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Continuous Glucose Monitoring in the Hospital

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Continuous glucose monitors (CGMs) have suddenly become part of routine care in many hospitals. The coronavirus disease 2019 (COVID-19) pandemic has necessitated the use of new technologies and new processes to care for hospitalized patients, including diabetes patients. The use of CGMs to automatically and remotely supplement or replace assisted monitoring of blood glucose by bedside nurses can decrease: the amount of necessary nursing exposure to COVID-19 patients with diabetes; the amount of time required for obtaining blood glucose measurements, and the amount of personal protective equipment necessary for interacting with patients during the blood glucose testing. The United States Food and Drug Administration (FDA) is now exercising enforcement discretion and not objecting to certain factory-calibrated CGMs being used in a hospital setting, both to facilitate patient care and to obtain performance data that can be used for future regulatory submissions. CGMs can be used in the hospital to decrease the frequency of fingerstick point of care capillary blood glucose testing, decrease hyperglycemic episodes, and decrease hypoglycemic episodes. Most of the research on CGMs in the hospital has focused on their accuracy and only recently outcomes data has been reported. A hospital CGM program requires cooperation of physicians, bedside nurses, diabetes educators, and hospital administrators to appropriately select and manage patients. Processes for collecting, reviewing, storing, and responding to CGM data must be established for such a program to be successful. CGM technology is advancing and we expect that CGMs will be increasingly used in the hospital for patients with diabetes.

Keywords: Blood glucose; COVID-19; Diabetes mellitus; Glucose; Hospitals; Intensive care units; Technology

INTRODUCTION

Recent escalating interest in the use of continuous glucose monitor (CGM) technology for hospitalized patients has been fueled by (1) improvements in the sensing and data management technology; (2) increasing popularity of these devices among outpatients with diabetes as well as others from the athlete community and the quantified self movement; (3) a recent surge of articles in leading diabetes journals describing both good accuracy and improved clinical outcomes in hospitalized patients using these devices; (4) a recent decision by the United States Food and Drug Administration (FDA) related to the coronavirus disease 2019 (COVID-19) pandemic to exercise enforcement discretion and not block hospitals from providing devices and technical support to hospitals wishing to use these systems; and (5) dissemination of guidelines and review articles describing policies for using CGMs in a hospital setting.

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DEFINITION OF A CONTINUOUS GLUCOSE MONITOR

A CGM is a device that measures the glucose concentration automatically around the clock [1]. The device must be attached to the body in some way and it can be either a wearable device or an implanted device. A CGM sensor can be situated in the subcutaneous space to measure the glucose concentration in interstitial fluid (ISF) or in a blood vessel and measure the glucose concentration in blood. Intravascular sensors are rarely used and confer a risk of bleeding and thrombosis and will not be covered in this article. Subcutaneous glucose sensors can require calibration anywhere from not at all up to four times daily [2]. One of the advantages of automatic glucose measurements is the time saved for the nurses who do not have to check blood glucoses as often, but a disadvantage is that compared to blood glucose monitors, these sensors track ISF glucose rather than reference blood glucose concentrations (which are used for registration studies) less closely. Therefore, if a particular CGM requires regular calibration with blood glucose testing and provides less accurate reading as well, then there will be little interest in using such a product for hospitalized patients.

A CGM sensor with two attractive features: (1) factory calibration and (2) accuracy close to that of most blood glucose monitors (which many clinicians and mathematicians consider to be a mean absolute relative difference (MARD) from reference of below 10%) [3] would be well received in a hospital setting, providing there are no special accuracy concerns about physiological states altering ISF composition in critically ill patients. Two currently available types of sensors, the FreeStyle Libre series (FreeStyle Libre 14 day and FreeStyle Libre 2) from Abbott Diabetes Care (Alameda, CA, USA) [4,5], and the Dexcom G6 from Dexcom (San Diego, CA, USA) [6] provide these two features for most patients. The FreeStyle Libre 3 has a Conformité Européenne (CE) mark, but is not cleared by the FDA. However, none of these products are cleared by the FDA for use by critically ill hospitalized patients. Table 1 presents a list of currently available (in the United States) factory-calibrated subcutaneous CGMs that have product labels available and their known interferences from chemical substances [7-14].

For a given glucose concentration, CGMs from different manufacturers might report different percentages of time spent below range and above range, and might generate different individual times spent below or above range that could lead to different therapy recommendations [15]. Some hospitalized patients are volume depleted or they can experience peripheral vasoconstriction from pressors, and it has not been clearly established whether CGMs that are currently intended for outpatient use can deliver adequately accurate results for these people [16]. More data will be needed about the analytical accuracy of CGMs in hospitalized patients before these devices will receive regulatory clearance for use in this setting.

