Endocrine CONNECTIONS

REVIEW

Continuous glucose monitoring for inpatient diabetes management: an update on current evidence and practice

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Abstract

Over the last few years, several exciting changes in continuous glucose monitoring (CGM) technology have expanded its use and made CGM the standard of care for patients with type 1 and type 2 diabetes using insulin therapy. Consequently, hospitals started to notice increased use of these devices in their hospitalized patients. Furthermore during the coronavirus disease 2019 (COVID) pandemic, there was a critical need for innovative approaches to glycemic monitoring, and several hospitals started to implement CGM protocols in their daily practice. Subsequently, a plethora of studies have demonstrated the efficacy and safety of CGM use in the hospital, leading to clinical practice guideline recommendations. Several studies have also suggested that CGM has the potential to become the standard of care for some hospitalized patients, overcoming the limitations of current capillary glucose testing. Albeit, there is a need for more studies and particularly regulatory approval. In this review, we provide a historical overview of the evolution of glycemic monitoring in the hospital and review the current evidence, implementation protocols, and guidance for the use of CGM in hospitalized patients.

Key Words

- continuous glucose monitoring
- inpatient diabetes
- glycemic monitoring
- hospital diabetes technology

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Introduction

Evolution of glycemic control in the hospital

The management of dysglycemia in the hospital has undergone a significant evolution over the last 30 years, with changes in glucose targets, advances in technology, and increased recognition of its importance to improve patient outcomes. In the 1990s, most patients with diabetes admitted to the hospital received no changes in their treatment or glucose monitoring during their hospital stay. Management of dysglycemia relied solely on the widespread use of insulin sliding scales, a reactive approach to management, waiting for hyperglycemia to occur to correct it (1, 2).

As new evidence became available, the optimal management of hyperglycemia in the hospital evolved. The landmark Leuven randomized controlled trial published in 2001 demonstrated improvement in outcomes with improved glycemic control in critically ill patients with the use of an intravenous insulin infusion (3). Subsequently, the observational study by Umpierrez *et al.* demonstrated that inpatient hyperglycemia among non-critically ill patients, with and without a known history of diabetes, was an independent marker of mortality and poor outcomes, with worse outcomes among those with stress hyperglycemia (4). Several studies further confirmed that dysglycemia was associated with

increased morbidity and mortality in both critically ill and non-critically ill patients (5, 6).

Historical overview of glycemic monitoring in the hospital

As new studies provided efficacy and safety evidence, basal-bolus insulin regimen became the standard of care for glycemic control for non-critically ill and continuous insulin infusion became the standard of care for the critically ill population, as recommended by several clinical practice guidelines (7, 8, 9, 10). Over the years, inpatient diabetes management was mostly based on insulin therapy, either as a sliding insulin scale, continuous intravenous infusion, or basal-bolus regimen. All requiring a need for frequent glucose monitoring. This was possible with the use of point-of-care (POC) capillary glucose testing via fingersticks, which replaced the delayed and non-practical venous/blood glucose testing, performed every 1–2 h in the intensive care units (ICUs) or before meals and at the bedtime in non-ICU settings (1, 11, 12).

While capillary glucose testing has been widely implemented in hospitals across the world and used for years, it has limitations. This approach only provides a limited evaluation of isolated glycemic excursions, based on specific glucose samples per day in non-ICU patients. It cannot reliably detect asymptomatic or nocturnal hypoglycemia and other potentially dangerous scenarios in the hospital (11, 13). In the ICU where glucose is tested more frequently (e.g., every 1–2 h), it becomes burdensome to patients and clinical staff (12). The use of capillary glucose testing also requires frequent education of nursing staff and other personnel, device calibrations, time for documentation, and quality control; all associated with increased costs (11, 14, 15, 16). At a large academic hospital, the median cost of bedside capillary glucose testing was estimated to be around US$5.52 per test, with a range of US$3.08–US$48.16, depending on the efficiency of the hospital unit (14). Furthermore, the use of POC capillary glucose testing in critically ill patients may be limited in scenarios commonly seen in hospitalized patients, such as hypothermia, hypotension, and change in volume status, where its use may lead to biased glucose values (17, 18). Many glucose meters have been tested in critically ill patients. However, until recently, only a few of them met the Food and Drug Administration (FDA) criteria for accuracy (19). In 2018, the FDA approved the first POC capillary glucose monitoring system in critical and non-critically ill patients, the StatStrip Glucose system (Waltham, MA, USA) (20). However, this device may not be available in many hospitals worldwide.

