# HOSPITAL MANAGEMENT OF DIABETES (A WALLIA AND JJ SELEY, SECTION EDITORS)



## CGM in the Hospital: Is It Ready for Prime Time?

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#### Abstract

**Purpose of Review** The use of continuous glucose monitoring (CGM) in the hospital setting is growing with more patients using these devices at home and when admitted to the hospital, especially during the COVID-19 pandemic.

**Recent Findings** Historically, most evidence for CGM use in the inpatient setting was limited to small studies utilizing outdated CGM technology and analyzing accuracy of sensor measurements. Previous studies have shown reduced sensor accuracy during extreme hypo- or hyperglycemia, rapid fluctuations of glucose, compression of the sensor itself, and in those who are critically ill. Studies that are more recent have shown CGM to have adequate accuracy and may be effective in reducing hypoglycemia in hospitalized patients; some studies have also showed improvement in time in target glycemic range. Furthermore, CGM may reduce nursing workload, cost of inpatient care, and use of personal protective equipment and face-to-face patient care especially for patients during the COVID-19 pandemic.

**Summary** This review will describe the evidence for use of CGM in hospitalized critically ill or non-critically ill patients, address accuracy and safety considerations, and outline paths for future implementation.

Keywords Continuous glucose monitoring · Diabetes · Inpatient glucose management

## Introduction

Diabetes is a burgeoning epidemic worldwide. In the USA, the prevalence has quadrupled between 1980 and 2020 with an estimated 21.9 million adults living with diabetes [1]. Hospitalizations among patients with diabetes account for 30% of the total medical cost of inpatient care with more than 7.8 million hospital discharges in 2017 in the USA [2].

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<sup>2</sup> The Ohio State University College of Nursing, Columbus, OH, USA Hypoglycemia, hyperglycemia, and glycemic variability in the hospital are associated with poor health outcomes including infection, acute renal failure, and death [3–7]. Traditional point of care (POC) capillary glucose monitoring measures glucose at one point in time often misses hypoglycemia [6, 8, 9], especially overnight or asymptomatic episodes, whereas continuous glucose monitoring (CGM) can help provide details of glucose continuously as well as velocity and direction of change over time. CGM devices measure glucose in interstitial fluid every 1-5 min depending on the device. Interstitial fluid correlates with plasma glucose, but at times of rapid glucose changes, there may be a 10–15 min lag time in respective interstitial glucose. Most CGM devices require insertion of an electrochemical enzymatic sensor subcutaneously by the patient every 7-14 days depending on the device. Benefits of CGM include being able to see the current sensor glucose as well as trend or direction and velocity of glucose change. Potential disadvantages of CGM use in hospitalized patients include the physiologic lag time between blood and interstitial glucose, added costs, and limited the current data that tighter glycemic control has favorable outcomes [10]. Hospitalized patients are much more likely to have conditions that would

be expected to impact sensor accuracy and it is important to establish the efficacy and safety of using such devices in the hospital in order to support more widespread approvals for use. Moreover, in previous studies, CGM systems were optimized for inpatient use [11]. Most current CGM devices are designed for home and patient use and may not be optimized for inpatient use; nevertheless, they are being repurposed for use in the COVID-19 pandemic so it is critical to understand how implementation would affect clinical workflows, nursing effort, and costs in the hospital setting. Table 1 displays the currently available subcutaneous CGM systems, which are commercially available in the USA [12–16]. The purpose of this review is to describe the latest and most salient evidence for use of CGM in the hospital, including an assessment of accuracy, efficacy, safety, and considerations for inpatient implementation, as well as to identify gaps in need of further study.

#### **Patients in Intensive Care Units**

Hyperglycemia is common in patients in the intensive care unit (ICU). The glucose range in ICU patients is recommended to be 140–180 mg/dl based on multi-center study data and until further data is obtained [4, 17]. Tighter glycemic targets (namely 80–110 mg/dl) have been associated with excess hypoglycemia and may increase mortality, although 110–140 mg/dl range may be reasonable for higher risk populations such as cardiothoracic surgery patients and at some institutions where it can be done safely. Glucoses higher than 180 mg/dl are to be avoided and have been associated with fluid and electrolyte shifts and impaired immune function. These glucose targets were based upon protocols that used intermittent POC or arterial blood gas testing. Thus, it is possible that CGM would be able to more safely support tighter glucose targets in the ICU without increasing the risk for hypoglycemia, though outcomes studies are needed to demonstrate this.

