia, PA, US210
- Wald M, Seftel A D, Ross L S et al. Computational models for detection of erectile dysfunction. *Br J Urol* 2005;173(1):167-170.
- Waldbaum R S. The safety of PDE5 inhibitors in ED treatment: Putting cardiovascular concerns to rest. *Cardiology Review* 2005;22(9):23-24.
- Wang Z L, Shao S X, Li B et al. Sildenafil versus prostaglandin E1 in the management of erectile dysfunction. *Journal of Clinical Urology* 2002;17(7):347-349.
- Wang Z, Liu B C, Chen B et al. Randomized controlled study on erectile dysfunction treated by trazodone. *Chinese Journal of Andrology* 2002;16(3):236-238.
- Ware J, Catesby Rose F, Vincent McBrayer et al. The acute effects of nefazodone, trazodone and buspirone on sleep and sleep-related penile tumescence in normal subjects. *Sleep: Journal of Sleep Research & Sleep Medicine* 1994;17(6):544-550.
- Watanabe T, Chancellor M B, Rivas D A et al. Epidemiology of current treatment for sexual dysfunction in spinal cord injured men in the USA model spinal cord injury centers. *J Spinal Cord Med* 1996;19(3):186-189.
- Webb D J, Muirhead G J, Wulff M et al. Sildenafil citrate potentiates the hypotensive effects of nitric oxide donor drugs in male patients with stable angina. *J Am Coll Cardiol* 2000;36(1):25-31.
- Wegner H E H, Knispel H H, Meier T et al. Nitric oxide donor, linsidomine chlorhydrate (SIN-1), in the diagnosis and treatment of erectile dysfunction: Critical appraisal and review of the literature. *International Urology & Nephrology* 1995;27(5):621-628.

- Weinhardt L S, Carey M P. Prevalence of erectile disorder among men with diabetes mellitus: Comprehensive review, methodological critique, and suggestions for future research. *J Sex Res* 1996;33(3):205-214.
- Weinsaft J W, Hickey K, Bokhari S et al. Effects of tadalafil on myocardial blood flow in patients with coronary artery disease. *Coron Artery Dis* 2006;17(6):493-499.
- Weiske W-H. Invasive diagnosis and therapy - Are they still reasonable in the age of sildenafil?. *Andrologia* 1999;31(SUPPL. 1):95-97.
- Wespes E, Rammal A, Garbar C. Sildenafil non-responders: haemodynamic and morphometric studies. *Eur Urol* 2005;48(1):136-139.
- Wessells H, Fuciarelli K, Hansen J et al. Synthetic melanotropic peptide initiates erections in men with psychogenic erectile dysfunction: double-blind, placebo controlled crossover study. *Br J Urol* 1998;160(2):389-393.
- Wessells H, Gralnek D, Dorr R et al. Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction. *Urology* 2000;56(4):641-646.
- Wheatley D. Triple-blind, placebo-controlled trial of Ginkgo biloba in sexual dysfunction due to antidepressant drugs. *Hum Psychopharmacol* 2004;19(8):545-548.
- Wilke D R, Parker C, Andonowski A et al. Testosterone and erectile function recovery after radiotherapy and long-term androgen deprivation with luteinizing hormone-releasing hormone agonists. *BJU Int* 2006;97(5):963-968.
- Williams T, Honeywell M, Branch E et al. Tadalafil in the treatment of erectile dysfunction. *P & T* 2004;29(5):
- Wilt T J, Fink H A. Is antidepressant plus sildenafil a recipe for priapism?. *Postgrad Med* 2004;116(6):11-12.
- Witt Deborah K. Yohimbine for erectile dysfunction. *J Fam Pract* 1998;46(4):282-283.
- Wood P L. Slow, tedious but essential: The need for incremental R&D. *Current Drug Discovery* 2004;(pp 31-35):-35.
- Wyllie M G. The hunt for pink Viagra. *BJU Int* 2005;95(1):181-182.
- Wyllie M G. Let's hope for more in 2004. *BJU Int* 2004;93(1):175-176.
- Wyllie M G. The Second International Consultation on Erectile Dysfunction: Highlights from the pharmaceutical industry. *BJU Int* 2003;92(6):645-646.
- Wyllie M G. The genesis of a phytopharmaceutical industry (Mark II). *BJU Int* 2003;91(7):721-722.
- Yajima T, Yajima Y, Koppiker N et al. No clinically important effects on intraocular pressure after short-term administration of sildenafil citrate (Viagra). *Am J Ophthalmol* 2000;129(5):675-676.
- Yaman O, Akand M, Gursoy A et al. The effect of diabetes mellitus treatment and good glycemic control on the erectile function in men with diabetes mellitus-induced erectile dysfunction: a pilot study. *Br J Sex Med* 2006;3(2):344-348.
- Yamanaka M, Shirai M, Shiina H et al. Vascular endothelial growth factor restores erectile function through inhibition of apoptosis in diabetic rat penile crura. *Br J Urol* 2005;173(1):318-323.
- Yan J Y, Yang W Z. A comparative effects of Sildenafil and Yohimbine for the treatment of erectile dysfunction. *Chinese Journal of Andrology* 2000;14(2):103-105.
- Yarkony G M. Enhancement of sexual function and fertility in spinal cord-injured males. [Review] [40 refs]. *Am J Phys Med Rehabil* 1990;69(2):81-87.
- Yassin A A, Saad F. Treatment of sexual dysfunction of hypogonadal patients with long-acting testosterone undecanoate (Nebido). [Review] [25 refs]. *World J Urol* 2006;24(6):639-644.
- Yassin A A, Saad F. Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. *Andrologia* 2006;38(1):34-37.
- Yasumoto R, Nishisaka N, Sakakura T et al. Ethanol embolization for impotent patients with venous leakage: A new technique and initial results. *Minimally Invasive Therapy & Allied Technologies: Mitat* 1996;5(6):564-566.
- Yeager J, Beihn R M. Retention and migration of alprostadil cream applied topically to the glans meatus for erectile dysfunction. *Int J Impot Res* 2005;17(1):91-95.
- Youssef A F, Fort F L, Ronsen B et al. Evaluation of apomorphine HCl effects on reproductive endpoints: Studies in male rats and dogs. *J Toxicol Sci* 1999;51(2):273-279.
- Zaslau S, Nicolis C, Galea G et al. A simplified pharmacologic erection program for patients with spinal cord injury. *J Spinal Cord Med* 1999;22(4):303-307.
- Zasler N D. Therapeutic approaches to sexual impotence. *Hospital Practice (Office Edition)* 1988;23(7):197, 200

Zhao L. Clinical observation on the therapeutic effects of heavy moxibustion plus point-injection in treatment of impotence. *J Tradit Chin Med* 2004;24(2):126-127.

Zhigang Long, Xiaowei Liu, Shengbo Lu. Therapy of impotence with traditional Chinese medicine. *Journal of Sex Education & Therapy* 1994;20(2):140-143.

Zini Dante, Carani Cesare, Baldini Augusto et al. Sexual behavior of men with isolated hypogonadotropic hypogonadism or prepubertal anterior panhypopituitarism. *Horm Behav* 1990;24(2):174-185.

Zusman R M. Cardiovascular data on sildenafil citrate: introduction.[erratum appears in *Am J Cardiol* 1999 Jul 15;84(2):244]. *Am J Cardiol* 1999;83(5A):1C-2C.

Zusman R M, Prisant L M, Brown M J. Effect of sildenafil citrate on blood pressure and heart rate in men with erectile dysfunction taking concomitant antihypertensive medication. Sildenafil Study Group. *J Hypertens* 2000;18(12):1865-1869.

Appendix E. Additional Acknowledgments

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Appendix F. Quality Assessment

Randomized Controlled Trials (RCTs)