Current recommendations for CGM use in the hospital

Newer factory-calibrated continuous glucose monitoring (CGM) systems have revolutionized the care of patients with diabetes, making it simpler, less burdensome, less painful, and providing a comprehensive overview of glycemic excursions (see Table 1). CGM has proven to be a valuable tool for glycemic control and has become the standard of care for diabetes care according to the American Diabetes Association (ADA) for people on multiple insulin injections per day or continuous subcutaneous insulin infusions in ambulatory settings (21, 22). Interestingly, there is also evidence of its benefits in reducing HbA1C in people with type 2 diabetes (T2D) on long-acting basal insulin (23). Despite its benefits in the outpatient setting, CGM use in the hospital for glycemic monitoring or optimization is not yet approved by regulatory entities, despite being widely used during and after the coronavirus disease 2019 (COVID-19) pandemic (12, 15).

Patients hospitalized with COVID-19 and severe hyperglycemia (adjusted HR 3.14; 95% CI 1.44–6.88) or hypoglycemia have an increased risk of mortality and complications (24), leading to efforts to improve glycemic control during the COVID pandemic. In 2020, the FDA granted non-objection to the use of CGM in the hospital setting, allowing for the introduction and expansion of this technology (see Fig. 1). This has provided valuable information about the accuracy and limitations of CGM in the hospital. The CGM systems that were most often tested included the Dexcom G6 (San Diego, CA, USA), Abbott FreeStyle Libre (Alameda, CA, USA), and Medtronic Guardian Connect (Northridge, CA, USA) (16, 25). Consequently, several medical societies have recently released evidence-based recommendations for the use of CGM in hospital settings, suggesting that CGM has the potential for becoming the standard of care for glycemic monitoring in the hospital (11, 26, 27, 28). In Table 2, we review recent indications, precautions, and considerations of several international guidelines.

The British Diabetes Society for Inpatient Care recommends keeping the 'time below range' (TBR) <1% in hospitalized patients and for those who are acutely ill a higher TIR (time in range) from 108 to 180 mg/dL to avoid hypoglycemia. These guidelines also recommend

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Table 1 Characteristics of currently available CGM systems (39, 40, 54, 55, 56).

Features	Dexcom G7	Dexcom G6	Dexcom One	Guardian 3	Guardian 4	Freestyle libre 3	Freestyle libre 2	Freestyle 14 days	Eversense XL
Real-time CGM / Intermittent scanning CGM	Real-time CGM	Real-time CGM	Real-time CGM	Real-time CGM	Real-time CGM	Real-time CGM	Intermittent scanning CGM	Intermittent scanning CGM	Real-time CGM
Glucose measurement	Every 5 min	Every 5 min	Every 5 min	Every 5 min	Every 5 min	Every 1 min	Every 1 min	Every 1 min	Every 5 min
Sensor life	10 days	10 days	10 days	7 days	7 days	14 days	14 days	14 days	180 days
Calibrations	Optional	Optional	Optional	Every 12 h	Optional	No	No	No	Every 12 h
Insertion site	Back of the arms	Abdomen, arms	Abdomen, arms	Abdomen, arms, upper buttocks	Abdomen, arms, upper buttocks	Back of the arms	Back of the arms	Back of the arms	Back of the arms
Warm up (h)	1/2	2	2	2	2	1	1	1	24
Indication (age)	>2 years	>2 years	>2 years	>2 years	>2 years	>18 years	>4 years	>4 years	>18 years
Web platform	Clarity	Clarity	Clarity	CareLink	CareLink	Libreview	Libreview	Libreview	Eversense DSM
Interferences	Hydroxyurea (falsely raise sensor glucose readings)	Hydroxyurea (falsely raise sensor glucose readings)	Hydroxyurea (falsely raise sensor glucose readings)	Acetaminophen (falsely raise sensor glucose readings) Hydroxyurea (falsely raise sensor glucose readings)	Acetaminophen (falsely raise sensor glucose readings)	Ascorbic acid (falsely raise glucose readings) Salycilic acid (falsely decreased)	Ascorbic acid (falsely raise glucose readings) Salycilic acid (falsely decreased)	Ascorbic acid (falsely raise glucose readings) Salycilic acid (falsely decreased)	Tetracycline (falsely decreased) Mannitol (falsely increased) Aspirin (high doses may falsely raise glucose readings)