The major barriers to glycemic control in the ICU include risk for hypoglycemia, particularly in patients who cannot communicate symptoms, and rapid fluctuations in glucose levels due to changes in illness severity, nutrition, and therapies that can affect glucose. Another barrier is the need for frequent monitoring which may cause blood loss, pain, and increased nursing effort, particularly since intravenous insulin is the preferred treatment modality during critical illness and generally requires hourly glucose testing. The use of CGM could mitigate some of these barriers. However, it is important to understand the potential limitations of interstitial glucose monitoring in the ICU in terms of accuracy, efficacy, and safety. In critically ill patients, factors leading to inaccuracy of capillary blood glucose measurements include low perfusion index, hypotension, hypothermia, hypoxia, vasopressor use, and edema [18]. Inaccuracy has not been associated with severity of illness, sepsis, albumin, lactate, plasma arterial concentration of CO2, pH, or hematocrit [18].

Table 1 List of FDA-approved CGM systems with features, limitations, and interfering substances

| CGM system  | Key features   | Limitations  | Salicylic acid         |  |
|---|--|--|------------------------|--|
| Abbott Diabetes Care FreeStyle<br>Libre 14 day System [13]  | <ul> <li>a). No calibration required</li> <li>b). 1-h warm-up</li> <li>c). 14-day sensor wear</li> <li>d). Range 40–500 mg/dl</li> </ul>   | <ul><li>a). Requires scanning every 8 h to<br/>preserve data</li><li>b). No threshold or predictive alerts</li></ul>                                 |                        |  |
| Abbott Diabetes Care Freestyle<br>Libre 2 [12]  | <ul> <li>a). No calibration required</li> <li>b). 1-h warm-up</li> <li>c). 14-day sensor wear</li> <li>d). Range 40–400 mg/dl</li> <li>e). Optional alarms for hypoglycemia, hyperglycemia, and signal loss</li> </ul> | <ul><li>a). Requires scanning every 8 h to<br/>preserve data</li><li>b). No predictive alarms</li><li>c). Limited ability to transmit data</li></ul> | Ascorbic acid          |  |
| Dexcom G6 [14]  | <ul> <li>a). No calibration required</li> <li>b). 10-day sensor wear</li> <li>c). 40–400 mg/dl range</li> <li>d). Predictive alerts for hypogly-<br/>cemia</li> </ul>  | a). 2-h warm-up  | Hydroxyurea            |  |
| Medtronic MiniMed Guardian Sen-<br>sor [15]   | <ul><li>a). 7-day sensor wear</li><li>b). Predictive alerts</li><li>c). Range 40–400 mg/dl</li></ul>   | <ul><li>a). 2–4 calibrations/day required</li><li>b). 2-h warm up</li><li>c). 7-day sensor wear</li></ul>  | Acetaminophen          |  |
| nseonics Eversense [16]<br>a). 90–180 day sensor wear<br>b). Predictive hypo- and hyperglyco<br>mia alerts<br>c). Conditional MRI compatibility |  | <ul><li>a). Implantable</li><li>b). 2 calibrations/day required</li><li>c). 24-h warm-up</li></ul>   | Mannitol, tetracycline |  |

Dozens of studies have assessed the accuracy and reliability of CGM systems in ICU patients. An excellent summary of studies has been published previously [19•]. Most studies are small, utilize intravenous or subcutaneous sensors, and/ or have older technology. The largest study to date assessed the accuracy of an intravascular glucose monitor (OptiScanner 5000) in 243 ICU patients who required glucose monitoring [20]. In this study, accuracy was excellent, including mean absolute relative difference (MARD) 7.6% and 99.9% of paired glucose readings which were within zones A and B of the Clarke Error Grid. However, intravenous sensors are invasive, may be associated with complications such as thrombosis or infection, and are more cumbersome than noninvasive monitors. By comparison, the accuracy of the Freestyle Navigator (with a subcutaneous sensor) was assessed in another large study of 155 mixed ICU patients and reported a MARD of 13.3%, which was magnified during hypoglycemia or hyperglycemia, and 96.8% of values fell in zones A or B of the Clarke error grid [21]. The study protocol required 5 calibrations with arterial glucose values within the first 72-80 h of use. Nearly 25% of subjects in the study had < 95% real-time sensor glucose display with almost 50% having gaps of > 30 min of sensor glucose readings [20].

