

**Evidence-based Practice Center  
Technology Assessment Protocol**

**Project Title: Short and Long Term Outcomes after Bariatric Therapies in the Medicare Population**

Project ID: OBST0816

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**I. Background and Objectives for the Systematic Review**

Obesity, an accumulation of excessive fat tissue, has been associated with morbidity (e.g., sleep apnea, diabetes, cardiovascular disease, osteoarthritis, hypertension),<sup>1-4</sup> mortality,<sup>5,6</sup> decreased quality of life,<sup>7</sup> and increased healthcare costs,<sup>2,4,8</sup> especially among older adults in whom chronic conditions are more prevalent. Obesity carries a substantial health burden,<sup>9</sup> and obesity-related conditions include preventable leading causes of death, such as type 2 diabetes, cardiovascular disease, and some cancers. There are indications that the risks of morbidity and mortality increase as obesity becomes more severe.<sup>1-4</sup> The estimated annual medical cost of obesity in the U.S. was \$147 billion in 2008 U.S. dollars and the medical costs for people who have a body mass index (BMI) over 30 Kg/m<sup>2</sup> were approximately \$1,400 higher than those with a normal BMI (between 18.5 and 24.9 Kg/m<sup>2</sup>).<sup>8</sup> This cost-of-care differential between people with high versus normal BMI is probably even higher for people with more severe obesity. Among employed Americans, the 3% who are severely obese account for 21% of the health care costs associated with obesity.<sup>8</sup>

Treatments for severe obesity include lifestyle modifications (exercise, diet), use of medications (e.g., orlistat, sibutramine), endoscopically-placed devices (e.g. gastric balloons), and bariatric surgery. Most non-surgical treatments for obesity fail to achieve long-term weight control.<sup>10</sup> In contrast, bariatric surgery is perceived to be an effective obesity treatment, especially long-term, and probably reduces morbidities.<sup>11-13</sup> It has become the preferred therapy for severely obese patients refractory to medical therapy.<sup>14</sup> According to a National Institutes of Health (NIH) Panel, bariatric surgery is indicated for patients with BMI  $\geq 40$  Kg/m<sup>2</sup> (obesity grade 3), or BMI  $\geq 35$  Kg/m<sup>2</sup> (obesity grades 2 or 3) with an obesity-related comorbidity who have not responded to lifestyle modification therapy.<sup>3</sup> Bariatric surgery has also been evaluated in moderately obese adults (obesity grade 1, BMI 30-34.9 Kg/m<sup>2</sup>).<sup>15</sup>

Bariatric surgery procedures result in anatomic manipulations of the gastrointestinal (GI) tract and more recently similar anatomic modifications can be achieved through the use of endoscopic technologies. Depending on the exact procedure, bariatric procedures are thought to achieve weight control through one or more of the following mechanisms: (1) a **restricting mechanism**, by restricting the diameter of the stomach's esophageal orifice, or restricting the stomach's effective volume, thereby reducing the volume and speed of food intake; (2) **endocrine or metabolic mechanisms** (e.g., removal of the stomach's fundus decreases secretion of hunger-inducing hormones such as ghrelin); (3) a **diversionary malabsorptive mechanism**, by diverting the physiological route of ingested food to more distal segments of the gastrointestinal tract, leading to malabsorption of ingested food; and (4) **conditioning mechanisms**, food restriction to avoid experiencing gastrointestinal disturbances (e.g., dumping syndrome, dysphagia,

vomiting, flatus) due to surgery-induced changes of the anatomy and function of the gastrointestinal tract.

Many older adults meet indications for bariatric treatment. Based on the U.S. National Health and Nutrition Examination Survey (NHANES), in 2012 people 60 years and older commonly had BMI  $\geq 30$  (prevalence 35%),  $\geq 35$  (14%), and  $\geq 40$  (6%) Kg/m<sup>2</sup>.<sup>16</sup> In these people, obesity was more prevalent among women than men, and varied across ethnicities, being highest among non-Hispanic blacks (49%) and Hispanics (47%), and lowest among Asians (9%).<sup>16</sup> Thus, a large number of Medicare-eligible people likely meet NIH indications for bariatric therapy either surgical or endoscopic.

Therefore, the comparative effectiveness and safety of bariatric surgery interventions is of great interest to the Centers for Medicare and Medicaid Services (CMS). The Brown Evidence-based Practice Center (EPC) has assembled a team comprising content experts (bariatric surgeon Beth Ryder and behavioral scientist Dale Bond) and in-house experts in systematic review (SR), hierarchical modeling, and network meta-analysis to address these questions.