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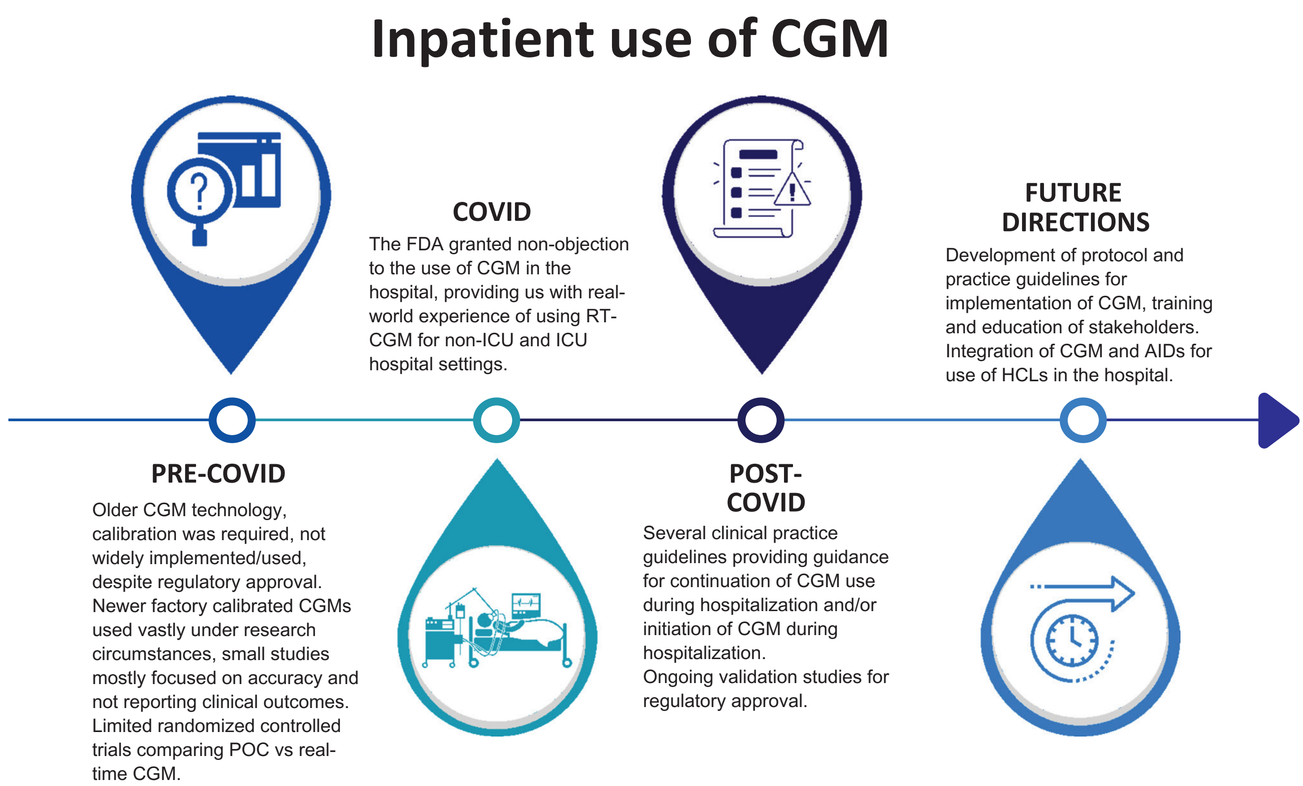
Inpatient use of CGM
COVID
The FDA granted non-objection to the use of CGM in the hospital, providing us with real-world experience of using RT-CGM for non-ICU and ICU hospital settings.
FUTURE DIRECTIONS
Development of protocol and practice guidelines for implementation of CGM, training and education of stakeholders.
Integration of CGM and AIDs for use of HCLs in the hospital.
PRE-COVID
Older CGM technology, calibration was required, not widely implemented/used, despite regulatory approval.
Newer factory calibrated CGMs used vastly under research circumstances, small studies mostly focused on accuracy and not reporting clinical outcomes.
Limited randomized controlled trials comparing POC vs real-time CGM.
POST-COVID
Several clinical practice guidelines providing guidance for continuation of CGM use during hospitalization and/or initiation of CGM during hospitalization.
Ongoing validation studies for regulatory approval.

Figure 1
Timeline of CGM research, implementation, and the use in the hospital.

caution with CGM interpretation when systolic blood pressure is <100 mmHg (29). The Diabetes Technology Society's consensus guideline recommends moving up the TBR to 80–85 mg/dL, if using real-time CGM, to avoid hypoglycemia and to avoid the use of CGM in hyperglycemic crisis (BG> 500 mg/dL), hypoglycemia (<40 mg/dL), or situations with rapidly changing BG (11). The American Diabetes Association (ADA) recommends always confirming CGM readings with POC testing (21). The Endocrine Society (ENDO) recommends avoiding using CGM in areas with extensive skin infections, in hypoperfusion and hypovolemia, or in those receiving vasopressor therapy (28). Finally, the American Association of Clinical Endocrinology (AACE) recommends that the patients should notify their primary team to confirm with a POC BG when CGM reads hypoglycemia (BG <70 mg/dL or <54 mg/dL) (27).