Table F-1. Quality Assesment of RCTs

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
Palmer 2000 ¹	1	0	0	1	0	2	Unclear
Seidman 2001 ²	1	0	1	1	1	4	Unclear
Kongkanand 2003 ³	1	0	1	1	1	4	Unclear
Stuckey 2003 ⁴	1	1	1	1	1	5	Adequate
Choi 2003 ⁵	1	0	1	1	1	4	Unclear
Levinson 2003 ⁶	1	0	1	0	1	3	Unclear
DeBusk 2004 ⁷	1	1	1	0	1	4	Unclear
Boolell 1996 ⁸	1	0	1	0	1	3	Unclear
Goldstein 1998 ⁹	1	0	1	1	1	4	Unclear
Tan 2000 ¹⁰	1	0	1	1	1	4	Unclear
Meuleman 2001 ¹¹	1	0	1	1	1	4	Unclear
Eardley 2001 ¹²	1	-1	1	1	0	2	Unclear
Young 2002 ¹³	1	0	1	1	0	3	Unclear
von Keitz 2002 ¹⁴	1	-1	1	0	1	2	Unclear
Goldstein 2003 ¹⁵	1	0	1	0	1	3	Unclear
Nurnberg 2003 ¹⁶	1	1	1	1	1	5	Adequate
Incrocchi 2003 ¹⁷	1	0	1	0	1	3	Unclear
Hellstrom 2003 ¹⁸	1	1	1	0	1	4	Adequate
Price 1998 ¹⁹	1	0	1	0	1	3	Unclear
Rendell 1999 ²⁰	1	1	1	1	1	5	Adequate
Christiansen 2000 ²¹	1	1	1	1	1	5	Adequate
Olsson 2000 ²²	1	0	1	0	1	3	Unclear
Chen 2001 ²³	1	0	1	1	1	4	Unclear
Boulton 2001 ²⁴	1	0	1	1	0	3	Unclear
Hussain 2001 ²⁵	1	0	1	0	0		Unclear
Lewis 2001 ²⁶	1	0	1	0	0	2	Unclear
Brock 2002 ²⁷	1	0	0	0	1	2	Unclear
Porst 2003 ²⁸	1	0	1	0	0	2	Unclear
Montorsi 2004 ²⁹	1	0	1	0	1	2	Unclear
Safarinejad 2004 ³⁰	1	1	1	0	1	4	Adequate
Webster 2004 ³¹	1	-1	1	0	1	2	Unclear
Giuliano 2005 ³²	1	-1	1	0	0	1	Unclear
Hatzichristou 2005 ³³	1	-1	1	0	0	2	Unclear
Eardley 2005 ³⁴	1	0	0	0	1	2	Unclear
Cavallini 2005 ³⁵	1	-1	1	1	1	3	Unclear
Diamond 2005 ³⁶	1	0	1	0	1	3	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
Hellstrom 2005 ³⁷	1	0	1	0	0	2	Unclear
Melman 2005 ³⁸	0	0	0	0	0	0	Unclear
Valiquette 2005 ³⁹	1	0	1	0	1	3	Unclear
Shabsigh 2005 ⁴⁰	1	0	1	0	0	2	Unclear
Ardicoglu 2005 ⁴¹	0	0	0	0	0	0	Unclear
Melnik 2005 ⁴²	1	1	0	0	1	3	Adequate
Seyam 2005 ⁴³	1	0	0	0	1	2	Unclear
Mirone 2005 ⁴⁴	1	0	0	0	1	2	Unclear
Nehra 2005 ⁴⁵	1	1	1	0	1	4	Unclear
Young 2005 ⁴⁶	1	-1	1	0	0	1	Unclear
McMahon 2005 ⁴⁷	1	1	1	1	1	5	Unclear
Fowler 2005 ⁴⁸	1	1	1	1	0	4	Adequate
Haren 2005 ⁴⁹	1	1	1	1	0	4	Unclear
Carson 2005 ⁵⁰	1	0	1	0	1	3	Unclear
Mahon 2005 ⁵¹	1	0	1	1	0	3	Unclear
Rosano 2005 ⁵²	1	0	1	1	1	4	Unclear
Kirby 2005 ⁵³	1	0	1	1	1	4	Unclear
De Rose 2005 ⁵⁴	1	1	0	0	1	3	Adequate
Gontero 2005 ⁵⁵	1	1	1	1	1	5	Adequate
Katz 2005 ⁵⁶	1	1	1	0	1	4	Unclear
Carson 2004 ⁵⁰	1	-1	1	1	1	4	Unclear
Fonseca 2004 ⁵⁷	1	0	1	0	0	2	Unclear
Wheatley 2004 ⁵⁸	1	1	1	1	0	4	Adequate
Abdel-Naser 2004 ⁵⁹	1	0	0	0	1	2	Unclear
Parsons 2004 ⁶⁰	1	1	1	0	0	3	Inadequate
Deveci 2004 ⁶¹	1	0	1	0	0	2	Unclear
Seftel 2004 ⁶²	1	0	0	0	0	1	Inadequate
Eardley 2004 ⁶³	1	0	0	0	0	1	Unclear
Gentile 2004 ⁶⁴	1	-1	1	0	0	2	Unclear
Staab 2004 ⁶⁵	1	-1	1	1	1	3	Adequate
Montorsi 2004 ⁶⁶	1	0	1	1	0	3	Unclear
Skoumal 2004 ⁶⁷	1	1	1	1	1	5	Unclear
Rosen 2004 ⁶⁸	1	-1	1	0	1	2	Unclear
Shabsigh 2004 ⁶⁹	1	0	1	1	0	3	Unclear
Seftel 2004 ⁷⁰	1	1	1	1	1	5	Unclear
Nagao 2004 ⁷¹	1	-1	1	1	1	3	Adequate
Perimenis 2004 ⁷²	1	-1	1	-1	1	1	Unclear
Tignol 2004 ⁷³	1	0	0	0	0	1	Unclear
Perimenis 2004 ⁷⁴	1	1	1	1	1	5	Unclear
Carson 2004 ⁷⁵	1	1	0	0	1	3	Unclear
Eardley 2004 ⁷⁶	1	0	1	0	1	3	Unclear
Stief 2004 ⁷⁷	1	1	0	0	0	2	Unclear
Hatzichristou	1	0	1	1	1	4	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
2004 ⁷⁸							
Cavallini 2004 ⁷⁹	1	1	1	1	1	5	Adequate
Rosen 2004 ⁸⁰	1	1	0	0	0	2	Adequate
von Keitz 2004 ⁸¹	1	0	1	1	0	3	Unclear
Leder 2004 ⁸²	1	0	1	1	1	4	Unclear
Diamond 2004 ⁸³	1	1	1	0	0	3	Unclear
Mancini 2004 ⁸⁴	1	0	1	1	0	3	Unclear
Perimenis 2004 ⁸⁵	1	0	1	0	1	3	Unclear
Govier 2003 ⁸⁶	1	-1	0	0	0	1	Unclear
Fox 2003 ⁸⁷	1	0	0	0	1	2	Unclear
Brock 2003 ⁸⁸	1	-1	1	0	1	2	Unclear
Padma-Nathan 2003 ⁸⁹	1	0	1	1	0	3	Unclear
Hellstrom 2003 ⁹⁰	1	1	1	1	1	5	Adequate
Montorsi 2003 ⁹¹	1	0	1	1	1	4	Unclear
Porst 2003 ⁹²	1	-1	0	0	1	1	Unclear
Boyanov 2003 ⁹³	1	0	1	0	0	2	Unclear
Anderson 2003 ⁹⁴	1	1	1	1	1	5	Unclear
Steidle 2003 ⁹⁵	1	0	0	0	1	2	Unclear
Gontero 2003 ⁹⁶	1	1	0	0	1	3	Unclear
Aversa 2003 ⁹⁷	1	-1	0	0	0	0	Unclear
Hagemann 2003 ⁹⁸	1	0	0	0	0	1	Unclear
Montorsi 2003 ⁹⁹	1	0	0	0	0	1	Unclear
McNicholas 2003 ¹⁰⁰	1	0	0	0	0	1	Unclear
Padma-Nathan 2003 ¹⁰¹	1	0	1	0	0	2	Unclear
Harding 2002 ¹⁰²	1	-1	1	0	0	2	Unclear
Steidle 2002 ¹⁰³	1	0	1	0	0	2	Unclear
Thadani 2002 ¹⁰⁴	1	0	1	0	1	3	Unclear
Saenz, I 2002 ¹⁰⁵	1	1	1	0	0	3	Inadequate
Hellstrom 2002 ¹⁰⁶	1	0	1	0	1	3	Unclear
Seibel 2002 ¹⁰⁷	1	0	1	0	1	3	Unclear
Bocchi 2002 ¹⁰⁸	1	0	1	0	1	3	Unclear
Ugarte 2002 ¹⁰⁹	1	1	1	0	1	4	Adequate
Gomez 2002 ¹¹⁰	1	1	1	1	1	5	Adequate
Becher 2002 ¹¹¹	1	0	1	0	1	3	Unclear
Glina 2002 ¹¹²	1	0	0	0	0	1	Unclear
Schanz 2002 ¹¹³	1	0	1	1	1	4	Unclear
Padma-Nathan 2002 ¹¹⁴	1	0	1	0	1	3	Unclear
Lebret 2002 ¹¹⁵	1	0	1	1	0	3	Unclear
Lindsey 2002 ¹¹⁶	0	0	0	0	0	0	Unclear
Lim 2002 ¹¹⁷	0	0	0	0	1	1	Unclear
van der Windt	1	1	1	0	0	3	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
2002 ¹¹⁸							
Kunelius 2002 ¹¹⁹	1	1	1	1	1	5	Unclear
Lammers 2002 ¹²⁰	1	0	1	1	1	4	Unclear
De Rose 2002 ¹²¹	1	0	0	0	1	2	Unclear
Eardley 2002 ¹²²	1	1	1	1	1	5	Inadequate
Hatzichristou 2001 ¹²³	1	0	1	0	0	2	Unclear
Incrocci 2001 ¹²⁴	1	1	0	0	1	3	Adequate
Stark 2001 ¹²⁵	1	0	1	1	1	4	Unclear
Choppin 2001 ¹²⁶	0	0	1	1	1	3	Unclear
Porst 2001 ¹²⁷	1	0	1	0	1	3	Unclear
Mann 2001 ¹²⁸	1	0	1	0	0	2	Unclear
Dula 2001 ¹²⁹	1	0	0	0	0	1	Unclear
Safarinejad 2001 ¹³⁰	1	0	1	1	1	4	Unclear
Gomaa 2001 ¹³¹	1	0	1	0	1	3	Unclear
Olsson 2001 ¹³²	1	0	1	0	0	2	Unclear
Padma-Nathan 2001 ¹³³	1	0	1	0	0	2	Unclear
Klotz 2001 ¹³⁴	1	0	1	1	0	3	Adequate
Goldstein 2001 ¹³⁵	1	0	1	0	0	2	Unclear
Kloner 2001 ¹³⁶	1	0	1	0	0	2	Unclear
Fu 2000 ¹³⁷	1	0	1	0	0	2	Unclear
Montorsi 2000 ¹³⁸	1	-1	1	1	1	3	Unclear
Enzlin 2000 ¹³⁹	1	0	1	0	0	2	Unclear
Baum 2000 ¹⁴⁰	1	0	0	0	0	1	Unclear
Wessells 2000 ¹⁴¹	1	0	1	1	1	4	Unclear
Cappelleri 2000 ¹⁴²	1	0	1	0	1	3	Unclear
Ekman 2000 ¹⁴³	1	0	0	0	0	1	Unclear
Dula 2000 ¹⁴⁴	1	0	1	0	1	3	Unclear
Rabkin 2000 ¹⁴⁵	1	0	1	0	0	2	Unclear
Shabsigh 2000 ¹⁴⁶	1	0	0	0	0	1	Unclear
Anderson 1999 ¹⁴⁷	1	0	1	1	1	4	Unclear
Palmer 1999 ¹⁴⁸	1	1	1	1	1	5	Adequate
Shokeir 1999 ¹⁴⁹	1	1	0	0	0	2	Unclear
Le Roux 1999 ¹⁵⁰	1	0	0	0	1	2	Unclear
Sandhu 1999 ¹⁵¹	1	0	1	1	1	4	Unclear
Costabile 1999 ¹⁵²	1	0	0	0	1	2	Unclear
Dinsmore 1999 ¹⁵³	1	0	1	1	1	4	Adequate
Chen 1999 ¹⁵⁴	1	0	1	0	0	2	Unclear
Montorsi 1999 ¹⁵⁵	1	1	1	0	0	3	Unclear
Dinsmore	1	0	1	0	0	2	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
1999 ¹⁵⁶							
Gramkow 1999 ¹⁵⁷	1	0	1	0	1	3	Unclear
Klotz 1999 ¹⁵⁸	1	0	1	1	1	4	Unclear
Eardley 1999 ¹⁵⁹	1	0	1	1	0	3	Unclear
Hartmann 1999 ¹⁶⁰	1	0	1	0	0	2	Unclear
Feldman 1999 ¹⁶¹	1	-1	0	0	0	1	Unclear
Young 1999 ¹⁶²	1	0	1	0	0	2	Unclear
Padma-Nathan 1998 ¹⁶³	1	0	1	0	1	3	Unclear
Williams 1998 ¹⁶⁴	1	0	1	0	0	2	Unclear
Foldvari 1998 ¹⁶⁵	1	0	1	0	0	2	Unclear
Costabile 1998 ¹⁶⁶	1	0	1	1	1	4	Unclear
Williams 1998 ¹⁶⁷	1	-1	1	0	0	1	Unclear
Engel 1998 ¹⁶⁸	1	0	1	1	0	3	Unclear
Peterson 1998 ¹⁶⁹	1	0	1	0	0	2	Unclear
Becker 1998 ¹⁷⁰	1	-1	1	0	0	2	Unclear
Buvat 1998 ¹⁷¹	1	0	1	0	0	2	Unclear
Montorsi 1998 ¹⁷²	1	0	1	0	0	2	Unclear
Sogari 1997 ¹⁷³	1	0	1	0	1	3	Unclear
Meinhardt 1997 ¹⁷⁴	1	0	1	1	1	4	Unclear
Vogt 1997 ¹⁷⁵	1	0	0	0	0	1	Unclear
Montorsi 1997 ¹⁷⁶	1	0	0	0	0	1	Unclear
Soderdahl 1997 ¹⁷⁷	1	0	1	1	1	4	Unclear
Schiavi 1997 ¹⁷⁸	1	0	1	0	1	3	Unclear
Bechara 1997 ¹⁷⁹	1	0	0	0	0	1	Unclear
Kunelius 1997 ¹⁸⁰	1	-1	0	0	0	0	Unclear
Rowland 1997 ¹⁸¹	1	0	1	0	0	2	Unclear
Padma-Nathan 1997 ¹⁸²	1	0	1	0	1	3	Unclear
Aversa 1996 ¹⁸³	1	0	1	0	0	2	Unclear
Hellstrom 1996 ¹⁸⁴	0	0	1	1	0	2	Adequate
Colli 1996 ¹⁸⁵	1	0	1	0	1	3	Unclear
Godschalk 1996 ¹⁸⁶	1	0	0	0	0	1	Unclear
Mann 1996 ¹⁸⁷	1	0	1	0	0	2	Unclear
Gheorghiu 1996 ¹⁸⁸	1	0	1	0	0	3	Unclear
Peskircioglu 1996 ¹⁸⁹	1	1	1	0	1	4	Unclear
Gomaa 1996 ¹⁹⁰	1	0	1	0	1	3	Unclear
Linet 1996 ¹⁹¹	1	0	1	0	0	2	Unclear
Bechara 1996 ¹⁹²	1	0	0	0	0	1	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
Knoll 1996 ¹⁹³	1	0	1	0	0	2	Unclear
Wegner 1995 ¹⁹⁴	1	0	1	1	1	4	Unclear
van Ahlen 1995 ¹⁹⁵	1	0	0	0	0	1	Unclear
Guay 1995 ¹⁹⁶	1	0	0	0	0	1	Unclear
Vanderschueren 1995 ¹⁹⁷	1	1	1	1	0	4	Unclear
Georgitis 1995 ¹⁹⁸	1	0	1	0	1	3	Unclear
el-Saleh 1995 ¹⁹⁹	1	1	1	1	0	4	Unclear
Ogrinc 1995 ²⁰⁰	1	0	1	0	0	2	Unclear
Kattan 1995 ²⁰¹	1	0	1	0	0	2	Unclear
Martinez-Pineiro 1995 ²⁰²	1	1	0	0	0	2	Unclear
Cavallini 1994 ²⁰³	1	0	1	0	0	2	Unclear
Lazzeri 1994 ²⁰⁴	1	0	1	1	1	4	Unclear
Wegner 1994 ²⁰⁵	1	0	0	0	0	1	Unclear
Montorsi 1994 ²⁰⁶	1	1	1	0	0	3	Unclear
Schramek 1994 ²⁰⁷	1	0	0	0	0	1	Unclear
Kurt 1994 ²⁰⁸	1	-1	0	0	0	1	Unclear
Godschalk 1994 ²⁰⁹	1	0	1	1	1	4	Adequate
Brennemann 1993 ²¹⁰	1	0	1	1	0	3	Unclear
von Heyden 1993 ²¹¹	1	0	1	0	1	3	Unclear
Moriel 1993 ²¹²	1	0	1	0	1	3	Unclear
Porst 1993 ²¹³	1	-1	1	1	1	3	Unclear
Korenman 1993 ²¹⁴	1	0	0	0	0	1	Unclear
Costa 1993 ²¹⁵	1	0	1	1	0	3	Unclear
Allen 1992 ²¹⁶	1	0	0	0	0	1	Unclear
Mahmoud 1992 ²¹⁷	1	0	1	0	0	2	Unclear
Cavallini 1991 ²¹⁸	1	1	1	0	1	4	Unclear
Kattan 1991 ²¹⁹	1	1	1	-1	0	2	Unclear
Segraves 1991 ²²⁰	1	0	1	0	0	2	Unclear
Floth 1991 ²²¹	1	1	1	0	0	3	Unclear
Sonda 1990 ²²²	1	0	1	1	0	3	Unclear
Roy 1990 ²²³	1	0	1	1	0	3	Unclear
Earle 1990 ²²⁴	1	0	0	0	0	1	Unclear
van Ahlen 2005 ²²⁵	0	0	1	1	1	3	Unclear
Goldstein 2005 ²²⁶	1	0	1	0	1	3	Unclear
Fisher 2005 ²²⁷	1	-1	0	0	0	0	Unclear
Carrier 2005 ²²⁸	1	0	1	1	1	4	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
Moncada 2005 ²²⁹	1	1	1	1	1	5	Unclear
Hatzichristou 2005 ²³⁰	1	1	1	1	1	5	Unclear
Patterson 2005 ²³¹	1	-1	1	1	1	3	Unclear
Albuquerque 2005 ²³²	1	0	0	0	0	1	Unclear
Yonessi 2005 ²³³	1	0	1	0	1	3	Unclear
Shamloul 2005 ²³⁴	1	0	1	1	1	4	Unclear
McMahon 2005 ²³⁵	1	1	1	1	1	5	Unclear
Speel 2005 ²³⁶	1	1	1	0	0	3	Unclear
Chen 2004 ²³⁷	1	0	0	0	0	1	Unclear
Rosen 2004 ²³⁸	1	1	0	0	1	3	Unclear
Donatucci 2004 ²³⁹	1	0	0	0	1	2	Unclear
Gingell 2004 ²⁴⁰	1	1	1	0	1	4	Unclear
Montorsi 2004 ²⁴¹	1	-1	1	0	1	3	Unclear
Pickering 2004 ²⁴²	1	-1	1	0	0	2	Unclear
Pavone 2004 ²⁴³	1	0	1	-1	1	3	Unclear
Bawa 2004 ²⁴⁴	1	-1	1	1	1	3	Unclear
Petrov 2003 ²⁴⁵	1	0	1	0	1	3	Unclear
Dunzendorfer 2002 ²⁴⁶	1	0	0	0	1	2	Unclear
Glina 2001 ²⁴⁷	1	0	1	0	0	2	Unclear
Giammusso 1996 ²⁴⁸	1	0	0	0	1	2	Unclear
Garceau 1996 ²⁴⁹	1	0	0	0	0	1	Unclear
Claes 1992 ²⁵⁰	1	0	1	1	1	4	Unclear
Valiquette 2005 ²⁵¹	1	0	1	0	0	2	Unclear
Reiter 1999 ²⁵²	1	0	1	0	0	2	Unclear
Kunelius 1998 ²⁵³	1	0	1	0	0	2	Unclear
Haslam 1992 ²⁵⁴	1	1	1	0	0	3	Unclear
Rosen 2006 ²⁵⁵	1	1	0	0	1	4	Unclear
Korenman 1994 ²⁵⁶	1	-1	1	0	0	1	Unclear
Clopper 1993 ²⁵⁷	1	0	1	1	1	4	Unclear
Wang 2000 ²⁵⁸	1	0	1	1	0	3	Unclear
Nickel 2007 ²⁵⁹	1	0	1	1	0	3	Unclear
Yassin 2006 ²⁶⁰	1	0	0	0	0	1	Unclear
Martin-Morales 2007 ²⁶¹	1	0	1	0	1	3	Unclear
Heiman 2007 ²⁶²	1	0	1	1	0	2	Unclear
Bank 2006 ²⁶³	1	0	0	0	1	2	Unclear
McVary 2007 ²⁶⁴	1	0	1	0	0	2	Unclear