PROSPERO registration number: *Pending*

## II. The Key Questions

With input from clinical experts, we have developed the following Key Questions (KQ) and study eligibility criteria for the systematic review:<sup>a</sup>

**KQ 1:** What are the theorized mechanisms of action of bariatric procedures on weight loss and on type 2 diabetes in the Medicare population?

**KQ 2:** In studies that are applicable to the Medicare population and enroll patients who have undergone bariatric therapy, what are

- a) the characteristics and indications of the patients including descriptives of age, BMI, and comorbid conditions
- b) the characteristics of the interventions, including the bariatric procedures themselves as well as pre- and/or post-surgical surgical work-ups (e.g., psychiatric evaluations, behavioral and nutritional counseling)
- c) the outcomes that have been measured, including peri-operative (i.e., 90 days or less after bariatric surgery), short-term (2 years or less from surgery), mid-term (more than 2 but 5 or less years), and long-term (more than 5 years after surgery) outcomes?

**KQ 3a:** In Medicare-eligible patients, what is the effect of different bariatric therapies (contrasted between them or vs. non-bariatric therapies) on weight outcomes (including failure to achieve at least minimal weight loss)?

**KQ 3b:** What patient- (KQ2a) and intervention-level characteristics (KQ2b) modify the effect of bariatric therapies on weight outcomes (including failure to achieve at least minimal weight loss)?

**KQ 3c:** In Medicare-eligible patients who have undergone bariatric therapy, what is the frequency and the predictors of failing to achieve at least minimal weight loss?

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<sup>a</sup> These KQs are semantically equivalent to preliminary Key Questions proposed by the Centers for Medicare and Medicaid Services (CMS), AHRQs sponsoring partner on this project.

**KQ 4a:** In Medicare-eligible patients, what is the comparative effectiveness and safety of different bariatric interventions (contrasted between them or vs. non-bariatric interventions) with respect to the outcomes in KQ2c?

**KQ 4b:** What patient- (KQ2a) and intervention-level (KQ2b) characteristics modify the effect of the bariatric therapies on the outcomes in KQ2c?

**KQ 5a:** In Medicare-eligible patients who have undergone bariatric therapy, what is the association between weight outcomes and eligible short- and long-term outcomes (other than weight outcomes)?

**KQ 5b:** In Medicare-eligible patients, what proportion of the bariatric intervention effect on eligible short- and long-term outcomes (other than weight outcomes) is accounted for by changes in weight outcomes?

### **Eligibility Criteria**

For all KQs, the Eligibility Criteria will be defined based on the PICOTS framework:

Population: Medicare-eligible population to include those age 65 and older and the disabled.

Interventions: Bariatric treatments including anatomic alteration, FDA-approved device placements, open surgical procedures, as well as laparoscopic and endoscopic procedures

#### **A. Surgical bariatric therapies**

1. Adjustable gastric banding (AGB)
  - a.LAP-band, pars flaccida technique
  - b.LAP-band, perigastric technique
  - c.Swedish-band (also known as REALIZE-band), pars flaccida technique
  - d.Swedish-band (also known as REALIZE-band), pars flaccida technique, single bolus filling
2. Gastroplasties
  - a.Horizontal banded gastroplasty
  - b.Vertical banded gastroplasty
  - c.Endoluminal vertical gastroplasty
3. Sleeve gastrectomy
4. Gastric plication (also referred to as gastric greater curvature plication or gastric imbrication)
5. Jejunioileal bypass
6. Biliopancreatic diversion (BPD)
  - a.Biliopancreatic diversion (BPD) with RYGB (BPD-RYGB)
  - b.BPD with duodenal switch (BPD-DS)
7. Roux-en-Y Gastric Bypass (RYGB)
8. Mini-gastric bypass
9. Single Anastomosis Duodeno-Ileostomy (SADI)
10. Vagal blockade
11. Omentum removal (omentectomy)
12. Gastric stimulation (also referred to as gastric pacing)
13. Mucosal ablation

- B. Endoscopic bariatric therapies
  - 1. Space-occupying endoscopic bariatric therapies
    - a. Intra-gastric balloons
    - b. Nonballoon devices
  - 2. Aspiration therapy
  - 3. Endoscopic sleeve gastropasty
  - 4. Endoscopic gastrointestinal bypass devices
    - a. Duodenojejunal bypass sleeve
    - b. Gastroduodenojejunal bypass sleeve
  - 5. Duodenal mucosal resurfacing
  - 6. Self-assembling magnets for endoscopy