Notably, there is still no consensus on what CGM parameters should be reported or used for treatment decisions, what CGM-related glucose targets should be recommended, or in what clinical inpatient scenarios their use and interpretation should be used with caution.

Current evidence for the use of CGM in the hospital

Non-ICU settings

Overall, the evidence for newer CGM systems and their use in non-ICU settings are mostly derived from observational studies (see Table 3). Several small, pilot studies have been published since the COVID pandemic. These studies have heterogenous populations, use different CGM protocols, and different metrics for data reporting. Furthermore, variable outcomes or metrics and the methods for calculating them are not standardized. Most studies focused on assessing accuracy, reporting MARD as the main measure, and used capillary glucose testing as the reference/comparator. The MARD for overall glucose values ranged from 6.6% to 30.5% for all glucose values (see Table 3) (30).

ICU settings

Similarly, the evidence for using subcutaneous factory-calibrated CGM in the ICU is largely derived from observational studies, with heterogenous populations, variable CGM metrics studied, different calibration

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Table 2 Summary of recommendation by international guidelines on the use of CGM in the hospital.

	CGM indications/ glycemic targets in the hospital	Special situations and cautions	Radiology	Perioperative period	Confirm with POC BG
British Diabetes Societies for Inpatient Care (UK) (29)	- All hospitalized patients: TBR <1% - Acutely unwell hospitalized patients: TIR 108–180 mg/dL - Hospitalized patients: TIR 70–180 mg/dL	- SBP <100 mmHg - Hyperthermia - Hypothermia - Volume depletion - Hyperglycemic Emergencies - In ICU settings	- CT, radiotherapy, electrocautery use: Individualized decision - MRI: Remove CGM	- May be considered to guide use of POC or ABG - Hold if hypotension or hemorrhage	Yes
Diabetes Technology Society Consensus Guideline (US) (11)	- All hospitalized patients TBR <80–85 mg/dL	- BG <40 mg/dL or > 500 mg/dL - Hyperglycemic crisis - Situations with rapidly changing glucose levels and fluid/ electrolyte shifts - Patients with poor tissue perfusion or using vasoactive agents	None	None	Yes
Standard of Care in Diabetes, American Diabetes Association (US) (21, 22)	- Always confirmed with POC - Individual capable to use the device safely and independently	None	None	None	Yes
The Endocrine Society (US) (28)	- Non-critically ill hospitalized patients: real-time CGM with confirmatory bedside POC-BG monitoring for adjustments in insulin dosing rather than POC-BG alone	- Extensive skin infections - Hypoperfusion, or hypovolemia - Those receiving vasoactive or pressor therapy	None	None	Yes
American Association of Clinical Endocrinology (US) Use of Advanced Technology (27) Comprehensive Diabetes Care Plan (57)	- With proper protocols, persons previously using CGM, should continue using the sensors during admission Therapy should be adjusted and hypoglycemia (BG <70 mg/dL or <54 mg/dL) should be confirmed with hospital-calibrated glucose meters	None	None	None	Yes

ABG, arterial blood glucose; BG, blood glucose; CGM, continuous glucose monitoring; CT, computer tomography; MRI, magnetic resonance imaging; POC, point of care; RTC-CGM, real-time CGM; SBP, systolic blood pressure; TBR, time below range; TIR, time in range.

protocols, and glucose measurement used making outcome comparisons difficult. Overall, MARD ranged from 6.6% to 14.8% (see Table 3), with a tendency to lower accuracy in the hypoglycemia range (30). However, the number of glucose pair references is smaller in that range which can impact the MARD calculation (31). Moreover, patients in the ICU present unique challenges to glycemic control, with highly fluctuating glucose levels influenced by factors such as nutritional support, steroid use, stress response, vasopressor use, and acute kidney injury. Nevertheless, the potential benefits of improved glycemic assessment and reduced nursing burden and capillary testing make the use of CGM in the ICU, an area of active research and development (16, 32, 33). With the advent of newer factory-calibrated CGM devices and standardization of appropriate protocols, the use of CGM, whether adjunctive or non-adjunctive, has the potential to overcome the limitations of the current approach with capillary glucose testing (28, 30).

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Table 3 Summary of recent studies using CGM in different hospital settings.

