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Clinical Practice Guideline

Management of Hyperglycemia in Hospitalized Adult Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline

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Abstract

Background: Adult patients with diabetes or newly recognized hyperglycemia account for over 30% of noncritically ill hospitalized patients. These patients are at increased risk for adverse clinical outcomes in the absence of defined approaches to glycemic management.

Objective: To review and update the 2012 Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline and to address emerging areas specific to the target population of noncritically ill hospitalized patients with diabetes or newly recognized or stress-induced hyperglycemia.

Methods: A multidisciplinary panel of clinician experts, together with a patient representative and experts in systematic reviews and guideline development, identified and prioritized 10 clinical questions related to inpatient management of patients with diabetes and/or hyperglycemia. The systematic reviews queried electronic databases for studies relevant to the selected questions. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to assess the certainty of evidence and make recommendations.

Results: The panel agreed on 10 frequently encountered areas specific to glycemic management in the hospital for which 15 recommendations were made. The guideline includes conditional recommendations for hospital use of emerging diabetes technologies including continuous glucose monitoring and insulin pump therapy; insulin regimens for prandial insulin dosing, glucocorticoid, and enteral nutrition–associated hyperglycemia; and use of noninsulin therapies. Recommendations were also made for issues relating to preoperative glycemic measures, appropriate use of correctional insulin, and diabetes self-management education in the hospital. A conditional recommendation was made against preoperative use of caloric beverages in patients with diabetes.

Conclusion: The recommendations are based on the consideration of important outcomes, practicality, feasibility, and patient values and preferences. These recommendations can be used to inform system improvement and clinical practice for this frequently encountered inpatient population.

Abbreviations: ARR, adjusted rate ratio; BBI, basal bolus insulin; BG, blood glucose; CHO, carbohydrate; CC, carbohydrate counting; CGC, Clinical Guidelines Committee; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DCESs, diabetes care and education specialists; DPP4i, dipeptidyl peptidase-4 inhibitor; DSMES, diabetes self-management education and support; EtD, evidence to decision; GC, glucocorticoid; GDP, Guideline Development Panel; HbA1c, hemoglobin A1c; ICR, insulin-to-carbohydrate ratio; IRR, incidence rate ratio; LOS, length of stay; MD, mean difference; MET, metformin; NPH, neutral protamine Hagedorn; POC-BG, point-of-care blood glucose; RCT, randomized controlled trial; RR, rate ratio; SC, subcutaneous; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SSI, sliding scale insulin; SU, sulfonylurea; T1D, type 1 diabetes; T2D, type 2 diabetes; TZD, thiazolidinediones.

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List of Recommendations

Question 1. *Should continuous glucose monitoring (with confirmatory point-of-care blood glucose monitoring for adjustments in insulin dosing) vs bedside capillary blood glucose monitoring be used for adults with diabetes hospitalized for noncritical illness?*

Recommendation 1.1

In adults with insulin-treated diabetes hospitalized for noncritical illness who are at high risk of hypoglycemia, we suggest the use of real-time continuous glucose monitoring (CGM) with confirmatory bedside point-of-care blood glucose (POC-BG) monitoring for adjustments in insulin dosing rather than point-of-care blood glucose (POC-BG) testing alone in hospital settings where resources and training are available. (2⊕⊕○○)

Remarks

- In hospitals where CGM is not available, monitoring of blood glucose (BG) levels can be continued with POC-BG testing as an alternative option.
- Patients identified as being at high risk for hypoglycemia include but are not limited to the following criteria: age ≥ 65 years; body mass index ≤ 27 kg/m^2; total daily dose of insulin ≥ 0.6 units/kg; history of stage ≥3 chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2), liver failure, cerebrovascular accident, active malignancy, pancreatic disorders, congestive heart failure, or infection; history of preadmission hypoglycemia or hypoglycemia occurring during a recent or current hospitalization; or impaired awareness of hypoglycemia.
- This recommendation does not apply to situations in which CGM may not be accurate, including in patients with extensive skin infections, hypoperfusion, or hypovolemia or those receiving vasoactive or pressor therapy. In addition, some medications can cause inaccurate continuous glucose monitoring readings (eg, acetaminophen > 4 g/day, dopamine, vitamin C, hydroxyurea).

Question 2. *Should neutral protamine Hagedorn insulin regimens vs basal bolus insulin regimens be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness receiving glucocorticoids?*

Recommendation 2.1

In adult patients who are hospitalized for noncritical illness and experience hyperglycemia while receiving glucocorticoids (GCs), we suggest glycemic management with either neutral protamine Hagedorn (NPH)-based insulin or basal bolus insulin (BBI) regimens. (2⊕⊕○○)

Remarks

- An NPH-based regimen may consist of NPH (with or without prandial insulin) given in divided doses depending on the timing, pharmacokinetics, and frequency of the specific GC being administered. NPH insulin may be added to BBI if the patient is already on this regimen.
- Management of patients with GC-associated hyperglycemia requires ongoing BG monitoring with adjustment of insulin dosing. All therapies require safeguards to avoid hypoglycemia when doses of GCs are tapered or abruptly discontinued.

Question 3. *Should continuous subcutaneous insulin infusion pump therapy be continued vs transitioning to scheduled subcutaneous insulin therapy for adults with diabetes on pump therapy who are hospitalized for noncritical illness?*

Recommendation 3.1

In adult patients using insulin pump therapy for diabetes management prior to admission for noncritical illness, we suggest that these patients continue insulin pump therapy rather than changing to subcutaneous (SC) basal bolus insulin (BBI) therapy in hospitals with access to personnel with expertise in insulin pump therapy. Where expertise is not accessible, we suggest that patients with anticipated hospital length of stay (LOS) of more than 1 to 2 days be transitioned to scheduled subcutaneous (SC) basal bolus insulin (BBI) before discontinuation of an insulin pump. (2⊕⊕○○)

Remarks

- Patients with an impaired level of consciousness, inability to appropriately adjust pump settings, critical illness (intensive care unit care), diabetic ketoacidosis, or hyperosmolar hyperglycemic state are not candidates for inpatient use of the insulin pump. Any change in a patient's condition that would interfere with their ability to safely self-manage the insulin pump device requires removal and transition to SC therapy (Table 3). Availability of supplies (provided by the patient or patient's family) over the course of the hospitalization is necessary. Adaptation of the basal rate may be needed at time of admission.
- Patients using hybrid closed-loop insulin pump therapy may be able to continue this at time of admission if they meet criteria similar to that for patients using insulin pump therapy independently of a CGM device as long as the CGM and insulin pump are able to function without interference of hospital care. If CGM fails or is removed from the patient, the insulin pump can be reverted to manual mode as long as basic criteria for pump use in hospital are still met.
- Hospitals need to have policies and procedures including patients' informed consent and standardized order sets in place as well as expertise from a healthcare professional who is knowledgeable in insulin pump therapy. These policies and procedures should include information for management of insulin pump devices during magnetic resonance imaging, computed tomography, or other imaging studies, in addition to any surgical procedures.

Question 4. Should inpatient diabetes education be provided vs not provided before discharge for adults with diabetes hospitalized for noncritical illness?

Recommendation 4.1

In adult patients with diabetes who are hospitalized for noncritical illness, we suggest providing inpatient diabetes education as part of a comprehensive diabetes discharge-planning process, rather than not providing inpatient diabetes education. (2⊕⊕⊕○)

Remarks

- Inpatient diabetes education is best provided by diabetes care and education specialists (DCES). Where availability of DCES is limited, DCES can serve as a resource to healthcare providers specifically tasked to provide inpatient diabetes education (eg, staff nurses, pharmacists, dieticians, etc.) by providing training and support.
- Ideally, the DCES should be Certified Diabetes Care and Education Specialists and/or hold the Board Certified-Advanced Diabetes Management credentials or be working toward 1 of these certifications.
- A comprehensive diabetes discharge-planning process includes education on and validation of diabetes survival skills, referral for outpatient diabetes self-management education and support, scheduling diabetes care follow-up appointments, and ensuring access to the medications and supplies required for diabetes self-management following discharge.
- In the case of limited personnel, healthcare providers providing diabetes education could prioritize education for patients at high risk for hospital readmission, those admitted for diabetes-related issues, and those newly diagnosed with diabetes or newly starting insulin.

Question 5. Should prespecified preoperative blood glucose and/or hemoglobin A1c levels be targeted for adults with diabetes undergoing elective surgical procedures?

Recommendation 5.1

For adult patients with diabetes undergoing elective surgical procedures, we suggest targeting preoperative hemoglobin A1c (HbA1c) levels < 8% (63.9 mmol/mol) and blood glucose (BG) concentrations 100 to 180 mg/dL (5.6 to10 mmol/L). (2⊕○○○)

Recommendation 5.2

For adult patients with diabetes undergoing elective surgical procedures, when targeting hemoglobin A1c (HbA1c) to < 8% (63.9 mmol/mol) is not feasible, we suggest targeting preoperative blood glucose (BG) concentrations 100 to 180 mg/dL (5.6 to 10 mmol/L). (2⊕○○○)

Remarks

- These recommendations apply only to patients who are scheduled for elective surgical procedures for whom it would be reasonable to allow time for implementation of therapies that target either a preoperative HbA1c or BG level.
- BG concentrations should be within the targeted range of 100 to 180 mg/dL (5.6 to 10 mmol/L) 1 to 4 hours prior to surgery.
- Factors that may affect HbA1c levels such as anemia, hemoglobinopathies, chronic renal failure, alcoholism, drugs, and large BG variations should be taken into account.

Question 6. Should basal or basal bolus insulin vs neutral protamine Hagedorn insulin be used for adults hospitalized for noncritical illness receiving enteral nutrition with diabetes-specific and nonspecific formulations?

Recommendation 6.1

In adult patients hospitalized for noncritical illness who are receiving enteral nutrition with diabetes-specific and nonspecific formulations, we suggest using neutral protamine Hagedorn (NPH)-based or basal bolus regimens. (2⊕○○○)

Question 7. Should noninsulin therapies [metformin, sulfonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter-2 inhibitors] vs scheduled insulin therapies be used for adults with hyperglycemia [with and without known type 2 diabetes] hospitalized for noncritical illness?

Recommendation 7.1

In most adult patients with hyperglycemia (with or without known type 2 diabetes (T2D)) hospitalized for a noncritical illness, we suggest that scheduled insulin therapy be used instead of noninsulin therapies for glycemic management. (2⊕⊕○○)

Remarks

- Dipeptidyl peptidase-4 inhibitors (DPP4is) may be appropriate in select patients with T2D (see Recommendation 7.2), including those with established noninsulin-requiring diabetes nearing hospital discharge.
- It may be reasonable to begin other noninsulin therapies in stable patients prior to discharge as a part of a coordinated transition plan.

Recommendation 7.2

In select adult patients with mild hyperglycemia and type 2 diabetes (T2D) hospitalized for a noncritical illness, we suggest using either dipeptidyl peptidase-4 inhibitor (DPP4i) with correction insulin or scheduled insulin therapy. (2⊕⊕○○)

Remarks

- Select patients include those with T2D that is moderately well-managed as reflected by a recent HbA1c < 7.5% (9.4 mmol/L), BG < 180 mg/dL (10 mmol/L), and, if on insulin therapy before hospitalization, to have a total daily insulin dose < 0.6 units/kg/day; this recommendation applies both to patients taking the DPP4i before admission and those who are not.

- Patients who develop persistently elevated BG [eg, >180 mg/dL (10 mmol/L)] on DPP4i therapy should be managed with scheduled insulin therapy; this recommendation does not apply to patients with type 1 diabetes (T1D) or other forms of insulin-dependent diabetes.
- As with all new therapies started in the hospital, a discussion with the patient about cost and overall acceptability is suggested if there are plans to continue the medication after discharge.

Question 8. Should caloric carbohydrate containing oral fluids vs noncaloric beverages be used preoperatively for adults with diabetes undergoing planned elective surgical procedures?

Recommendation 8.1

In adult patients with type 1 diabetes (T1D), type 2 diabetes (T2D), or other forms of diabetes undergoing surgical procedures, we suggest not administering carbohydrate (CHO) containing oral fluids preoperatively. (2⊕○○○)

Question 9. Should carbohydrate counting for prandial insulin dosing vs no carbohydrate counting (other insulin-dosing regimen) be used for adults with diabetes hospitalized for noncritical illness?

Recommendation 9.1

In adult patients with noninsulin-treated type 2 diabetes (T2D) hospitalized for noncritical illness who require prandial insulin therapy, we suggest not using carbohydrate counting (CC) for calculating prandial insulin doses. (2⊕○○○)

Recommendation 9.2

In adult patients with type 1 diabetes (T1D) or insulin-treated type 2 diabetes (T2D) hospitalized for noncritical illness, we suggest either carbohydrate counting (CC) or no carbohydrate counting (CC) with fixed prandial insulin dosing. (2⊕○○○)

Remarks

- Patients who perform CC in the outpatient setting, including those with insulin-treated T2D, may prefer to continue this method of calculating prandial insulin doses during hospitalization. An insulin-to-carbohydrate ratio (ICR) is used to calculate the prandial dose of insulin when using CC.
- A policy to guide CC for calculating prandial insulin dosing in the hospital is necessary for safe implementation, as is expertise from a healthcare professional knowledgeable in diabetes management.
- In hospitals where expertise, resources, and training are available, either CC or fixed prandial insulin dosing can be implemented.
- Adjustments to the ICR may be needed in the hospital setting to address the impact of illness or treatments on insulin requirements (eg, glucose-interfering medications, infection, surgery, insulin resistance).