Author Year	Jadad Q-1	Jadad Q-2	Jadad Q-3	Jadad Q-4	Jadad Q-5	Total Scores	Allocation Concealment
Saylan 2006 ²⁶⁵	1	1	1	0	1	4	Inadequate
Zinner 2007 ²⁶⁶	1	0	1	1	0	3	Unclear
Edwards 2006 ²⁶⁷	1	0	1	0	1	3	Unclear
Rajfer 2007 ²⁶⁸	1	0	1	0	1	3	Unclear
Valiquette 2006 ²⁶⁹	1	0	1	0	0	2	Unclear
Wespes 2007 ²⁷⁰	1	0	1	0	1	3	Unclear
Porst 2006 ²⁷¹	1	0	1	0	1	3	Unclear
Yip 2006 ²⁷²	1	0	1	1	0	3	Unclear
Safarinejad 2006 ²⁷³	1	0	0	0	0	1	Unclear
Agostini 2006 ²⁷⁴	1	0	1	0	1	3	Unclear
Mazo 2006 ²⁷⁵	1	0	1	0	1	3	Unclear
El-Shafey 2006 ²⁷⁶							
Tolra 2006 ²⁷⁷	1	0	1	1	0	3	Unclear
Ziegler 2006 ²⁷⁸	1	0	1	0	0	2	Unclear
Ishii 2006 ²⁷⁹	1	0	1	0	0	2	Unclear
Guo 2006 ²⁸⁰	1	0	0	0	1	2	Unclear
Nagao 2006 ²⁸¹	1	0	1	1	1	4	Unclear
Padma-Nathan 2006 ²⁸²	1	0	1	1	1	4	Unclear
Dean 2006 ²⁸³	1	0	1	0	1	3	Unclear
Seidman 2006 ²⁸⁴	1	0	1	0	1	3	Unclear
Demir 2006 ²⁸⁵	1	1	1	0	0	3	Unclear
Althof 2006 ²⁸⁶	1	0	0	0	0	1	Unclear
Buvat 2006 ²⁸⁷	1	0	0	0	1	2	Unclear
McMahon 2006 ²⁸⁸	1	0	0	0	0	1	Unclear
Fava 2006 ²⁸⁹	1	0	1	0	1	3	Unclear
Gopalakrishnan 2006 ²⁹⁰	1	0	0	0	0	1	Unclear
Herrmann 2006 ²⁹¹	1	1	1	0	1	4	Unclear
Titta 2006 ²⁹²	1	1	1	0	1	4	Unclear
Sommer 2006 ²⁹³	1	1	1	1	1	5	Inadequate
Rochira 2006 ²⁹⁴	1	0	1	1	0	3	Unclear
O'Leary 2006 ²⁹⁵	1	0	0	0	0	1	Unclear
Viswaroop 2005 ²⁹⁶	1	0	1	0	0	2	Unclear
Carson 2005 ²⁹⁷	1	0	0	0	0	1	Unclear
Kaplan 2007 ²⁹⁸	1	1	1	0	0	3	Unclear
Choi 2006 ²⁹⁹	1	1	0	0	0	2	Unclear
Gomaa 2006 ³⁰⁰	1	0	1	0	0	2	Unclear