Study	Population/Country	Design	Study type	Type of CGM	Performance measurement	Outcome
General wards (non-critically ill people)						
Dillman *et al.* 2022 (58)	*n* = 53/UK	Prospective	Feasibility	Guardian	none	Increased TIR, no change in TBR
Wright *et al.* 2022 (59)	*n* = 77 USA	Prospective	Accuracy		POC	Libre 1 MARD 21.4%, Libre 2 MARD 17.7%
Davis *et al.* 2021 (60)	*n* = 218/USA	Retrospective	Accuracy	Dexcom G6	POC	MARD 12.8%
Reutrakal *et al.* 2020 (61)	*n* = 9/USA	Prospective	Accuracy	Dexcom G6	POC	MARD 9.77%,
Galindo *et al.* 2020 (13)	*n* = 97/USA	Prospective	Accuracy	FreeStyle Libre Pro	POC	Overall MARD 14.8% Increased TIR, reduced TAR
Singh *et al.* 2020 (62)	*n* = 12/USA	RCT	Prevention of hypoglycemia	Dexcom G4	Blinded CGM	No difference in BG
Fortmann *et al.* 2020 (63)	*n* = 110/UK	RCT	Effectiveness	Dexcom G6	POC	Increased TIR, reduced TAR
Singh *et al.* 2020 (46)	*n* = 72/UK	RCT	Prevention of hypoglycemia	Dexcom G4	Blinded CGM	Reduced TBR
Shehav-Zaltzman *et al.* 2020 (64)	*n* = 4/Israel	Observational	Feasibility	Guardian,	POC	Reduced mean BG
Gomez *et al.* 2015 (65)	*n* = 38/Colombia	Prospective	Accuracy	iPro system,	POC	Higher number hypoglycemia detected compared to POC No difference in daily average glucose.
Schuapp *et al.* 2015 (66)	*n* = 84/Austria	Prospective	Accuracy	iPro system,	POC	Higher number hypoglycemia detected overnight compared to POC
Dungan *et al.* 2012 (67)	*n* = 43/USA	Prospective	Accuracy	iPro system,	POC	MARD in heart failure and severe hyperglycemia was 9.6% and 16.2%, respectively.
Burt *et al.* 2013 (68)	*n* = 26/Australia	Prospective	Accuracy	System Gold,	POC	CGM identified more episodes of postprandial hyperglycemia and hypoglycemia
ICU +/– general ward						
Boeder *et al.* 2022 (42)	*n* = 24	Retrospective	Accuracy	Dexcom G6	Capillary by POC	Overall MARD 14.8%
Longo *et al.* 2021 (69)	*n* = 28/USA	Prospective	Accuracy	Dexcom G6	POC/ whole blood Lab	Overall MARD for ITU 12.1% Overall MARD for medical wards 14%
Gomez *et al.* 2021 (70)	*n* = 60/Colombia	Prospective	Glycemic control	FreeStyle Libre (unknown type)	none	TIR: 72.5%, 22% TAR, 3% were TBR (<70 mg/dL People with TAR >180 mg/dL had higher rates of a composite of complications
Tingsarat *et al.* 2021 (71)	*n* = 12/Thailand	Prospective	Accuracy	Medtronic	POC/whole blood Lab	Overall MARD 6.6%
Faulds *et al.* 2021 (44)	*n* = 18	Prospective	Feasibility	Dexcom G6	none	Hybrid protocol resulted in feasible good glycemic control, but accuracy was suboptimal for standalone use
Agarwal *et al.* 2021 (72)	*n* = 11 (= 493)	Prospective	Accuracy	Dexcom G6	POC	Overall MARD 12.6% CGM reduced POC testing by ~60%
Surgical/ Perioperative period						
Herzig *et al.* 2023 (34)	*n* = 16	Prospective	Accuracy	Dexcom G6	POC	Intrasurgery MARD of 23.8%, during hypothermia MARD 29.1%.
Sweeney *et al.* 2022 (73)	*n* = 11/USA	Prospective	Accuracy	Dexcom G6	POC	Overall MARD 14.8%

(Continued)

Table 3 Continued.

Study	Population/Country	Design	Study type	Type of CGM	Performance measurement	Outcome
Perez-Guzman *et al.* 2021 (32)	n = 15/USA	Prospective	Accuracy	Blinded Dexcom G6	POC	Overall MARD 12.9% signal loss was common in OR and was not always regained postoperatively
Nair *et al.* 2020 (74)	n = 10/USA	Prospective	Accuracy	Blinded Dexcom G6	POC	Overall MARD 9.4%
Tripyla *et al.* 2020 (36)	n = 20/Switzerland	Prospective	Accuracy	Dexcom G6	POC	Overall MARD 12.7%
Schierenbeck *et al.* 2017 (75)	n = 26/Sweden	Prospective	Accuracy	FreeStyle Libre	POC POC	Overall MARD 30.5 (12.4)%
Radiology						
Migdal *et al.* 2020 (37)	n = 49/USA x-rays (n = 28); CT scan (n = 13)	Prospective	Accuracy	Dexcom G6	POC	Overall MARD 13.3% pre-imaging; 12.7% post-imaging.