Question 10. Should correctional insulin vs correctional insulin and scheduled insulin therapy (as basal bolus insulin or basal insulin with correctional insulin) be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness?

Recommendation 10.1

In adults with no prior history of diabetes hospitalized for noncritical illness with hyperglycemia [defined as blood glucose (BG) > 140 mg/dL (7.8 mmol/L)] during hospitalization, we suggest initial therapy with correctional insulin over scheduled insulin therapy (defined as basal or basal/bolus insulin) to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). For patients with persistent hyperglycemia [≥2 point-of-care blood glucose (POC-BG) measurements ≥ 180 mg/dL (≥10.0 mmol/L) in a 24-hour period on correctional insulin alone], we suggest the addition of scheduled insulin therapy. (2⊕OOO)

Recommendation 10.2

In adults with diabetes treated with diet or noninsulin diabetes medications prior to admission, we suggest initial therapy with correctional insulin or scheduled insulin therapy to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). For hospitalized adults started on correctional insulin alone and with persistent hyperglycemia [≥2 point-of-care blood glucose (POC-BG) measurements ≥ 180 mg/dL in a 24-hour period (≥10.0 mmol/L)], we suggest addition of scheduled insulin therapy. We suggest initiation of scheduled insulin therapy for patients with confirmed admission blood glucose (BG) ≥ 180 mg/dL (≥10.0 mmol/L). (2⊕OOO)

Recommendation 10.3

In adults with insulin-treated diabetes prior to admission who are hospitalized for noncritical illness, we recommend continuation of the scheduled insulin regimen modified for nutritional status and severity of illness to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). (1⊕⊕OO)

Remarks

Reductions in the dose of basal insulin (by 10% to 20%) at time of hospitalization may be required for patients on basal heavy insulin regimens (defined as doses of basal insulin ≥ 0.6 to 1.0 units/kg/day), in which basal insulin is being used inappropriately to cover meal-related excursions in BG.

Introduction

Adult patients with diabetes account for 25% of noncritically ill hospitalized patients (1, 2). Another 12% to 25% of hospitalized patients experience hyperglycemia, defined as blood glucose (BG) > 140 mg/dL (2-4). Both diabetes and hyperglycemia in the hospital are associated with prolonged hospital stay, increased incidence of complications, and disability after hospital discharge (5, 6). Glycemic management protocols that target recommended BG levels of 100 to 180 mg/dL in noncritically ill patients with diabetes have the potential to ameliorate these observed adverse outcomes (4, 7).

Following the publication of the 2012 Endocrine Society Clinical Guideline for Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Settings, several important studies have been published that address issues for

which scant data were previously available to support specific approaches to therapy. In addition, the emergence of continuous glucose monitoring (CGM) as the standard of care for outpatients with insulin-treated diabetes has raised questions regarding the ability to use this technology in hospitalized patient populations as a way of facilitating glycemic management and avoiding hypoglycemia.

This emergence of new data and new technologies guiding glycemic management in the hospital necessitated a review and update of the 2012 guideline (4). Recognizing the magnitude of the problem and the continued variability that persists in managing hospitalized patients with diabetes and/or newly recognized hyperglycemia, the Endocrine Society convened a Guideline Development Panel (GDP) comprised of healthcare professionals involved in inpatient diabetes care to review published data and make recommendations specific to frequently encountered glycemic management issues (1, 8, 9).

The purpose of this guideline is to address emerging areas that are specific to the target population of the noncritically ill hospitalized adult patient population with diabetes and/or with newly recognized or stress-induced hyperglycemia. This guideline is targeted to all healthcare professionals involved in the inpatient care of this group of patients. This includes healthcare providers and other key stakeholders including hospital administrators, healthcare payors, and regulators who are responsible for providing the resources that foster an environment focused on improved management of hyperglycemia in inpatient settings.

The Endocrine Society's guideline development process was recently refined to improve methodological rigor and enhance guideline trustworthiness (10). Because the Society's current guideline development process is substantially more labor- and resource-intensive than what was used for prior guidelines, the panel could not address all of the 2012 recommendations in this update. Instead, the GDP prioritized the 10 most important current clinical questions, which address the following areas: CGM, continuous subcutaneous insulin infusion (CSII) pump therapy, inpatient diabetes education, prespecified preoperative glycemic targets, use neutral protamine Hagedorn (NPH) insulin for glucocorticoid (GC) or enteral nutrition-associated hyperglycemia, noninsulin therapies, preoperative carbohydrate (CHO)-containing oral fluids, carbohydrate counting (CC) for prandial insulin dosing, and correctional and scheduled (basal or basal bolus) insulin therapies. Topics that were not addressed in this guideline but which may be addressed in a future update include glycemic targets, intra- and postoperative glycemic management, treatment of hyperglycemia in patients receiving total parenteral nutrition, and prevention and management of hypoglycemia.

Definition of Terms Used for This Clinical Guideline

1. Sliding scale insulin (SSI): reactive approach to insulin therapy in which a rapid-acting insulin analogue or regular insulin (Table 1) is administered for an elevated BG level often without regard to timing of food or meal ingestion, the presence or absence of preexisting insulin administration, or individualization of the patient's sensitivity to insulin. SSI doses range from 0 units to a prespecified maximum dose for BG levels below and above a defined level. BG measures for SSI are usually obtained by a hospital point-of-care blood glucose (POC-BG) monitoring device.
2. Correction insulin therapy: administration of a rapid-acting analogue or regular insulin (Table 1) based on POC-BG readings obtained prior to a meal in patients who are eating or at 4- to 6-hour intervals in patients who are nil per os. Correction insulin can be used alone in specific situations or in combination with scheduled insulin therapy.
3. Scheduled insulin therapy: a combination of an intermediate- or long-acting basal insulin (Table 1) with prandial administration of a rapid- or short-acting insulin prior to meals or as a combination of basal insulin with correction insulin administered every 4-6 hours based on POC-BG levels.
4. Basal bolus insulin (BBI) therapy: an approach to scheduled insulin therapy that combines

   A. basal insulin administered once or twice a day with
   B. prandial insulin in combination with correction insulin.

5. CC: method used to calculate prandial insulin doses based on the anticipated amount of CHO to be consumed as part of a meal. When using CC as scheduled prandial insulin therapy, insulin is dosed according to a prespecified ratio between the insulin dose and the grams of CHO consumed (eg, 1 unit of insulin for every 15 g of planned CHO consumption).

Recommendations

Question 1. Should CGM (with confirmatory POC-BG monitoring for adjustments in insulin dosing) vs bedside capillary BG monitoring be used for adults with diabetes hospitalized for noncritical illness?

Background

The increasing use of CGM devices in the outpatient setting has led to significant improvements in glycemic measures and

Table 1. Currently available injectable insulin preparations

Preparations	Currently available
Prandial or correctional insulin preparations	
Very rapid-acting insulin	Faster aspart Lispro–aabc
Rapid-acting insulins	Aspart Glulisine Lispro[a]
Short-acting insulin	Regular insulin
Basal insulin preparations	
Intermediate-acting insulin	NPH
Long-acting insulins	Glargine[b] Detemir Degludec[a]

[a]Available in U100 and U200 preparations.
[b]Available in U100 and U300 preparations.

variability. Emerging data have led to increasing interest in incorporating CGM in the hospital setting.

Recommendation 1.1

In adults with insulin-treated diabetes hospitalized for noncritical illness who are at high risk of hypoglycemia, we suggest the use of real-time CGM with confirmatory bedside POC-BG monitoring for adjustments in insulin dosing rather than POC-BG testing alone in hospital settings where resources and training are available. (2⊕⊕OO)

Remarks

- In hospitals where CGM is not available, monitoring of BG levels can be continued with POC-BG testing as an alternative option.
- Patients identified as being at high risk for hypoglycemia include but are not limited to the following criteria: age ≥ 65 years; body mass index ≤ 27 kg/m^2; total daily dose of insulin ≥ 0.6 units/kg; history of stage ≥3 chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2), liver failure, cerebrovascular accident, active malignancy, pancreatic disorders, congestive heart failure, or infection; history of preadmission hypoglycemia or hypoglycemia occurring during a recent or current hospitalization; or impaired awareness of hypoglycemia.
- This recommendation does not apply to situations in which CGM may not be accurate, including in patients with extensive skin infections, hypoperfusion, or hypovolemia or those receiving vasoactive or pressor therapy. In addition, some medications can cause inaccurate CGM readings (eg, acetaminophen > 4 g/day, dopamine, vitamin C, hydroxyurea).

Summary of evidence

The evidence-to-decision (EtD) framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/EploP2iQ86g.

Benefits and harms

The systematic review identified 5 randomized controlled trials (RCTs) and 4 non-RCTs to address this question (11). Although the evidence is uncertain from both RCTs and non-RCTs, using CGM may increase the detection of hypoglycemic events [non-RCT incident rate ratio (IRR) 3.48 (95% CI 1.99 to 6.11); very low level of certainty] than POC-BG testing alone (12-15). CGM also may increase the detection rate of patients with hypoglycemia defined as BG < 70 mg/dL [rate ratio (RR) 2.05 (95% CI 0.76 to 5.50)], corresponding to 23 fewer to 425 more patients per 1000, and as BG < 54 mg/dL [RR 1.86 (95% CI 0.36 to 9.74)], corresponding to 24 fewer to 330 more patients per 1000 identified as experiencing hypoglycemia (both with moderate level of certainty) (16). The evidence also suggests that CGM reduces the percentage of time with BG > 180 mg/dL [>10.0 mmol/L; mean difference (MD) −9.24% (95% CI −26.29% to 7.82%)] and > 250 mg/dL [13.9 mmol/L; MD −2.91% (95% CI −9.37% to 3.55%); both with low level of certainty]. Three RCTs demonstrated reductions in time spent in hypoglycemia [defined variably in the different studies as BG < 70 (<3.9 mmol/L) or < 54 mg/dL (3.0 mmol/L)] with CGM compared to POC-BG testing (13, 17, 18). Four RCTs demonstrated reductions in mean daily BG compared to POC-BG monitoring alone; the MD from 4 RCTs is −14.76 mg/dL [0.82 mmol/L (95% CI −25.39 to −4.12 mg/dL); moderate level of certainty] (12-14, 16-20). Similar findings for all outcomes were observed with observational (non-RCT) studies.

Other evidence to decision criteria and considerations

Panel members placed a high value on the moderate benefits that may occur with CGM use, including early detection and avoidance of hypoglycemia, and less on the trivial undesired effects. The majority of patients included in studies comparing CGM with POC-BG had type 2 diabetes (T2D). The baseline risk of hypoglycemia may be similar in insulin-treated patients with T2D to what occurs with type 1 diabetes (T1D), suggesting that hospitalized patients with T1D would derive similar benefits with CGM use (21). The acceptability of CGM depends in part on the moderate cost of this intervention. Hospitals will need to consider costs associated with CGM devices, training of personnel who will be using these devices, and increased costs that could occur with repeated sensor malfunctions or need for replacement in patients undergoing magnetic resonance imaging or other radiologic procedures (13, 15). However, potential cost savings are possible, attributable to reductions in nurse time for performing POC-BG testing, reducing hypoglycemic events, and lowering laboratory costs for verifying POC-BG measures (22). A recent study found that transmission of information from CGM devices to a nursing station with alerts for upward or downward trends in BG values could reduce time with glucose values out of desired range (17).

Many of the studies investigating CGM in the inpatient setting represent externally funded research studies, which could lead to concern about potential equity issues for hospitals without described resources and barriers to safe implementation of CGM. However, several reported studies included minority populations in underserved areas, many of whom had chronic kidney disease stages 3 to 5, demonstrating the feasibility of CGM in high-risk populations (15, 17). Overall, the panel determined that the feasibility of introducing CGM for noncritically ill patients at high risk for hypoglycemia will vary by institution, and if implemented, a protocol for guiding the process is necessary for success (Table 2) (23, 24).

The accuracy of CGM devices when compared to POC-BG measures in the inpatient setting has been demonstrated as moderate to good in several RCT and non-RCT studies in the inpatient setting (12, 19, 20). The lower accuracy of CGM for BG < 70 mg/dL (<3.9 mmol/L) raises some concern for overtreating low BG; however, the benefit of avoiding significant hypoglycemia outweighs this concern. The lower accuracy at higher BG levels supports recommendations to confirm results with POC-BG prior to making insulin adjustments. Currently, there are no available data that directly compare accuracy or clinical outcomes between the several different types of CGM devices in hospitalized patients. Calibration of any CGM device with POC-BG within the first 12 hours following initial placement of the sensor device is important for validating the reliability or accuracy of glucose readings obtained using CGM.