There are few randomized controlled trials demonstrating the efficacy and safety of CGM in ICU patients. A study [22] of 124 ventilated patients receiving IV insulin with an infusion protocol randomized 63 patients to real-time CGM with the Medtronic Guardian CGM yielding sensor glucose values every 5 min and the control group of 61 patients using standard of care with glucose measurements at least every 2 h. The Medtronic CGM system was calibrated four times daily with a POC glucose level. This study demonstrated that severe hypoglycemia (defined as < 40 mg/dl) was lower in the CGM group compared to the control group (1.6% vs 11.5%, p = 0.031), while glycemic control (namely average sensor glucose and time spent < 110 mg/dl) was not significantly different between groups [22]. In contrast, another randomized study [23] of 177 patients randomized to realtime CGM using the FreeStyle Navigator or blinded CGM control group reported no significant difference in severe glycemia or time in target range. However, there was a much lower incidence of hypoglycemia compared to the previous study, likely due to a higher target glucose range (90-160 mg/dl vs. 80-110 mg/dl) and the use of a computerized insulin infusion algorithm. In a randomized study [24] of 35 severely ill medical ICU patients, the GlucoDay CGM demonstrated acceptable accuracy (MARD 11.2%, 98.6% of values in zones A and B or the Clarke error grid Analysis), but similar mean glucose and % time in range as the control group. However, the device did not provide alerts for hypoglycemia or hyperglycemia, and CGM values were not used to make treatment decisions but to prompt an arterial glucose measure if the glucose rate of change exceeded 25 mg/dl over 30 min.

Thus, while accuracy may not be optimal with respect to subcutaneous monitoring devices in the ICU, these studies suggest that CGM may be useful adjunctively in ICU populations as a means of reducing POC tests and improving time in target glucose range. Newer systems are more accurate and can provide alerts for hypoglycemia or hyperglycemia as well as predictive alerts for impending glucose excursions. Moreover, increased frequency of glucose monitoring has been shown to compensate for accuracy concerns [25]. Additional high-quality studies are needed using newer technology.

### General Medical and Surgical Ward Patients Without COVID-19 Infection

There have been several clinical trials (total n = 345 subjects) evaluating CGM use in non-COVID patients hospitalized patients [26-31] prior to the start of the COVID-19 pandemic. Historically, most of these studies have analyzed the accuracy, efficacy, and safety of the CGM compared to POC glucose testing and enrolled patients without COVID-19 infection. In a post-hoc analysis of a 2011-2012 prospective cohort study, Gomez et al. evaluated 38 general ward patients with type 2 diabetes and demonstrated no significant difference in mean glucose between sensor and POC glucose values, but more hypoglycemia was detected by the CGM (55 vs 12 episodes, p < 0.01)[29]. Nearly 92% of sensor glucose measurements fell within the Clarke error grid zones A and B, which is a measure of clinically correct or benign errors in treatment decisions [29]. In Galindo's 2020 nonrandomized study of 100 subjects with type 2 diabetes in the general medicine and surgery wards without COVID-19 infection, the FreeStyle Libre Pro CGM demonstrated lower mean sensor glucose (176.1  $\pm$  46.9 vs 188.9  $\pm$ 37.3 mg/dL) and identified more hypoglycemia compared to POC glucose monitoring alone, including overnight and prolonged hypoglycemia [31]. Furthermore, CGM accuracy was lowest in the hypoglycemic range. Davis et al. reported Dexcom G6 accuracy in 218 hospitalized general medicine and surgery patients, most with type 2 diabetes and found a MARD of 12.8%, 68.7% of values within 15% of the POC reference for blood glucose > 100 mg/dl or within 15 mg/ dl of the POC reference for blood glucose  $\leq 100 \text{ mg/dl}$ , and 81.7% within 20% or 20 mg/dl. Clarke error grid analysis demonstrated 98.7% of values in zones A and B. There was a trend for lower accuracy in the first 12 and 24 h, during hypoglycemia, and severe anemia (hemoglobin < 7 g/dL) [32]. Accuracy of the sensor was comparable across race, body mass index, renal function, or sensor placement on arm versus abdomen.