Quality Assessment of Observational Studies

Table F-2. Quality assessment on 8 Out of 14 QUADAS questions for each included study

STUDY ID	Q1: Spectrum	Q2. Selection criteria	Q5. Reference standard?	Q8. Details of index test described	Q10. Index test interpreted without knowledge of RS	Q12. Same clinical data available	Q13. Uninterpretable test results reported	Q14. Withdrawals explained	TOTAL ("YES")
Jaffe 1996 ³⁰¹	yes	no	no	yes	yes	yes	No	no	4
Netto 1993 ³⁰²	yes	no	no	yes	yes	yes	No	no	4
Citron 1996 ³⁰³	no	yes	yes	yes	yes	no	No	no	4
Hatzichristou 2002 ³⁰⁴	yes	yes	no	yes	yes	yes	No	no	5
Martinez- Jabaloyas 2006 ³⁰⁵	yes	no	no	yes	yes	yes	no	no	4
Acar 2004 ³⁰⁶	unclear	no	no	yes	yes	yes	no	no	3
Earle 2003 ³⁰⁷	yes	no	no	yes	yes	yes	no	no	4
Rhoden 2002 ³⁰⁸	no	yes	no	yes	yes	no	no	no	3
Bunch 2002 ³⁰⁹	yes	yes	unclear	yes	yes	yes	no	no	5
Fahmy 1999 ³¹⁰	yes	no	no	yes	yes	yes	no	no	4
Buvat 1997 ³¹¹	yes	no	no	yes	yes	yes	no	no	4
Akpononu 1994 ³¹²	unclear	yes	yes	yes	unclear	yes	no	yes	5
Drinka 1993 ³¹³	no	yes	no	yes	yes	yes	no	yes	5
Johnson 1992 ³¹⁴	yes	no	no	yes	yes	yes	no	no	4
El-Sakka 2005 ³¹⁵	no	yes	no	yes	yes	yes	No	no	4
Tsujimura 2005 ³¹⁶	yes	yes	no	yes	yes	yes	No	no	5
Guay 1991 ³¹⁷	no	yes	no	yes	yes	no	No	no	3
Forsberg 1990 ³¹⁸	yes	yes	no	yes	yes	yes	No	no	5

STUDY ID	Q1: Spectrum	Q2. Selection criteria	Q5. Reference standard?	Q8. Details of index test described	Q10. Index test interpreted without knowledge of RS	Q12. Same clinical data available	Q13. Uninterpretable test results reported	Q14. Withdrawals explained	TOTAL ("YES")
Reyes-Vallejo 2006 ³¹⁹	no	yes	no	yes	yes	no	No	no	3
El-Sakka 2006 ³²⁰	no	yes	no	yes	yes	yes	No	no	4
Hwang 2007 ³²¹	yes	no	no	yes	yes	yes	No	no	4
Low 2006 ³²²	yes	yes	no	yes	yes	yes	No	no	5
Guay 2007 ³²³	unclear	no	no	no	yes	yes	No	no	2
Zohdy 2007 ³²⁴	unclear	yes	yes	yes	unclear	yes	No	no	4

Appendix G. Funnel Plots

Sildenafil

Figure G-1. Sildenafil (any dose) vs. Placebo: mean IIEF-Q3 score

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 02 Mean IIEF-Q3 score

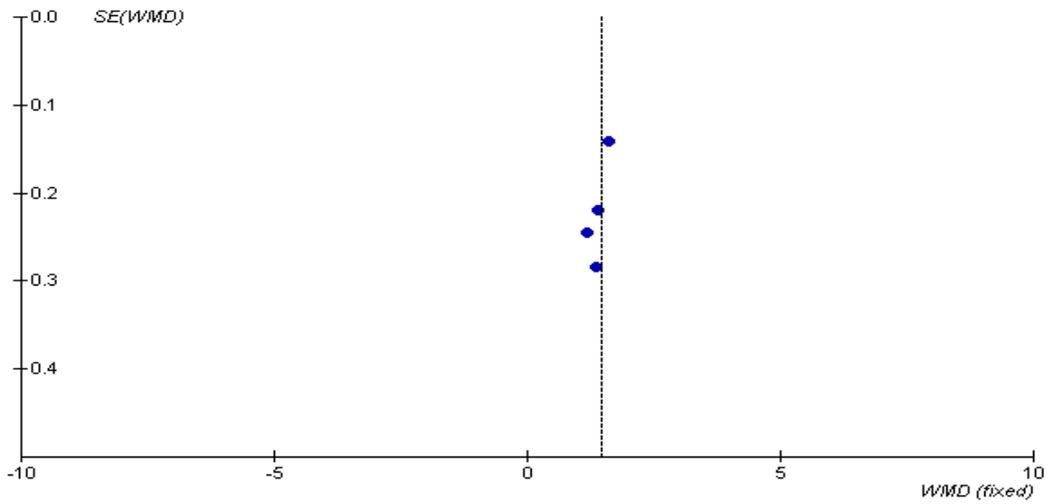


Figure G-2. Sildenafil (any dose) vs. Placebo: mean IIEF-Q4 score

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 03 Mean IIEF-Q4 score

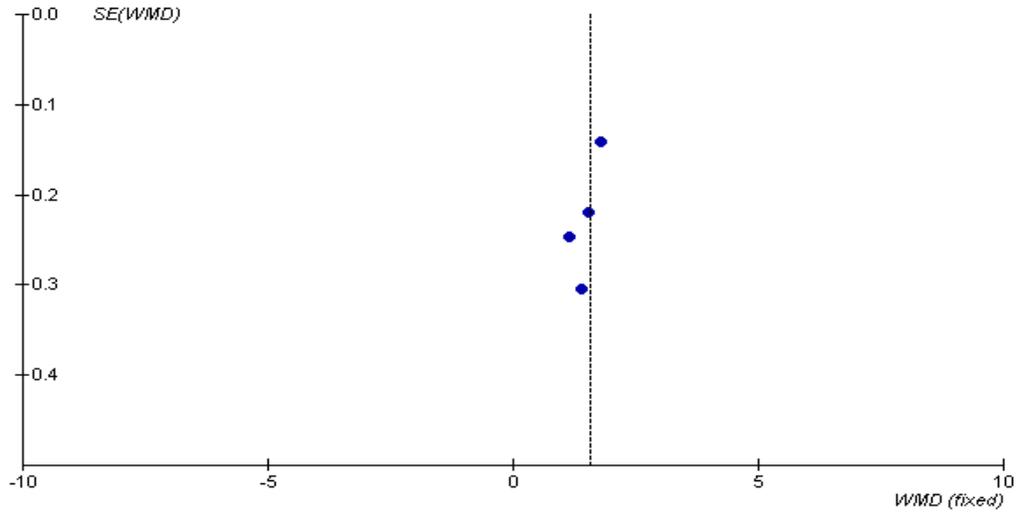


Figure G-3. Sildenafil (any dose) vs. Placebo: participants with improved erection (GEQ-Q1)

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 05 Patients with Improved Erections (GEQ-Q1)