Justification for the recommendation

The panel agreed that based on low-certainty evidence for a higher detection rate of hypoglycemia, lower percentage time

Table 2. Resources required for safe implementation of continuous glucose monitoring in the noncritical care hospital setting

Engagement, training, and education of nursing personnel
Patient education regarding care of the device and how to respond to alarms for high or low BG
Purchase of equipment (eg, sensors, transmitters, receivers)
Expertise from healthcare professionals knowledgeable in this technology
Oversight and guidance for CGM use
Integration of CGM data with the hospital electronic medical record
Clarity of assigned responsibility for interpreting and acting on CGM data

Abbreviation: CGM, continuous glucose monitoring
Source: Galindo RJ et al. *J Diabetes Sci Technol*, 2020; (14)4. © Diabetes Technology Society (24).

spent with hypoglycemia and hyperglycemia, and lower mean BG (moderate level of certainty) with the use of CGM in patients at high risk for hypoglycemia, CGM use is preferred over POC-BG testing alone.

Comments

The panel acknowledges that an increasing number of patients are using their own CGM device in combination with a BBI regimen or insulin pump therapy at time of hospitalization. Many of these patients may wish to continue to use their own CGM device while in the hospital. Patients can continue to use their own CGM device following established hospital protocols as long as the device is able to function without interference or interfere with hospital care. If the CGM fails or is removed, patients can be transitioned to a hospital CGM device if available or to POC BG monitoring. For patients using sensor augmented insulin pump therapy, the pump device can be placed in manual mode in the event of failure or insufficient supplies to continue to use the patient-owned CGM.

Research considerations

The rapid increase in technology for glycemic management in patients with diabetes emphasizes the need for ongoing large-scale investigations into how use of these technologies translates from the outpatient to the inpatient settings. Proposed areas for research with CGM in the inpatient setting include:

1. Accuracy and safety of using these devices in surgical areas and critical care units.
2. Use of these devices in hospitalized patients with T1D.
3. Identification of patient populations who would be most likely to benefit from use of CGM, including patients requiring intravenous insulin infusions or GC therapy.
4. Evaluation of the impact of CGM education and use by patients at discharge on transitions of care and readmission rates.
5. Use of CGM devices in combination with hybrid sensor–augmented insulin pump devices.
6. Cost-effectiveness of CGM vs POC BG monitoring in the hospital setting.
7. Nurse satisfaction and level of confidence with CGM devices.

Question 2. Should NPH insulin regimens vs BBI regimens be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness receiving GCs?

Background

Hyperglycemia occurs in 56% to 86% of hospitalized patients receiving supraphysiologic doses of GCs (25, 26). GC-associated hyperglycemia, independent of preexisting diabetes, is associated with increased risk of mortality, cardiovascular events, and infections (27). The optimal insulin regimen for preventing GC-associated hyperglycemia and maintaining glycemic measures in hospitalized patients is not known.

Recommendation 2.1

In adult patients who are hospitalized for noncritical illness and experience hyperglycemia while receiving GCs, we suggest glycemic management with either NPH-based insulin or BBI regimens. (2⊕⊕OO)

Remarks

- An NPH-based regimen may consist of NPH (with or without prandial insulin) given in divided doses depending on the timing, pharmacokinetics, and frequency of the specific GC being administered. NPH insulin may be added to BBI if the patient is already on this regimen.
- Management of patients with GC-associated hyperglycemia requires ongoing BG monitoring with adjustment of insulin dosing. All therapies require safeguards to avoid hypoglycemia when doses of GCs are tapered or abruptly discontinued.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/SiErNHqAS9M.

Benefits and harms

The systematic review identified 6 RCTs and 1 non-RCT to address this question (11). Much variability occurred among the studies regarding the insulin regimens used in both the NPH-based groups and the comparator groups. In the 3 RCTs involving 148 patients comparing NPH added to a BBI regimen with BBI alone (28-30), the mean daily BG was 40.6 mg/dL (2.3 mmol/L) lower in the NPH group (95% CI −75.1 to −6.0; very low certainty of evidence). Similarly, in a study comparing NPH added to home therapy vs home therapy alone (31), mean daily BG was 42.5 mg/dL (2.4 mmol/L) lower in the NPH group (95% CI −63.2 to −21.7; very low certainty of evidence). No differences were found in 2 other RCTs (19, 32)

or an observational (non-RCT) study (33) whose design involved comparing NPH administered with prandial bolus vs basal bolus therapy. One RCT (19) demonstrated more total hypoglycemic events with the NPH-based regimen; however, this study dosed NPH every 8 hours [RR 1.93 (95% CI 0.58 to 6.40); very low level of certainty]. No differences occurred in rates of hypoglycemia measured as the number of patients with an event or the number of events per patient in the 5 other studies that reported these data (all with very low certainty of evidence). In 2 RCTs (19, 31), no differences occurred in hospital length of stay (LOS) (very low certainty of evidence).

Other evidence to decision criteria and considerations

Panel members placed a high value on the importance of addressing GC-associated hyperglycemia and less on the type or complexity of the insulin regimen. The studies included in this analysis used doses of GCs ranging from 10 to 100 mg of prednisone equivalency administered with a frequency of 1 to 3 times a day. Approaches varied for both NPH and BBI dosing, which made direct comparisons between the studies difficult. The feasibility of implementing complex insulin regimens may be difficult for nursing personnel, placing additional burdens that have potential to affect patient safety (28). However, from a patient perspective, a once-daily morning NPH regimen may be easier to learn than multiple daily injections, particularly for patients who will be discharged home on GC therapy (34).

Patients receiving any type of supraphysiologic GC who are treated with a basal-bolus regimen require a higher percentage of nutritional insulin to achieve normoglycemia (35). However, although experts commonly recommend that pharmacodynamic profiles of insulin should be reconciled ("matched") with corresponding profile of GCs, this has not been well-studied in the literature.

Barriers to addressing GC-associated hyperglycemia may be bridged by establishing protocols and guidelines that outline best practices for achieving and maintaining glycemic control, such as administration of NPH at the same time as intermediate-acting GCs, such as prednisone or methylprednisolone (36-38). Establishing these protocols may incur additional costs associated with training of providers and nurses to use complex insulin regimens that require more intensive monitoring.

Justification for the recommendation

The panel based its recommendation on low-certainty evidence demonstrating similar glycemic outcomes for mean BG, hyperglycemia, hypoglycemia, and hospital LOS with NPH- and BBI-based regimens for patients with GC-associated hyperglycemia in the hospital. Therefore, the panel suggests either NPH- or BBI-based regimens for glycemic management of GC-associated hyperglycemia. Neither regimen demonstrated cost, feasibility, acceptability, or equity advantages.

Comments

- The purpose of this guideline was not to provide comprehensive strategies for selecting doses of insulin treatment of GC-induced hyperglycemia; however, the reader can refer to recently published review papers (39-41) for suggestions regarding insulin dosing adjustments for upward or downward titrations of GC therapy.
- An important consideration for selecting an NPH- or BBI-based regimen is a patient's nutrition status. The studies reviewed included only patients who were eating regular meals. Patients who were in a fasting state and those receiving total parenteral or enteral nutrition were excluded in these studies.
- If an NPH-based insulin regimen is used, nurses and patients need education on proper rolling of NPH vials or pens to ensure adequate mixing of this insulin suspension.

Research considerations

The frequent occurrence of GC-associated hyperglycemia in hospitalized patients emphasizes the need for further research to determine the best therapeutic approach. Proposed areas for future research include

1. Designing studies using targeted insulin therapy that matches pharmacokinetic profiles of specific GCs.
2. Developing protocols with demonstrated acceptability to nurses as well as safety and efficacy for patients.
3. Developing implementation strategies to ensure safe and effective protocol utilization.
4. Evaluating efficacy of hybrid closed-loop insulin delivery systems in management of GC-associated hyperglycemia.
5. Evaluating the efficacy of noninsulin agents for treatment of GC-associated hyperglycemia.

Question 3. Should CSII pump therapy be continued vs transitioning to scheduled subcutaneous (SC) insulin therapy for adults with diabetes on pump therapy who are hospitalized for noncritical illness?

Background

An increasing number of people with T1D (insulin-deficient diabetes mellitus), and more recently with T2D, are using insulin pump therapy, also known as CSII therapy. It is estimated that more than 400 000 people with T1D in the United States are using insulin pumps, which has resulted in an increase in the number of patients who are using these devices at the time of hospitalization.

Recommendation 3.1

In adult patients using insulin pump therapy for diabetes management prior to admission for noncritical illness, we suggest that these patients continue insulin pump therapy rather than changing to SC BBI therapy in hospitals with access to personnel with expertise in insulin pump therapy. Where expertise is not accessible, we suggest that patients with anticipated hospital LOS > 1 to 2 days be transitioned to scheduled SC BBI before discontinuation of an insulin pump. (2⊕⊕OO)

Remarks

- Patients with an impaired level of consciousness, inability to appropriately adjust pump settings, critical illness (intensive care unit), diabetic ketoacidosis, or hyperosmolar hyperglycemic state are not candidates for inpatient use of the insulin pump. Any change in

Table 3. Methodology for converting continuous subcutaneous insulin infusion to scheduled basal bolus insulin

	Dosing suggestions[a]	
	Basal insulin dose	**Prandial and/or correctional insulin dose[b]**
Basal rate settings on pump known	Refer to the pump's active basal profile to determine the 24-hour basal insulin dose. Administer this dose as glargine U100 insulin as a single daily dose or in equally divided doses administered every 12 hours.	For patients who perform CC at home, allow patients to continue using the settings provided in the pump's active insulin profile for prandial and correctional insulin dosing. For patients not using CC, use weight-based fixed premeal insulin doses (0.2 to 0.4 units/kg divided into 3 prandial insulin doses with correctional insulin administered for BG above target range. For patients who are not eating, hold prandial insulin and continue correctional insulin dosing.
Basal rate settings on pump not known	Calculate basal insulin dose of 0.2 to 0.4 units/kg per day administered as glargine U100 given as a single daily dose or in equally divided doses administered every 12 hours.	Use weight-based fixed premeal insulin doses (0.2 to 0.4 units/kg divided into 3 prandial insulin doses). Hold if patient is not eating.

Abbreviations: BG, blood glucose; CC, carbohydrate counting.
[a]Basal insulin should be administered 2 hours prior to discontinuation of insulin pump. Rapid-acting or regular insulin should be administered at least 30 minutes prior to discontinuation of an insulin pump.
[b]Correctional insulin dosing can be administered before meals in addition to prandial insulin for patients who are eating or every 4 to 6 hours in patients who are not eating. For patients with a known correction factor, correction insulin may be prescribed as either a correction factor calculated toward a glucose target or a correction scale that uses a correction factor for the interval.

a patient's condition that would interfere with their ability to safely self-manage the insulin pump device requires removal and transition to SC therapy (Table 3). Availability of supplies (provided by the patient or patient's family) over the course of the hospitalization is necessary. Adaptation of the basal rate might be needed at time of admission.

- Patients using hybrid closed-loop insulin pump therapy may be able to continue this at time of admission if they meet criteria similar to that for patients using insulin pump therapy independently of a CGM device as long as the CGM and insulin pump are able to function without interference with hospital care. If CGM fails or is removed from the patient, the insulin pump can be reverted to manual mode as long as basic criteria for pump use in hospital are still met.
- Hospitals need to have policies, procedures including patients' informed consent, and standardized order sets in place as well as expertise from a healthcare professional who is knowledgeable in insulin pump therapy. These policies and procedures should include information for management of insulin pump devices during magnetic resonance imaging, computed tomography, or other imaging studies, in addition to any surgical procedures.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/0WWdIMKqa78.

Benefits and harms

The systematic review identified 2 non-RCTs to address this question (11, 42, 43). These studies, performed predominantly in patients with T1D, suggest that in select patients insulin pump use is safe with no increased risk of hypoglycemia or diabetic ketoacidosis. The number of hypoglycemic or hyperglycemic events per patient may not be different between those continuing CSII compared and those discontinuing CSII during hospitalization (42, 43). One study showed a lower percentage of BG measurements < 40 mg/dL (2.2 mmol/L; 0.5% vs 1.0%), and BG measurements > 300 mg/dL (16.7 mmol/L), >350 mg/dL (19.4 mmol/L), and > 400 mg/dL (22.2 mmol/L; 11% vs 18%) in "pump on" vs "pump off' cases (43). Mean BG adjusted for hospital LOS was not different between the patients continuing pump therapy compared to those transitioned to scheduled insulin therapy (42, 43). Although these observational (non-RCT) studies included predominantly patients with T1D, the panel concurred that the evidence can be applied to patients with T2D or other forms of insulin-deficient diabetes who use insulin pump therapy prior to hospital admission.

Other evidence to decision criteria and considerations

The studies were performed in hospitals with expertise in the management and oversight of patients who continued to use insulin pump therapy in the hospital. The panel also acknowledges that many patients who use insulin pump therapy as outpatients may be more knowledgeable in the use of their devices than hospital healthcare providers.

Justification for the recommendation

The panel agreed that the evidence suggests little difference in benefits and harms of continued use of insulin pump therapy compared to SC injections in the hospital setting. Continued use of insulin pump therapy may be acceptable for patients who are able to self-manage these devices adequately, and a protocol needs to be in place guiding the inpatient use of this form of insulin delivery.

Research considerations

Proposed areas for future research include

1. Evaluating the safety, efficacy, and cost-effectiveness of continuing CSII compared to changing to SC BBI therapy in patients using insulin pump prior to admission.

2. Use of CGM devices in combination with hybrid sensor–augmented insulin pump devices.

Question 4. Should inpatient diabetes education be provided vs not provided before discharge for adults with diabetes hospitalized for noncritical illness?