Comparisons of interest include comparisons between different surgical interventions, or between surgical and non-surgical interventions

Outcomes will be classified as peri-operative (i.e., 90 days or less after bariatric surgery), short-term (2 years or less from surgery), mid-term (more than 2 but 5 or less years), and long-term (more than 5 years after surgery). The following outcome categories are of interest:

- A. Mortality
- B. Weight loss
- C. Reoperations/need for revisional bariatric surgery
- D. Postoperative complications including mortality
- E. Metabolic/diabetes-related outcomes
  - i. Correction of glucose tolerance, including elimination of all medications with Hemoglobin A1c (HbA1c) <6
  - ii. Diabetes: new onset diabetes; treatment of diabetes; diabetic complications (microvascular disease, kidney disease, retinopathy)
  - iii. Hypoglycemic-like syndromes such as nesidioblastosis, post-gastric surgery hypoglycemia, and dumping syndrome
  - iv. Non-alcoholic steatohepatitis (NASH) and/or non-alcoholic fatty liver disease (NAFLD)
- F. Reflux
- G. Cardiovascular outcomes
  - i. Myocardial infraction
  - ii. Stroke
  - iii. Hypertension
- H. Respiratory disease
  - i. Asthma
  - ii. COPD
- I. Orthopedic outcomes
  - i. Fractures
  - ii. Falls
  - iii. Osteoporosis/bone-mineral density (DEXA, DEEG)

- J. Sleep apnea including the discontinuation of CPAP or BiPAP
- K. Incidence of specific cancers (breast, colorectal cancer, endometrial cancer, esophageal adenocarcinoma, gall bladder cancer, and renal cell cancer)
- L. Nutritional deficiencies including zinc, iron, thiamine, and vitamin D, and associated disorders such as neuropathy and bone disease
- M. Renal function as measured by creatinine clearance or urinary albumin excretion
- N. Compliance to follow-up
- O. Mental health outcomes
  - i. Incidence of suicide and suicide attempts
  - ii. Incidence of depression
  - iii. Alcohol addiction after surgery/Substance abuse
  - iv. Psychiatric hospitalizations
  - v. Anxiety
  - vi. Panic disorder
  - vii. Borderline personality disorder
  - viii. PTSD
  - ix. Bipolar disorder
- P. Function and quality of life (validated measurements only), e.g.,
  - i. Cognitive functioning
  - ii. Sexual functioning
  - iii. Ability to participate in an exercise program
  - iv. Ability to return to work
  - v. Physical performance test pain (joint pain, joint aches)
  - vi. Regular daily activities
  - vii. Polypharmacy
  - viii. Admission to a skilled-nurse facility
- Q. Access to plastic surgery
- R. Readmissions/rehospitalizations

Timing:

- No time limit

Setting:

- Any

Depending on the volume of the literature, and after discussions with the Technical Expert Panel and AHRQ, we may revise the exact definitions of eligible outcomes in the aforementioned categories, and may prioritize some outcome categories over others for more detailed descriptions or analyses.

**Comments About the Eligibility Criteria**

Because the interest is in Medicare-eligible individuals, we will exclude studies in pediatric populations (ages 0-18 years) and of the remaining we will further exclude those studies with no Medicare-eligible participants (i.e. age 65 or older; disabled) and studies on pregnant women.

For all Key Questions, we will include studies of bariatric therapies as those are defined in the current protocol (see section VI). Eligible will be any surgical (open or laparoscopic) as well as endoscopic procedure that result in anatomic and/or functional alteration of the gastrointestinal system and which may or may not involve device placement. Studies will be ineligible if they focus exclusively on non-bariatric therapies (i.e., pharmacological, behavioral, nutritional); and studies in which subjects are not candidates for bariatric surgery or have not undergone bariatric surgery. We will also exclude studies on the effects of revisional bariatric surgery as well as studies of the management of bariatric therapy complications (e.g. anastomosis leak, post-surgical hernias etc.) since these studies address clinical questions that are distinct from the effects of bariatric therapies. Studies reporting on hormonal, biochemical, and other molecular changes in relation to bariatric therapies will be included only if these changes are related to health outcomes. Last, we will exclude case-control studies, case series, case reports, letters, comments, animal studies, and data available only on abstracts.