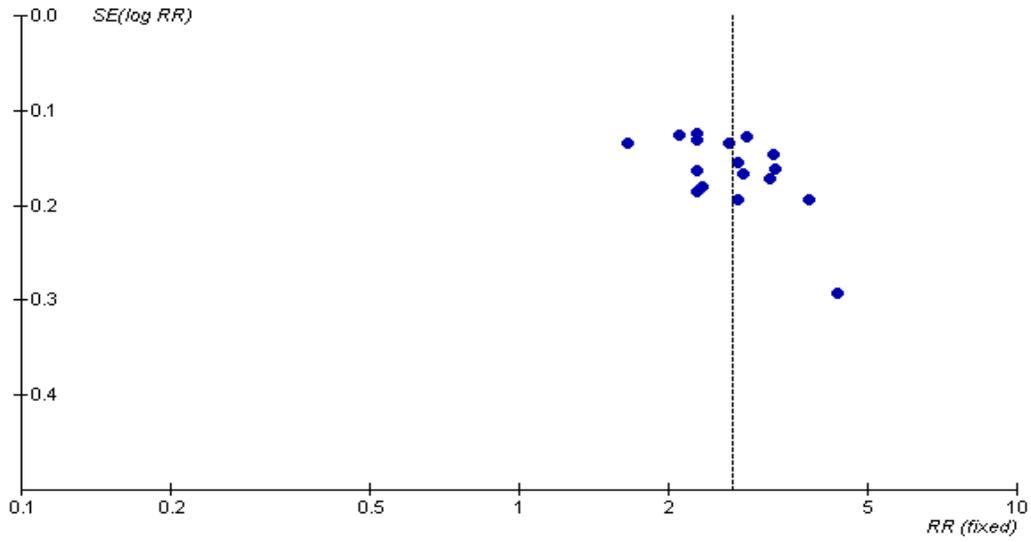


Figure G-4. Sildenafil (any dose) vs. Placebo: mean IIEF-Q3 score
Participants with type I-II diabetes

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 02 Mean IIEF-Q3 score

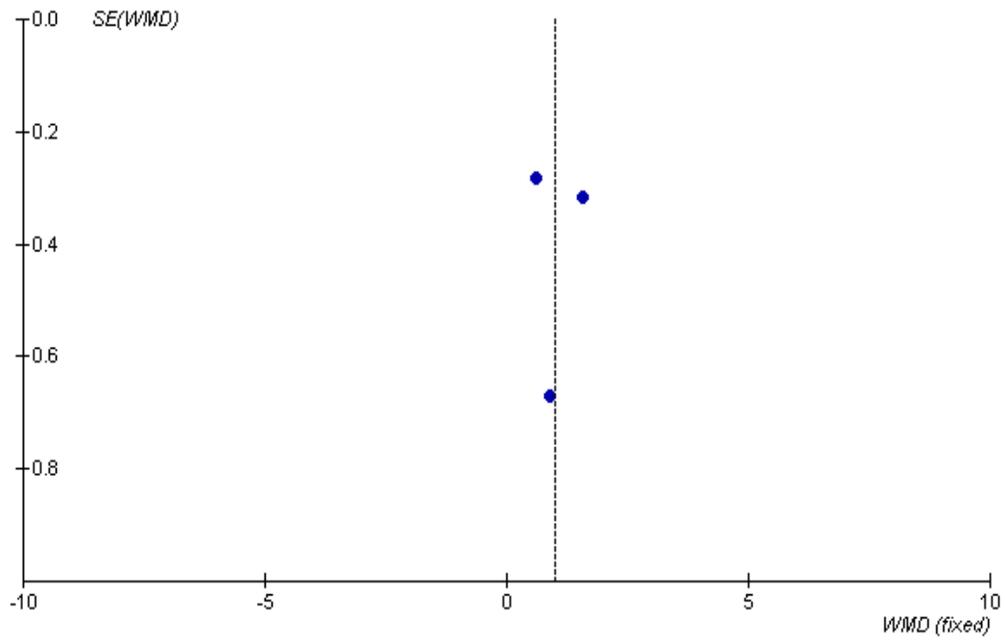
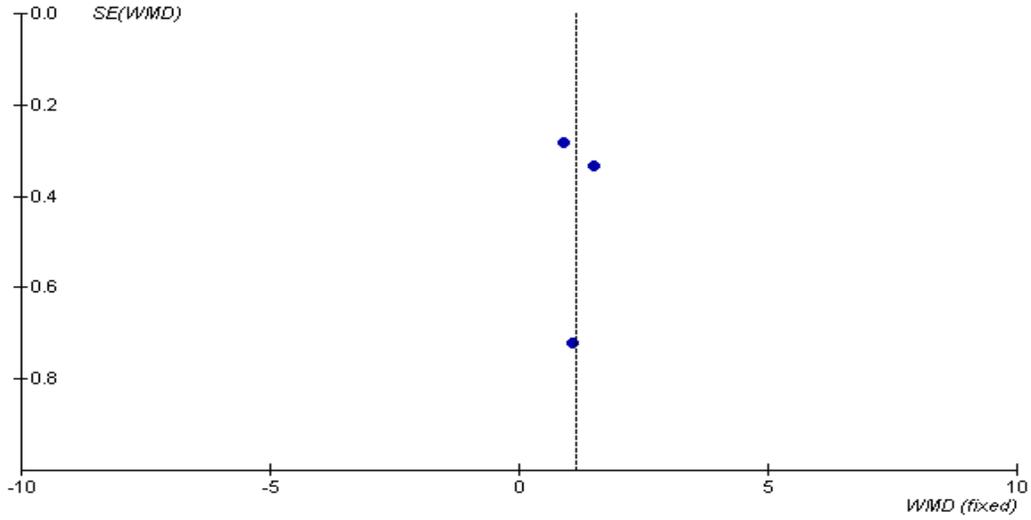


Figure G-5. Sildenafil (any dose) vs. Placebo: mean IIEF-Q4 score
Participants with type I-II diabetes

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 03 Mean IIEF-Q4 score



**Figure G-6. Sildenafil (any dose) vs. Placebo: patients with improved erection (GEQ-Q1)
Participants with type I-II diabetes**

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 05 Patients with Improved Erections (GEQ-Q1)

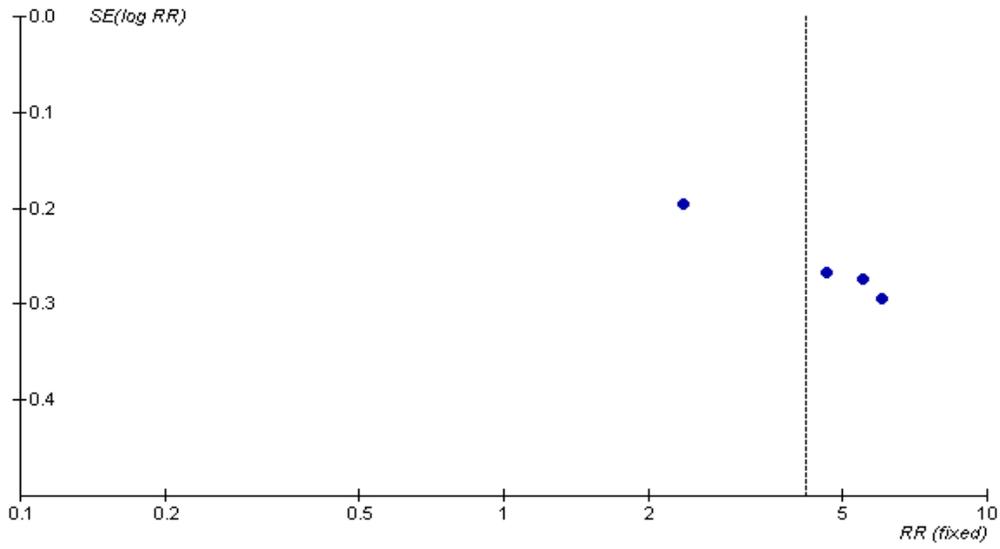


Figure G-7. Sildenafil (any dose) vs. Placebo: participants with improved erection (GEQ-Q1)
Participants with type II diabetes

Review: Sildenafil
Comparison: 01 Sildenafil (any dose/dosing) vs. Placebo
Outcome: 05 Patients with Improved Erections (GEQ-Q1)

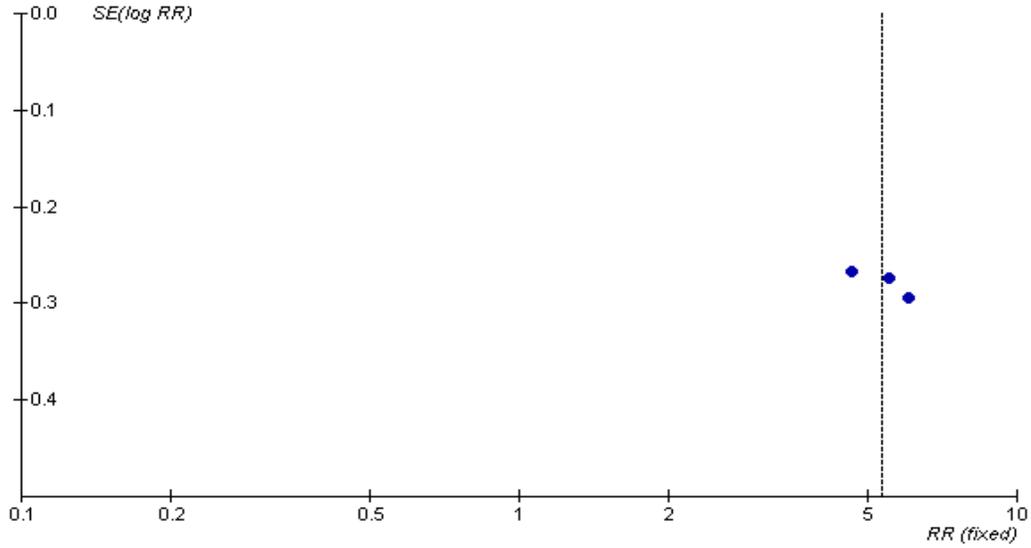
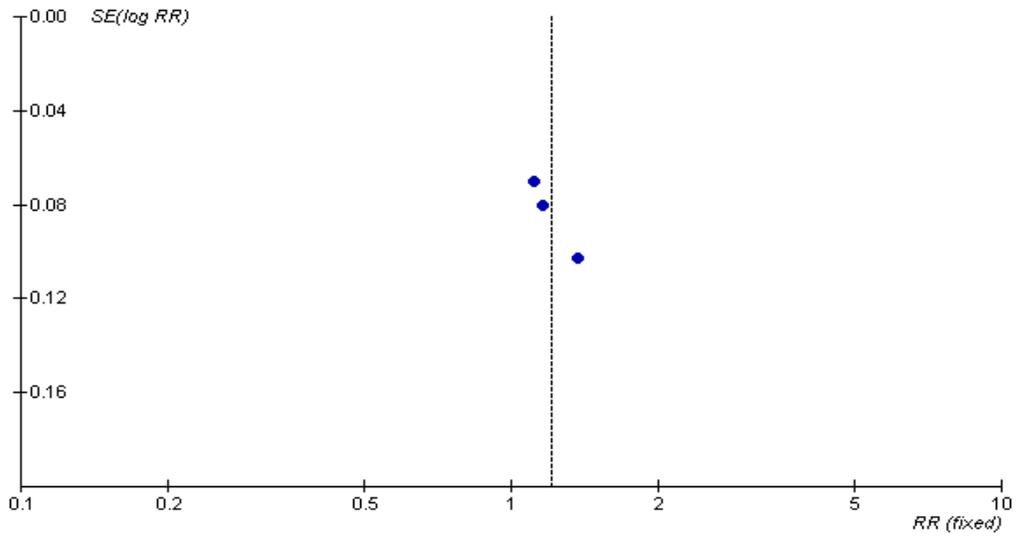