Background

Diabetes Self-Management Education and Support (DSMES) provides people with diabetes the knowledge, skills, resources, and confidence to successfully self-manage their diabetes. The percentage of people receiving DSMES, however, is low (44). Although hospitalization is often considered a suboptimal environment for patient education, it is considered 1 of the 4 critical times that DSMES should be provided (44). Hospitalization represents an opportunity to begin DSMES for patients who have not received it in the past or to reinforce previously provided DSMES (44, 45).

Recommendation 4.1

In adult patients with diabetes who are hospitalized for noncritical illness, we suggest providing inpatient diabetes education as part of a comprehensive diabetes discharge-planning process, rather than not providing inpatient diabetes education. (2⊕⊕⊕O)

Remarks

- Inpatient diabetes education is best provided by diabetes care and education specialists (DCESs). Where availability of DCESs is limited, DCESs can serve as a resource to healthcare providers specifically tasked to provide inpatient diabetes education (eg, staff nurses, pharmacists, dieticians, etc.) by providing training and support.
- Ideally, the DCESs should be Certified Diabetes Care and Education Specialists and/or hold the Board Certified-Advanced Diabetes Management credentials or be working toward 1 of these certifications.
- A comprehensive diabetes discharge-planning process includes education on and validation of diabetes survival skills, referral for outpatient DSMES, scheduling diabetes care follow-up appointments, and ensuring access to the medications and supplies required for diabetes self-management following discharge.
- In the case of limited personnel, healthcare providers providing diabetes education could prioritize education for patients at high risk for hospital readmission, those admitted for diabetes-related issues, and those newly diagnosed with diabetes or newly starting insulin.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/IX6WasWxx-Q.

Benefits and harms

The systematic review identified 4 RCTs and 6 non-RCTs to address this question (11, 45-54). Evidence from RCTs shows that providing inpatient diabetes education as part of a comprehensive diabetes discharge-planning program likely reduces hemoglobin A1c (HbA1c) at 3 months by 1.25% (95% CI –2.08 to –0.42) and 6 months by 0.8% (95% CI –1.07 to –0.54) following discharge (moderate level of certainty) (46-48). In addition, evidence from 3 non-RCTs suggests a moderate benefit in readmission rates [RR 0.72 (95% CI: 0.60 to 0.88)] with an estimated 43 fewer hospital readmissions per 1000 patients (95% CI –61 to –18); very low level of certainty] when inpatient diabetes education was part of a comprehensive diabetes discharge-planning process (49-51). Inpatient diabetes education may increase patient satisfaction (45, 46) without increasing hospital LOS (49, 50, 53, 54). The studies did not identify any negative effects of inpatient diabetes education.

Other evidence to decision criteria and considerations

Panel members placed high value on the moderate benefits of improved HbA1c and reduced readmissions with inpatient diabetes education provided as part of a comprehensive diabetes discharge-planning process. Providing diabetes education during a hospital stay may help socioeconomically challenged patients who do not have access to this resource as outpatients and who typically have higher hospital readmission rates (51). The panel acknowledged that although it may not be feasible for all patients with diabetes in the hospital to receive diabetes education directly from a DCES, healthcare personnel providing diabetes education should optimally have a DCES as a readily available resource. It has been shown that formally trained diabetes resource nurses who have support from a DCES can decrease hospital readmission rates (49, 55). Additionally, in the setting of limited availability of educators, alternative approaches may be considered, including the use of tablets or other technologies to deliver standardized education to select patients (56), with the understanding that many patients may have difficulty navigating these devices independently due to physical limitations, lack of technology experience, or lack of interest in using technology (57).

Justification for the recommendation

The panel agreed that inpatient diabetes education likely lowers HbA1c postdischarge, may reduce hospital readmissions, may enhance patient satisfaction, and may improve health inequities for those who may not have access to outpatient education. Although inpatient diabetes education is associated with costs related to the employment and training of personnel, the panel agreed that, overall, the benefits may outweigh these costs.

Comments

- Diabetes survival skill education in the hospital includes an assessment of patient-specific needs and identification of barriers to learning such as disabilities, health literacy, and numeracy limitations. The training is then individualized to the patient, their family and/or caregivers. DSMES focuses on the Association of Diabetes Care & Education Specialists self-management model known as the ADCES7 Self-Care Behaviors (58). Although these behaviors provide the framework for optimal diabetes self-management in the outpatient setting, inpatient education focuses

on the basic education and skills needed for safe transition from hospital to home. Inpatient DSMES can be considered a part of the diabetes care and education continuum. At a minimum, survival skill education includes

- Teaching how to take/administer medications, including, but not limited to, insulin.
- BG monitoring including when to test and goals of treatment.
- Basic meal planning.
- Prevention, identification, and treatment of hypoglycemia and hyperglycemia.
- Who to contact for emergent questions or concerns following hospital discharge.

- Within the included studies, patient education was typically coupled with other interventions aimed at improving the transition of the patient from the inpatient to outpatient setting—for example, establishing follow-up diabetes care and education appointments, providing telephone follow-up following discharge, and facilitating patient access to the appropriate medications and supplies needed for diabetes self-management.

Research considerations

Proposed areas for future research include

1. Evaluating effectiveness of different models of education delivery (face-to-face, virtual visit, videos, interactive modules).
2. Identifying criteria for selecting high-risk patients who are given priority for inpatient education by a DCES.
3. Performing cost-benefit and cost-effective analyses (comparing salary of DCESs to reimbursement for pay for performance, value-based care, and cost of readmission).
4. Comparing impact of DCES- vs staff nurse–delivered diabetes education on patient outcomes and readmission rates.

Question 5. Should prespecified preoperative BG and/or HbA1c levels be targeted for adults with diabetes undergoing elective surgical procedures?

Background

Although it is commonly accepted that preoperative in addition to perioperative glycemic management affects surgery outcomes, it is still a matter of debate as to whether specifically defined preoperative HbA1c or BG concentrations should be recommended prior to elective surgical procedures.

Recommendations 5.1

For adult patients with diabetes undergoing elective surgical procedures, we suggest targeting preoperative HbA1c levels < 8% (63.9 mmol/mol) and BG concentrations 100 to 180 mg/dL (5.6 to 10 mmol/L). (2⊕OOO)

Recommendations 5.2

For adult patients with diabetes undergoing elective surgical procedures when targeting HbA1c to <8% (63.9 mmol/mol) is not feasible, we suggest targeting preoperative BG concentrations 100 to 180 mg/dL (5.6 to 10 mmol/L). (2⊕OOO)

Remarks

- These recommendations apply only to patients who are scheduled for elective surgical procedures for whom it would be reasonable to allow time for implementation of therapies that target either a preoperative HbA1c or BG level.
- BG concentrations should be within the targeted range of 100 to 180 mg/dL (5.6-10 mmol/L) 1 to 4 hours prior to surgery.
- Factors that may affect HbA1c levels such as anemia, hemoglobinopathies, chronic renal failure, alcoholism, drugs, and large BG variations should be taken into account.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/zu8Z1OQDk-k.

Benefits and harms

The systematic review identified 44 observational (non-RCT) studies to address this question (11). A minority of patients with T1D were included, a single study recruited only patients with T1D (59), and many studies did not specify the type of diabetes. The majority of studies were performed in patients undergoing cardiac and orthopedic surgery, but other surgeries were included. Studies also used different cutoff values for HbA1c and BG concentrations and different strategies and interventions for peri- and intraoperative glucose control, which are likely to have affected outcomes.

A meta-analysis of 11 non-RCTs that measured hospital LOS comparing patients with a preoperative HbA1c < 7% vs ≥ 7% (<53 mmol/mol vs ≥53 mmol/mol) reported a shorter LOS [MD –0.45 days (95% CI –0.89 to 0.00); very low level of certainty] (60-70).

In 10 non-RCTs, postoperative infections were less frequent in patients with a preoperative HbA1c < 7% vs ≥ 7% [<53 mmol/mol vs ≥53 mmol/mol; odds ratio 0.54 (95% CI 0.40 to 0.73); very low level of certainty] (60, 61, 66, 71-77). Similar findings were observed in 2 non-RCTs that compared patients with a preoperative HbA1c < 8% vs ≥ 8% [<63.9 mmol/mol vs ≥63.9 mmol/mol; odds ratio 0.83 (95% CI 0.15 to 4.63); very low level of certainty] (78, 79). One study reported a HbA1c ≥ 7.8% (61.7 mmol/mol) as the threshold above which a significantly higher rate of wound complications occurred (78). The incidence of postoperative infections may also be reduced in patients with better glycemic measures in studies using different HbA1c cutoff levels (<6.5% vs ≥6.5%, <7.5% vs ≥7.5%, and < 8% vs ≥8%; <48.6 mmol/mol vs ≥48.6 mmol/mol, <58.5 mmol/mol vs ≥58.5 mmol/mol, and < 63.9 mmol/mol vs ≥63.9 mmol/mol, respectively) (80-84). However, the need for reoperations was

higher in 6 studies that included patients with preoperative HbA1c < 7% vs ≥ 7% [<53 mmol/mol vs ≥53 mmol/mol; RR 1.40 (95% CI 1.03 to 1.92); very low level of certainty] (62, 65-67, 72, 85).

In comparing patients with a preoperative HbA1c level of < 7% vs ≥ 7% (<53 mmol/mol vs ≥53 mmol/mol), respiratory complications may be reduced [6 observational (non-RCT) studies: RR 0.88 (95% CI 0.63 to 1.23); very low level of certainty] (61, 64-66, 73, 85). Reductions in neurologic complications [11 observational (non-RCT) studies: RR 0.57 (95% CI 0.41 to 0.78); very low level of certainty] (60, 61, 64-68, 72, 86-88), postoperative renal failure [12 observational (non-RCT) studies: RR 0.83 (95% CI 0.59 to 1.17); very low level of certainty] (60, 61, 64, 66, 67, 69, 72, 73, 86, 88-90), and cardiac complications [14 observational (non-RCT) studies: RR 0.99 (95% CI 0.73 to 1.33); very low level of certainty] (60, 61, 64, 65, 67, 68, 72, 73, 85-87, 89, 91, 92) were also observed. Other studies using different HbA1c cutoff levels [from<6.5% (<48.6 mmol/mol) to <8% (<63.9 mmol/mol) and <10% (85.8 mmol/mol)] also observed an increased postoperative complication rate in patients with poorer glycemic measures (79, 88, 90).

Other evidence to decision criteria and considerations

Among the studies that evaluated the effect of preoperative BG concentrations on postoperative outcomes (83, 93-96), only 2 provided data on BG concentrations on the day of surgery (95, 96). Preoperative glycemic measures and presence of diabetes were significant determinants of total cost of hospital care (97). The effects of race and sex were evaluated in only 2 studies (90, 97) with neutral results. Nevertheless, the panel discussed that patients living in rural areas or who have low socioeconomic status may have less access to optimal diabetes care and be more likely to have higher HbA1c and BG measures, which could interfere with their ability to receive timely surgical interventions that may impact health-related quality of life. Acceptability and feasibility were not addressed specifically in any of the studies but may be comparable to the situation in all patients with diabetes or assumed to be even somewhat increased in motivated patients and their caregivers in advance of elective surgery.

Justification for the recommendations

The panel agreed that the evidence suggests that patients with better preoperative glucose management have better outcomes. While the majority of studies compared outcomes associated with HbA1c < 7% or ≥7 % (<53 mmol/mol vs ≥53 mmol/mol), the panel suggests a target HbA1c of >8 % (63.9 mmol/mol) as a feasible goal for identifying patients at higher risk for postoperative complications. In addition, although very limited data exist on the effect of preoperative BG levels on postoperative outcomes, the panel suggests a BG target 100 to 180 mg/dL (5.6 to 10 mmol/L) 1 to 4 hours preoperatively, which is also the recommended target for intra- and postoperative glycemic management.

Research considerations

Proposed areas for research regarding preoperative glucose management include

1. Evaluating the effect of preoperative fasting glucose concentration vs HbA1c on postoperative outcomes.
2. Evaluating the association between preoperative time in range (CGM sensor data) and postoperative outcomes.
3. Evaluating the effect of perioperative glucose control vs preoperative glucose control on postoperative outcomes.
4. Evaluating the effect of 2-day, 1-week, or 2-week period of strict glycemic control for patients with HbA1c ≥ 8% (63.9 mmol/mol) on postoperative outcomes.

Question 6. Should basal or BBI vs NPH insulin be used for adults hospitalized for noncritical illness receiving enteral nutrition with diabetes-specific and nonspecific formulations?

Background

Hyperglycemia frequently occurs in hospitalized patients receiving enteral nutrition and is associated with a higher risk of complications and mortality (4, 98-100). Effective management of hyperglycemia in patients on enteral nutrition decreases adverse outcomes but also increases the risk of hypoglycemia (4, 99). It has been proposed that NPH insulin, due to the shorter half-life and duration of action compared to long-acting insulin preparations, may be appropriate for patients on enteral nutrition. Basal insulins or BBI therapy is safe and effective in managing inpatient hyperglycemia in adults hospitalized for noncritical illness. However, an effective and safe insulin regimen to reduce hyperglycemia and avoid hypoglycemia in hospitalized patients receiving enteral nutrition therapy has not been established.

Recommendation 6.1

In adult patients hospitalized for noncritical illness who are receiving enteral nutrition with diabetes-specific and nonspecific formulations, we suggest using NPH-based or basal bolus regimens. (2⊕OOO)

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/Jjgoz8CiQVM.