BG, blood glucose; CT, computerized tomography scan; MARD, mean absolute relative difference; POC, point-of-care testing; RCT, randomized controlled trial; TAR, time above range; TBR, time below range; TIR, time in range.

Special hospital clinical settings

Fewer studies have been published on scenarios specific to hospital settings. The use of CGM during the perioperative period may be beneficial by providing frequent glucose readings, allowing for closer monitoring, and helping anesthesiologists to optimize insulin treatment or to avoid hypoglycemia. Notably, potential limitations related to signal interference with the use of electrocautery (32), medications (16), hypothermia (34), and compression of the devices may also exist (35).

Recent studies have reported on the accuracy of CGM during the perioperative period and during imaging studies. Herzig *et al.* reported on the accuracy of Dexcom G6 among adult patients undergoing cardiac surgery with hypothermic extracorporeal circulation. They found an intrasurgery MARD of 23.8% which increased to 29.1% during hypothermia. However, the accuracy was improved after surgery (MARD 15.0%) (34). Triplya *et al.* compared the accuracy of Dexcom G6 with POC glucose in patients undergoing elective abdominal surgeries from the induction of anesthesia up to 2 h post-surgery and reported a MARD of 12.7% (s.d. ± 8.7%) (36).

Few observational studies have been published evaluating the accuracy or performance of CGM during radiology procedures. In one single-center observational study performed during hospital admission, they reported good accuracy with MARD of 12.7% after x-ray and computed tomography (CT) scans (37). Thomas *et al.* reported recently that Dexcom G6 sensors retain basic functionality and data integrity after exposure to x-rays but during simulated *in vitro* situations (38). However, at the present time, Abbott (the manufacturer) (39) recommends to remove the sensor before magnetic resonance imaging (MRI), CT scans, x-rays, or high-frequency electrical heat (diathermy) treatment. For Dexcom G7 (40), the manufacturer's recommendation is not to wear any CGM component during MRI or diathermy and to keep the sensor during CT scan but to maintain the CGM sensor out of the CT scan area and cover it with a lead apron during the scan (40). Therefore, until more information is available, it is recommended that perioperative CGM readings be confirmed with blood glucose measurements before making any treatment decisions, especially for major surgeries. Hence, CGM may not need to be removed and used to track patterns and trends except for MRI or diathermy procedures.

In situations where rapid glucose fluctuation is expected, such as diabetes ketoacidosis, hyperglycemic hyperosmolar state, or severe hyperglycemia with very

high glucose levels (CGM maximum reporting range is often limited to 400 mg/dL), CGM use is not recommended, or clinicians should consider a hybrid protocol with confirmatory capillary or venous glucose testing. We provide further descriptions of hybrid protocols below. The evidence in patients with anasarca, with skin lesions on CGM insertion areas, using vasoconstrictive drugs, receiving hyperbaric oxygen treatments or taking potential interfering substances is still limited.

Adjunctive and non-adjunctive use of CGM in the hospital: hybrid protocols

Traditionally new 'approaches to care' are implemented after extensive research has been done. But in the case of CGM use in the hospital, most of the innovative approaches were implemented and studied at the same time. On April 1, 2020, the FDA granted a temporary enforcement discretion approval to allow hospitals to use CGM. The first hospitals in the US to start using CGM were in New York City, where the pandemic was hitting the hardest. Soon after, other institutions started using CGM, implementing new protocols, and analyzing their real-world evidence (RWE), including usability and applicability of CGMs for inpatients. Subsequently, pre-planned research protocols were published. Thus, most of the recent advances in the use of CGM in hospitals were derived from 'reversed' implementation of the scientific process. In other means, new processes were implemented, and new research data was then obtained from that. For the last 3 years, there have been many publications related to the real-world experience of using rt-CGM for inpatients (41, 42, 43, 44) (Fig. 1).

