8. Harms Due to Diabetic Agents

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Introduction

In this chapter, two different kinds of diabetes patient safety practices are addressed—both intended to improve diabetes medication management. One practice focuses on provider administration of medication in the hospital setting when patients are ill. The other focuses on patient self-management in settings where patients are well enough to comprehend information about diabetes medication, typically outpatient settings.

The research on standardized protocols to reduce insulin administration errors that result in hypoglycemia is more robust than the research on the teach-back method, a communication confirmation method. However, in both cases, additional research is needed that is adequately powered and presents a study design that can detect an effect on hypoglycemia in the inpatient setting due to standardized protocols or a change in blood glucose levels in the outpatient setting due to teach-back. Key findings for both practices are located in the box on the next page.

Background

Individuals who have diabetes are not usually hospitalized for glucose control but are for other acute and chronic conditions. As inpatients, they are at risk for hypoglycemia and hyperglycemia by having their blood glucose levels (BGL) outside the recommended ranges for hospitalized patients (a target glucose range of 140–180 mg/dL); they may not have available or be consulting with a specialized diabetes or glucose management team skilled in diabetes medication administration.[1,2] Diabetes exacerbations are known to contribute to morbidity and mortality, and can be avoided through better medication management, including through the use of standardized insulin protocols. During the past decade, the United Kingdom—more than any other Nation—has documented diabetes medication errors through the National Diabetes Audit and instituted quality improvement projects to reduce errors and improve outcomes.[3] The data compiled through the National Diabetes Audit constitute one of the best sources of information on safety practices and are referred to below.

Diabetes is a growing chronic condition in the United States. Ambulatory patients with diabetes too frequently experience poor management of BGL, hypoglycemia (blood glucose below 70 mg/dL) and hyperglycemia (200 mg/dL or a fasting blood glucose level above 126 mg/dL).[4] In the 2013 Making Health Care Safer report, the Agency for Healthcare Research and Quality (AHRQ) focused on diabetes management as a patient safety practice. In this update, we more narrowly focus on medication management in hospitals and how to better equip both providers and patients to maintain recommended BGL levels and avoid instances of hypo- and hyperglycemia.

In addition, we examine the teach-back method used in settings where patients are able to self-manage their diabetes, generally in outpatient settings. The teach-back method is used for many different conditions and diseases, and has shown promise in helping patients and caregivers avoid medical mistakes.[5,6]

Importance of Harm Area

The clinical standards regarding BGL have evolved over the past two decades, beginning with a 2001 landmark study by Van den Berghe[7] that documented increased morbidity and mortality due to hyperglycemia in the inpatient setting. The study catalyzed a change in inpatient diabetes medication management toward standard protocols based on the American Diabetes Association's recommendations and away from the practice of sliding-scale insulin. In addition, there has been a move away from aggressive glycemic targets; adherence to strict targets has led to an increase in episodes of hypoglycemia. Tight glucose control is not indicated in the hospital setting. BGL <180 mg/dL is associated with lower rates of mortality and stroke compared with a target glucose <200 mg/dL, whereas no significant additional benefit was found with more strict glycemic control (<140 mg/dL).[8,9] Thus, the ranges for acceptable BGL have eased over time.[10,11]

There are numerous reasons that standardized insulin protocols or other ways of reducing medication administration errors are important patient safety practices (PSPs). A growing number of aging U.S. residents have diabetes, contributing to increases in the number of inpatients with multiple chronic conditions, which make diabetes even more difficult to manage and control.[4] If diabetes is well controlled during inpatient stays, other conditions can be more effectively treated and instances of BGL out of recommended range can be reduced.[12] These practice changes have implications for inpatient costs, quality of care, readmission rates, and patient reported outcomes.

The United Kingdom has made safety for diabetes inpatients a priority through DiabetesUK, a program that has collected data on medication errors and worked to decrease error rates. In 2017, one in six people in a hospital bed in England had diabetes, an estimated 270,000 individuals with diabetes suffered a medication error, 58,000 suffered an episode of severe hypoglycemia, and 9,600 required rescue treatment after falling into a coma as a result of severe hypoglycemia.[3] The country has been conducting the National Diabetes Audit since 2010, and based on the results, England instituted a multipronged patient safety program that includes: multidisciplinary diabetes teams in hospitals with strong clinical leadership, diabetes training, patient support and empowerment, better technology for identifying diabetes patients and those at increased risk for hypoglycemia, electronic prescribing, monitoring medication, and learning techniques to help hospitals learn from mistakes.

Key Findings for Insulin Protocol:

- Several studies have found that standardized protocols reduce hypoglycemic events in hospitalized patients in both acute and intensive care.
- Results are not uniform, and some studies using standardized protocols did not lead to a reduction in hypoglycemic events.
- Nurses are able to administer new, standardized protocols in most cases, even if the protocols take more time and are more complicated than prior protocols.
- The existing studies suffer from small numbers and weak study designs.
- The diversity of types and modes of protocols, study settings, and study designs makes the studies difficult to compare or synthesize.

Key Findings for Teach-Back:

- Teach-back has not been proven to improve Hemoglobin A1c levels or other clinical outcomes for diabetes patients.
- A greater number of studies and higher quality studies in diverse settings are needed to test the effects of teach-back in diabetes medication management.

There are several other trends that underscore the importance of reducing diabetes medication management errors. The Centers for Medicare & Medicaid Services (CMS) has established quality measures, and financial penalties in some cases, for unnecessary hospital readmissions. The pressure to

avoid readmissions has intensified, and hospitals and hospital systems are creating and using new protocols that can improve care coordination and healthcare access and help keep patients, including diabetes patients, out of the hospital. Since 2010, the Centers for Disease Control and Prevention (CDC) has funded the National Diabetes Prevention Program, a public-private partnership to disseminate a research-based lifestyle change program intended to prevent or delay type 2 diabetes. In recognition of the importance of diabetes prevention, CMS is currently conducting a project that implements and evaluates the diabetes prevention program among Medicare and Medicaid recipients on a large scale.

Methods for Selecting PSPs

Initial literature searches for PSPs in the harm area of medication management and diabetes agents were conducted, focusing on systematic reviews and guidelines. Results of these searches were reviewed by harm-area task leads to identify PSPs, and as needed, searches were refined. Then the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to AHRQ for review. After several rounds of review with AHRQ, two PSPs on medication management—diabetes agents were selected.

What's New/Different Since the Last Report?