Benefits and harms

The systematic review identified 2 systematic reviews, 1 RCT, and 3 non-RCTs that address this question (11, 98, 101-103). Studies found little to no difference in mean daily BG between basal or BBI vs NPH-based regimens with correctional (sliding scale) insulin. One observational (non-RCT) study found that the average hospital LOS may be reduced by 1.57 days with NPH regimens compared to basal bolus (95% CI –1.71 to 4.85), and another found that the number of hypoglycemic events may result in an increase of 41% with basal-bolus compared to 70/30-biphasic insulin [IRR 2.92 (95% CI 0.70 to 12.20)], but these results are uncertain. No studies reported outcomes related to nurse time and effort.

Other evidence to decision criteria and considerations

The panel was unable to identify any evidence for acceptability, equity, resources, or feasibility. However, the panel agreed that both regimens are likely acceptable, would require equivalent resources, and be feasible depending on the expertise in the hospital to provide either regimen. The panel agreed that the pharmacokinetics and pharmacodynamic

profile of the insulin regimen should be matched with the mode of the enteral nutrition delivery (continuous, bolus, cyclic, etc.) (104).

Justification for the recommendation

The panel agreed that based on the very low certainty evidence, no important differences were seen in the outcomes with either regimen. There are probably no advantages of either regimen related to cost, feasibility, acceptability, or equity, although no research evidence exists to support this.

Research considerations

Proposed areas of research include

1. Designing studies using targeted insulin therapy that matches glycemic profiles of the modes of enteral nutrition delivery (continuous, bolus, cyclic, etc.).
2. Evaluating noninsulin injectables and oral antihyperglycemic agents in patients receiving enteral nutrition.
3. Assessing the feasibility and efficacy of CGM devices combined with hybrid closed-loop insulin pump devices in patients receiving enteral nutrition.

7. *Should noninsulin therapies (metformin (MET), sulfonylureas (SUs), thiazolidinediones (TZDs), DPP4is, glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium-glucose cotransporter-2 inhibitors (SGLT2is)) vs scheduled insulin therapies be used for adults with hyperglycemia (with and without known T2D) hospitalized for noncritical illness?*

Background

Insulin therapy is the standard practice for management of patients in the hospital with hyperglycemia due to its effectiveness and flexible dosing. Insulin therapy also requires expertise on the part of healthcare personnel involved in the care of patients with diabetes or hyperglycemia to optimize effectiveness and minimize harm (eg, hypoglycemia). Given the increasing number of noninsulin therapies available for addressing glycemic management primarily in outpatients with T2D, alternative strategies have been proposed and investigated for the inpatient setting.

Recommendation 7.1

In most adult patients with hyperglycemia (with or without known T2D) hospitalized for a noncritical illness, we suggest that scheduled insulin therapy be used instead of noninsulin therapies for glycemic management. (2⊕⊕OO)

Remarks

- DPP4is may be appropriate in select patients with T2D (see Recommendation 7.2), including those with established noninsulin-requiring diabetes nearing hospital discharge.
- It may be reasonable to begin other noninsulin therapies in stable patients prior to discharge as a part of a coordinated transition plan.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/H1DpdlMZ-94.

Benefits and harms

The systematic review identified 5 RCTs that compared the effects of a noninsulin agent without scheduled insulin in comparison to an insulin-only approach (11, 105-109). All studies enrolled patients with established T2D. There were no RCTs in hospitalized patients comparing insulin therapy to MET, SUs, TZDs, or SGLT2is. Two RCTs comparing GLP-1RAs with insulin therapy in select patient populations found a small absolute reduction in risk of hypoglycemia [RR 0.09 (95% CI 0.01 to 0.66); adjusted RR (ARR) 100 fewer events per 1000 (95% CI −109 to −37); low-certainty evidence] and lower mean daily BG [15.1 mg/dL lower (95% CI −65.2 to 34.9 mg/dL); very low certainty]. These findings were outweighed by a nearly 6-fold increase in nausea and/or vomiting [RR 5.95 (95% CI 1.07 to 33.03); ARR 50 more per 1000 (95% CI 1 to 320); low certainty]. Several retrospective analyses identified SU use as a risk factor for hypoglycemia in the hospital, indicating more harm than benefit. Since interrupted nutrition and other hypoglycemia risk factors are common in hospitalized patients, SUs are generally not advisable for inpatient use. Theoretical concerns derived from the use of some noninsulin glucose-lowering therapies in the outpatient setting, including rare and known adverse events, were considered as being more likely to occur in the acute care setting. These include lactic acidosis (MET), euglycemic ketoacidosis, and acute kidney injury especially in the perioperative setting (SGLT2is) and acute heart failure (TZDs).

Other evidence to decision criteria and considerations

The panel placed a high value on glycemic outcomes (ie, reduced hyper- and hypoglycemia) and safety. The panel was unable to identify any evidence regarding cost-effectiveness, acceptability, feasibility, and healthcare equity. However, overall, the panel considered that the acceptability and feasibility of using noninsulin agents in patients without a defined insulin requirement (such as those with T1D) over insulin favorable. This consideration is based in part on the inherent complexity of insulin therapy compared with the ease of administration of noninsulin agents.

Justification for the recommendation

The panel agreed that there was very low level evidence to suggest the general use of noninsulin agents in hospitalized patients. In the case of GLP-1RAs and SUs, evidence suggested harm. Although the panel assumed some impact on health equity with the use of GLP-1RAs, other criteria were generally equivocal between noninsulin and insulin therapies.

Recommendation 7.2

In select adult patients with mild hyperglycemia and T2D hospitalized for a noncritical illness, we suggest using either DPP4i with correction insulin or scheduled insulin therapy. (2⊕⊕OO)

Remarks

- Select patients include those with T2D that is moderately well-managed as reflected by a recent HbA1c < 7.5% (9.4 mmol/L), BG < 180 mg/dL (10 mmol/L), and, if on insulin therapy before hospitalization, to have a total daily insulin dose < 0.6 units/kg/day; this recommendation applies both to patients taking the DPP4i before admission and those who are not.
- Patients who develop persistently elevated BG [eg, >180 mg/dL (10 mmol/L)] on DPP4i therapy should be managed with scheduled insulin therapy; this recommendation does not apply to patients with T1D or other forms of insulin-dependent diabetes.
- As with all new therapies started in the hospital, a discussion with the patient about cost and overall acceptability is suggested if there are plans to continue the medication after discharge.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/H1DpdlMZ-94.

Benefits and harms

Based on a metanalysis of 3 RCTs performed in individuals with established T2D prior to hospitalization, DPP4i dosed once daily compared with BBI therapy may provide no benefit on glycemic management (11). In select patients, there may be a reduced insulin requirement and lower frequency of hypoglycemic events [RR 0.27 (95% CI 0.09 to 0.84); low certainty evidence]. The incidence of hypoglycemia was reduced with use of DPP4i in several trials; however, patients with impaired renal function and those considered to be at higher risk of hypoglycemia and hyperglycemia were excluded from enrollment. DPP4is are approved for use and considered safe in patients with any degree of kidney disease (note that dose adjustment for renal dysfunction is required for select DPP4is; eg, sitagliptin and alogliptin). Therefore, while patients with advanced kidney disease may benefit from reduced hypoglycemia, this remains unknown. Of importance, the metaanalysis excluded those studies in which the intervention was a combination of DPP4i and scheduled insulin. However, all RCTs except 1 comparing DPP4i to BBI allowed the use of correction insulin for intermittent hyperglycemia. Finally, all RCTs included criteria for conversion to scheduled insulin therapy in the case of persistent hyperglycemia.

Other evidence to decision criteria and considerations

As noted in Recommendation 7.1, the panel found no additional evidence for cost-effectiveness or equity favoring either DPP4i or insulin.

Justification for the recommendation

The panel agreed that DPP4i dosed once daily compared with BBI therapy may provide no benefit on glycemic management. However, in select patients treated with a DPP4i, there may be reduced insulin requirements and lower frequency of hypoglycemic events. Due to uncertainty of the difference in effects, cost, acceptability, and feasibility between DPP4is and insulin therapy, the panel made a conditional recommendation for using either DPP4is or insulin therapy in select adults requiring management of hyperglycemia. The panel determined that the recommendation would not apply to patients with T1D or with significant risk of hyperglycemia.

Research considerations

Future trials of noninsulin therapies for use in hospitalized patients with hyperglycemia should include strictly defined patient groups with clear and generalizable protocols. Proposed areas for research on noninsulin therapies to manage hyperglycemia in the hospital include

1. Comparing continuation vs discontinuation of a noninsulin therapy in medical or surgical patients who were already established on an agent prior to hospitalization and who do not have a contraindication.
2. Examining use of noninsulin therapies for nonglycemic indications (eg, SGLT2i or GLP-1 RA for cardiac disease) in a general inpatient diabetes population that includes prespecified outcomes related to glycemic measures.
3. Evaluating safety and effectiveness of restarting a noninsulin regimen prior to discharge from the hospital.
4. Assessing patient-, provider-, and nursing-reported outcome measures to assess preference and acceptability.

Question 8. Should caloric CHO-containing oral fluids vs noncaloric beverages be used preoperatively for adults with diabetes undergoing planned elective surgical procedures?

Background

To improve surgical outcomes, Enhanced Recovery after Surgery pathways have been rapidly accepted in many institutions. This multipronged approach includes more than 20 elements, such as the management of fluids, pain, and early mobilization. One of the components has been to optimize perioperative nutrition with administration of CHO-containing beverages within a few hours before surgery. This practice is based on a hypothesis that the insulin resistance and muscle catabolism induced by surgical stress can be dampened by preoperative oral CHO administration. The potential benefits, such as decreased insulin resistance, would not be expected in patients with diabetes who have insulin resistance and/or insulinopenia. There are also potential harms associated with administration of CHO-containing beverages to patients with diabetes, such as hyperglycemia with potential cancellation of scheduled procedures. In the majority of published studies, patients with diabetes were specifically excluded. Nevertheless, the practice of preoperative oral CHO administration is often used in patients with diabetes.

Recommendation 8.1

In adult patients with T1D, T2D, and other forms of diabetes undergoing surgical procedures, we suggest not administering CHO-containing oral fluids preoperatively. (2⊕OOO)

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/BzXkdFhGCw4.

Benefits and harms

The systematic review identified 1 RCT and 2 non-RCTs to address this question in patients with diabetes (11, 110-112). With low to very low certainty, evidence suggests little to no differences in hypoglycemia, mean daily BG, and hospital LOS with or without oral caloric fluids. Based on 1 study of 169 patients, the risk for hypoglycemia with CHO drinks may not be importantly increased [RR 1.33 (95% CI 0.42 to 4.21); very low level of certainty; 19 more per 1000 hypoglycemia events (95% CI −33 to 180)]. In another observational (non-RCT) study, mean daily BG may also not be importantly increased with a CHO drink [increase of 7.2 mg/dL (0.4 mmol/L) (95% CI −14.05 to 28.44)]. From these 2 studies, LOS was also not importantly changed [increase of 0.29 days with CHO drinks (95% CI −0.72 to 1.3)]. In 1 RCT (112) comparing preoperative administration of intravenous dextrose with oral carbohydrate ingestion, measures of patient satisfaction were higher [MD 5.0 (95% CI 0.85 to 9.15)] in the latter group (low level of certainty).

Other evidence to decision criteria and considerations

There are potential moderate costs for administering oral CHO preoperatively. There is the potential need for additional interventions for patients who require endocrine consultation for hyperglycemia that can occur following CHO administration. The guideline panel agreed that there is variability in this practice among surgeons, anesthesiologists, and endocrinologists, some of whom discourage this practice for patients with diabetes. From the patient's standpoint, they may enjoy having something to drink, and it would be acceptable to provide this in some circumstances. Finally, the lack of data and guidance has created differences in the acceptability of this practice among institutions.

Justification for the recommendation

The guideline panel agreed that there may be no benefit and instead potential harm with use of preoperative caloric oral fluids in patients with diabetes. Oral CHO administration may be harmful if it causes preoperative hyperglycemia in patients with all forms of diabetes. Given the uncertainty of benefit and potential for harm, the panel made a conditional recommendation suggesting against preoperative oral caloric fluids.

Research considerations

The areas for future research include

1. Performing randomized, prospective, controlled studies in patients with diabetes.
2. Enrolling patients with all types of diabetes and all levels of preoperative BG control.
3. Studying specific procedures separately (eg, colorectal surgery, orthopedic surgery, short and long procedures).
4. Controlling for postoperative dexamethasone used to control for nausea or pain.
5. Evaluating outcomes including pre- and postoperative glucose levels, elective surgery cancellations due to hyperglycemia, and benefits such as hospital LOS.

Question 9. Should carbohydrate counting for prandial insulin dosing vs no carbohydrate counting (other insulin-dosing regimen) be used for adults with diabetes hospitalized for noncritical illness?

Background

CC is a strategy used for calculating prandial doses of insulin often used by nonhospitalized patients with T1D or T2D receiving multiple daily insulin injections or insulin pump therapy (113). This method calculates doses of premeal rapid- or short-acting insulin based on the anticipated CHO content of the food to be consumed (114), potentially offering more flexibility in insulin dosing and improved postprandial glycemic excursions when compared to fixed premeal dosing (115). CC is used less frequently in the inpatient setting in part due to the few studies evaluating this approach in hospitalized patients.