With the recent COVID-19 pandemic straining hospital resources in 2020, the FDA notified Abbott Diabetes Care and Dexcom that they would exercise enforcement discretion and not object if these companies provided devices and technical support to hospitals who used CGMs for off-label use [17-19]. This plan has allowed many hospitals to assign nurses to use these devices for remote monitoring of glucose concentrations in COVID-19 patients with diabetes without needing to spend time performing fingerstick testing, having as much contact with contagious patients, and using up as much (in some cases limited) personal protective equipment (PPE) during fingerstick testing. Furthermore these programs have benefitted both these two manufacturers and the FDA by facilitating collection of real world data on large numbers of patients, whereas in clinical trials of these products in a hospital setting testing protocols would have been expensive and time consuming.

ESTABLISHING A CGM PROGRAM

The implementation of a CGM program in the hospital demands the interaction of multiple stakeholders including hospital leadership, physicians (many times including endocrinologists), nursing leadership, information technologists, quality implementation officers, laboratories representatives, pharmacists, and risk management officers. Ideally, information technology services can facilitate the documentation of CGM in the electronic health records (EHRs) to facilitate the comparison of point of care (POC) tests with CGM values and confirm periodically that CGM readings used for patient care are within an acceptable range [20]. Steps for a successful implementation in the hospital were recently described by Galindo et al. [21].

Current platforms for CGM implementation with factory-calibrated devices (that do not need a confirmatory test for decisions in the outpatient setting) include apps for the patient, apps for remote followers of glucose values, and platforms for population-based management. The Dexcom G6 device from Dexcom can transmit glucose data via Bluetooth to a receiver or smartphone (Android or iOS) within 20 feet. If using a compatible smartphone, then information can then be shared via the "Follow" app to up to 10 selected people, such as clinicians at a

Table 1. List of Currently Available (in the United States) Factory-Calibrated Subcutaneous CGMs That Have Product Labels Available and Their Known Interferences from Chemical Substances

CGM system	Warm up time, hr	No. of wear, day	Technical features [7]	Can the device be connected to an AID system?	Associated mobile app	Known interferences from chemical substances
Abbott Diabetes Care FreeStyle Libre 14 day system [8]	1	14	Range 40–500 mg/dL; no predictive alerts; glucose measured every minute and real-time data can be viewed by scanning sensor which holds 8 hours of data	No	Freestyle LibreLink, LibreLinkUp [9]	Ascorbic acid Salicylic acid
Abbott Diabetes Care FreeStyle Libre 2 [10,11]	1	14	Range 40–400 mg/dL; optional real-time alarms for hypoglycemia, hyperglycemia, and signal loss; no predictive alerts, since the sensor monitors glucose every minute; real-time data can be viewed by scanning sensor which holds 8 hours of data	No	FreeStyle Libre 2 app (currently under FDA review), LibreLinkUp [9]	Ascorbic acid
Dexcom G6 [12,13]	2	10	Range 40–400 mg/dL; sensor monitors glucose every 5 minutes; urgent low alarm (55 mg/dL) and optional hypoglycemia predictive alert, hypoglycemia and hyperglycemia threshold alerts, and rate of change alerts	Yes	Dexcom G6 app, Follow app [14]	Hydroxyurea

CGM, continuous glucose monitor; AID, automated insulin delivery; FDA, U.S. Food and Drug Administration.

nursing station (who can use a dedicated tablet), the primary care team, bedside nurses, pharmacists, and/or endocrinologists that follow remotely. The data can also be transferred to online platforms, such as Dexcom CLARITY, that generates CGM-based glucose reports and summarizes data on a daily basis or over any specified period of time [14]. With the FreeStyle Libre 14 day and FreeStyle Libre 2 systems, a similar approach can allow the use of this technology in the hospital. With the FreeStyle Libre 14 day system the information can be transferred to a receiver or a smartphone via the FreeStyle Librelink app, which then sends data to FreeStyle LibreView. Data on FreeStyle LibreView can be viewed by the patient and clinicians. Data can be viewed by patients via the LibreLink app, then to followers via the LibreLinkUp app, and then to Libreview.com to monitor multiple patients [9,22]. It should be noted that the both of the FreeStyle Libre systems measure glucose every minute; real-time glucose data including the trend and retrospective information is available by scanning the sensor, which holds 8 hours of data. The FreeStyle Libre 2 system has real-time optional alarms, which alert the user to high and low glucose levels without scanning.

Even though CGMs often appear to be reliable in the hospital, we believe regular routine POC blood glucose testing is still needed plus additional confirmatory POC tests are needed when: (1) glucose values are <85 mg/dL or >300 mg/dL; (2) hypoglycemic symptoms occur; (3) glucose readings and/or glucose trend arrows are not present on the monitor; (4) a blood drop symbol appears on the monitor; (5) hemodynamic instability occurs; and (6) a patient is in the immediate postoperative period.