The focus of PSPs has shifted from the last report to the current report, which more narrowly highlights diabetes medication management in inpatient settings. Recent studies to predict which patients are likely to experience hypoglycemia while hospitalized have led to development of screening tools,[13] identification of risk factors, [14,15] and identification of specific phenotypes[16] to help address this important potential patient-harm area.

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8.1 PSP1: Use of Standardized Insulin Protocols To Reduce Risk of Serious Hypoglycemia in Hospitals Due to Administration Errors

8.1.1 Practice Description

Standardized protocols are used in many situations because they reduce variability in human behavior and thus reduce the chance of error. Standardized insulin protocols and the insulin regimens to which they apply are intended to maintain relatively constant BGL in a person and reduce fluctuations. However, insulin medication must be adjusted based on an individual's activity and nutrition intake; an insulin bolus may be needed at mealtime, for example. Insulin regimens include basal insulin or a basal plus bolus correction insulin, which is the preferred treatment for non-critically ill hospitalized patients with poor oral intake. An insulin regimen with basal, prandial, and correction components is the preferred treatment for non-critically ill hospitalized patients who are able to intake nutrition orally. Standardized protocols are implemented through different forms, including specialized medical teams and paper and electronic order sets. Sole use of sliding-scale insulin in the inpatient hospital setting is strongly discouraged.[1]

8.1.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "insulin," "insulin administration," "hypoglycemic agents," and related synonyms, as well as "standing orders," "standard order set," and "standardized insulin protocol." Articles included were published from 2008 to 2018. The initial search yielded 145 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 132 articles were screened for inclusion, and full-text articles were retrieved. Of those, 14 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

8.1.3 Review of Evidence

Fourteen studies met the evidence criteria for this review in that they involved a standardized insulin protocol intended to reduce insulin medication administration errors in the inpatient setting and specifically targeted hypoglycemia. The types of studies were diverse in terms of populations, settings, countries, study design, sample size, type of standardized protocol, and outcomes (implementation and clinical).

Populations included individuals with type 1 or 2 diabetes who were admitted to acute care, intensive care, surgical, emergency department, and critical care units. Sample sizes ranged from 47 to 5,530, but most were small studies; eight of the studies included 200 or fewer patients.

The study designs included one interrupted time series (Wong et al., 2017),[2] three comparative effectiveness studies,[3-5] four prospective studies that used retrospective controls,[6-9] three pre-post studies,[10-12] one retrospective review,[13] one intervention with control group,[14] and one prospective

observational study in conjunction with a quality improvement effort. There were no randomized control studies.

8.1.3.1 Clinical Outcomes

Of the 14 studies, 7 demonstrated lower hypoglycemia rates when a standardized protocol was introduced. (Two of the studies drew findings from the same overall study.[6,8]) In some of these studies hypoglycemia was reduced, although time in target BGL was not statistically significant between the intervention and nonintervention groups. The seven studies are briefly described below.

In a study of 131 intensive care unit (ICU) patients, 65 received a static sliding-scale protocol, and 66 received a dynamic insulin infusion protocol. The dynamic protocol resulted in a lower rate of hypoglycemic events than the static protocol, although the time in target BGL ranges was low compared to other computer-assisted protocols. Twice as many nurses felt that the dynamic protocol, although more time consuming, was more effective than those who preferred the static one. However, the study population was small and conducted in a single hospital.[5]

A study of 552 acute and subacute trauma intensive care unit (TICU) patients who received an automated nurse-driven computer-based protocol was compared with retrospective data from patients at the same hospital who were treated with a manual, paper-based protocol. Hypoglycemia was lower in the computerized protocol group, and more patients were in the target BGL range. The computerized protocol worked with nursing workflows, and overall compliance was good.[9]

Two pilot studies were conducted—one in the cardiology and the other in the nephrology units of a Canadian hospital. Both studies used pre-printed insulin orders intended to standardize insulin prescribing practices, promote basal and mealtime insulin, reduce reliance on sliding-scale insulin, and standardize hypoglycemic management. Hypoglycemia rates decreased after the first pilot of 47 patients but not after the second.[10]

A small study of 96 ICU patients receiving parenteral nutrition compared a group receiving a transition order set with a retrospective comparison group (n=153) that did not receive the transition order set. Hypoglycemia rates decreased for the intervention group, and nurses reported that the new protocol was more time consuming but was a useful and instructive tool for maintaining BGL.[6]

In another sub-study based on the same overall study described above, a nurse-led self-adjusting standardized intravenous insulin protocol in an ICU led to a substantial reduction in hypoglycemic events, and fewer patients experienced more than one hypoglycemic event. The study examined the outcomes for the intervention compared with a retrospective control group. ICU length of stay was also lower for the protocol group.[8]

Another study using retrospective controls implemented a basal-bolus-booster insulin protocol in 57 patients known to be hyperglycemic in non-critical hospital units. Hypoglycemia was lower in the intervention group. Staff compliance with implementation of the basal-bolus portion of the protocol was good, while compliance with the bedtime booster was poor.[7]

In a study embedded in a quality improvement effort, 5,530 inpatients in an academic medical center were given a structured subcutaneous insulin order set that encouraged the use of scheduled basal and nutritional insulin, and provided guidance for monitoring glucose levels and insulin dosing. A hypoglycemia protocol and standardized correction insulin table were embedded in the order set. The

intervention was conducted over three time periods with slight changes each time. The percent of patients who suffered one or more hypoglycemic events over the course of their inpatient stay was 11.8 percent, 9.7 percent, and 9.2 percent, for time points (TP) 1, 2, and 3, respectively. The rate ratio (RR) of patients suffering from a hypoglycemic event was significantly improved in the intervention time periods compared to baseline, with an RR of TP3:TP1=0.77 (confidence interval [CI], 0.65-0.92). TP3 to TP2 showed no statistically significant difference. Of the monitored patient days in the baseline, TP1, 3.8 percent contained a hypoglycemic value. With the introduction of the structured insulin orders, TP2 hypoglycemia decreased to 2.9 percent, and in TP3 it was 2.6 percent.[15]

8.1.3.2 Process Outcomes

Four of the studies measured whether or not the protocol could be easily administered by nurses.[4-7] In all four cases, the new protocol was acceptable to nurses and integrated into workflows. However, in two of the studies, the nurses found the new protocol to be more time consuming than the prior protocols.[5,6]

8.1.3.3 Summary of Evidence on Implementation

Most of the studies were small, and several used retrospective data as the comparison group. Most suffered from weak designs. Standard protocols included both electronic and paper versions. None of them used sliding-scale methods. Nurses found the standardized protocols to take more time. In some cases, they were more complicated than usual care yet could be integrated into the workflow, and nurses supported them.