Recommendation 9.1

In adult patients with noninsulin-treated T2D hospitalized for noncritical illness who require prandial insulin therapy, we suggest not using CC for calculating prandial insulin doses. (2⊕OOO)

Recommendation 9.2

In adult patients with T1D, insulin-treated T2D hospitalized for noncritical illness, we suggest either CC or no CC with fixed prandial insulin dosing. (2⊕OOO)

Remarks

- Patients who perform CC in the outpatient setting, including those with insulin-treated T2D, may prefer to continue this method of calculating prandial insulin doses during hospitalization. An insulin-to-carbohydrate ratio (ICR) is used to calculate the prandial dose of insulin when using CC.
- A policy to guide CC for calculating prandial insulin dosing in the hospital is necessary for safe implementation, as is expertise from a healthcare professional knowledgeable in diabetes management.
- In hospitals where expertise, resources, and training are available, either CC or fixed prandial insulin dosing can be implemented.
- Adjustments to the ICR may be needed in the hospital setting to address the impact of illness or treatments on insulin requirements (eg, glucose-interfering medications, infection, surgery, insulin resistance).

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/ycsH14NDvvo.

Benefits and harms

The systematic review identified 1 RCT and 2 non-RCTs addressing this question (11, 116-118). Most patients represented in these studies had T2D. Evidence from the RCT found that mean daily BG values may be lower by 8.3 mg/dL (0.5 mmol/L) with CC compared to fixed meal dosing (95% CI −22.76 to 6.16; very low certainty), while a combined analysis of the 2 observational (non-RCT) studies found little to no difference (very low certainty). Results from the RCT and non-RCT studies conflicted for hypoglycemia. The RCT found 158 more hypoglycemia events per 1000 patients with CC [95% CI −4 to 444; RR 1.71 (95% CI 0.98 to 3.00)] (116). One observational (non-RCT) study found fewer hypoglycemia events with CC [RR 0.04 (95% CI 0.00 to 0.72)]

(117), and 1 found little to no difference in the number of events with CC (118). All results are based on very low certainty evidence. Hospital LOS between CC and no CC may not differ (very low certainty) (116, 117). Only the RCT assessed patient satisfaction using the Diabetes Treatment Satisfaction Questionnaire for Inpatients, and it suggests no difference using or not using CC (low certainty).

Other evidence to decision criteria and considerations

Panel members placed high value on mean daily BG, hypoglycemic events, LOS, and measures of patient satisfaction. Panel members recognized the variability in the timing of when prandial insulin was administered within the available studies and the potential impact on BG levels. Barriers to appropriate timing of any prandial insulin dosing regimen in the hospital setting include the medical complexity of hospitalized patients, nurse-to-patient staffing ratios, the prevalence of patients requiring insulin, and variability in methods of meal delivery. Although most nurses trained in CC report being confident with calculating insulin doses, the opposite is true of administering doses on time (119).

Successful implementation of CC requires the prerequisite of nutrition and nursing education, development of menus that include information regarding the CHO content of foods, and development of protocols to guide this approach. Panel members acknowledge that CC requires expertise that has potential to increase costs to an institution. The panel agreed, however, that there is a distinction between implementing CC for all noncritically ill hospitalized patients requiring prandial insulin and patients who practice CC at home who may be comfortable continuing this practice in the hospital, provided their condition permits them to safely and independently continue to do so.

Justification for the recommendations

The panel agreed that based on the very low certainty evidence for mean daily BG, hypoglycemia, hospital LOS, patient satisfaction, and other EtD criteria that the balance did not favor either CC or other insulin-dosing regimens for prandial insulin dosing.

Research considerations

Proposed areas for future research include

1. Comparing CC to fixed mealtime doses in patients with T1D and T2D requiring a BBI regimen in the hospital.
2. Determining whether CC is more valuable for patients eating low vs high CHO meals (<50 g vs >50 g of CHO per meal), those who consume wide variations in CHO intake from meal to meal, or those on a liquid diet.
3. Comparing the effect of pre- vs postprandial insulin dosing (fixed and/or with CC) on BG management.
4. Examining patient preferences and satisfaction with CC vs fixed insulin dosing in hospitalized patients with T1D and T2D.

Question 10. Should correctional insulin vs correctional insulin and scheduled insulin therapy (as BBI or basal insulin with correctional insulin) be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness?

Background

The phrase "correctional insulin" is used in place of "SSI," the definition of which is not consistent between providers and researchers and has evolved over the decades. As originally used, SSI usually referred to a set amount of insulin administered for hyperglycemia without regard to the timing of the food, the presence or absence of preexisting insulin administration, or even individualization of the patient's sensitivity to insulin. With modern-day insulin regimens, correction-dose insulin or correctional insulin is usually provided before meals for above-target glycemia. Many of the studies refer to this definition of correctional insulin with the older term of SSI. The panel made the decision to define correctional insulin as rapid-acting analogue or regular insulin dosing based on preprandial BG readings in patients who are eating or at every 4- to 6-hour intervals in patients who are nil per os. Studies not clearly describing this process for correctional insulin were not included in the analysis.

Recommendation 10.1

In adults with no prior history of diabetes hospitalized for noncritical illness with hyperglycemia [defined as BG > 140 mg/dL (7.8 mmol/L)] during hospitalization, we suggest initial therapy with correctional insulin over scheduled insulin therapy (defined as basal or basal/bolus insulin) to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). For patients with persistent hyperglycemia [≥2 POC-BG measurements ≥ 180 mg/dL (≥10.0 mmol/L) in a 24-hour period on correctional insulin alone], we suggest the addition of scheduled insulin therapy. (2⊕OOO)

Recommendation 10.2

In adults with diabetes treated with diet or noninsulin diabetes medications prior to admission, we suggest initial therapy with correctional insulin or scheduled insulin therapy to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). For hospitalized adults started on correctional insulin alone and with persistent hyperglycemia [≥2 POC-BG measurements ≥ 180 mg/dL (≥10.0 mmol/L) in a 24-hour period], we suggest addition of scheduled insulin therapy. We suggest initiation of scheduled insulin therapy for patients with confirmed admission BG ≥ 180 mg/dL (≥10.0 mmol/L). (2⊕OOO)

Recommendation 10.3

In adults with insulin-treated diabetes prior to admission who are hospitalized for noncritical illness, we recommend continuation of the scheduled insulin regimen modified for nutritional status and severity of illness to maintain glucose targets in the range of 100 to 180 mg/dL (5.6 to 10.0 mmol/L). (1⊕⊕OO)

Remark

Reductions in the dose of basal insulin (by 10% to 20%) at time of hospitalization may be required for patients on basal heavy insulin regimens (defined as doses of basal insulin ≥ 0.6 to 1.0 units/kg/day), in which basal insulin is being used inappropriately to cover meal-related excursions in BG.

Summary of evidence

The EtD framework with a detailed summary of the evidence can be found online at https://guidelines.gradepro.org/profile/t_SV6L7iSYk.

Benefits and harms

The systematic review identified 9 studies (6 RCTs and 3 non-RCTs) to address this question (11). The populations studied, definitions, and study protocols were variable between studies. For example, insulin "rescue therapy" for BG values above 180 to 240 mg/dL (10.0 to 13.3 mmol/L) was used for some but not all studies. Correction insulin used alone likely results in a 16 mg/dL (0.9 mmol/L) increase in mean daily glucose over BBI (95% CI 10.62 to 21.42; moderate certainty) (103, 120-122) or BBI plus correctional insulin (95% CI 4.96 to 27.04; low certainty) (123, 124). Similar findings were observed with observational (non-RCT) studies (125-127). Correction insulin may, however, reduce the number of hypoglycemic events compared to BBI ± correctional insulin [IRR 0.23 (95% CI 0.09 to 0.57) from 2 RCTs; low certainty] or basal insulin + correctional insulin [MD 2.9 (95% CI −5.56 to −0.24); low certainty]. It may also reduce the number of patients experiencing hypoglycemia compared to BBI [IRR 0.38 (95% CI 0.10 to 1.38) from 2 RCTs; low certainty]. Two RCT studies showed hospital LOS may be slightly shortened with correctional insulin compared to basal plus correctional insulin by 0.5 days (95% CI −2.01 to 1.01; very low certainty of evidence).

The panel also investigated clinical outcomes in patients receiving basal plus correctional insulin vs BBI therapy. The evidence is very low certainty, but the number of patients experiencing hypoglycemia may be lower for patients receiving basal plus correctional insulin [IRR 0.79 (95% CI 0.43 to 1.43) from 2 RCTs], and the number of hypoglycemic events per patient may be lower [MD −0.5 (95% CI −2.97 to 1.97)]. However, the mean daily BG may be slightly higher in patients receiving basal plus correctional insulin compared to BBI (MD 7 mg/dL (0.4 mmol/L) (95% CI −1.61 to 15.61)]. In several studies, patients receiving correctional insulin alone had more frequent BG levels > 300 mg/dL (>16.7 mmol/L) and > 400 mg/dL (>22.2 mmol/L).

Other evidence to decision criteria and considerations

Little information was available regarding other EtD factors for acceptability or feasibility of the intervention.

Justification for the recommendations

Overall glycemic differences between the 2 strategies (correctional insulin vs scheduled insulin therapy) for patients with newly recognized hyperglycemia or with T2D may be small and outweighed by the undesired effects of hyperglycemia. The panel agreed that ensuring glycemic safety (avoiding excessive hyperglycemia or hypoglycemia) is more important than nurse time and effort or patient satisfaction. Therefore, when correctional insulin is used alone, and patients demonstrate persistent BG values ≥ 180 mg/dL (≥10.0 mmol/L), the recommendation is to use scheduled insulin therapy. Furthermore, due to large differences in patient insulin requirements among patients with T1D or T2D and patients with normal glucose tolerance preadmission, it was necessary to split the recommendations into 3, based on presence or absence of diabetes prior to admission and need for insulin therapy prior to admission. Some patients who are using basal insulin alone without prandial insulin preadmission may require this in the hospital.

Comments

- The panel had strong and not always consistent views given the frequency with which this topic occurs in the hospital.
- The nomenclature of insulin therapy has evolved further adding to the difficulty of this question; panel members were not consistent in basic definitions such as "BBI."
- There was general but not unanimous agreement that premix insulin preparations (eg, 70/30, 50/50, 75/25) not be considered as BBI.

Research considerations

The overall certainty of the evidence for this question is very low. There is a question as to the need for further studies to strengthen the evidence or with our growing understanding of physiologic insulin replacement if future studies should instead focus on types of insulin used for correctional insulin. Proposed areas for future research include

1. Comparing the efficacy of ultra-rapid–acting insulins with rapid-acting analogs as correctional insulin or part of scheduled insulin therapy.
2. Using CGM to better assess glycemic efficacy and safety of different insulin regimens in different groups of patients.
3. Using correctional insulin as part of a scheduled insulin regimen for patients with T1D using multiple daily injections or automated insulin delivery systems.

Methods of Development of Evidence-based Clinical Practice Guidelines

This guideline was developed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology (128). A detailed description of the Endocrine Society guideline development program can be found online at https://www.endocrine.org/clinical-practice-guidelines/methodology. This methodology includes the use of EtD frameworks to ensure all important criteria are considered when making recommendations (129, 130). The process was facilitated by the GRADEpro Guideline Development Tool (GRADEpro GDT) (131). The GDP consisted of 11 content experts representing the following specialties: endocrinology, internal medicine, primary care, nursing, pharmacy, and diabetes education. A patient representative was also included on the panel. Members were identified by the Endocrine Society Board of Directors and the Clinical Guidelines Committee (CGC) and were vetted according to the conflict-of-interest policy (132), which was adhered to throughout the guideline process to manage and mitigate conflicts of interest. Detailed disclosures of panel members and the management strategies implemented during the development process can be found in Appendix A. In addition, the group included a clinical practice guideline methodologist from the Mayo Evidence-Based Practice Center, who led the team that conducted the systematic reviews and meta-analyses, and a methodologist from the McMaster University GRADE Centre, who advised on methodology and moderated the application of the EtD framework and development of the recommendations.

Two GDP members were assigned to lead each guideline question. The questions addressed in this guideline were prioritized from an extensive list of potential questions through a survey and discussion; 10 questions were identified as most important. The Mayo Evidence-Based Practice Center conducted a systematic review for each question and produced GRADE evidence profiles that summarized the body of evidence for

Table 4. GRADE certainty of evidence classifications

Certainty of evidence	Interpretation
High ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate ⊕⊕⊕O	We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low ⊕⊕OO	Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very Low ⊕OOO	We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Source: Reprinted from Eds: Schünemann HJ, Brożek J, Guyatt, GH, Oxman AD. *GRADE handbook: Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach*. Updated October 2013. Accessed March 2, 2022. https://gdt.gradepro.org/app/handbook/handbook.html#h.9rdbelsnu4iy (135).

Table 5. GRADE strength of recommendation classifications and interpretation

Strength of recommendation	Criteria	Interpretation by patients	Interpretation by healthcare providers	Interpretation by policymakers
1—Strong recommendation for or against	Desirable consequences *clearly outweigh* the undesirable consequences in most settings (or vice versa)	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.	The recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guidelines could be used as a quality criterion or performance indicator.
2—Conditional recommendation for or against	Desirable consequences *probably outweigh* undesirable consequences in most settings (or vice versa)	The majority of individuals in this situation would want the suggested course of action, but many would not.	Clinicians should recognize that different choices will be appropriate for each individual and that clinicians must help each individual arrive at a management decision consistent with the individual's values and preferences. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values and preferences.	Policymaking will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision making is appropriate.