WHO IS A CANDIDATE FOR USING A CGM IN THE INTENSIVE CARE UNIT

Reports are emerging on the use of wearable CGMs in the intensive care unit (ICU) setting during the COVID-19 pandemic. CGMs may be practical in the ICU for patients that require continuous intravenous insulin infusion, where hourly POC blood glucose testing is not practical. CGMs can be attractive alternatives to hourly POC capillary blood glucose testing because of the exposure risk of healthcare workers performing assisted monitoring of blood glucose [23], the amount of time needed to don and doff PPE in order to perform a POC capillary blood glucose test, and the depletion of scarce PPE used up just to perform a single POC capillary blood glucose test. Also, at some hospitals there can be a shortage of POC blood glucose monitors. Careful monitoring of POC blood glucose along with CGM readings are required to identify potential mechanical interference [24], such as pressure induced sensor attenuation [25]. Table 2 presents a review of the literature of clinical trials of CGM use in ICU settings for adult patients [26-68]. Table 3 presents a review of the literature of clinical trials of CGM use

Table 2. Clinical Trials of CGM Use in ICU Settings for Adult Patients

Study	Year	First author country	Population	CGM type	CGM manufacturer	Performance measurement	Comparator
Goldberg et al. [30]	2004	USA	ICU (n=22)	CGMs	Medtronic MiniMed	Accuracy	Capillary by POC
Vriesendorp et al. [31]	2005	Netherlands	OR, SICU (n=8)	CGMs and GlucoDay	Medtronic MiniMed and A. Menarini Diagnostics (A. Menarini Diagnostics Ltd., Florence, Italy)	Accuracy and feasibility	Arterial by blood gas analyzer
Corstjens et al. [32]	2006	Netherlands	MICU (n=45)	System Gold	Medtronic MiniMed	Accuracy	Arterial by blood gas analyzer, YSI (YSI 2300 STAT Plus glucose and lactate analyzer, YSI Life Science, Yellow Springs, OH, USA) and POC
De Block et al. [33]	2006	Belgium	MICU (n=50)	Glucoday	A. Menarini Diagnostics	Reliability	Arterial
Price et al. [34]	2008	UK	Mixed ICU (n=17)	Guardian	Medtronic MiniMed	Accuracy	Arterial by blood gas analyzer and POC
Logtenberg et al. [35]	2009	Netherlands	Cardiac surgery ICU (n=30)	Paradigm	Medtronic MiniMed	Accuracy and glycemic control	Capillary, arterial, and venous by POC
Yamashita et al. [36]	2009	Japan	ICU (n=50)	STG 22	Nikkiso Co. Ltd. (Tokyo, Japan)	Accuracy	Arterial by blood gas analyzer
Rabiee et al. [37]	2009	USA	SICU/Burn (n=19)	Dexcom STS	Dexcom	Accuracy and reliability	Capillary by POC and serum by lab
Holzinger et al. [38]	2009	Austria	MICU (n=50)	System Gold	Medtronic MiniMed	Accuracy and reliability	Arterial by blood gas analyzer
Holzinger et al. [39]	2010	Austria	ICU, mechanical ventilation (n=24)	Guardian	Medtronic MiniMed	Glycemic control (% time at glucose <110 mg/dL), LOS, mortality	Arterial by blood gas analyzer and blinded Medtronic MiniMed System Gold CGM
Jacobs et al. [40]	2010	USA	ICU (n=29)	Guardian RT	Medtronic MiniMed	Accuracy and feasibility	Capillary by POC
Brunner et al. [41]	2011	Austria	MICU (n=174)	Guardian & System Gold	Medtronic MiniMed	Accuracy and reliability	Arterial by blood gas analyzer
Kalmovich et al. [42]	2012	Israel	Perioperative cardiac surgery (n=32)	System Gold Blinded	Medtronic MiniMed	Accuracy and feasibility	Venous by blood gas analyzer
Lorencio et al. [43]	2012	Spain	ICU (n=41)	Guardian	Medtronic MiniMed	Accuracy	Arterial by blood gas analyzer
Kopecky et al. [44]	2013	Czech Republic	Cardiac ICU (n=24)	Guardian RT	Medtronic MiniMed	Accuracy and glycemic control	Arterial by blood gas analyzer and computer (enhanced model predictive control) algorithm alone