The most accepted protocol at this time is the combination of the available tools; a blood glucose meter, in conjunction with the use of CGM guiding the appropriate time to perform a POC rather than measuring at strict time points. CGM is able to indicate to the healthcare team when the patient is trending low or high and converts POC testing to an on-demand system, reducing the number of POC and the burden of care. This has been called the 'hybrid protocol'. Faulds *et al.* were among the first to use it, and published their approach for managing glycemia excursions and providing appropriate treatment for inpatients. In this report, they not only explained the procedure that they established at Ohio State University Medical Center but also described in detail the benefits and barriers they encountered with this innovative approach (45). This protocol has been adopted in other institutions with variations, such as the protocol used by Dr. Davis *et al.* at Emory University (see the section 'CGM and computerized decision support systems for insulin administration' below) (35).

For the last 3 years, CGM has become part of the regular care for glycemic management for hospitalized patients mainly not only in the US but also in the UK and Europe. Consequently, societies are developing guidelines to create a consensus on the use of CGM for inpatient hospital use, and manufacturers are pursuing formal regulatory approval to allow current and new users access to CGM during hospitalization. The sole use of CGM or in combination with POC will be determined by care team experience and precise guidelines. What is certain at this time is the capability of CGM to provide better tools in predicting patient glucose trends which will guide appropriate treatment decisions and achieve better glycemic control for patients experiencing dysglycemia while in the hospital.

Innovative approaches using CGM in the hospital

Glucose telemetry system

Before the COVID pandemic, few investigators were performing research using CGM for inpatients. One of the most innovative approaches was Glucose Telemetry System (GTS) developed by Dr. Ilias Spanakis at the University of Maryland. The initial studies using real-time, remote, GTS monitoring (46) showed that rt-CGM has the potential to reduce dysglycemic excursions, hypoglycemia in particular, in hospitalized high-risk patients with diabetes treated with insulin.

A second larger, multicenter RCT was conducted at the University of Maryland and Emory University in non-ICU participants who were treated with basal-bolus insulin to target a fasting and premeal glucose between 70 and 180 mg/dL. Subjects were randomly assigned to use a blinded Dexcom G6 CGM with insulin dose adjustment based on POC glucose testing (before meals and at bedtime) or to use real-time (factory-calibrated) Dexcom G6 CGM (RT-CGM) with insulin adjustment based on daily review of CGM data. The use of rt-CGM improved the prevention of recurrent hypoglycemia events (1.80 ± 1.54 vs 2.94 ± 2.76 events/patient; $P = 0.03$) They concluded that the inpatient use of real-time Dexcom G6 CGM is safe and effective, resulting in the

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reduction of hypoglycemic events compared with POC-guided insulin adjustment (47). This allows for real-time monitoring and alarm setting, helping clinicians detect and address glucose excursions more quickly.

Integrating CGM and insulin delivery systems

CGM and computerized decision support systems for insulin administration

CGM integrated with computerized insulin administration has the potential to improve glycemic control and reduce the risk of hypoglycemia in hospitalized patients. Computerized insulin administration systems (CIASs) are software systems that use algorithms to calculate insulin doses based on a patient's glucose level, indicate the need for glucose testing, and can automatically adjust insulin delivery based on real-time glucose data. Integrating CGM with CIAS allows for more accurate and precise insulin dosing, as the system can adjust insulin delivery in real time based on the changes in glucose levels. This can help to reduce the risk of hypoglycemia and hyperglycemia (12).

Davis *et al.* implemented a hybrid protocol using CGM and POC integrated with Glucommander® (Glytec, Waltham, MA, USA) in nine patients admitted with COVID-19 in a critical care unit. The implementation of this strategy resulted in 63% decrease in POC testing by nursing personnel. Despite the patients being on nutritional support, using steroids, and being on mechanical ventilation, glucose control was significantly improved, with a mean TIR (70–180 mg/dL) of 71.4 ± 13.9%, TAR (time above average) (>250 mg/dL) of 7.5 ± 7.3%, and TBR (<70 mg/dL) of 0.6 ± 0.9%. However, the authors pointed out some limitations of using CGM, such as signal loss, sensor malfunction due to mechanical compression or hypoperfusion, or malfunction in hypothermia protocols (35).

Overall, integrating CGM with CIAS has the potential to significantly improve glycemic control and reduce the use of POC in critically ill patients. However, further research is needed to determine the optimal CGM and CIAS systems for use in different clinical settings and to evaluate the long-term benefits and safety of these systems.

CGM with continuous subcutaneous insulin infusion: HCLs or automated insulin delivery (AID) systems

While there is increased interest in the use of closed-loop insulin delivery systems in hospitalized patients with diabetes, there are limited studies. The benefits of closed-loop insulin delivery systems have been studied in patients with T1D (48) and in patients with other forms of diabetes. However, few prospective studies have assessed the efficacy and safety of starting HCLs in the hospital.