There are few randomized controlled trials in general medical patients. In a 2020 interim analysis of a randomized study by Spanakis et al., 72 patients with insulin-requiring type 2 diabetes with additional risk factors for hypoglycemia were randomized to standard of care (POC glucose checks) versus real-time CGM using the Dexcom G6 [33]. Treatment decisions were based upon POC glucose testing which was performed 4 times daily in all patients. In the intervention group, the glucose telemetry system resulted in lower time below range (< 70 mg/dl), fewer hypoglycemic events (< 70 mg/dl), and less clinically significant hypoglycemic events (< 54 mg/dL) compared to the POC glucose group [33].

A 2017 study of 40 general medicine patients with type 2 diabetes randomized to closed loop subcutaneous insulin delivery without meal-time boluses versus standard of care found improved time in range at 72 h for the closed loop (59.8% versus 38.1% with an absolute difference of 21.8% [95% *CI* 10.4–33.1], p = 0.0004) compared to the control group [34]. POC glucose measures were obtained in both groups according to usual practice but were only used for insulin dosing in the standard of care group. There were no episodes of hypoglycemia or hyperglycemia with ketonemia in either group.

In a sentinel, an independently funded study by Fortmann [35] et al. published in November 2020, 110 non-ICU inpatients with type 2 diabetes were provided with Dexcom G6 RT-CGM versus usual care (and blinded CGM). Hospital telemetry (using an iPad at the nursing station which displayed sensor values) was used to monitor CGM data and alerted nursing of glucoses (< 90 mg/dL and > 250 mg/dl) and glycemic trends. The study showed improved time in range (+11.26%), time in hyperglycemia > 250 mg/dl (-11.41%), and lower mean glucose (-18.5 mg/dl) compared with usual care (p < 0.05) [35].

Thus, current data from above-referenced research suggests that CGM use in patients with diabetes provides more complete information regarding glucose trends and velocity of change compared to POC glucose testing. Moreover, accuracy is acceptable though may be limited on the first day of sensor wear, in the hypoglycemic range or in case of severe anemia. CGM may help prevent hypo- or hyperglycemia in select patients and settings. However, additional, larger randomized studies in more diverse populations are needed to establish efficacy and safety for stand-alone use.

#### **Patients Undergoing Surgical Procedures**

There have been few studies of CGM use in the operating room. A 2021 study by Perez-Guzman and colleagues evaluated 15 patients undergoing cardiopulmonary bypass graft (CABG) receiving IV insulin and admitted to the cardiac ICU [36]. This study found the mean absolute relative difference was 12.9% and median absolute relative difference of 10.5%. Sensors seemed accurate preoperatively, but in the operating room, signal loss was common and was not always regained postoperatively. Of the sensors that did regain accuracy postoperatively, they remained accurate with vasopressor therapy. Nair et al. recently published data on 10 non-ICU COVID-19 negative patients using Dexcom G6 intraoperatively with data showing mean absolute relative difference of 9.4% [37].

There have been several other peri-COVID-19 (pre and post) pandemic studies examining CGM use in hospitalized patients with COVID-19 infection, which will be reviewed in the subsequent section.

## **COVID-19 Considerations**

During the COVID-19 pandemic, there was an urgent need to conserve personal protective equipment and limit exposure to COVID-19. More than 25% of hospitalized patients with COVID-19 were reported to have diabetes [38], and diabetes was associated with higher mortality [39], especially in the setting of known microvascular or macrovascular complications and hyperglycemia [40]. The Food and Drug Administration (FDA) allowed for in-hospital use of home glucometers and CGM devices by patients during the COVID-19 pandemic to reduce patient and provider interaction and exposure to COVID-19 [41•]. Due to the rapid need to reduce personal protective equipment and change diabetes management algorithms related to the COVID-19 pandemic, an open access initiative was created to share information regarding diabetes management plans [42]. For inpatients with hyperglycemia, management plans to avoid IV insulin if possible (and the resultant need for hourly glucose checks and insulin infusion rate adjustments) for less severe hyperglycemia were created.