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Table 2. Continued

Study	Year	First author country	Population	CGM type	CGM manufacturer	Performance measurement	Comparator
Leelarathna et al. [45]	2013	UK	Neurosurgical ICU (*n*=24)	FreeStyle Navigator	Abbott Diabetes Care	Glycemic control	Arterial by blood gas analyzer
Rodriguez-Quintanilla et al. [46]	2013	Mexico	ICU (*n*=16)	Guardian RT	Medtronic MiniMed	Time to normoglycemia	Venous and capillary by POC
Schuster et al. [47]	2014	USA	SICU (*n*=24)	Guardian	Medtronic MiniMed	Accuracy	Capillary by POC
Kosiborod et al. [48]	2014	USA	Cardiac ICU (*n*=21)	Sentrino	Medtronic MiniMed	Accuracy and reliability	Central venous by POC or lab
Boom et al. [49]	2014	Netherlands	MICU/SICU (*n*=156)	FreeStyle Navigator	Abbott Diabetes Care	Accuracy and glycemic control	Arterial by blood gas analyzer, and POC
Umbrello et al. [50]	2014	Italy	MICU (*n*=6)	OptiScanner 5000	OptiScan Biomedical	Glycemic control	Central venous by blood gas analyzer or lab (reported elsewhere)
van Hooijdonk et al. [51]	2015	Netherlands	ICU (*n*=50)	Sentrino	Medtronic MiniMed	Accuracy and reliability	Arterial by blood gas analyzer
Sechterberger et al. [52]	2015	Netherlands	Cardiac ICU (*n*=8)	FreeStyle Navigator	Abbott Diabetes Care	Accuracy	Arterial by blood gas analyzer
Punke et al. [53]	2015	Germany	SICU (*n*=14)	Sentrino	Medtronic MiniMed	Accuracy	Arterial by blood gas analyzer
Ballesteros et al. [54]	2015	Spain	MICU (*n*=18)	Soft Sensor	Medtronic MiniMed	Accuracy	Capillary by POC
De Block et al. [55]	2015	Belgium	MICU (*n*=35)	GlucoDay S	A. Menarini Diagnostics	Accuracy and glycemic control	Arterial by blood gas analyzer and blinded microdialysis-based CGM
Gottschalk et al. [56]	2016	Germany	Extracorporeal cardiac life support (*n*=25)	Sentrino	Medtronic MiniMed	Accuracy	Arterial by blood gas analyzer
Nohra et al. [57]	2016	USA	SICU (*n*=23)	Optiscanner 5000	Optiscan Biomedical	Accuracy	Central venous by YSI
Righy Shinotsuka et al. [58]	2016	Belgium	ICU (*n*=88)	OptiScanner 5000	Optiscan Biomedical	Accuracy	Arterial by YSI
Wollersheim et al. [59]	2016	Germany	MICU (*n*=20)	Sentrino	Medtronic MiniMed	Accuracy and feasibility	Arterial, central venous, or venous by blood gas analyzer
Schierenbeck et al. [60]	2017	Sweden	Cardiac ICU (*n*=26)	FreeStyle Libre Subcutaneous-CGM vs. Eirus Intravascular	Abbott Diabetes Care and Maquet Getinge Group	Accuracy	Arterial by blood gas analyzer and capillary by POC
Song et al. [61]	2017	Republic of Korea	OR, ICU (*n*=22)	Guardian	Medtronic MiniMed	Accuracy and reliability	Arterial by blood gas analyzer
Ancona et al. [62]	2017	Australia	ICU (*n*=8)	FreeStyle Libre CGM	Abbott Diabetes Care	Accuracy and feasibility	Arterial by blood gas analyzer or capillary by POC

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Table 2. Continued

Study	Year	First author country	Population	CGM type	CGM manufacturer	Performance measurement	Comparator
Bochicchio et al. [63]	2017	USA	ICU (n=243)	OptiScanner 5000	OptiScan Biomedical	Accuracy	Arterial, central venous, or venous by YSI
Rijkenberg et al. [64]	2018	Netherlands	Mixed ICU (n=155)	FreeStyle Navigator	Abbott Diabetes Care	Accuracy and reliability	Arterial by blood gas analyzer
Nukui et al. [65]	2019	Japan	Acute stroke (n=39)	FreeStyle Pro CGM	Abbott Diabetes Care	Accuracy and efficacy	Capillary by POC
Furushima et al. [66]	2020	Japan	ICU (n=40)	FreeStyle Libre CGM	Abbott Diabetes Care	Determine the mean amplitude of glycemic excursions	Arterial by blood gas analyzer
Chow et al. [67]	2020						
	USA	ICU (n=1)	Dexcom G6	Dexcom	Accuracy	Capillary by POC and venous (methods not specified)	
Sadhu et al. [29]	2020	USA	ICU (n=11)	Guardian Connect Dexcom G6	Medtronic MiniMed Dexcom	Accuracy and feasibility	Capillary, venous, and arterial by POC
Garelli et al. [68]	2020	Argentina	ICU patients with COVID-19 (n=3) (2 other pediatric patients were also studied)	Dexcom G6 for the ICU patients	Dexcom	Glycemic control using a new multisensor platform	None
Agarwal et al. [27]	2020						
	USA	ICU (n=47)	Dexcom G6	Dexcom	Accuracy	Capillary by POC	
Chow et al. [28]	2021	USA	ICU patients with COVID-19 (n=30)	Dexcom G6	Dexcom	Clinical utility and accuracy	Arterial by POC
Perez-Guzman et al. [26]	2021	USA	OR and cardiac ICU patients without diabetes undergoing scheduled or urgent coronary artery bypass surgery	Dexcom G6	Dexcom	Accuracy	Capillary by POC

CGM, continuous glucose monitor; ICU, intensive care unit; POC, point of care; OR, operating room; SICU, surgical ICU; MICU, medical ICU; COVID-19, coronavirus disease 2019.