Source: Adapted from Schünemann HJ et al. *Blood Adv*, 2018; 2(22) © by The American Society of Hematology (136).

each question and the certainty of the evidence (11). The systematic searches for evidence were conducted on July 2020 and updated in December 2021. In parallel to the development of the evidence summaries, the GDP members searched for and summarized research evidence for other EtD criteria, such as patients' values and preferences, feasibility, acceptability, costs/resource use, cost-effectiveness, and health equity. Research evidence summaries noted in the EtD frameworks were compiled using standardized terminology templates for clarity and consistency (133). During a series of video conferences, the GDP judged the balance of benefits and harms, in addition to the other EtD criteria, to determine the direction and strength of the recommendation (Table 4 and 5) (133-136).

The draft recommendations were posted publicly for external peer review and were reviewed internally by Endocrine Society members, the Society's CGC, representatives of any cosponsoring organizations, a representative of the board of directors, and an expert reviewer. Revisions to the guideline were made based on submitted comments and approved by the CGC, the expert reviewer, and the board of directors. Finally, the guideline manuscript was reviewed before publication by the *Journal of Clinical Endocrinology and Metabolism*'s publisher's reviewers.

This guideline will be reviewed annually to assess the state of the evidence and determine if there are any developments that would warrant an update to the guideline.

Acknowledgments

The Endocrine Society and the GDP thank Christopher McCartney, MD, in his role as CGC chair for the contributions he made through his leadership and shared expertise. We are also grateful for the methodological support provided by the McMaster GRADE Centre in the Endocrine Society's efforts to enhance adherence to GRADE standards, including Holger Schünemann, MD, PhD; Thomas Piggott, MD, MSc; Nancy Santesso, RD, PhD; and Wojtek Wiercioch, MSc, PhD. We also thank M. Hassan Murad, MD, for his methodological support for this guideline and his team at the Mayo Evidence-based Practice Center, especially Mohamed Seisa, MD, for their contribution in conducting the evidence reviews for the guideline. The Endocrine Society and the GDP are grateful to the ACP for their appointment of a primary care representative to the panel. Lastly, we would like to thank the Diabetes Patient Advocacy Coalition for their help in identifying a patient representative to provide valuable contributions to this guideline.

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Disclaimer

The Endocrine Society's clinical practice guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The guidelines should not be considered as an all-encompassing approach to patient care and not inclusive of all proper approaches or methods, or exclusive of others. The guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgement of healthcare providers and each patient's individual circumstances. THE ENDOCRINE SOCIETY MAKES EVERY EFFORT TO PRESENT ACCURATE AND RELIABLE INFORMATION. THIS PUBLICATION IS PROVIDED "AS IS," AND THE SOCIETY MAKES NO WARRANTY, EXPRESS OR IMPLIED, REGARDING THE ACCURACY AND RELIABILITY OF THESE GUIDELINES AND SPECIFICALLY EXCLUDES ANY WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR USE OR PURPOSE, TITLE, OR NONINFRINGEMENT OF THIRD PARTY RIGHTS. THE SOCIETY, ITS OFFICERS, DIRECTORS, MEMBERS, EMPLOYEES, AND AGENTS SHALL NOT BE LIABLE FOR DIRECT, INDIRECT, SPECIAL, INCIDENTAL, OR CONSEQUENTIAL DAMAGES, INCLUDING THE INTERRUPTION OF BUSINESS, LOSS OF PROFITS, OR OTHER MONETARY DAMAGES, REGARDLESS OF WHETHER SUCH DAMAGES COULD HAVE BEEN FORESEEN OR PREVENTED, RELATED TO THIS PUBLICATION OR THE USE OF OR RELIANCE ON THE INFORMATION CONTAINED HEREIN.

Disclosures

See Appendix A for all author disclosures.

Data Availability

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Appendix A: Endocrine Society's Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting Continuous Glucose Monitoring

Guideline Development Panel Makeup, Roles, Conflicts, and Management Plans

Summary

Role	Name[a]	Relevant COI?[b]	Representative
Chair	Mary T. Korytkowski	No	
Co-Chair	Ranganath Muniyappa	No	
Members	Kellie Antinori-Lent	Yes	ADCES
	Amy C. Donihi	No	
	Andjela T. Drincic	No	
	Irl B. Hirsch	Yes	ADA
	Anton Luger	Yes	ESE
	Marie E. McDonnell	No	
	Craig Nielsen	No	ACP
	Claire Pegg	No	Patient representative
	Robert J. Rushakoff	No	
	Guillermo E. Umpierrez	Yes	AACE and DTS
Methodologists	M. Hassan Murad	No	
	Nancy Santesso	No	

Abbreviations: AACE, American Association of Clinical Endocrinologists; ACP, American College of Physicians; ADA, American Diabetes Association; ADCES, Association of Diabetes Care & Education Specialists; COI, conflict of interest; ESE, European Society of Endocrinology; DTS, Diabetes Technology Society; GDP, Guideline Development Panel.
[a]Total number of GDP members = 14.
[b]Percentage of total GDP members with relevant (or potentially relevant) conflicts of interest = 29%.

Individual Disclosures, Conflicts, and Management Strategies

Chairs

Chair: Mary T. Korytkowski, MD

University of Pittsburgh, Pittsburgh, PA, USA
Disclosures (2019-2022):

- American Board of Internal Medicine: Endocrinology, Diabetes, Metabolism Exam Committee and Board Member

- Journal of Clinical Endocrinology & Metabolism: Editorial Board Member
- American Diabetes Association: Speaker and Clinical Centers and Programs Interest Group Chair
- Department of Defense: IDSMB Chair
- Leona Helmsley Foundation: DSMB
- National Institutes of Health: grant support

Open Payments Database: https://openpaymentsdata.cms.gov/physician/266061

Assessment and Management

- No relevant conflicts in 12 months prior to selection.

Co-Chair: Ranganath Muniyappa, MD, PhD
National Institutes of Health, Bethesda, MD, USA
Disclosures (2019-2022): None.
Open Payments Database: No entries
Assessment and Management

- No relevant conflicts in 12 months prior to selection.

Guideline Development Panel Members

Kellie Antinori-Lent, RN, MSN, CDE
University of Pittsburgh Medical Center (UPMC) Shadyside Hospital, Pittsburgh, PA, USA
Expertise: Diabetes Clinical Nurse Specialist
Other: American Association of Diabetes Educators (AADE) representative
Disclosures (2019-2022):

- Association of Diabetes Care and Education Specialists (formerly AADE): president-elect (2019), president (2020), immediate past president (2021)
- BD (Becton, Dickinson and Company): Consultant. BD manufactures insulin needles, insulin syringes, and self-injecting systems.
- Valeritas: Trainer in 2020

Open Payments database entries: Not applicable (N/A)
Assessment and Management

- Regarding the relationship with BD, K.A-L. participated in a 1-day advisory panel on injection therapy in Fall 2018. This was a 1-time occurrence, and the monetary payment to K.A-L. was ~$1000. BD manufactures insulin needles, insulin syringes, self-injecting systems.
- There was some uncertainty regarding whether the relationship with BD should be considered relevant to the CPG. On the one hand, it is plausible that BD could have a stake in at least some of the CPG's recommendations (eg, a recommendation related to CSII vs insulin injections). On the other hand, this was a 1-time occurrence (ie, it is not an ongoing relationship), and many would consider the monetary payment to K.A-L. to be nominal/minimal. In the end, the CGC Chair decided that it would be most prudent to consider the relationship to be *potentially* relevant for the purposes of CPG conflict of interest (COI) accounting. (According to the CPG COI policy, a "relevant" COI is defined as a potential COI that could plausibly influence (or could have the appearance of influencing) the direction or strength of 1 or more guideline recommendations.) However, the CGC Chair judged that the risk of bias was minimal, and thus no COI management would be required.
- Regarding the relationship with Valeritas, K.A-L. served as a Clinical Training Specialist on an ad hoc basis. This relationship was deemed relevant to the CPG in that Valeritas manufactured insulin pumps. At the time, this relationship was identified, and appropriate management was planned around recommendations regarding pump technology. However, this relationship ended when the company went bankrupt in February 2020.
- No COI management required.

Amy C. Donihi, PharmD, BC-ADM
University of Pittsburgh School of Pharmacy, Pittsburgh, PA, USA
Expertise: Clinical pharmacy specialist
Disclosures (2019-2022): None
Open Payments database entries: N/A
Assessment and management

- No COI relevant to this CPG.
- No COI management required.

Andjela T. Drincic, MD
University of Nebraska Medical Center, Omaha, NE, USA
Expertise: Adult endocrinology
Disclosures (2019-2022):

- Corcept Therapeutics: Advisory Board (providing medical opinions related to treatment of Cushing's syndrome). A.T.D. received compensation for attending a single meeting in December 2018. Corcept does not manufacture pharmaceutical products relevant to inpatient diabetes care.
- WellCare Health Plans, Inc: Behavioral Health Provider Advisory Committee. Wellcare is a managed healthcare organization. In essence, the Behavioral Health Provider Advisory Committee is a Quality Assessment and Process Improvement Committee related to provision of diabetes care for the Wellcare ambulatory patient population. A.T.D. received compensation for attending quarterly meetings last year.
- REPOWER: Grant support in 2020
- Toyota: Grant support in 2020
- DARPA-NARI: Grant support in 2020
- Endocrine Society: Special Programs Committee Member
- Pituitary Society: Pituitary Centers of Excellence Committee Member
- Chiasma, Inc: Grant support and Advisory Board Member in 2021. Chiasma, Inc. is part of Amryt Pharma Group, which does not manufacture products relevant to inpatient diabetes care.
- OPKO Pharmaceuticals: Research funding in 2019. OPKO Pharmaceuticals does not manufacture pharmaceutical products relevant to inpatient diabetes care.

Open Payments Database: https://openpaymentsdata.cms.gov/physician/160937

Assessment and management

- No industry relationships relevant to this CPG.
- No COI management required.

Irl B. Hirsch, MD

University of Washington Diabetes Institute, Seattle, WA, USA

Expertise: Adult endocrinology

Other: American Diabetes Association (ADA) representative

Disclosures (2019-2022):

- Abbott Diabetes Care: Consulting. Abbott manufactures and markets glucose monitoring systems (FreeStyle, FreeStyle Libre) and nutrition products (eg, Ensure, Glucerna).
- Adocia: Consulting. Adocia is developing BioChaperone Lispro, BioChaperone Combo (lispro + glargine), HinsBet (BioChaperone human insulin), BioChaperone Glugacon, BioChaperone Glargine GLP-1 (dulaglutide/liraglutide), ADO09 pramlintide + insulin.
- Roche: Consulting. Roche markets glucose monitoring systems, namely Accu-Chek products (360 diabetes management software, Aviva Expert meter, Aviva meter, Aviva Nano meter, Combo system, Compact Plus system, Connect diabetes management system, FastClix lancing device, Lancing Devices for Professionals, Smart Pix device reader model 2, Softclix Lancet Device).
- BD (Becton, Dickinson and Company): Consulting. BD manufactures insulin needles, insulin syringes, and self-injecting systems.
- BigFoot Biomedical: Consulting. Bigfoot Biomedical is developing an automated, closed-loop insulin delivery system ("artificial pancreas").
- Medtronic Diabetes: Grant support. Medtronic manufactures and markets insulin pumps, continuous glucose monitors, and an automated, closed-loop insulin delivery system (MiniMed 670G).
- Insulet: Grant support. Insulet manufactures and markets the Omnipod insulin delivery system.
- UptoDate: Diabetes Editor
- Sanofi: Research funding. Sanofi manufactures and markets Adlyxin (lixisenatide), Lantus (glargine), Toujeo (glargine U-300), Apidra (glulisine), Admelog (lispro), Siliqua (glargine + lixisenatide), and Amaryl (glimepiride).
- National Institutes of Health: Research funding
- Helmsley Charitable Trust: Grant support

Open Payments Database: https://openpaymentsdata.cms.gov/physician/311840

Assessment and management

- I.B.H. has industry relationships relevant to this CPG.
- I.B.H. was allowed to participate in the Guideline Development Panel because he is a renowned expert in the area of diabetes care and since the ADA nominated him as their representative.
- Divestment: I.B.H. agreed to not speak on behalf of any pharmaceutical or technology companies until publication.
- COI management I.B.H.'s industry relationships are primarily relevant to glucose monitoring and diabetes technology (CGM, insulin pumps), standard insulin injection supplies, and the use of biochaperones for drug delivery. [According to the CPG COI policy, GDP members are prohibited from drafting guideline sections directly related to their COI, determining the strength and direction of a recommendation directly related to their COI, and voting on matters directly related to their COI.]
    - I.B.H. was not involved in systematic reviews for PICO questions directly related to the previously described considerations.
    - I.B.H. was not involved in determining the strength and direction of a recommendation directly related to the previously described considerations.
    - I.B.H. did not vote on matters directly related to the previously described considerations.
    - I.B.H. did not draft guideline sections directly related to the previously described considerations.
    - All GDP participants were made aware of I.B.H.'s COI related to the previously described considerations.