Primary outcome categories will be weight loss, mortality, type 2 diabetes, quality of life, and ability to perform daily activities. All other outcomes will be secondary.

For Key Question 1, we will focus on biological, pathophysiological, and mechanistic studies.

For Key Question 2, we will include comparative and non-comparative studies (registries, cross-sectional studies, cohort studies).

Because Key Questions 3a, 3b, 4a, and 4b are about comparative effectiveness and/or safety, only comparative studies, including randomized controlled trials (RCTs) and nonrandomized comparative studies, will be eligible.

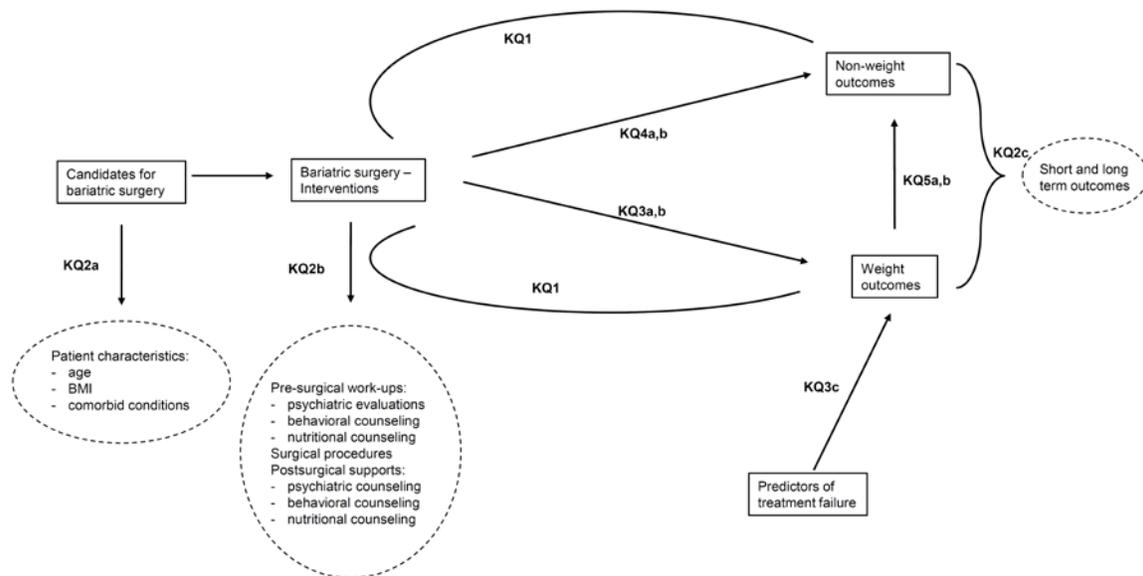
For Key Question 3c, we will include prospective cohort studies that report on predictive models for the success or failure of bariatric surgery in regards to weight outcomes. We may also consider only comparative studies in which the information on predictive factors comes only from the intervention arm.

For Key Question 5a, we will include both comparative and non-comparative studies, while for Key Question 5b we will include randomized and non-randomized comparative studies.

### **III. Analytic Framework**

To guide the assessment of studies, the analytic framework maps the specific linkages associating the populations of interest, the interventions, and outcomes of interest. The analytic framework depicts the chains of logic that evidence must support to link the studied interventions studied.

**Figure 1: Analytic Framework for Short and Long Term Outcomes after Bariatric Surgery in the Medicare Population**



#### IV. Methods

The Evidence-based Practice Center (EPC) will conduct the review based on a systematic review of the published scientific literature using established methodologies as outlined in the Agency for Healthcare Research and Quality’s (AHRQ) Methods Guide for Comparative Effectiveness Reviews.<sup>17</sup> We will use a combination of review of the published literature, interviews with key informants, grey literature review, evidence mapping (i.e., a systematic description of the characteristics of the published studies), and quantitative methods to answer the key questions.

**Criteria for Inclusion/Exclusion of Studies in the Review:** Please refer to Section II *The Key Questions*, where the Eligibility Criteria are listed after the KQs.