in ICU settings for pediatric patients [68-74]. Every table in this article presenting studies of CGM trials in hospital settings refers to protocols where these devices are intended to determine insulin doses administered manually rather than by way of automated delivery. In these intended settings, patients are already being closely monitored and there is no convincing data currently that CGM technology will be useful in this setting. Furthermore, patients in an intensive care setting frequently require pressors, which can cause peripheral vasoconstriction. It is possible that in such patients the circulation to the skin where CGMs are placed might be decreased and the CGM readings might or might not be accurate. Recently, Perez-Guzman et al. [26] performed a prospective study with the Dexcom G6 in the ICU, for 15 patients with stress hyperglycemia treated with continuous insulin infusion and vasopressors. The reported accuracy was a MARD of 12.9%. Agarwal et al. [27] conducted a retrospective analysis of 11 diabetes patients who were using Dexcom G6 CGMs. Their series included patients who had anasarca and/or were receiving renal replacement therapy, vasopressors, mechanical ventilation support, or high-dose glucocorticoids.

Table 3. Clinical Trials of CGM Use in ICU Settings for Pediatric Patients

Study	Year	First author country	Population	Type of CGM	CGM manufacturer	Performance measurement	Comparator
Bridges et al. [69]	2010	USA	ICU (n=47)	Guardian	Medtronic MiniMed	Accuracy	Arterial, venous, and capillary by iSTAT POC and lab
Steil et al. [70]	2011	USA	Cardiac ICU (n=311)	Guardian	Medtronic MiniMed	Accuracy and hypoglycemia prevention	Arterial by POC and lab
Prabhudesai et al. [71]	2015	UK	ICU (n=19)	Guardian	Medtronic MiniMed	Accuracy	Arterial by lab
Kotzapanagiotou et al. [72]	2020	Greece	ICU (n=16)	FreeStyle Libre	Abbott Diabetes Care	Accuracy	Arterial by blood gas analyzer capillary by POC, biochemical serum by lab
Sopfe et al. [73]	2020	USA	Stem cell transplantation (n=29)	FreeStyle Libre Pro	Abbott Diabetes Care	Accuracy	Central venous by lab
Garelli et al. [68]	2020	Argentina	ICU patients with COVID-19 (n=2) (3 other adult patients were also studied)	Dexcom G6 for the ICU patients	Dexcom	Glycemic control using a new multisensor platform	None
Chesser et al. [74]	2021	USA	Children with postprandial hypoglycemia due to late dumping syndrome following gastric surgeries (n=3)	Dexcom G4 Dexcom G5 Dexcom G6	Dexcom	Diagnose hypoglycemia due to late dumping syndrome. Also to determine best treatment strategies and feeding regimens.	None

AID, automated insulin delivery; CGM, continuous glucose monitoring; ICU, intensive care unit; POC, point of care; COVID-19, coronavirus disease 2019.

The MARD of these CGMs was 12.58% [27]. In a different cohort of 30 critically ill patients, Chow et al. [28] found a decrease in mean glucose in 77% of the patients after Dexcom G6 monitoring was started. For the full cohort, there was a 14% decrease (235.7 to 202.7 mg/dL, P=0.0003) in mean sensor glucose. Sadhu et al. [29] reported similar accuracy between the Medtronic Guardian Connect (Medtronic Minimed, Northridge, CA, USA) and Dexcom G6 devices in a cohort of 11 ICU patients. This ICU data is promising for eventual routine use of CGMs in an ICU setting. However, these studies have limitations, including small sample sizes, inconsistent reference matrices (either capillary or arterial blood), and little information on glycemic or clinical outcomes.

As the information about CGMs in the ICU is evolving, we currently recommend using CGM in the ICU for selected candidates, such as patients with COVID-19, who (1) are treated with continuous intravenous insulin infusion; (2) develop steroid-induced hyperglycemia; or (3) have medical nutrition therapy-induced hyperglycemia or high glycemic variability. We also recommend using a hybrid approach (combining CGM with periodical POC blood glucose testing) in the ICU to ensure consistent accuracy. CGM is currently not widely used for non-COVID patients outside of research settings.

WHO IS A CANDIDATE FOR USING A CGM IN THE WARDS

An emerging use for CGM in the hospital will be detection and prevention of hypoglycemia on the wards among insulin-treated patients. This is a new application of CGM and the early evidence from trials to detect this complication of hospitalizations are promising. Table 4 presents a review of the literature of clinical trials of CGM use in non-ICU settings for adult patients [75-89]. Ward patients sometimes need to have their ongoing