Anton Luger, MD

Medical University and General Hospital of Vienna, Vienna, Austria

Expertise: Adult endocrinology

Other: European Society of Endocrinology (ESE) representative

Disclosures (2019-2022):

- ESE: Focus Area Lead—Diabetes, Endocrinology, Metabolism
- ESE Membership Committee Co-chair
- ESE Executive Committee as representative of the ESE Council of Affiliated Societies
- ESE Policy and Advocacy Task Force 2020-2024
- ESE Nominations Committee 2020-2024
- ESE European Hormone and Metabolism Foundation 2020-2024
- European Union of Medical Specialists: President of the Section of Endocrinology, Diabetes and Metabolism (ended 2018)
- Austrian Society for Endocrinology: Executive Board member
- Boehringer Ingelheim: Advisory Board (not an ongoing activity, most recent occurrence in November 2018); speaker/lecturer in 2018. Boehringer Ingelheim manufactures and markets Jardiance (empafliglozin), Glyxambi (empafliglozin + linagliptin), Jentaduento (linagliptin + metformin), Synjarti (empagliflozin + metformin), and Tranenta (linagliptin).
- Novo Nordisk: Speaker/lecturer in 2018. Novo Nordisk manufactures and markets Ozempic (semaglutide), Fiasp (insulin aspart), Victoza (liraglutide), Tresiba (insulin degludec), Levemir (insulin detemir), Xultophy (insulin degludec + liraglutide), Novolog (insulin aspart), NovoLog Mix 70/30 (insulin aspart protamine and insulin aspart), Novolin 70/30 (human NPH + regular insulin), Novolin N (human NPH insulin), Novolin R (human regular insulin), Prandin (repaglinide), and GlucaGen HypoKit (glucagon).

- Novartis: Speaker/lecturer in 2018. Novartis manufactures and markets Starlix (nateglinide).
- Hexal: Speaker/lecturer in 2018. Hexal AG appears to be a division of Novartis.
- big5health: Honoraria and Expert Panel Member

Open Payments database entries: N/A
Assessment and management

- A.L. has industry relationships relevant to this CPG.
- A.L. was allowed to participate in the Guideline Development Panel because he is a renowned expert in the area of diabetes care and because the ESE nominated him as their representative.
- Divestment (According to the CPG COI policy, WC members must refrain from participating in the marketing activities or advisory boards of entities that may have a potential financial interest in the contents of the guideline; such divestment must be maintained at least until guideline publication):
  - A.L. has not served on any advisory board since November 2018, and he agreed to not serve on any advisory board until CPG publication.
  - A.L. has not provided a lecture for a pharmaceutical company since late 2018, and he agreed to not speak on behalf of any pharmaceutical or technology companies until CPG publication.
- COI management: A.L.'s industry relationships are primarily relevant to use/nonuse of SGLT2 inhibitors, use/nonuse of DPP4 inhibitors, use/nonuse of GLP1 receptor agonists, use/nonuse of meglitinides, and choice of specific insulin products (eg, analog vs nonanalog insulin for mealtime coverage, degludec vs other basal insulins). Therefore:
  - A.L. was not involved in determining the strength and direction of a recommendation directly related to the previously described considerations.
  - A.L. did not vote on matters directly related to the previously described considerations.
  - A.L. did not draft guideline sections directly related to the previously described considerations.
  - All GDP participants were made aware of A.L.'s recent COI related to the previously described considerations.

Marie E. McDonnell, MD
Brigham and Women's Hospital and Harvard Medical Center, Boston, MA, USA
Expertise: Adult endocrinology
Disclosures (2019-2022):

- American Association of Clinical Endocrinologists:
  - Associate Editor, Endocrine Practice
  - Coordinating committee for American Association of Clinical Endocrinologists (AACE) regional primary care day (2017)
- Eisai (Belviq):
  - Adjudicator for clinical trial CAMELLIA TIMI-61 ("Effect of Lorcaserin on Prevention and Remission of Type 2 Diabetes in Overweight and Obese Patients")
- National Institutes of Health: Grant support
- Alosa Health: Speaker. Alosa Health is a nonprofit that produces educational materials for healthcare professionals.
- Everlywell: Advisory Board. Everlywell does not manufacture products relevant to inpatient diabetes care.
- Abbott: Stock. Abbott develops, manufactures, and distributes CGM systems.
- Endocrine Society: Clinical Guidelines Committee Chair
- American Diabetes Association: Speaker

Open Payments Database: https://openpaymentsdata.cms.gov/physician/346015
Assessment and management

- No industry relationships relevant to this CPG in past 12 months.
- Regarding the stock in Abbott, the value of the shares was considered minimal and not likely to represent a potential source of bias. Regardless, M.E.M. sold these shares prior to work beginning on the guideline.
- No COI management required.

M. Hassan Murad, MD
Mayo Clinic Evidence-Based Practice Center: Rochester, MN, USA
Expertise: Clinical practice guideline methodology
Disclosures (2019-2022):

- Society for Vascular Surgery: Methodology Consultant
- American Society of Hematology: Methodology Consultant
- CHEST: Methodology Consultant
- World Health Organization: Methodology Consultant
- Evidence Foundation: Board Member

Open Payments Database: No entries
Assessment and management

- No industry relationships relevant to this CPG.
- No management required.

Claire Pegg
Patient representative
Disclosures (2019-2022):

- Diabetes Patient Advocacy Coalition: Advocate
- Sanofi: Travel reimbursement (Food and Drug Administration testimony regarding a research trial of sotagliflozin)

Open Payments database: N/A
Assessment and management

- The Endocrine Society guidelines staff contacted the Diabetes Patient Advocacy Coalition for assistance

in identifying a patient representative to serve on this Guideline Development Panel. The Diabetes Patient Advocacy Coalition nominated C.P.

- C.P. was in a clinical research trial for sotagliflozin (Sanofi)—the Barbara Davis Center was a participating site. Sanofi had contacted Barbara Davis Center looking for trial participants to talk to about their experience on the drug and to possibly be interviewed about it. C.P. agreed to be contacted. After a phone interview with a Sanofi representative, C.P. was asked if she would be interested in sharing her experience at the Food and Drug Administration Advisory Committee meeting. She agreed. Sanofi did not preview or edit her remarks in any way. Sanofi offered to pay her travel expenses, but no other payment was provided.
- The CPG Chairs and the CGC Chair agreed that C.P. disclosed relationship with Sanofi did not represent relevant COI for this CPG. C.P. agreed to do this as a way to be helpful. She did not receive any personal income from this activity, only travel expenses. This is not an ongoing activity or income source that C.P. would need to protect.
- No COI management was required.

Craig Nielsen, MD
Cleveland Clinic, Cleveland, OH, USA
Expertise: General Internal Medicine
Other: American College of Physicians representative
Disclosures (2019-2022): None
Open Payments Database: https://openpaymentsdata.cms.gov/physician/583645
Assessment and management

- No industry relationships relevant to this CPG.
- No management required.

Robert J. Rushakoff, MD
University of California San Francisco, San Francisco, CA, USA
Expertise: Adult endocrinology
Disclosures (2019-2022):

- ADA: Interest Group Advisor

Open Payments Database: https://openpaymentsdata.cms.gov/physician/106136
Assessment and management

- No industry relationships relevant to this CPG.
- No management required.

Nancy Santesso, MD
McMaster University, Ontario, Canada
Expertise: Clinical practice guideline methodology
Disclosures (2019-2022):

- World Health Organization: Primary/Coinvestigator

Open Payments Database: N/A
Assessment and management

- No industry relationships relevant to this CPG.
- No management required.

Guillermo E. Umpierrez, MD
Emory University, Atlanta, GA, USA
Expertise: Adult endocrinology
Other: AACE and Diabetes Technology Society (DTS) representative; Chair of prior CPG (2012)
Disclosures (2019-2022):

- ADA: National Board of Directors Member 2020-2022
- ADA: President, Medicine Science
- AACE: National Board of Directors Member, 2019-2021
- Sanofi: Grant support
- Novo Nordisk: Grant support
- Merck: Grant support. Merck manufactures and markets Janumet (sitagliptin + metformin), Janumet XR (sitagliptin + metformin ER), Januvia (sitagliptin), Segluromet (ertugliflozin + metformin), Steglatro (ertugliflozin), and Steglujan (ertugliflozin + sitagliptin).
- Insulcloud: Grant support. Insulcloud is a technology-based startup that developed Insulclock, a small electronic device that can be plugged into an insulin injection pen, tracking dates, times, and dosages.
- Dexcom: Hospital Clinical Evidence Virtual Advisory Board Meeting (no payment). This relationship occurred during the development of the guideline and was managed appropriately. It was not evaluated as a preexisting COI. Dexcom develops, manufactures, and distributes CGM systems.
- Dexcom: Grant support
- Abbott: Health Disparities Advisory Board Meeting (no payment). This relationship occurred during the development of the guideline and was managed appropriately. It was not evaluated as a preexisting COI.
- BMJ Open Diabetes Research & Care: Editor-in-Chief
- AstraZeneca: Grant support. AstraZeneca manufactures and markets Onglyza (saxagliptin) and Bydureon (exenatide).
- Bayer: Grant support. Bayer manufactures and markets the Breeze2 inpatient glucose meter.

Open Payments Database: https://openpaymentsdata.cms.gov/physician/908864
Assessment and management

- G.E.U. has industry relationships relevant to this CPG.
- G.E.U. was allowed to participate in the Guideline Development Panel because he was the Chair of the 2012 version of this guideline, he is a renowned expert in the area of diabetes care—inpatient diabetes management in particular—and because AACE and DTS nominated him as their representative.
- Divestment: G.E.U. was not to speak on behalf of any pharmaceutical or technology companies or participate on any advisory boards at least until CPG publication.
- COI management: G.E.U's industry relationships are primarily relevant to use/nonuse of SGLT2 inhibitors, use/nonuse of DPP4 inhibitors, use/nonuse of GLP1 receptor agonists, use/nonuse of SUs, use/nonuse of SGLT2 inhibitors SGLT2 inhibitors, use/nonuse of meglitinides, choice of specific insulin products (eg, analog vs nonanalog insulin for mealtime coverage, degludec vs other basal insulins), and the use of technology to convert an insulin pen to a smart pen. Therefore:

- G.E.U. was not involved in systematic reviews for PICO questions directly related to the previously described considerations.
- G.E.U. was not involved in determining the strength and direction of a recommendation directly related to the previously described considerations.
- G.E.U. did not vote on matters directly related to the previously described considerations.
- G.E.U. did not draft guideline sections directly related to the previously described considerations.
- All GDP participants were made aware of G.E.U.'s recent COI related to the previously described considerations.
- During the development of the guideline, it came to the attention of the CGC chair that G.E.U. participated on advisory boards for Dexcom and Abbott. Although no payment was accepted, it still was in violation of the COI policy and constituted a relationship that had to be managed. Since the advisory board meetings took place after the development of the recommendations and the main writing of the manuscript had occurred, it was the decision of the CGC chair that G.E.U. could remain on the panel and as an author of the guideline but that he could not participate in further editing of the recommendations or the guideline manuscript.

PICO Questions vis-a-vis Potential Guideline Development Panel Member Conflicts

PICO question	GDP members with potentially pertinent conflicts related to the PICO
1. Should continuous glucose monitoring (with confirmatory point of care blood glucose monitoring for adjustments in insulin dosing) vs bedside capillary blood glucose monitoring be used for adults with diabetes hospitalized for noncritical illness?	Hirsch
2. Should neutral protamine hagedorn insulin regimens vs basal bolus insulin regimens be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness receiving glucocorticoids?	Luger, Umpierrez
3. Should continuous subcutaneous insulin infusion pump therapy be continued vs transitioning to scheduled subcutaneous insulin therapy for adults with diabetes on pump therapy who are hospitalized for noncritical illness?	Hirsch
4. Should inpatient diabetes education be provided vs not provided before discharge for adults with diabetes hospitalized for noncritical illness?	None
5. Should prespecified preoperative blood glucose and/or hemoglobin A1c levels be targeted for adults with diabetes undergoing elective surgical procedures?	None
6. Should basal or basal bolus insulin vs neutral protamine hagedorn insulin be used for adults hospitalized for noncritical illness receiving enteral nutrition with diabetes-specific and nonspecific formulations?	Luger, Umpierrez
7. Should noninsulin therapies (metformin, sulfonylureas, thiazolidinediones, dipeptidylpeptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter-2 inhibitors) vs scheduled insulin therapies be used for adults with hyperglycemia (with and without known type 2 diabetes) hospitalized for noncritical illness?	Luger, Umpierrez
8. Should caloric carbohydrate–containing oral fluids vs noncaloric beverages be used preoperatively for adults with diabetes undergoing planned elective surgical procedures?	None
9. Should carbohydrate counting for prandial insulin dosing vs no carbohydrate counting (other insulin-dosing regimen) be used for adults with diabetes hospitalized for noncritical illness?	None
10. Should correctional insulin vs correctional insulin and scheduled insulin therapy (as basal bolus insulin or basal insulin with correctional insulin) be used for adults with hyperglycemia (with and without known diabetes) hospitalized for noncritical illness?	Luger, Umpierrez

Abbreviation: GDP, Guideline Development Panel.

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