Figure G-8. Sildenafil (25 mg) vs. Sildenafil (50 mg): participants with improved erection (GEQ-Q1)

Review: Sildenafil
Comparison: 02 Sildenafil (25 mg) vs. Sildenafil (50 mg)
Outcome: 01 Proportion of patients with improved erection (GEQ-Q1)



Vardenafil

Any dose vs. Placebo

Figure G-9. Vardenafil (any dose) vs. Placebo: mean IIEF 'EF domain' score at week 12

Review: Vardenafil
Comparison: 01 Vardenafil (any dose) vs. Placebo
Outcome: 01 Mean IIEF 'EF domain' Score at week 12

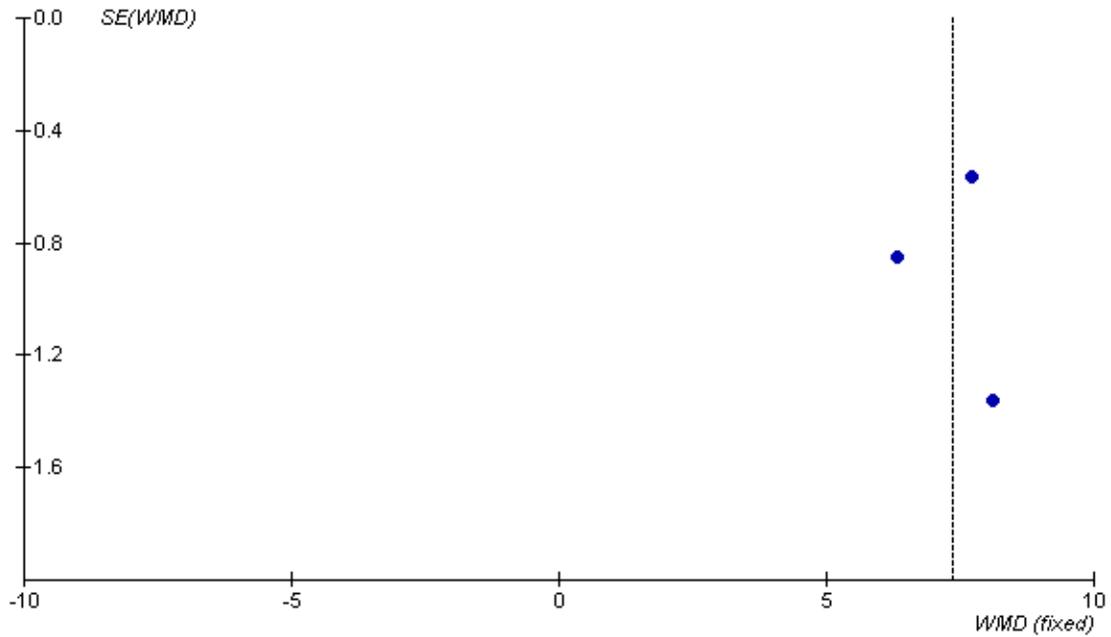


Figure G-10. Vardenafil (any dose) vs. Placebo: patients with mean IIEF 'EF domain' score ≥ 26

Review: Vardenafil
Comparison: 01 Vardenafil (any dose) vs. Placebo
Outcome: 05 Patients with Mean IIEF 'EF domain' Score \Rightarrow 26 at weeks 10-12

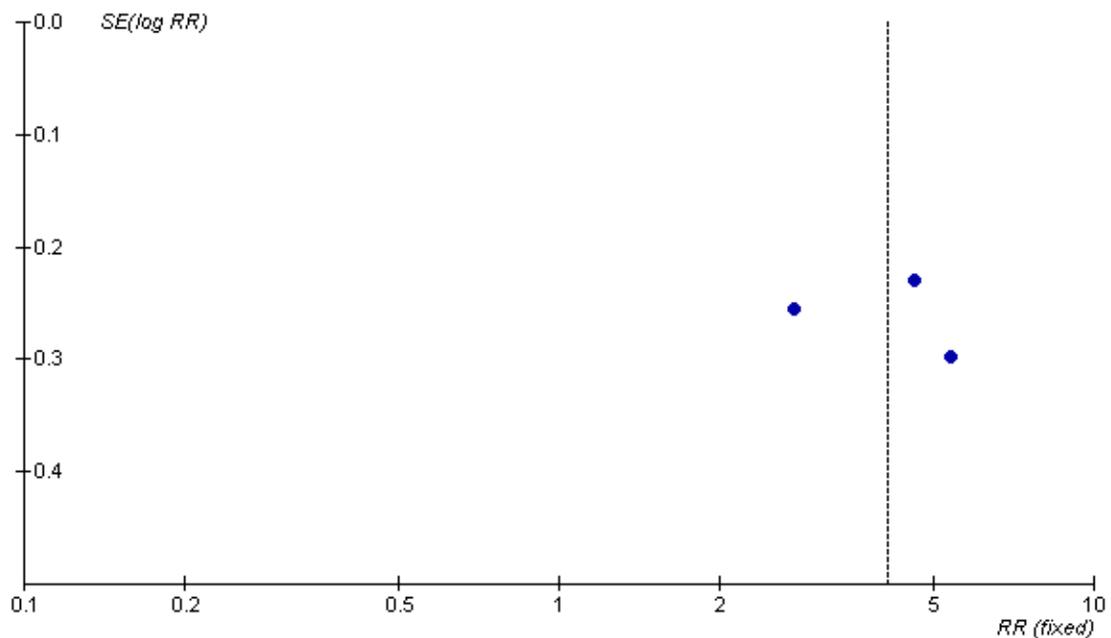
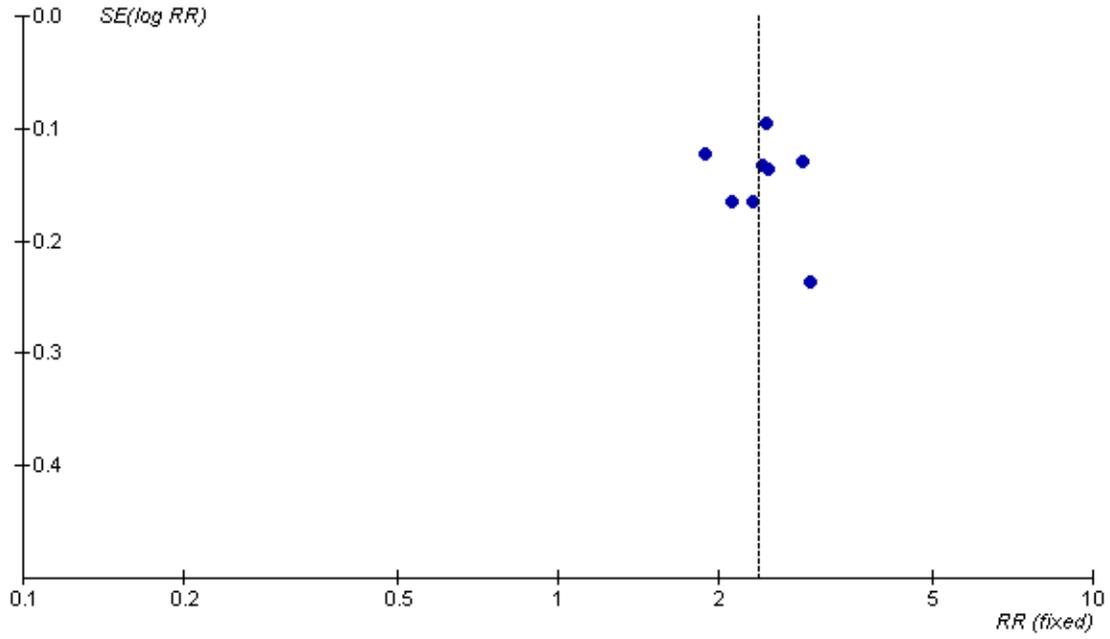


Figure G-11. Vardenafil (any dose) vs. Placebo: patients with improved erection (GAQ-Q1)

Review: Vardenafil
Comparison: 01 Vardenafil (any dose) vs. Placebo
Outcome: 04 Patients with improved erection (GAQ-Q1) at week 12