Table 4. Clinical Trials of CGM Use in Non-ICU Settings for Adult Patients

Study	Year	First author country	Patient population	CGM type	CGM manufacturer	Performance measurement	Comparator
Dungan et al. [77]	2012	USA	T1DM and T2DM (n=58), on intravenous or subcutaneous insulin	iPro system	Medtronic MiniMed	Accuracy	Capillary by POC
Burt et al. [78]	2013	Australia	T1DM and T2DM, on basal bolus insulin (n=26)	System Gold	Medtronic MiniMed	Accuracy and glycemic control	Capillary by POC
Gomez et al. [79]	2015	Colombia	T2DM, on basal bolus insulin (n=38)	iPro2 system	Medtronic MiniMed	Glycemic control and hypoglycemia detection	Capillary by POC
Schaupp et al. [80]	2015	Austria	T2DM, on basal bolus insulin (n=84)	iPro2 system	Medtronic MiniMed	Accuracy	Capillary by POC
Spanakis et al. [81]	2018	USA	T2DM, on insulin therapy (n=5)	Dexcom G4 CGM with Share2 application	Dexcom	Glucose telemetry system feasibility	None
Migdal et al. [82]	2020	USA	Adult medicine and surgery patients with T1DM and T2DM (n=49)	Dexcom (CGM type unspecified)	Dexcom	Precision and accuracy	Capillary by POC
Shehav-Zaltzman et al. [83]	2020	Israel	T1DM on CSII (n: 1) and T2DM on basal bolus (n=3), COVID-19 wards (n=5)	Guardian	Medtronic MiniMed	Feasibility	None
Singh et al. [84]	2020	USA	T2DM, on basal-bolus insulin (n=13)	Dexcom G4 Platinum CGM	Dexcom	Feasibility and prevention of hypoglycemia	Blinded CGM
Tripyla et al. [75]	2020	Switzerland	Prediabetes patients undergoing elective abdominal surgery (n=20)	Dexcom G6	Dexcom	Accuracy	Capillary by POC
Reutrakul et al. [85]	2020	USA	Diabetes (unspecified type) on subcutaneous insulin injection with COVID-19 (n=1)	Dexcom G6	Dexcom	Feasibility	Capillary by POC
Galindo et al. [86]	2020	USA	T2DM, on basal-bolus insulin (n=97)	FreeStyle Libre Pro CGM	Abbott Diabetes Care	Accuracy and hypoglycemia detection	Capillary by POC
Nair et al. [76]	2020	USA	Surgical ward (n=10)	Dexcom G6 Blinded	Dexcom	Accuracy	Capillary by POC
Singh et al. [87]	2020	USA	T2DM, on basal-bolus insulin (n=72)	Dexcom G6	Dexcom	Prevention of hypoglycemia	Blinded CGM
Fortmann et al. [88]	2020	USA	T2DM on subcutaneous insulin (n=110)	Dexcom G6	Dexcom	Effectiveness	Capillary by POC
Ushigome et al. [89]	2021	Japan	Diabetes (unspecified type) with COVID-19 (n=1)	Dexcom G4 Platinum	Dexcom	Safety and effectiveness	Lab

CGM, continuous glucose monitor; ICU, intensive care unit; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; POC, point of care; CSII, continuous subcutaneous insulin infusion; COVID-19, coronavirus disease 2019.

insulin dose significantly decreased suddenly if they miss a meal or if they are receiving a regimen of corticosteroids or parenteral nutrition, which is suddenly curtailed or discontinued, and the communication between the physicians, nurses, and pharmacists is not optimal. Hypoglycemia detection is particularly useful in a setting where ward nurses are not always with

Table 5. Clinical Trials of CGM Use to Detect Hypoglycemia in Hospitalized Patients

Study	Year	First author country	Patient population	CGM type	CGM manufacturer	Definition of hypoglycemia	Outcome
Steil et al. [70]	2011	USA	Cardiac ICU (n=311)	Guardian	Medtronic MiniMed	Blood glucose <60 mg/dL (3.3 mmol/L)	No reduction if CGM alarm was set at 60 mg/dL. 18 out of 40 episodes of hypoglycemia detected when the alarm threshold set to 70 mg/dL. One to two false hypoglycemia alarms in each patient
Gomez et al. [79]	2015	Colombia	T2DM, on basal bolus insulin (n=38)	iPro2 system	Medtronic MiniMed	Hypoglycemia was defined as blood glucose <70 mg/dL (3.9 mmol/L) or <60 mg/dL (3.3 mmol/L).	CGM is more effective than POC testing for detecting hypoglycemic episodes and asymptomatic hypoglycemia using either definition of hypoglycemia.
Singh et al. [84]	2020	USA	T2DM, on basal-bolus insulin (n=13)	Dexcom G4 Platinum CGM	Dexcom	Blood glucose <70 mg/dL (3.9 mmol/L)	A hypoglycemia prevention protocol using a specific Glucose Telemetry System can reduce incidence of inpatient hypoglycemia
Galindo et al. [86]	2020	USA	T2DM, on basal-bolus insulin (n=97)	FreeStyle Libre Pro CGM	Abbott Diabetes Care	Hypoglycemia was defined as <70 mg/dL (3.9 mmol/L) or <54 mg/dL (3.0 mmol/L).	Hypoglycemic events were detected more often by CGM use than POC testing.
Singh et al. [87]	2020	USA	T2DM, on basal-bolus insulin (n=72)	Dexcom G6	Dexcom	Hypoglycemia was defined as blood glucose <70 mg/dL (3.9 mmol/L) for over 15 minutes. Clinically significant hypoglycemia was defined as blood glucose <54 mg/dL (3.0 mmol/L).	In patients with type 2 diabetes who have been treated with insulin, hypoglycemia can be decreased by a combination of RT-CGM use with a protocol for hypoglycemia prevention.
Chesser et al. [74]	2021	USA	Children with postprandial hypoglycemia due to late dumping syndrome following gastric surgeries (n=3)	Dexcom G4 Dexcom G5 Dexcom G6	Dexcom	Hypoglycemia was not explicitly defined, but one patient whose glucose level was up to 65 mg/dL was considered hypoglycemic.	CGM can be used for early diagnosis of dumping syndrome by revealing glycemic dysregulation. It can also be used to evaluate the effectiveness of treatments and feeding regimens for postprandial hypoglycemia due to late dumping syndrome.