8.1.3.4 Gaps and Future Directions

8.1.3.4.1 Gaps

Studies with stronger designs and larger sample sizes were more likely to show an effect in terms of reducing hypoglycemia.

8.1.3.4.2 Future Directions

The evidence that standardized inpatient protocols lead to reduced hypoglycemia is growing. However, larger prospective studies with more robust methods are still needed. Other areas of future research include examination of standardized protocols that include intravenous insulin protocols versus subcutaneous protocols. Similarly, for the future, standardized protocols that include real-time continuous glucose monitoring (CGM) may improve patient safety. Real-time CGM would provide frequent measurements of interstitial glucose levels, as well as direction and magnitude of glucose trends, and may have an advantage over point-of-care glucose testing in detecting and reducing the incidence of hypoglycemia in the hospital setting. A recent review has recommended against using CGM in adults in a hospital setting until more safety and efficacy data become available.[16]

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8.2 PSP2: Use of Teach-Back in Diabetes Medication Management

8.2.1 Practice Description

The teach-back method is also called "closing the loop" and can be effective in increasing patients' ability to retain knowledge that helps them manage health conditions.[1,2] Teach-back tests comprehension by asking patients to say in their own words what they understand the clinician has instructed them to do. Teach-back has been utilized with many different kinds of patients; we sought to find examples of using teach-back with diabetes patients to improve their self-care. A recent AHRQ publication, Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families, includes a section on the teach-back method.[3] It is important to note that teach-back can occur in multiple settings, but to be effective, the patient must have the cognitive ability to comprehend the information, the physical skills to successfully self-administer insulin and other diabetes medication, be able to perform self-monitoring of blood glucose, and have adequate oral intake. The setting for teach-back is typically an outpatient setting.

8.2.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "diabetes" or "diabetes mellitus" as well as "teach-back communication," "teach-back," "teach back," and other related terms. Articles included were published from 2008 to 2018. The initial search yielded 161 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 155 articles were screened for inclusion, and full-text articles were retrieved. Of those, four were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

8.2.3 Review of Evidence

Four studies that used the teach-back method for diabetes patients met the inclusion criteria for this review. Three were small studies with 12 to 171 subjects,[4-6] and one included 442 subjects.[7] Most studies were conducted in one or two provider organizations and consequently were difficult to generalize. Two studies measured clinical outcomes, and the others measured changes in knowledge. A main purpose of three of the studies was to assess the effectiveness of specific education methods in patient cohorts with low literacy. Below we review each of the four studies.

Coulter's (2018) study of 12 patients with type 2 diabetes in a rural clinic in Northern Illinois used a pre- and post-test design. Patients received standard teaching at baseline during face-to-face office visits, and the teach-back method was delivered via phone. Patients filled out surveys to assess their perceived understanding of diabetes management, patient actions that would help manage diabetes, and participant goals. The study found statistically significant decreases in hemoglobin A1C (HbA1c) cover

the 3-month study period. While the authors noted that patients improved their understanding of diabetes management, no data were provided on measures of understanding or statistical significance.[4]

Kandula et al. (2011) conducted two experiments with patients in a health center and academic medical center, both located in Chicago. In one experiment, 112 patients were tested before and after receiving diabetes education Module One, and tested again after receiving diabetes education Module Two. In the second experiment with 58 patients, a pre- and post-test were administered before and after Module One, and the patients discussed their answers with a provider and were allowed to correct them. Both groups were tested 2 weeks after the initial test. The teach-back method did not have a statistically significant effect on diabetes knowledge scores.[5]

Negarandeh et al. (2013) conducted a randomized control trial in Kurdistan with 45 type 2 diabetes patients in each of three arms: one that received usual care, one that received diabetes education with a pictorial representation, and one that received diabetes education with teach-back. The analysis of variance indicated that there were statistically significant differences between the three groups in terms of knowledge, adherence to medication, and adherence to dietary regimen in the followup measurement ($p<0.05$). Both the pictorial and teach-back groups had better self-reported medication and dietary adherence than the control group. There was no statistically significant difference in HbA1c outcome measures.[6]

The largest study we identified randomized patients from the Carilion Clinic Department of Family and Community Medicine in southwest Virginia into two groups. One group included 217 patients who viewed a 60- minute DVD on diabetes prevention and then received a teach-back telephone call, while 225 patients attended a 120-minute group seminar and then received a teach-back telephone call. DVD participants performed significantly better across teach-back questions, demonstrated comprehension in fewer teach-back rounds, and answered more questions correctly on the first try. Among participants with low health literacy (LHL), the differences between the DVD and class groups were not significant. The approximately 18 percent of DVD participants and 16 percent of class participants with LHL did not achieve the teach-back goal after the teach-back was completed.[7]

8.2.3.1 Clinical Outcomes

Two of the studies measured changes in HbA1c levels over the course of the education and teach-back periods. One included only 12 patients, but there was a positive and statistically significant change in the patients BGL before and after teach-back was applied.[4] A second study found no difference in HbA1c levels before and after the intervention.[6]

8.2.3.2 Process Outcomes

All four studies measured changes in knowledge, and all found an increase in knowledge. However, the knowledge change could be attributed to the teach-back method in only two of the studies.[4,7]

8.2.3.3 Economic Outcomes

None of the studies investigated economic costs or outcomes.

8.2.4 Gaps and Future Directions

The studies with diabetes patients using teach-back as a method to improve diabetes medication knowledge or HbA1c levels are limited, and the results are mixed. However, most of the studies suffer

from small numbers and weak study designs. Larger, more robust studies might be able to shed more light on this patient safety practice. Additionally, adaptations for health literacy and cultural and other social barriers need to be controlled for.