Tadalafil

20 mg vs. Placebo

Figure G-12. Tadalafil (20 mg) vs. Placebo: mean IIEF-'EF domain' score change

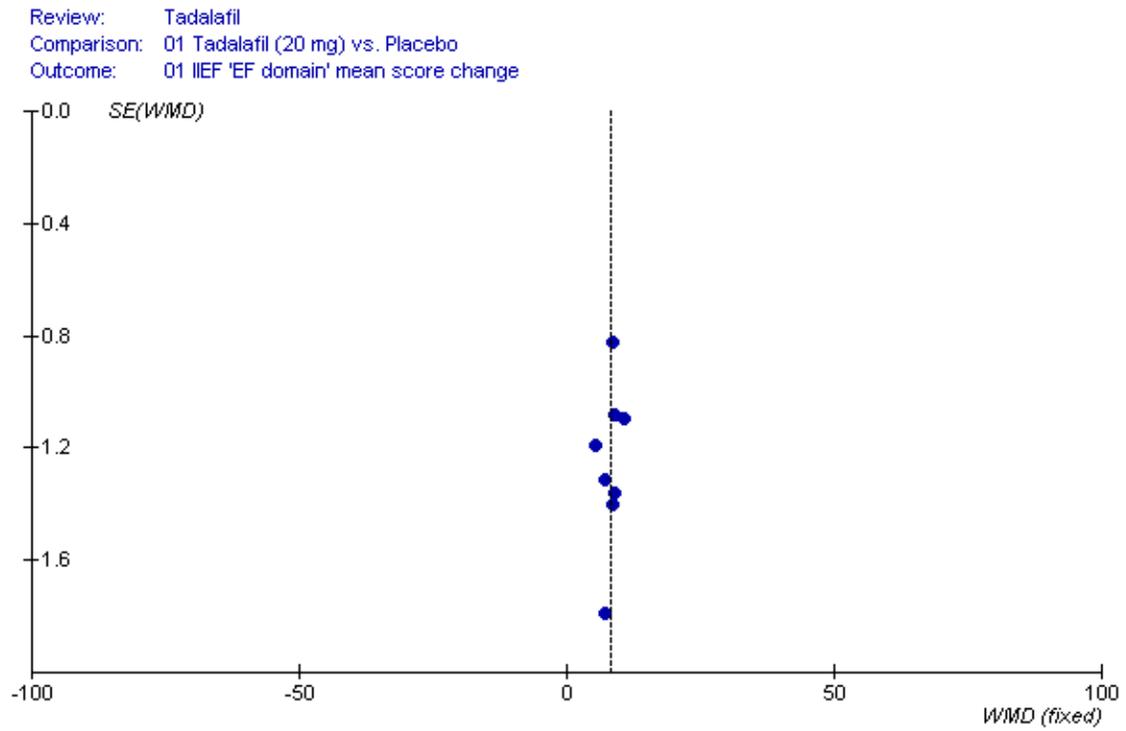


Figure G-13. Tadalafil (20 mg) vs. Placebo: % mean SEP-Q2 score change

Review: Tadalafil
Comparison: 01 Tadalafil (20 mg) vs. Placebo
Outcome: 02 Per-patient % mean change on SEP-Q2

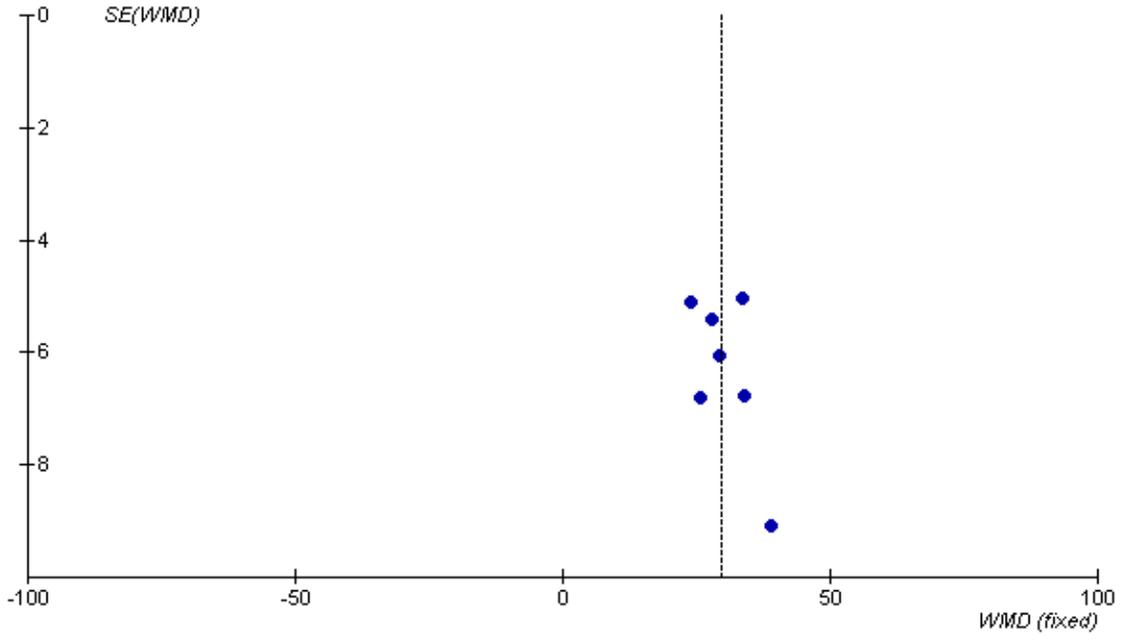
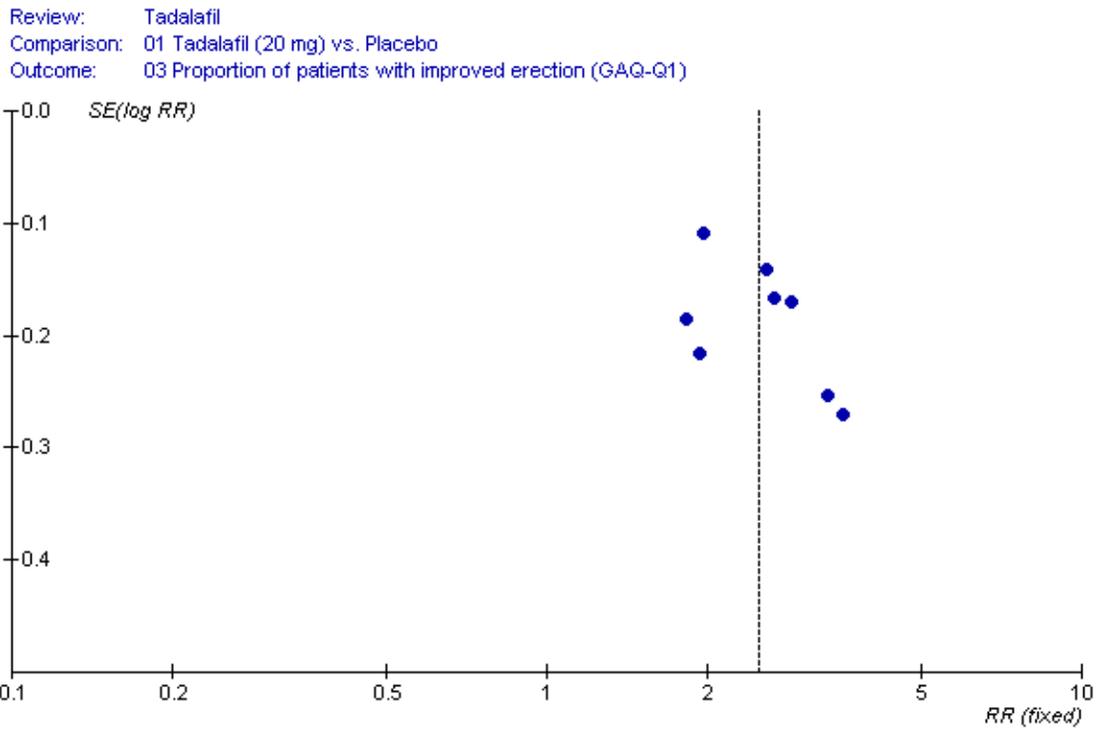


Figure G-14. Tadalafil (20 mg) vs. Placebo: patients with improved erection (GAQ-Q1)



20 mg vs. 10 mg

Figure G-15. Tadalafil (20mg) vs. Tadalafil (10mg): mean IIEF 'EF domain' score

Review: Tadalafil
Comparison: 03 Tadalafil (20 mg) vs. Tadalafil (10 mg)
Outcome: 01 IIEF 'EF domain' mean score change

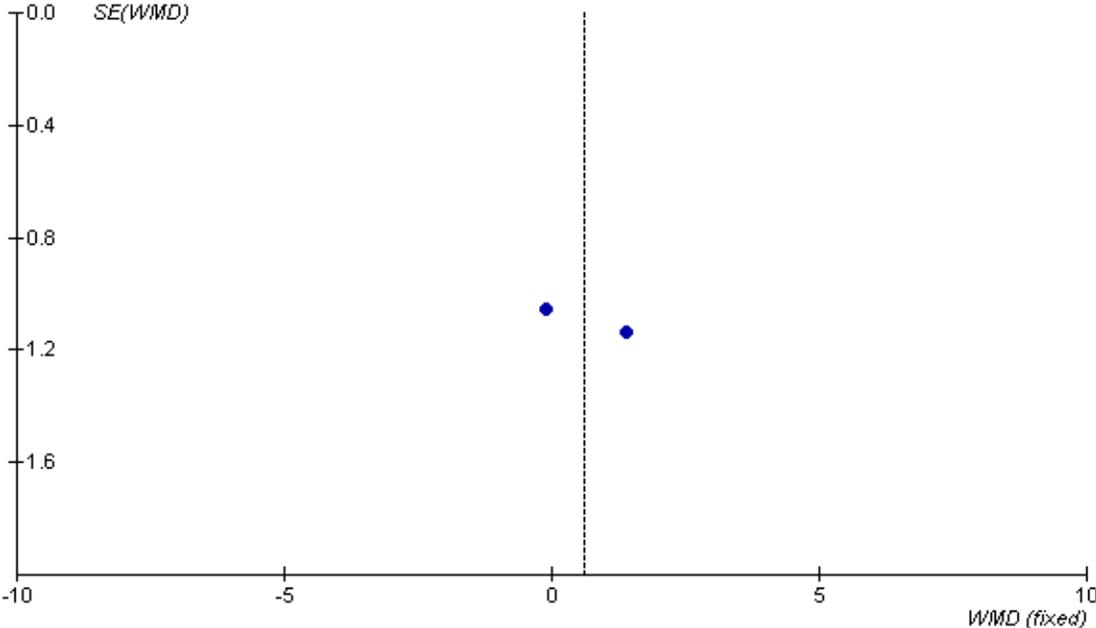
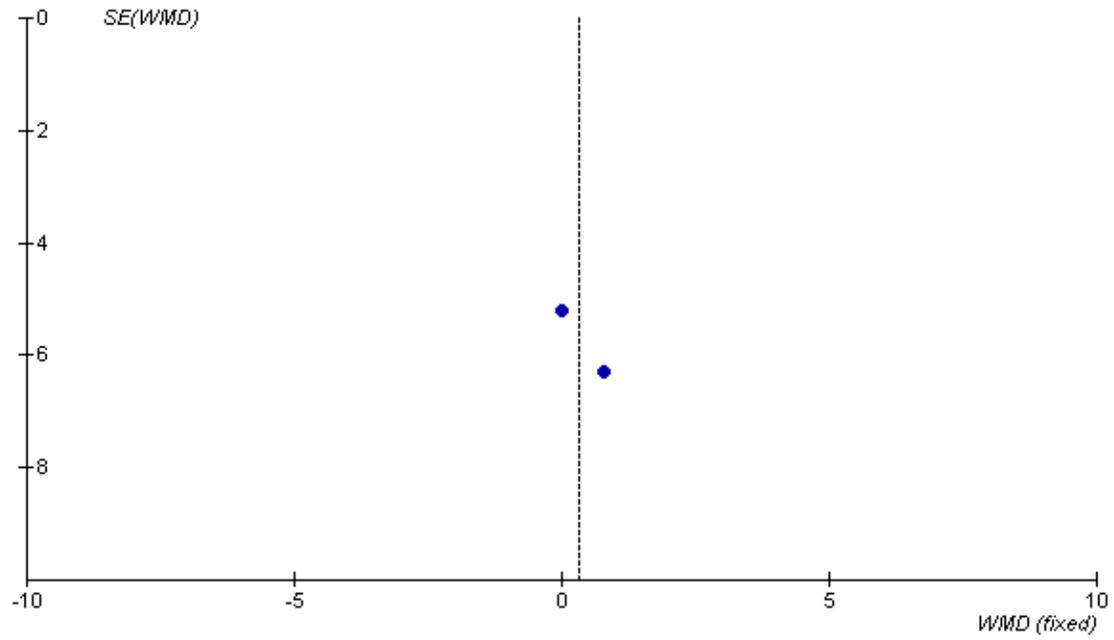