CGM, continuous glucose monitor; ICU, intensive care unit; T2DM, type 2 diabetes mellitus; POC, point of care; RT-CGM, real-time continuous glucose monitor.

the patient and where a patient might have hypoglycemia unawareness or might fail to complain of hypoglycemic symptoms and then slowly become confused or even unconscious. Table 5 presents a review of the literature of clinical trials of CGM use to detect hypoglycemia in hospitalized patients [70,74,79,84,86,87]. It is likely that CGM technology will be used frequently for this purpose in the future.

Based on our experience and the results of recent studies of currently available CGM systems, we believe that selected types of patients could benefit from wearing a CGM in a medical or surgical ward. These include patients with (1) a high risk of hypoglycemia (e.g., with a fragile habitus, end stage renal disease, advanced age, or poor nutrition); (2) type 1 diabetes; (3) a requirement for multiple daily insulin injections; (4) high glycemic variability; (5) steroid-induced hyperglycemia; and (6) enteral or parenteral feeding-induced hyperglycemia.

WHO IS A CANDIDATE FOR USING A CGM IN SURGERY

The opportunity to see a full glycemic profile during the operative time will be ideal for an anesthesiologist (who will receive

glucose readings every 5 to 15 minutes) managing patients with or without diabetes (including those with stress hyperglycemia). However, until recently, accuracy and performance data of CGMs during surgery has been unreliable. One recent study by Tripyla et al. [75] reported a MARD of 12.7% with the Dexcom G6 during elective abdominal surgery. Nair et al. [76] performed a prospective pilot study, in which they included 10 adult patients with a diagnosis of diabetes who were undergoing elective general surgery. They found that postoperatively, Dexcom G6 had a MARD of 9.4%. In 15 patients undergoing coronary artery bypass graft surgery, Perez-Guzman et al. [26] noted that CGM technology was not consistently reliable in the operating room (OR), which they attributed to electrocautery interference. They observed signal loss and negative bias during surgery in 60% of their patients. However, some sensors recovered immediately after surgery and had sustained accuracy postoperatively, even during exposure to vasopressors in the ICU. Based on these results they suggested avoiding the use of a CGM to make clinical decisions during surgery unless adequate accuracy of the device is confirmed and the possibility of needing a new sensor is excluded [26]. We do not recommend that any patient in the OR should be managed with a CGM system. For patients undergoing surgery who are already using a CGM, we recommend confirming accuracy in the immediate postoperative period, because interference due to electrocautery may occur in the OR causing temporary or permanent device dysfunction [26].

RESPONSIBILITIES OF PHYSICIANS, HOSPITALS, AND INDUSTRY

In September 2020, Diabetes Technology Society published the '*Continuous glucose monitors and automated insulin dosing systems in the hospital consensus guideline*' to address how and when to best use both subcutaneous CGMs and automated insulin delivery (AID) systems, as well as to promote clinical research utilizing these devices [21]. The consensus panel of 24 international experts in the use of CGM developed recommendations for physicians (which the guideline referred to as healthcare professionals), nurses, and hospitals, as well as for industry. The panel covered five topics: (1) continuation of home CGMs after hospitalization; (2) initiation of CGMs in the hospital; (3) continuation of automated insulin dosing systems in the hospital; (4) logistics and hands-on care of hospitalized patients using CGMs and automated insulin dosing systems; and (5) data management of CGMs. The panelists voted on 78 proposed recommendations and 77 recommendations were endorsed and classified as either strong (80% to 100% agreement) or mild (60% to 79% agreement). One recommendation failed to reach consensus.

IMPLICATIONS OF CGM USE FOR BEDSIDE NURSES

As inpatient CGM use increases in people with both type 1 and type 2 diabetes, the bedside nurse needs to become familiar with this technology and its advantages and limitations. Understanding that ISF glucose lags behind capillary glucose is important when recognizing and treating hypoglycemia. For example, a patient may feel fine after receiving an appropriate hypoglycemia treatment, and the fingerstick value may be above the recommended threshold of 80 to 100 mg/dL, but the sensor glucose may still reflect a value under 70 mg/dL. Any discrepancies between patients' symptoms and sensor numbers require a confirmatory finger stick POC capillary blood glucose measurement.