#### Institutional Experience from the Author

At the authors' institution, among non-critically ill inpatients requiring glucose monitoring, POC glucose checks and subcutaneous insulin doses coincide with standard medication administration times, meal tray delivery, in order to minimize the need for frequent re-entry into patient rooms [43]. In patients who were awake, patients were allowed to use their home glucometer and/or hospital supplied Freestyle Libre CGM with self-administered glargine and lispro. However, there were several barriers which impeded implementation of flash continuous glucose monitoring that require the user (i.e., patient, nurse) to scan the device. These include a patient population that was very ill, older, not equipped with smart phones (and there were insufficient receivers), and/ or non-English speaking. In contrast, patients who initiated Rt-CGM (Dexcom G6) in the MICU successfully continued CGM when transferred to a COVID-19 medical surgical floor. In these cases, MICU nurse leaders directly communicated with the medical surgical nurse leaders, frequently personally transferred the patient, and provided bedside orientation to the system and protocol.

Patients at the authors' institution who had COVID-19 and refractory hyperglycemia, diabetic ketoacidosis (DKA), or hyperglycemic nonketotic state (HNK) were treated with IV insulin using a hybrid protocol consisting of Dexcom G6 CGM in combination with POC glucose checks. Details of the implementation have been described previously [40] and were shared via an open access initiative (www.covid indiabetes.org) and implemented by others [44]. Each new sensor required validation prior to nonadjunctive use. Initial validation criteria were met if two consecutive hourly sensor glucose values were within 20% of the POC glucose if > 100 mg/dl or within 20 mg/dl of the POC glucose if <100 mg/dl [45]. If the sensor was validated, the CGM was then used to adjust IV insulin with ongoing POC glucose validation of accuracy at least every 6 h. A POC glucose was also obtained if there was no CGM value, no trend arrow, an urgent low soon or low threshold alert, signs and symptoms that did not match the sensor glucose, change in clinical status (such as intubation, hemodynamic compromise, nutrition change), or a new sensor placement. Thus, the potential risk of using CGM in the ICU was reduced through multiple means, including initial sensor validation, a higher alert threshold (100 mg/dl), predictive alerts, continuous data, use of clinical context, and requiring a diabetes consult. Our initial cohort of 19 patients included 89% on ventilators, 37% on vasopressors, and 42% on hemodialysis [43]. Median time to validation was 137 min (interquartile range 114-206 min), and in 17 patients was less than 24 h. MARD was 13.9% with no apparent association with oxygen

saturation, mean arterial pressure, vasopressor use, renal replacement, anticoagulation, or ventilator support. Time in range (70–180 mg/dl) on day 1 was 64+/-23%, and on days 2–7 was 72+/-16%. Time below range (< 70 mg/dl) was 1.5+/-4.1% on day 1 and 0.16+/-0.35% on days 2–7 [43]. Focus group feedback from nursing staff demonstrated positive perceptions regarding CGM accuracy, sensor validation, and ability to use the data to titrate insulin [40].

#### Other Published Studies Involving Subjects with COVID-19 Infection

Hybrid protocols of POC glucose checks with CGM use have been used in other small studies of ICU patients with COVID-19 (n = 61 subjects total in four studies) [44, 46–48] as displayed in Table 2. These studies have found decreased accuracy with sensor compression, hypothermia, and cardiac arrest [44]. The accuracy of the sensor in these studies of ICU patients is less than in studies of non-critically ill patients. In particular, MARD ranged between 11.1 and 13.9% for Dexcom G6 in several studies [43, 47, 48] and 13.1% in 6 patients using Medtronic CGM, but with Clarke error grid analysis showing 98–98.2% in zones A+B [47, 48]. A recent 2021 study of 52 hospitalized non-ICU subjects using the Freestyle Libre CGM compared results between capillary blood glucose readings obtained by the POC glucometer and the serum glucose values obtained by the hospital laboratory [49].