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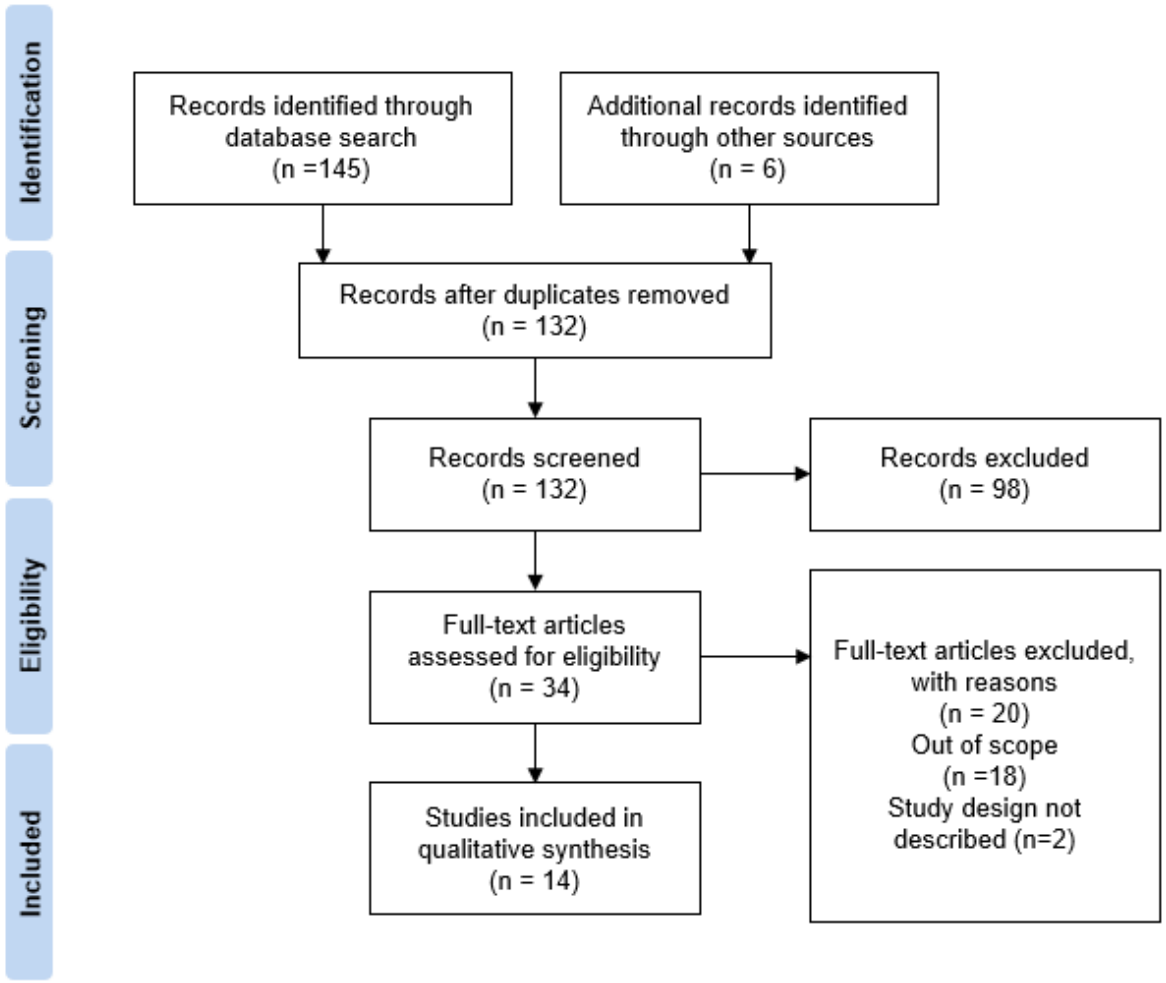
Conclusion and Comment

Diabetes is a growing chronic condition in all age groups, and strategies for improving medication management will have significant impact on mortality and morbidity. Using standardized insulin protocols to reduce hypoglycemia in the hospital and teach-back methods in other settings to improve the ability of diabetes patients to better understand and self-manage their own insulin and other antihyperglycemic medication needs are both patient safety practices that have potential. There is more and stronger evidence to support standardized hospital insulin protocols to prevent hypoglycemia than there is to support teach-back methods to improve medication management. However, better-designed studies on both patient safety practices are needed to establish a firm evidence base.

Larger, better-designed studies on reducing hypoglycemia would lead to stronger clinical evidence and also to improved implementation of feedback. Teach-back is in a formative stage in that enhanced definitions and typologies of teach-back methods are needed before it will be possible to collate the clinical evidence.

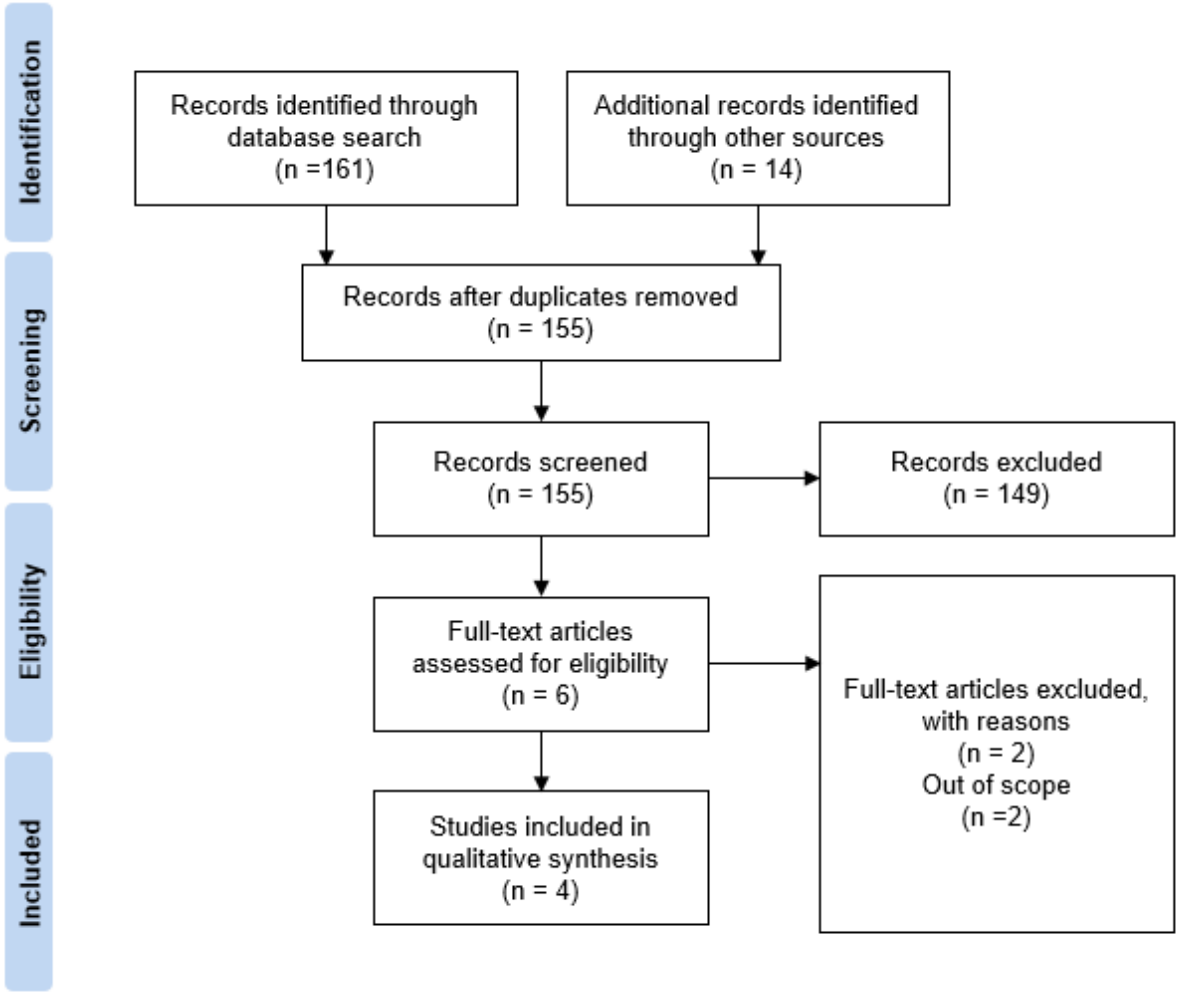
Appendix A. Harms Due to Diabetic Agents PRISMA Diagrams