Figure G-16. Tadalafil (20mg) vs. Tadalafil (10mg): % mean SEP-Q2 score change

Review: Tadalafil
Comparison: 03 Tadalafil (20 mg) vs. Tadalafil (10 mg)
Outcome: 02 Per-patient % mean change on SEP-Q2



Appendix H. Instruments Used in the Assessment of Treatment Outcomes

International Index of Erectile Function (IIEF)

Individual items of International Index of Erectile Function Questionnaire and response options (US version):*

Q1: How often were you able to get an erection during sexual activity?

- 0 = No sexual activity
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q2: When you had erections with sexual stimulation, how often were your erections hard enough for penetration?

- 0 = No sexual activity
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q3: When you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?

- 0 = Did not attempt intercourse
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q4: During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?

- 0 = Did not attempt intercourse
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q5: During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?

- 0 = Did not attempt intercourse
- 1 = Extremely difficult
- 2 = Very difficult
- 3 = Difficult
- 4 = Slightly difficult
- 5 = Not difficult

Q6: How many times have you attempted sexual intercourse?

- 0 = No attempts
- 1 = One to two attempts
- 2 = Three to four attempts
- 3 = Five to six attempts
- 4 = Seven to ten attempts

5 = Eleven+ attempts

Q7: When you attempted sexual intercourse, how often was it satisfactory for you?

- 0 = Did not attempt intercourse
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q8: How much have you enjoyed sexual intercourse?

- 0 = No intercourse
- 1 = No enjoyment
- 2 = Not very enjoyable
- 3 = Fairly enjoyable
- 4 = Highly enjoyable
- 5 = Very highly enjoyable

Q9: When you had sexual stimulation or intercourse, how often did you ejaculate?

- 0 = No sexual stimulation/intercourse
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q10: When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?

- 0 = No sexual stimulation/intercourse
- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q11: How often have you felt sexual desire?

- 1 = Almost never/never
- 2 = A few times (much less than half the time)
- 3 = Sometimes (about half the time)
- 4 = Most times (much more than half the time)
- 5 = Almost always/always

Q12: How would you rate your level of sexual desire?

- 1 = Very low/none at all
- 2 = Low
- 3 = Moderate
- 4 = High
- 5 = Very high

Q13: How satisfied have you been with your overall sex life?

- 1 = Very dissatisfied
- 2 = Moderately dissatisfied
- 3 = About equally satisfied and dissatisfied
- 4 = Moderately satisfied
- 5 = Very satisfied

Q14: How satisfied have you been with your sexual relationship with your partner?

- 1 = Very dissatisfied
- 2 = Moderately dissatisfied
- 3 = About equally satisfied and dissatisfied
- 4 = Moderately satisfied
- 5 = Very satisfied

Q15: How do you rate your confidence that you could get and keep an erection?

- 1 = Very low
- 2 = Low
- 3 = Moderate
- 4 = High
- 5 = Very high

** All questions are preceded by the phrase "Over the past 4 weeks."*

IIEF domains and the scoring

Domain	Items	Score Range	Minimum Score	Maximum Score
Erectile Function	1,2, 3, 4, 5, 15	0 (or 1)-5	1	30
Orgasmic Function	9, 10	0-5	0	10
Sexual Desire	11, 12	1-5	2	10
Intercourse Satisfaction	6, 7, 8	0-5	0	15
Overall Satisfaction	13, 14	1-5	2	10

IIEF-5 scoring system

Question	Score				
	1	2	3	4	5
Over the past six months:					
How do you rate your confidence that you could get and keep an erection?	Very low	Low	Moderate	High	Very high
When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always
During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always
During sexual intercourse how difficult was it to maintain your erection to the completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always

The IIEF-5 score is the sum of questions 1 to 5. The lowest score is 5 and the highest score 25.

Sexual Encounter Profile (SEP- Questions 2 and 3)

SEP-Q2: Were you able to insert your penis into your partner's vagina?

SEP-Q3: Did your erection last long enough for you to have successful intercourse?

Global Assessment Question (GAQ)

GAQ-Q1: Has the treatment you have been taking improved your erectile function?

GAQ-Q2: If yes, has the treatment improved your ability to engage in sexual activity?

Appendix I. List of Unobtained Articles

Anonymous. Sublingual apomorphine: new preparation. In erectile disorders: a narrow therapeutic margin. *Prescrire Int* 2002; 11(59):76-79.

De Siati M., Saugo M, Franzolin N. The start of pharmacological activity after sublingual administration of sildenafil citrate in 30 patients affected by erectile dysfunction. *Arch Ital Urol Androl* 2003; 75(1):18-20.

Gogtay NJ, Bichile SK, Pinto CJ et al. Erectile dysfunction and sildenafil citrate.[comment]. *J Assoc Physicians India* 2001; 49:871-872.

Guay AT, Perez JB, Velasquez E et al. Clinical experience with intraurethral alprostadil (MUSE) in the treatment of men with erectile dysfunction. A retrospective study. Medicated urethral system for erection. *Eur Urol* 2000; 38(6):671-676.

Tsai YS, Lin JS, Lin YM. Safety and efficacy of alprostadil sterile powder (S. Po., CAVERJECT) in diabetic patients with erectile dysfunction. *Eur Urol* 2000; 38(2):177-183.

Cecchi M, Sepich CA, Felipetto R et al. Vacuum constriction device and topical minoxidil for management of impotence. *Arch Esp Urol* 1995; 48(10):1058-1059.

Brooks DP, Giuliano F. Genitourinary diseases. *Drug Discovery Today: Therapeutic Strategies* 2005; 2(1):iii-iv.

Anonymous. Erratum: Efficacy and tolerability of sildenafil in Indian males with erectile dysfunction: A double-blind, randomized, placebo controlled, crossover study (*Indian Journal of Pharmacology* (2004) vol. 37 (5) (317)). *Indian Journal of Pharmacology* 2004; 36(6):391.

Bayes M, Rabasseda X, Prous JR. Gateways to Clinical Trials. *Methods & Findings in Experimental & Clinical Pharmacology* 2004; 26(9):723-753.

Martinez-Jabaloyas JM, Gil-Salom M, Villamon-Fort R et al. Prognostic factors for response to sildenafil in patients with erectile dysfunction. *Eur Urol* 2001; 40(6):641-647.

Grover JK, Vats V, Ajeeta. Sildenafil (Viagra(TM)). *Medico-Legal Update* 1998; 3(1-2):67-78.

Canale D, Giorgi PM, Lencioni R et al. Long-term intracavernous self-injection with prostaglandin E1 for the treatment of erectile dysfunction. *Int J Androl* 1996; 19(1):28-32.

Chiang H-S, Kao YH, Sheu MT. Papaverine and prostaglandin E1 gel applications for impotence. *Ann Acad Med Singapore* 1995; 24(5):767-769.

Anonymous. Alprostadil for erectile impotence. *Drug Ther Bull* 1995; 33(8):61-62.

Cara AM, Lopes-Martins RAB, Antunes E et al. The role of histamine in human penile erection. *Br J Urol* 1995; 75(2):220-224.

Shabsigh R. Efficacy of sildenafil citrate (VIAGRA) is not affected by aetiology of erectile dysfunction. *Int J Clin Pract* 1999; 102(Jun.):19-20.

Padma-Nathan H. Oral sildenafil citrate (VIAGRA) in the treatment of erectile dysfunction: assessment of erections hard enough for sexual intercourse. *Int J Clin Pract* 1999; 102(Jun.):13-15.

McMahon C. Comparison of erectile responses to differing doses of prostaglandin PGE1 in an attempt to standardise pharmacological diagnosis of impotence. *Journal of Assisted Reproduction & Genetics* 1992; 9:265A.

Bartlik BD, Kaplan P, Kaplan HS. Psychostimulants apparently reverse sexual dysfunction secondary to selective serotonin re-uptake inhibitors. *J Sex Marital Ther* 1995; 21(4):264-271.

El Malik EMA. Erectile dysfunction: An update of diagnosis and management. Qatar Medical Journal 2000; 9(2):9-17.

Varela SM, Cadarso SC, Garcia R, V et al. Sildenafil citrate in treatment of 100 patients with erectile dysfunction. Actas Urologicas Espanolas 2001; 25(5):335-340. N.

Wespes E, Sternon J, Hirsch E et al. Sildenafil (Viagra(TM)). Revue Medicale de Bruxelles 1998; 19(5):437-441. N.