Since the onset of the COVID-19 epidemic, CGM use in the inpatient setting has been more widely used and studied in patients in the ICU and non-ICU setting especially those with COVID-19 infection. In Denmark, Klarskov et al. performed an open-label randomized controlled trial of Dexcom G6 RT-CGM or blinded CGM in 64 non-critically ill

 Table 2
 Data from hybrid protocols of POC and CGM glucose during the COVID-19 pandemic

| Study  | N  | Device                  | Protocol  | $\downarrow$ POC glucose testing | Other findings  |
|--------|----|-------------------------|---|----------------------------------|---|
| 1 [44] | 30 | Dexcom                  | Masked RT-CGM ×24 h, then NA use if SG < 20% of BG              | $\downarrow$ in 50%, not overall | NA use: achieved in 100%<br>SG↓236 → 203 mg/dl<br>Nurses reported CGM helpful (64%), reduced<br>PPE (49%) |
| 2 [46] | 9  | Dexcom                  | NA use if SG < 20%/20 mg/dl of BG, deci-<br>sion support in her | 63%                              | 76% of SG < 20% of POC<br>TIR 71%<br>↓ Accuracy: compression, hypothermia,<br>cardiac arrest              |
| 3 [47] | 11 | Dexcom                  | NA use if SG < 20%/20 mg/dl of BG, com-<br>mittee               | 60%                              | 78% of SG < 20% of POC<br>MARD 12.6%<br>EGA A+B: 98.2%  |
| 4 [48] | 11 | 5 Dexcom<br>6 Medtronic | Reduced POC to q 4 h if SG 100–200 mg/dl without alerts         | 33%                              | Concordance R: 0.89 vs 0.79 (D vs M)<br>MARD 11.1 vs 13.1%<br>EGA A+B: 98 vs 100%                         |

*POC*, point of care blood glucoses; *NA*, neoadjunctive use (without need for confirmatory POC glucose); *EHR*, electronic health record; *MARD*, mean absolute relative difference; *EGA*, Clarke error grid analysis

inpatients quarantined due to COVID-19 or other infection with diabetes. While CGM did not improve time in range or other glycemic outcomes, CGM did reduce the frequency of hospital personnel and patient contact {Klarskov, 2021 #2922}. Furthermore, most health care providers preferred CGM (28 out of 30 surveyed) [50]. MARD between Libre CGM and POC AccuChek glucoses was 15.6% with a mean relative difference between Libre CGM and AccuCheck -11.4% [49]. A second study of Freestyle Libre flash CGM in 60 ICU and non-ICU patients with COVID-19 infection and hyperglycemia or diabetes showed that glycemic monitoring using flash CGM (scanned at least 3 times daily) and a basal bolus insulin regimen was effective in achieving time in range of 72.5% [51]. Higher time above range > 180 mg/dl was associated with greater rates of a composite of complications [51]. This study confirms other studies showing acceptable agreement between the POC glucose values and CGM values and serum glucose and CGM values.

### Other Safety Considerations and Interference

Overall, CGM devices are safe with risk of use similar to other subcutaneous procedures including infection, bleeding, pain, or discomfort at sensor insertion site. Additionally, reaction or irritation from adhesive is possible. For any hospital system utilizing CGM values for treatment decisions, the sensor glucose value should be confirmed with POC glucose testing if the patient clinically appears to be having hypoglycemia or hyperglycemia not indicated on the CGM, change in hemodynamic status, change in nutrition or mental status. No CGM is approved for use with exposure to any radiation, including X-rays, computed tomographic (CT) scans, diathermy, radiation therapy, electrocautery, or other sources of radiation. Magnetic resonance imaging (MRI) carries further risk of damage via the magnetic field. In the hospital, patients often are instructed to remove the CGM prior to these procedures, although some sites allow for the sensor to be covered with a lead shield [19]. However, several studies have shown that the Dexcom G6 sensor and the Freestyle Libre Pro are accurate when exposed to X-ray, CT, radiotherapy [52-54], and possibly MRI (in the case of the Freestyle Libre Pro) [55].

Exposure to several substances may impair the accuracy of CGM (Table 1). Acetaminophen can reduce the accuracy of CGM measurements from certain CGM systems (Dexcom G5, Medtronic Guardian) but does not interfere with sensor glucose measurement by the Dexcom G6 CGM or Freestyle Libre. Accuracy may be decreased with other substances (namely maltose, ascorbic acid, dopamine, mannitol, heparin, and salicylic acid) with certain devices [10].