Figure A.1: Harms Due to Diabetic Agents, Insulin Protocol—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.2: Harms Due to Diabetic Agents, Teach-Back—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Appendix B. Harms Dues to Diabetic Agents Evidence Tables

Table B.1: Harms Due to Diabetic Agents, Insulin Protocols–Single Studies

Note: Full references are available in the Section 8.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Cavalcanti et al., 2009[4]	Computer-assisted insulin protocol (CAIP) to maintain blood glucose levels between 100 and 130 mg/dL	The study compared three types of protocols used to obtain glucose control during an intensive care unit stay. The sample size was 165 patients.	Five intensive care units from five different Brazilian institutions	The mean of patients' median blood glucose was 125.0 (plus/minus 17.7) for CAIP, 127.1 (plus/minus 32.2) for Leuven, and 158.5 (plus/minus 49.6 mg/dL) for conventional treatment. The incidence of hypoglycemia was lower in the CAIP group than in the Leuven group, but higher in the CAIP than the conventional treatment. When episodes of hypoglycemia were considered in relation to the number of blood glucose (BG) measurements done, patients in CAIP protocol had a mean of 0.43 percent of glucose measurements below 40 mg/dL compared with 0.55 percent in Leuven group (P=04) and 0.03 percent in conventional group (P=.007).	Although the CAIP group when compared with Leuven had a lower risk of hypoglycemia, the risk was still considerable.	Acceptance of the insulin protocol by the nursing staff is critical for smooth implementation. The nurses who implemented the treatment judged it in terms of complexity and time spent to execute the protocol tasks: 11.7% found the CAIP difficult or very difficult as compared with 38.4% for Leuven protocol and 13.3% for conventional treatment.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Clergeu et al., 2017[5]	Use of a paper-based dynamic insulin infusion protocol (DP). The DP is a paper-based dynamic sliding-scale insulin protocol (SP).	One-year prospective study that compared two continuous intravenous insulin infusions—(1) dynamic insulin infusion protocol, (2) sliding scale static protocol—and the effects on glucose variability and hypoglycemia. One hundred thirty-one patients were included: SP (n=65), DP (n=66). Outcomes of interest included: mean BG (mmol/L), time spent in the target range (140-180 mg/dL to 7.7-9.9 mmol/L), time spent at greater and less than target range, and time before the first glucose value in the target range, low blood glucose (BG) episodes (<80 mg/dL-4.4 mmol/L), hypoglycemia (<60 mg/dL-3.3 mmol/L), and severe hypoglycemia (<40 mg/dL-2.2 mmol/L).	Intensive care unit (ICU) of French university hospital	Low BG (<4.4 mmol/L) and hypoglycemia (<3.3 mmol/L) were more frequent in the SP group than in the DP group. In cases of hypoglycemia, direct intravenous dextrose infusion (triggered by glucose values less than 3.3 and 4.1 mmol/L) occurred more frequently in the SP group than the DP group (0.17 plus/minus 0.49 and 0.03 plus/minus .17 dextrose injection per patient; P=0.03).	SP is not recommended because it was previously demonstrated to provide less control of parameters (blood glucose variability, hyperglycemia, and hypoglycemia).	Twenty-eight percent of nurses who completed the satisfaction survey felt that SP was suitable for ICU patients, compared with 66% of nurses who selected DP. The DP was also found to be more complex.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Donsa et al., 2017[11]	An algorithm-driven basal-bolus insulin regimen implemented through a computerized workflow and decision support system	A post-hoc analysis that used a before and after study design. The study included data from 70 type 2 diabetes patients. Diabetes management with a paper-based protocol for an algorithm-driven basal-bolus insulin therapy was compared to diabetes management with a computerized protocol for an algorithm-driven basal-bolus insulin therapy.	Division of Endocrinology and Metabolism at the Department of Internal Medicine at the Medical University of Graz, Austria.	Detection of Error Outcomes: Number of BG documentation errors and median absolute error were similar in both groups (p>0,2), 64.7% paper and 43.4% computer. Effect on Insulin Dose Outcomes: 11.1% of paper and 23.9% of computer of the BG documentation errors affected the results of bolus insulin dose calculations. Clinical Impact Outcomes: In the paper group, insulin dosing errors had a statistically significant influence on hypoglycemia. In the computer group, no statistically significant effects of insulin dosing errors on hypo or hyperglycemia were noted.	Not provide	Nurses performed 85% of all tasks and 80% of tasks including insulin dose calculations. The majority of errors affecting insulin dose calculations were from nurses when using the paper protocol. The relative frequency and absolute amount of insulin dosing errors were higher for physicians.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dortch et al., 2008[9]	Automated nurse-driven computer-based protocol	A retrospective investigation of patients treated with a manual, paper-based, nurse-driven, glycemic control protocol compared to an automated nurse-driven computer-based protocol. Five hundred fifty-two patients were included in the study.	A 31-bed integrated acute and subacute ICU	The computerized protocol group was associated with lower rates of hypoglycemia. The absolute rate of hypoglycemic glucose levels was significantly lower in the computerized protocol group than with the manual protocol: 23 of 10,0003 (0.2%) vs. 60 of 11,175 (0.5%). Proportionately fewer patients among the computerized protocol group experienced 2 or more hypoglycemic events: 3 patients of 243 (1.2%) vs. 13 of 309 (4.2%), p=.04.	Computerized protocol group experienced a greater rate of nosocomial infections.	After implementation of the computerized protocol, the proportion of study glucose values in the ideal range improved in all patients, regardless of the need for insulin. It also worked with nursing workflows, and overall compliance was good.	Not provided	None
Doyle et al., 2014[10]	Implementation of pre-printed insulin orders to standardize insulin-prescribing practices, promote use of basal and mealtime insulin, reduce reliance on sliding-scale insulin as the only form of diabetes treatment, and standardize hypoglycemic management.	Two pilot phases involving two inpatient units (cardiology and nephrology) and the implementation of pre-printed insulin orders.	Bilingual Canadian multicampus tertiary care hospital with more than 1,100 beds and 47,000 patient admissions yearly	The rate of hypoglycemia was reduced after the implementation of the intervention. The number of high BG days (2 or more documented BG readings over 11 mmol/L in 24 hours) did not improve on either unit.	Small increase in the number of days with 2 BG readings over 11 mmol/L was observed	Utilization of the order forms increased with additional education, development, and dissemination of decision-support tools and improved access to forms. It went from 11% in nephrology and 38% in cardiology to 68% and 74%, respectively.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Jakoby et al., 2012[6]	Transition order set	Prospective study with a retrospective control group	Nine-bed medical ICU at Hadassah Hospital in Jerusalem Israel.	Hypoglycemia in the protocol group was rare. Of the 9,893 blood glucose measurements, only 11 measurements (0.11%) in six patients were less than 70 mg/dL.	Not provided	Protocol was more time consuming for nurses, but nurses reported protocol was useful and an instructive tool for glucose control.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Joyner Blair et al., 2018[13]	Utilization of evidence-based diabetic ketoacidosis order set	Purpose of study: whether utilization of an evidence-based diabetic ketoacidosis order set vs. an individualized provider approach decreases resolution time and occurrences of hypoglycemia and improves clinical outcomes. Design: retrospective chart review of demographic and outcome variables for nonpregnant patients admitted and treated for diabetic ketoacidosis during two periods (2/2016 to 7/2016 and 8/2016 to 12/2016). A team of hospital experts developed, implemented, and evaluated the evidence-based order set. The sample included 150 nonpregnant adults, 19 years or older, with type 1 or type 2 diabetes presenting to the emergency department and diagnosed with diabetic ketoacidosis during the data collection periods.	