**Searching for the Evidence:** We will conduct literature searches of studies in PubMed, EMBASE, CINAHL, PsycINFO, the Cochrane Central Trials Registry (CENTRAL), and the Cochrane Database of Systematic Reviews, to identify primary research studies meeting our criteria. These databases should adequately cover the published literature on this topic. We anticipate using the search strategy in **Appendix A**, adapted as needed for each database. The search strategy will be peer reviewed by an independent, experienced information specialist/librarian. We will send a list of included studies to the Technical Expert Panel (see section X below for a description of the role of the Technical Experts) and ask them to provide citations of potentially relevant articles that we may have missed. Additionally, we will peruse the reference lists of published clinical practice guidelines, relevant narrative and systematic reviews, and Scientific Information Packages (SIP) from manufacturers or other stakeholders. We will also search ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for ongoing studies and studies that are not published in the medical literature. In addition, we will search the FDA drugs and devices portals for unpublished data. We will

use existing systematic reviews primarily as sources of studies; we will extract and incorporate all studies *de novo* and will not summarize or incorporate existing systematic reviews, per se. All articles identified through these sources will be screened for eligibility, using the same criteria as was used for articles identified through literature searches. Peer-review will provide an additional opportunity for the TEP and other experts in the field to ensure that no key publications have been missed. The search will be updated upon submission of the draft report for peer and public review.

All citations found by literature searches and other sources will be independently screened by two researchers. At the start of abstract screening, we will implement a training session, in which all researchers will screen the same articles and conflicts will be discussed. During double-screening, we will resolve conflicts as a group. All screening will be done in the open-source, online software Abstrackr (<http://abstrackr.cebm.brown.edu/>).<sup>18, 19</sup> All potentially relevant studies will be rescreened in full text to ensure eligibility.

**Data Extraction and Data Management:** Each study will be extracted by one methodologist. The extraction will be reviewed and confirmed by at least one other experienced methodologist. Any disagreements will be resolved by discussion among the team. Data will be extracted into a customized form in Systematic Review Data Repository (SRDR) online system (<http://srdr.ahrq.gov>) designed to capture all elements relevant to the Key Questions. Upon completion of the review, the SRDR database will be made accessible to the general public (with capacity to read, download, and comment on data). The basic elements and design of the extraction form will be the similar to those used for other AHRQ comparative effectiveness reviews and will include elements that address population characteristics, including characteristics of pre- and post-surgical work-ups; descriptions of patients; descriptions of the interventions, exposures, outcomes, and comparators analyzed; outcome definitions; effect modifiers; enrolled and analyzed sample sizes; study design features; funding source; results; and risk of bias questions.

**Assessment of Methodological Risk of Bias of Individual Studies:** We will assess the methodological quality of each study based on predefined criteria. For RCTs, we will use the Cochrane risk of bias tool,<sup>20</sup> which asks about risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. For observational studies, we will use relevant questions from the Newcastle Ottawa Scale.<sup>21</sup> Quality/risk of bias issues pertinent to specific outcomes within a study will be noted and considered when determining the overall strength of evidence for conclusions related to those outcomes. To assess the number of unpublished articles, we will record the number of studies found through the ClinicalTrials.gov search that are completed but unpublished.

**Data Synthesis:** All included studies will be summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, and results. These included descriptions of the study design, sample size, populations, interventions, follow-up duration, outcomes, results, funding source, and study quality. We will include studies found in ClinicalTrials.gov and studies submitted to the FDA whose reports are publicly accessible that give results but do not have a published report.

For KQ 1, we will conduct a narrative review by searching editorials, published narrative and systematic reviews in specialty journals, and textbooks in relevant medical specialties.

Our synthesis will involve a two-phase approach. At the first phase, we will build an evidence map to address KQ2 and subsequently based on the evidence map we will determine for which outcomes there is sufficient evidence to conduct quantitative analyses. We will build the evidence map based on our search strategy and inclusion/exclusion criteria; at this stage, outcomes will be described at the category level. An evidence map aims to summarize the extent and distribution of evidence in a broad clinical area. A systematic and replicable, but non-exhaustive, methodology is employed to efficiently appraise the available evidence on a topic of interest as well as identify major knowledge gaps.<sup>22</sup> The goal is to provide stakeholders with information about the type and amount of research available, the characteristics of that research, and the topics where a sufficient amount of evidence has accumulated for synthesis. Evidence mapping can inform users of the current state of research findings that could be used to generate hypotheses, inform ongoing research, and identify research gaps. Descriptive analyses for KQ2 will be done at the outcome-category level, and not for each individual outcome. For example, we will describe studies reporting “orthopedic outcomes” all together, instead of separately describing studies reporting outcomes such as fractures (e.g., of the knee, hip, spine), need for joint replacement surgery (knee or hip), or falls.