Bally *et al.* demonstrated that patients with T2D who used the automated closed-loop system (model predictive control algorithm version 0.3.70) had significantly higher in-hospital TIR (70–80 mg/dL) compared to those who received standard subcutaneous insulin therapy, without increasing the risk for hypoglycemia (65.8 ± 16.8% vs 24.3% ± 2.9%, $P < 0.001$) (49). Heriz *et al.* studied patients with diabetes, excluding those with T1D, who underwent elective surgery and evaluated whether the use of a closed-loop subcutaneous insulin delivery system without the need for bolus for nutritional support could improve glucose control compared to standard insulin therapy according to local clinical practice. The authors reported an increased proportion of in-hospital TIR in the closed-loop subcutaneous insulin delivery group compared to the control group (76.7 ± 10.1% vs 54.7 ± 20.8%, $P < 0.001$) (34). Boughton *et al.* had similar results in patients with diabetes, excluding those with T1D, receiving enteral or parenteral nutrition, reporting higher in-hospital TIR in the closed-loop subcutaneous insulin delivery group compared to a control group (68.4 ± 15.5% vs 36.4 ± 26.6%, $P < 0.001$) (50). These studies have shown the potential use of closed-loop subcutaneous insulin delivery systems to maintain euglycemia in high-risk hyperglycemic in-hospital clinical scenarios.

Pelkey *et al.* recently published a retrospective analysis comparing three hospitalized patient groups: HCL users, manual-mode insulin pump users, and pump-removed to basal-bolus insulin users. The authors confirmed in this real-world observational study that the continuation of the use of a HCLs in the inpatient setting was safe compared to the use of insulin pumps in manual mode (pumps not integrated into CGM) or basal-bolus insulin therapy (51). In order to consider the use of HCLs in hospitalized patients, we recommend that each hospital implement CGM and insulin pump policies and include their inpatient diabetes teams in treatment planning for better inpatient outcomes.

Future areas of research

While there is increasing interest in the continuation of CGMs upon admission in patients who previously were

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using these devices in ambulatory settings, there is still a need for more education of the hospital clinical and administrative personnel, patients, and family members/caregivers. It is recommended to have established protocols or clinical guidelines in hospitals where CGM will be initiated and used during the hospitalization (15, 28). Training should include patient education on how to respond to alarms and to notify hospital personnel in situations of malfunction, how to discern discordance between symptoms and glucose values/alarms, and when to have confirmatory venous or capillary glucose testing. As recommended by experts and guidelines, engagement, training, and education of nursing personnel is required for safe implementation of CGM in the hospital (11, 16).

In a recent multi-center survey in the US, including hospitalists (76%), advanced practice providers (10%), and primary care physicians (6%) from large academic and community hospitals, Madhun *et al.* demonstrated that the most common barrier for the use of insulin pumps in the hospital was the lack of familiarity and education of physicians and nurses. Furthermore, the majority of respondents were not aware of institutional policies for the use of CGM, despite all institutions having implemented such policies, with only 43.8% of the respondents reviewing CGM data upon admission of a patient (52).

Recently, there has been an increasing number of patients with type 1 diabetes (T1D) using HCLs in ambulatory settings. Similar to CGM, many patients would benefit from continuing the use of their HCLs during the hospitalization (11) if no contraindications exist and if supplies are available. While some new pilot studies are emerging (34, 49) with promising results, there is a still no guidance or consensus on how to approach this. Many institutions have allowed patients to continue using their automatized insulin delivery (AID) during hospitalization with in-house protocols and patient agreements, but the majority recommend not to use the 'AID' mode and prefer the 'manual mode' (11). This is driven by the lack of regulatory approval for using (adjunctive or non-adjunctive) CGM in the hospital at this time, which will be needed for HCLs' use.

While there are established guidelines for CGM metrics and targets for clinical care in the ambulatory setting (53), there is a need for standardized recommendations on what CGM metrics and glucose targets are appropriate for the hospital setting (30).

Conclusion

Over the last few years, CGM has revolutionized the care of patients with diabetes in the ambulatory setting, increasing its use and replacing self-monitored glucose testing as standard of care for some patients. It is expected that these innovative changes will need to be translated to the hospital setting. While this process usually takes time, since the COVID pandemic, there has been an urgency to move this field forward dictated by patient and clinical needs and limited resources and staffing. We have seen the rapid and exciting spread of CGM use in the hospital setting over the last few years, and optimistically anticipate a continued movement to improve glycemic monitoring and diabetes care in hospitalized patients with newer diabetes technology.

Declaration of interest

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