Level II trauma cent/ED and/or critical care unit of a 500-bed acute care academic medical center in West Central Georgia	Length of stay, arrival to intravenous fluid time, intravenous insulin initiation to discontinuation time, arrival to subcutaneous insulin administration time, time from initial to sequential laboratory testing, use of basal, prandial, and correction insulin approach, and the frequency of hypoglycemia. None of the t-tests were significant.	Not provided	Team members were expected to implement and follow the approved order set, but utilization was not required and the ability of providers to follow and adhere to protocol was not assessed.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Khalaila et al., 2011[8]	Nurse-led self-adjusting, standardized intravenous insulin protocol	Prospective study with a retrospective control group. There were 96 patients in the prospective study and 153 patients in the retrospective control group	Nine-bed medical intensive care unit	Hypoglycemia in the protocol group was rare. Of the 9,893 blood glucose measurements, only 11 measurements (0.11%) in six patients were less than 70 mg/dL (hypoglycemic). The mean blood glucose levels in these measurements was 57.0 (standard deviation, 11.5 mg/dL). Hypoglycemic events occurred less often in the protocol group than in the control group (7/10,000 measurements vs. 83/10,000 measurements), and fewer patients experienced one or more episodes of hypoglycemia (6% vs 30%, P<.001).	Not provided	Studies on tight glycemic control (80-110 mg/dL) in intensive care unit patients have shown conflicting results, with both improved outcomes and increased morbidity and mortality reported.	High	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Manders et al., 2016[14]	Nurse-driven diabetes in-hospital protocol (N-DIABIT)	Study population included adult patients with type 1 or type 2 diabetes admitted to 1 of the 11 participating wards at the hospital. Intervention group included 210 patients and the control group included 200 patients. Intervention group was exposed to the nurse-driven diabetes in-hospital protocol.	University Medical Centre in Amsterdam, Netherlands	In the total study population, no significant differences were found between the intervention group and control group in mean BG level, fasting BG level, the occurrence of severe hypoglycemia, consecutive hypoglycemia, or very severe hyperglycemia, and number of BG measurements.	Not provided	Nurses can successfully implement the protocol.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Perera et al., 2011[7]	Triple B (basal-bolus-booster [BBB]) subcutaneous insulin protocol	Study evaluated standardized subcutaneous insulin regimen throughout non-critical areas in hospital. Study included 57 patients who were recognized as significantly hyperglycemic. Results of study were compared with retrospective controls (n=45) treated with sliding-scale insulin.	Prince Alfred Hospital, Sydney, Australia	The mean BG level was lower in in the BBB group compare to the sliding-scale insulin group (11.7 plus/minus 2.6 vs. 13.6 plus/minus 2.4 mmol/L). The number of hyperglycemic episodes per patient was less with BBB (median 3 vs. 7). Patients who experienced hypoglycemic were less likely to have a repeat episode when managed using BBB compared to the sliding-scale insulin protocol (median 1 vs. 3). No severe hypoglycemic episode requiring intervention occurred while on the BBB protocol.	Not provided	Education about protocol was given to nursing and junior medical staff. Overall the protocol is user-friendly and can be implemented by staff who are not experts in managing diabetes. Staff was good at monitoring BGLs at scheduled times and administering basal/bolus insulin doses, but there was poor compliance with adding the booster dose insulin, especially with the bedtime booster dose.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Schroeder et al., 2012[3]	Intensive subcutaneous insulin protocol, which targeted fasting blood glucose of 110 mg/dL and postprandial glucose level of <180 mg/dL	All patients with previously diagnosed diabetes or suffering from recurrent hyperglycemia (2 or more measurements for blood glucose levels >180 mg/dL) who were admitted to the orthopedic surgery department via the emergency room were assigned to either ward A or ward B. Patients in ward A were treated with glycemic control intervention (n=35), and patients assigned to ward B were treated with standard sliding- scale insulin protocol (n=30). All patients had their blood glucose levels monitored four times a day.	Department of Orthopedic Surgery, Hebrew University Medical Center, Jerusalem Israel	No significant difference was noted in hypoglycemic rates between the two groups (p=0.6).	Protocol included staff training and the use of patient education from the diabetologist.	Low	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Maynard et al., 2009[15]	Structured subcutaneous insulin order sets and insulin management protocols	Prospective observational research in parallel with performance improvement efforts. Study population included all adult inpatients on non-critical care units with electronically reported point of care glucose testing. Sample size: 9,314 patients were included in the study, and of those 5,530 were included in the secondary analysis of glycemic control and hypoglycemia.	Four hundred-bed academic center	The percent of patients' days that was uncontrolled (> than or equal to 180 mg/dL) was reduced over the three time periods (37.8% vs. 33.9% vs. 30.1%, P<.005). Percent of patients with uncontrolled patient stays (mean glucose > than or equal to 180 mg/dL) was also reduced over the three time periods (41.5% vs. 36.7% vs. 34.2%). The percent of patients who suffered one or more hypoglycemic event over the course of their inpatient stay was 11.8%, 9.7%, and 9.2% for time points (TPs) 1, 2, and 3, respectively. The rate ratio (RR) of patients suffering from a hypoglycemic event was significantly improved in the intervention time periods compared to baseline with RR of TP3:TP1=0.77 (confidence interval, 0.65-0.92). TP3 to TP2 did not have statistical significance (<0.05).	Not provided	Fear of hypoglycemia is the most significant barrier to glycemic control efforts.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Schnipper et al., 2009[12]	Glycemic management protocol	Prospective before-after trial. Sixty-three patients for preintervention and 106 patients for postintervention.	Brigham and Women's Hospital	The mean percent of glucose readings between 60 and 180 mg/dL per patient was 59.1% for preintervention and 64.7% postintervention (=0.13). There was no significant difference in percent of patient days with any hypoglycemia or severe hypoglycemia. There were also no significant differences in the mean number of hypoglycemic events per patient day or severe hypoglycemic events per patient day.	Not provided	Protocols should promote the continuous use of intravenous insulin infusions or scheduled basal-bolus subcutaneous insulin regimens.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Wong et al., 2017[2]	Computerized provider order entry with integrated insulin order sets	An interrupted time series design with 2,217 pre-implementation patient encounters and 2,330 post-implementation patient encounters.	A large tertiary and quaternary facility with 550 inpatient beds; non intensive care. unit patients	Introduction of computerized provider order entry-integrated insulin order sets did not lead to significant change in glycemic control. With respect to hypoglycemia, on average 2% of blood glucose measurements were considered hypoglycemic in pre and post interventions. There was no significant change in glycemic control with the intervention. It did improve adherence to evidence-based practices via an increase in basal-bolus-correctional insulin ordering behavior.	Lack of change in overall glycemic outcomes was most likely attributable to low order set uptake of only 51.5%. Prior study in 2012 did show change in outcomes.	Low	Not provided	None