Most medical centers still require finger stick values for dosing insulin as a safety precaution, as if the devices are intended for adjunctive use, even though for outpatients the FDA-cleared factory-calibrated CGMs are approved for non-adjunctive use. Hospitals need a written policy and/or care guideline to provide medical and nursing staff with a system for charting decisions based on CGM data because these devices are not cleared for hospital use and it may be difficult to enter sensor values into the EHR.

Another care concern is documentation of the sensor placement location and inspection of the site any time from every shift to daily. For all radiologic studies, the sensor will need to be removed from the skin and the transmitter and/or receiver should be safely stored. As most medical centers do not carry sensor supplies, patients being admitted should be advised to bring additional sensor supplies.

HOSPITAL CGM DATA

CGM data for a hospitalized patient cannot be confirmed through a test using a reference method because it is almost impossible to assay ISF. Many hospital clinical chemists consider CGM data analogous to vital sign information, which is being monitored frequently but which cannot be individually confirmed for accuracy. A CGM can be calibrated in the factory for outpatient use, but it is not known whether this type of calibration will be adequate for a hospitalized patient.

CGM data is currently not compatible with the vast majority of EHRs. A screen shot of a tracing cannot be searched and

therefore, this type of record will have only limited value after the day it is collected. The selection of which types of CGM data to store will likely be various 24-hour or 14-day metrics, such as time in range, glycemic variability, or percentage of time spent in a slightly low, extremely low, slightly high, and extremely high range [90], because the amount of storage space needed to save every data point (up to 288 glucose readings per day or more) could overwhelm many hospital EHRs. Hospitals, CGM manufacturers, and EHR vendors must work together to integrate the most useful CGM data into the EHR. This data acquisition process must be compliant with regulatory privacy rules and sound cybersecurity policies. Successful integration of real-time CGM data into the EHR has been reported in a limited number of cases, so there is hope for the future [91,92]. If CGM data of a hospitalized patient must reside on the website of a CGM manufacturer or a software integrator of data from multiple CGM manufacturers, then the hospital might have concerns about how the data is protected from cyber breaches and who is liable if such data from a hospitalization is lost.

FUTURE TECHNOLOGY

It is likely that future CGM sensors will be more accurate with continued improvements in sensor sensitivity and algorithm fidelity for converting a signal to a glucose concentration. These sensors will likely have a smaller form factor, a longer life, and louder alarms for out of range glucose concentrations. With longer-duration sensors, it will be necessary to develop better adhesives that are less likely to cause a rash [93]. In order to prolong viable implantation time, it will be necessary to develop better coatings that will minimize the foreign body response that limits integration of the sensor into the subcutaneous space [94]. Future CGM data will become interconnected with multiple other data streams to provide a more nuanced pattern of how behavior affects glycemia and to better predict glucose patterns [95]. Data fusion technology will be combined with decision support and behavioral modification software for real-time management and in the hospital this management will be in the form of warnings and treatment recommendations for the hospital staff [96].

Just as in the past, many did not expect that a subcutaneous glucose sensor would ever provide accurate glucose readings comparable to blood glucose testing, many now believe that a wearable optical noninvasive glucose monitor [97] or a monitor that is based on noninvasive collection and measurement of a body fluid (such as sweat, saliva, or tears) [98] cannot be developed to measure glucose almost as accurately as an invasive blood test. These doubters of optical noninvasive technology might prove to be just as wrong as the doubters of subcutaneous minimally invasive technology were 20 years ago. Whether these new technologies can become established will depend significantly on whether human physiology will allow for body compartments other than blood or skin to be measured without significant lag during periods of dynamic fluctuations—not on the expected accuracy of future sensors to measure these matrices. Eventually it will become clear which individual or composite metrics for CGMs (if any) and which definitions of a hypoglycemic episode will best correlate with specific hospital outcomes [99].

CONCLUSIONS

CGMs are gradually migrating from the outpatient setting into the inpatient setting because these devices are becoming more compatible with the needs of the healthcare team that cares for these inpatients. The trend accelerated because of the COVID-19 pandemic, which necessitated collecting data remotely from patients when possible. It is too soon to know whether the accuracy and clinical benefits of CGMs will result in widespread adoption or regulatory clearance of this technology for hospital use. CGMs work extremely well on outpatients and there is reason to believe that they could prove to be effective to achieve well-defined endpoints for hospitalized patients.

CONFLICTS OF INTEREST

M. Citlalli Perez-Guzman, Trisha Shang, and Jennifer Y. Zhang have nothing to disclose. Donna Jornsay was a speaker for Abbott Diabetes Care and BD, and holds Medtronic stock. David C. Klonoff is a consultant for EOFlow, Fractyl, Lifecare, Novo, Roche, Samsung, and Thirdwayv.

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