To address KQ 3a and 4a we will conduct quantitative syntheses for all primary outcome categories and for those secondary outcome categories for which at least 4 studies are available based on the evidence map. We expect to conduct random-effects model meta-analyses of comparative studies, if they are sufficiently similar in population, interventions, and outcomes. Specific methods and metrics (summary measures) to be meta-analyzed will depend on available, reported study data, but we expect to summarize odds ratios for categorical outcomes; hazard ratios for time-to-event analyses; and standardized mean differences for continuous outcomes. Possible reasons for statistical heterogeneity will be explored qualitatively and, if appropriate data are available, we may also conduct meta-regression analyses to evaluate study, patient, and intervention features (e.g., open, laparoscopic procedure, or endoscopic). We will explore subgroup differences within (and possibly across) studies. We also plan to conduct a network meta-analysis to compare all treatment alternatives across studies. We will analyze networks of interventions defined at different degrees of granularity corresponding to different levels of the hierarchical description of interventions in PICOTS.

We anticipate to conduct a series of subgroup analyses by including in our synthesis only procedures that are contemporary by focusing on the studies conducted after 2000; however, synthesis of studies before 2000 can also provide useful insights for the comparative effectiveness/safety of modern procedures. Similarly, other subgroup analyses will involve only bariatric therapies that have been approved by the FDA and are implemented in the U.S. clinical practice.

For Key Question 3b and 4b, we will examine heterogeneity of treatment effects for the patient- and intervention-level characteristics in Key Questions 2a and 2b through meta-regression and subgroup analyses.

For Key Question 3c, we will identify studies that develop and/or validate predictive models for the change in weight outcomes before and after bariatric surgery. We will summarize the variables used as predictors of treatment effects, the populations in which the models have been developed, whether any validation attempts have been undertaken, and metrics of models performance (e.g. calibration, discrimination etc.).

For Key Question 5a, we will synthesize the metrics of association between weight loss and short- or long-term outcomes. Specific methodology will depend upon the available studies and the reported data.

For Key Question 5b, we will summarize mediation analyses to estimate the proportion of the bariatric surgical effect on outcomes other than weight loss that is accounted for by weight loss (indirect treatment effect).<sup>23</sup>

### **Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes:**

We will grade the strength of the body of evidence as per the AHRQ methods guide on assessing the strength of evidence.<sup>17</sup> We plan to assess the strength of evidence for each outcome. Following the standard AHRQ approach, for each intervention and comparison of intervention, and for each outcome, we will assess the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, and the overall findings across studies. Based on these assessments, we will assign a strength of evidence rating as being either high, moderate, or low, or there being insufficient evidence to estimate an effect. The data sources, basic study characteristics, and each strength-of-evidence dimensional rating will be summarized in a “Summary of Evidence Reviewed” table detailing our reasoning for arriving at the overall strength of evidence rating

**Assessing Applicability:** We will assess the applicability within and across studies with reference to demographics of enrolled participants (e.g. age and sex distributions), the degree of obesity, and the availability of treatments (e.g. contemporary treatments; availability/FDA approval of devices; established clinical practices in the U.S.).

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## **VI. Definition of Terms**

**Bariatric therapy** is the collective term used for a heterogeneous set of surgical (open or laparoscopic) and endoscopic procedures that modify the process of digestion by altering the anatomy and/or function of the gastrointestinal system, thus resulting in weight loss.

## **VII. Summary of Protocol Amendments**

This is the draft protocol and no amendments are applicable at the pre-review stage. In the event of amendments following public review comments, we will report all applicable amendments.

## **VIII. Review of Key Questions**

The EPC will refine and finalize the Key Questions after further input from Technical Experts. This input is intended to ensure that the Key Questions are specific and relevant.

## **IX. Key Informants**

There were no key informants for this project.

## **X. Technical Experts**

Technical Experts constitute a multidisciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore, study questions, design, and methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor do they contribute to the writing of the report. They have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

## **XI. Peer Reviewers**

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published 3 months after the publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

## **XII. EPC Team Disclosures**

EPC core team members must disclose any financial conflicts of interest greater than \$1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than \$1,000 will usually disqualify EPC core team investigators.