Table B.2: Harms Due to Diabetic Agents, Teach-Back–Single Studies

Note: Full references are available in the Section 8.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Coulter, 2018[4]	Educational intervention that uses the teach-back method to reduce HbA1c levels between baseline and 3 months among individuals receiving care for type 2 diabetes in a rural setting	Pre-test and post-test design. Data were collected over a 3-month period. Standard teaching was delivered at baseline during face-to-face office visits and intervention using a standardized survey, and teach- back method was delivered via phone dialogue. Dependent t-test compared the pre- and post-HbA1c mean scores. Patient sample, n=12.	Rural clinic in northern Illinois	The HbA1c levels decreased from pre-test (mean=9.26%, standard deviation=1.46) to post-test (mean=8.26% standard deviation=1.56). The mean difference of 1.00167 was statistically significant at t(11)=2.099, p<.05.	Not provided	Behavior modification and lifestyle changes are the mainstay treatment for people with diabetes.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Kandula et al., 2011[5]	Teach-back	Experiment 1 (n=113) included a pre-test and post-test. The evaluation was the Short Test of Functional Health Literacy in Adults. Experiment 2 (n=58) included pre-test and post-test, then another post-test. At the end the Short Test of Functional Health Literacy was administered. Two-sided test with a p value of .05 or less was used to determine statistical significance. The diabetes knowledge score was the main outcome of interest.	Federally Qualified Health Center and academic medical center outpatient clinic in Chicago	Experiment 1: Pre-test: median knowledge score, 5 points; post-test: 12 (p<.001). At the 2-week follow-up the median score was 9 (p<.001). There were no significant differences by literacy level in median knowledge gained from the pre-test to the post-test Experiment 2: Pre-test: median score was 4 points, post-test: 11. After teach-back, score was 16. Teach-back did not improve knowledge retention at the 2-week follow-up period.	Not provided	An individual with more education and more health background knowledge may have an easier time integrating new information into longer term memory.	Low	Lack of control groups, small sample size, and limited generalizability because patients were recruited from two clinics
Negarandeh et al., 2013[6]	Teach-back	Randomized controlled trial compared the impact of the teach-back method and pictorial image on diabetes-specific knowledge Intervention (pictorial), sample=45. Intervention group with teach-back had 45 patients, and the control group receiving the usual diabetes intervention had 45 patients.	Hospital in Kurdistan	The mean literacy scores for pictorial image, teach-back, and control group were 34.84, 34.71, and 33.58. Significant difference between baseline and follow-up measurement scores demonstrating differences in participants' diabetes-specific knowledge to self- management and patients' adherence to dietary regimen.	Not provided	Tailored strategies are needed for people with low health literacy levels to enhance treatment adherence and improve diabetes control.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Goessl et al., 2019[7]	DVD diabetes prevention intervention followed by a teach-back call	The small-group diabetes prevention class (120 minutes) focused on prevention objectives and the creation of an individualized action plan. The class was followed by a teach back call. The DVD diabetes prevention intervention was a 60 minute DVD designed to cover the same content presented in the small-group diabetes prevention class. After watching the DVD, participants also received a teach-back call. Participants also completed the Newest Vital Sign tool to assess health literacy.	Outpatient	Eighteen percent of participants had a low health literacy score, and 82 percent of participants had an adequate or high level adequacy score. Participants with low health literacy were older and significantly more likely to be African American (30%). There were significant differences in overall score performances between the two groups (the higher, the better). DVD: 15.4 plus/minus 2.5; class: 14.8 plus/minus 2.6. (p<0.001).	Not provided	Need for interventions that include strategies to address participants with varied levels of health literacy. Even when information is presented with the use of clear communication strategies, it may not be enough to ensure information uptake. Improved comprehension is achieved with multiple rounds f teach-back.	Low	None