### **Accuracy and Regulatory Concerns**

Accuracy of glucose measurement is of utmost significance and however is difficult to achieve. The Food and Drug Administration currently approves POC glucometers that have 95% of results within  $\pm$  12% of the measured capillary glucose, while 98% should be within  $\pm$  15 mg/ dl [56, 57]. Even under optimal conditions, CGM does not meet this standard [58]. However, standards for POC devices do not specifically apply to CGM because the additional features, including frequency of measurement, trend data, and alerts provide additional information that compensates for point accuracy. In a more recent statement, the FDA defined overall accuracy as 87% of values within  $\pm$  20% of the reference standard [59]. Currently, there are no standards for CGM accuracy in the inpatient setting.

#### Implementation

Prior to the COVID-19 pandemic, few studies included or reported implementation factors. The pandemic created a need for rapid implementation of CGM within health systems and subsequently an opportunity to examine realworld strategies for integration of CGM into the clinical environment. Many institutions relied heavily on the endocrinology team for nursing/clinician training, patient selection, device placement/set-up, and ongoing support [46–48]{Chow, 2021 #2947). While in other institutions, including the authors', these tasks shifted rapidly to nursing [44, 45, 60]. A need for strong ongoing endocrinology support has been mentioned as a potential barrier to widespread implementation of CGM in the hospital setting [10, 35], yet it appears many factors of CGM use can be independently integrated into nursing practice. The use of CGM was particularly successful when combined with other implementation initiatives such as externalization of IV infusion pumps, which when combined with external CGM placement allowed IV insulin to be monitored and titrated from outside the patient's room [45, 60, 61]. Placing the CGM receiver outside of the room had been reported before the COVID-19 epidemic [33, 62]. In the few studies describing nursing acceptance and perceptions regarding CGM use, results are inconsistent. At the authors' institution, nurses expressed a high degree of satisfaction with the use of CGM, felt that CGM presented a safer alternative to POC glucose due to the availability of continuous data, and became principal drivers of use within the ICU [45]. In another pandemic era study, 63% of nurses surveyed (N = 66) felt that CGM improve

#### Table 3 Summary of recommendations from expert groups

| ADA [4, 64]  | Patients using diabetes devices should be allowed to use them in an inpatient setting when proper supervision is available.   |
|--|---|
| AACE [65]  | <ul> <li>Continuation of home CGM after admission in patients who:</li> <li>Are cognitively intact</li> <li>Who have a family member who is knowledgeable and educated on the use of CGM device</li> <li>Or with a specialized diabetes inpatient consult team available for advice and support</li> </ul>  |
| Consensus panel — diabetes technology society<br>[19•] | <ul> <li>Continuation of home CGM after admission</li> <li>Consult with inpatient team</li> <li>Avoid relying on CGM if glucose is &lt; 40 mg/dl or &gt; 500 mg/dl</li> <li>Avoid neadjunctive use with DKA, rapid glucose fluctuation, or fluid/electrolyte shifts</li> <li>Avoid use near skin infections, areas of edema or poor perfusion, with vasoactive agents</li> <li>Use a CGM checklist preoperatively</li> <li>Encourage patients to bring supplies for any preplanned hospitalization</li> <li>Continue use in pregnant women</li> <li>Use approved POC glucose measures post-procedure or during critical illness</li> <li>Use trend arrows and rate of change to guide the need for POC BG testing</li> <li>Set alert thresholds commensurate with inpatient targets</li> <li>Nursing should document CGM in the electronic medical records</li> <li><i>Initiation of CGM during hospitalization</i></li> <li>Consider CGM to reduce the need for frequent POC testing for patients on isolation with highly contagious infectious disease</li> <li>Logistics of managing CGM</li> <li>Document interfering medications</li> <li>Ensure that off-label use of CGM is consistent with medical practice; appropriate precautions are in place</li> <li>Document hands-on nursing training through technology certification</li> <li>Nursing should inspect and document the insertion site every shift</li> <li>Nursing should administer patient competency assessment or survey to assess patient ability to safely assist with managing CGM</li> <li>Nursing should administer patient competency assessment or survey to assess patient ability to safely assist with managing CGM</li> <li>Nursing should administer patient competency assessment or survey to assess patient ability to safely assist with managing CGM</li> <li>Nursing should administer patient competency assessment or survey to assess patient ability to safely assist with managing CGM</li> <li>Nursing should measure POC glucose to confirm or supplement CGM at least 4 times daily and at patient reques Trend arrows and rate of change</li></ul> |

clinical care and 49% believed the devices reduced their use of PPE. However, in previous studies involving older technology, 79% nurses (N = 43) rated CGM as not beneficial in the ICU [11]. The discrepancy in nursing perception may be related to device accuracy and design as nurses reported inadequate alarm performance (23.3%). Additionally, in the study, CGM systems were used adjunctively with no reduction in POC, whereas in both studies with positive nursing responses, the CGM systems were used non-adjunctively within a hybrid protocol thereby reducing POC testing and likely nursing burden.

electronic health record

There is a pressing need for research specifically focused on how health systems and clinicians integrate CGM into routine care for hospitalized patients. Additionally, researchers should routinely report implementation factors (e.g., nursing/clinician training, device set-up/insertion, team composition, protocol use/fidelity) for those studies not focused on implementation. Integration of these elements can accelerate translational gains, promote effective implementation strategies, and create a roadmap for health systems and regulators [63].

### **Workflow Optimization and Cost**

In addition, the cost of hospitalization was also reportedly reduced by 12 Euro per patient per day with the use of CGM [23]. As noted in the COVID-19 ICU data above, nurses reported CGM to be helpful and used fewer personal protective equipment items [45, 46]. Daily patient blood loss was also significantly less in the intervention group compared to the control group, 15.3 mL vs 60 mL per day, p < 0.001 [23]. In Spanakis et al.'s study of 72 hospitalized patients with type 2 diabetes, the study team developed a glucose telemetry system whereby CGM readings were transmitted from the patient's room to an iPad at the nursing station. A low-glucose threshold alert of 85 mg/dl or lower aimed to allow nursing staff to treat impending hypoglycemia [33].

#### **Current Guidelines**

Guidance from expert groups is summarized in Table 3. The ADA recommends that patients using diabetes devices be allowed to continue use in the hospital with appropriate supervision but caution that CGM has not been approved by the FDA for inpatient use [4, 64]. AACE recommended continuation of personal CGM devices in patients who are cognitively intact, particularly if there is a family member who is knowledgeable in use or a specialized diabetes consult service available [65]. A recent consensus guideline provided more detailed expert recommendations, including 78 proposed recommendations regarding use of CGM and automated insulin delivery in the hospital setting [19]. Recommendations addressed continuation of home CGM after admission, initiation of CGM during admission, logistics of managing CGM, and data management. Recommendations spanned from clinical practice, to research, to hospital policy. A summary of the strong clinical practice recommendations is provided in Table 3.

## Conclusions

Further research is needed to determine if CGM can replace POC glucose checks (nonadjunctive use) in some hospitalized patient populations. Appropriate studies facilitating FDA approval in the inpatient setting are needed, including assessment of glucose control, hypoglycemia, as well as hospital outcomes including length of stay, mortality, and cost effectiveness. There is a need to address potential interferences with compression of the sensor site or cautery. Furthermore, research addressing how to optimally use CGM while performing imaging procedures is needed, as currently a sensor has to be removed and is wasted, particularly when MRI is performed. Once FDA approval is granted, education for staff and health care providers is needed on how best to implement CGM systems in the hospital setting. Future studies should include remote monitoring access, integration with the electronic medical record, decision support algorithms with respect to trend arrows, and validation of CGM glucose. Ultimately, improvement in CGM technology and automated insulin delivery systems may improve glycemic control and reduce risk of hypo- or hyperglycemia among inpatients with diabetes.

Author Contribution The idea for the article came from KD. EB performed the literature search. The first draft of the manuscript was written by EB and EF helped revise the draft. KD and EF assisted with the literature review and writing the manuscript. All authors read and approved the final manuscript.

#### Declarations

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