## **XIII. Role of the Funder**

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## Appendix A. Preliminary Literature Searches

((Anastomosis, Roux-en-Y"[Mesh]  
OR "Gastroenterostomy"[Mesh]  
OR ((obes\* or antiobesity or anti-obesity or "anti obesity" or gastric or restrictive or gastrointestinal or malabsorpti\*) and surg\*))  
OR (bariatric AND (operation or operations or procedure\*))  
OR ((gastric or silicon) AND (band or bands or banding))  
OR ((gastric or stomach) and stapl\*)  
OR ((gastrointestinal or biliopancreatic) and diversion)  
OR ((jejunoileal or "jejuno-ilial" or "jejuno ilial" or biliopancreatic or ileojejunal or intestinal or gastroileal or gastric) and bypass\*)  
OR ((vertical-banded or "vertical banded" or collis) and gastroplasty)  
OR Endoluminal vertical gastroplasty  
OR "duodenal switch"  
OR Stomach banding  
OR "Bariatric surgery"[Mesh]  
OR "biliopancreatic diversion"[Mesh]  
OR "Gastric bypass"[Mesh]  
OR (gastric and (sleeve or bypass or band or banding or bands))  
OR "gastroplasty"[Mesh]  
OR "Jejunoileal bypass"[Mesh]  
OR pancreatobiliary bypass  
OR roux-en-y  
OR "sleeve gastrectomy"  
OR bariatric surg\*  
OR duodenal next switch\*  
OR gastroenterostomy  
OR gastrogastrostomy  
OR gastrojejunostom\*  
OR gastroplasty  
OR laparoscopic adjustable gastric banding  
OR malabsorpti\* procedure\*  
OR "Gastric Balloon"[Mesh]  
OR "gastric balloon" or "Intragastric balloon"  
OR "Vagal blockade"  
OR "Aspiration therapy"  
OR Swedish band  
OR realize band)

Not ("Child"[Mesh] NOT "Adult"[Mesh]))

AND

("Cohort Studies"[Mesh] OR cohort OR "Clinical Trial" [Publication Type] OR "Clinical Trials as Topic"[Mesh] OR (follow-up or followup) OR longitudinal OR "Placebos"[Mesh] OR placebo\* OR "Research Design"[Mesh] OR "Evaluation Studies" [Publication Type] OR "Evaluation Studies as Topic"[Mesh] OR "Comparative Study" [Publication Type] OR ((comparative OR Intervention) AND study) OR "Intervention Studies"[Mesh] OR pretest\* OR pre test\* OR posttest\* OR post test\* OR prepost\* OR pre post\* OR "before and after" OR interrupted time\* OR time serie\* OR intervention\* OR ((quasi-experiment\* OR quasiexperiment\* OR quasi experiment\*) and (method or study or trial or design\*)) OR "Case-Control Studies"[Mesh] OR (case and control) OR "Clinical Studies" [Publication Type] OR "Clinical Studies as Topic"[Mesh] OR random allocation [mh] OR double-blind method[mh] OR single-blind method[mh] OR random\* OR "Clinical Trial" [Publication Type] OR "Clinical Trials as Topic"[Mesh] OR "Placebos"[Mesh] OR placebo OR ((clinical OR controlled) and trial\*) OR ((singl\* or doubl\* or trebl\* or tripl\*) and (blind\* or mask\*)) OR rct OR Observational Study [Publication Type] OR "Epidemiologic Studies"[Mesh] OR "Cohort Studies"[Mesh] OR cohort OR (observational and (study or studies)) OR Longitudinal OR Retrospective OR "Prospective Studies"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Follow-Up Studies"[Mesh] OR ((follow-up or followup or "follow up") and (study or studies)) OR "Registries"[Mesh] OR Evaluation Studies [Publication Type] OR Validation Studies [Publication Type]) NOT ("addresses"[pt] or "autobiography"[pt] or "bibliography"[pt] or "biography"[pt] or "case reports"[pt] or "comment"[pt] or "congresses"[pt] or "dictionary"[pt] or "directory"[pt] or "editorial"[pt] or "festschrift"[pt] or "government publications"[pt] or "historical article"[pt] or "interview"[pt] or "lectures"[pt] or "legal cases"[pt] or "legislation"[pt] or "letter"[pt] or "news"[pt] or "newspaper article"[pt] or "patient education handout"[pt] or "periodical index"[pt] or "comment on" OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] or cow[tw] or cows[tw] or chicken\*[tw] or horse[tw] or horses[tw] or mice[tw] or mouse[tw] or bovine[tw] or sheep or ovine or murinae)

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