Appendix C. Harms Due to Diabetic Agents Search Terms

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study	Standard Insulin Protocol	((MH "Insulin/AD" OR "Insulin, Long-Acting/AD" OR "Insulin, Short-Acting/AD") AND (MH"Drug Therapy, Computer-Assisted" OR "Insulin Infusion Systems") OR (AB "Standardized Orders" OR "Standardized Order" OR "Clinical Algorithm" OR "Clinical Algorithms" OR "Standard Order Set" OR "Standard Order Sets" OR "Insulin Protocol" OR "Insulin Protocols" OR "Standard Insulin Protocol" OR "Standard Insulin Protocols" OR "Standing Order" OR "Standing Orders" OR "Standardized Insulin Protocol" OR "Standardized Insulin Infusion Protocol" OR "Treatment Protocol" OR "Order Set")) AND (MH Hypoglycemia) AND ((MH "Hospitals" OR "Inpatients" OR "Intensive Care Units" OR "Hospitalization") OR (AB Inpatient OR Hospital* OR "Acute Care" OR "Critical Care" OR "Intensive Care" OR "Emergency Department" OR "Emergency Room")) NOT ((MH "Hyperglycemia" OR "Fatty Liver" OR "Fatty Liver, Alcoholic" OR "Non-alcoholic Fatty Liver Disease" OR "Heart Transplantation") OR	(((MH "Insulin/AD" OR "Insulin, Long-Acting/AD" OR "Insulin, Short-Acting/AD") AND ((MH "Standing Orders" OR "Clinical Protocols" OR "Drug Therapy, Computer-Assisted" OR "Insulin Infusion Systems") OR (AB "Standardized Orders" OR "Standardized Order" OR "Clinical Algorithm" OR "Clinical Algorithms" OR "Standard Order Set" OR "Standard Order Sets" OR "Insulin Protocol" OR "Insulin Protocols" OR "Standard Insulin Protocol" OR "Standard Insulin Protocols" OR "Standing Order" OR "Standing Orders" OR "Standardized Insulin Protocol" OR "Standardized Insulin Infusion Protocol" OR "Treatment Protocol" OR "Order Set")) AND (MH Hypoglycemia) AND ((MH Hospitals OR Inpatients OR "Intensive Care Units" OR "Hospitalization) OR (AB Inpatient OR Hospital* OR "Acute Care" OR "Critical Care" OR "Intensive Care" OR "Emergency Department" OR "Emergency Room"))) NOT ((MH "Hyperglycemia" OR "Fatty Liver" OR "Fatty Liver, Alcoholic" OR "Non-alcoholic Fatty Liver Disease" OR "Heart Transplantation") OR	((("Insulin/Administration and Dosage"[MeSH] OR "Insulin, Long-Acting/Administration and Dosage"[MeSH] OR "Insulin, Short-Acting/Administration and Dosage"[MeSH]) AND ("Standing Orders"[MeSH] OR "Clinical Protocols"[MeSH] OR "Drug Therapy, Computer-Assisted"[MeSH] OR "Insulin Infusion Systems"[MeSH] OR "Standardized Orders"[tiab] OR "Standardized Order"[tiab] OR "Clinical Algorithm" [tiab] OR "Clinical Algorithms"[tiab] OR "Standard Order Set" [tiab] OR "Standard Order Sets"[tiab] OR "Insulin Protocol" [tiab] OR "Insulin Protocols"[tiab] OR "Standard Insulin Protocol"[tiab] OR "Standard Insulin Protocols"[tiab] OR "Standing Order" [tiab] OR "Standing Orders"[tiab] OR "Standardized Insulin Protocol"[tiab] OR "Standardized Insulin Infusion Protocol"[tiab] OR "Treatment Protocol"[tiab] OR "Order Set"[tiab]) (("Hypoglycemia"[MeSH]) AND ("Hospitals"[MeSH] OR "Inpatients"[MeSH] OR "Intensive Care Units"[MeSH] OR "Hospitalization"[MeSH] AND Inpatient[tiab] OR Hospital*[tiab] OR "Acute Care"[tiab] OR "Critical Care"[tiab] OR "Intensive Care"[tiab] OR "Emergency Department"[tiab] OR "Emergency Room"[tiab])) NOT ("Hyperglycemia"[MeSH] OR "Fatty Liver"[MeSH] OR "Fatty Liver, Alcoholic"[MeSH] OR "Non-alcoholic Fatty Liver Disease"[MeSH] OR "Heart

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
• Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review		(AB Hyperglycemia OR Hyperglycemic OR Neonatal OR "Fatty Liver" OR Heart OR Transplant OR "Heart Transplantation")))	(AB Hyperglycemia OR Hyperglycemic OR Neonatal OR "Fatty Liver" OR Heart OR Transplant OR "Heart Transplantation")))	Transplantation"[MeSH] OR Hyperglycemia[tiab] OR Hyperglycemic[tiab] OR Neonatal[tiab] OR "Fatty Liver"[tiab] OR Heart[tiab] OR Transplant[tiab] OR "Heart Transplantation"[tiab]))

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study	Teach-Back	((MH “Diabetes Mellitus” OR AB “Diabetes”) AND (AB “Teach-Back” OR “Teach Back” OR Teachback))	((MH “Diabetes Mellitus” OR AB “Diabetes”) AND (MH “Teach-Back Communication” OR AB “Teach-Back” OR “Teach Back” OR Teachback))	(“Diabetes Mellitus”[MeSH] OR “Diabetes”[tiab]) AND (“Teach-Back Communication”[MeSH] OR “Teach-Back”[tiab] OR “Teach Back”[tiab] OR Teachback[tiab]))

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
• Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review				

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed