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REVIEW

Use of Continuous Glucose Monitors to Manage Type 1 Diabetes Mellitus: Progress, Challenges, and Recommendations

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Abstract: Type 1 diabetes (T1D) management has been revolutionized with the development and routine utilization of continuous glucose monitoring (CGM). CGM technology has allowed for the ability to track dynamic glycemic fluctuations and trends over time allowing for optimization of medical therapy and the prevention of dangerous hypoglycemic events. This review details currently-available real-time and intermittently-scanned CGM devices, clinical benefits, and challenges of CGM use, and current guidelines supporting its use in the clinical care of patients with T1D. We additionally describe future issues that will need to be addressed as CGM technology continues to evolve.

Keywords: continuous glucose monitoring, type 1 diabetes, time in range, hemoglobin A1c

Introduction

Type 1 diabetes (T1D) management has evolved significantly over the past several years, particularly with the widespread use of continuous glucose monitoring (CGM). Frequent glucose monitoring is a cornerstone of clinical management. Even though capillary blood glucose monitoring (BGM) systems have become more accurate and easier to use, they only offer static information about blood glucose levels. Conversely, CGM technology is able to capture dynamic changes in glucose over time, hypo- and hyperglycemic fluctuations, trends, and patterns, which enables clinicians to perform a more comprehensive analysis of glycemic trends and therefore to more effectively guide therapy.[1] Significant progress has been made over the years, and multiple studies have demonstrated that CGM-derived time in range (TIR, 70–180 mg/dL or 3.9–10.0 mmol/L) levels correlate with hemoglobin A1c (HbA1c).[2] Emerging data also suggest that TIR can be used as a surrogate marker to predict diabetes-related complications.[3] CGM has proven to be effective in achieving glycemic goals while minimizing risk of hypoglycemia and contributing to improvement in quality of life.[4,5]

Although implementation of CGM is not without its own challenges, CGM has been recognized as the standard of care for patients with T1D by various professional societies, including the Endocrine Society, American Diabetes Association, and the American Association of Clinical Endocrinology.[6–8]

Continuous Glucose Monitoring Systems

CGM systems measure interstitial fluid glucose levels continuously or semi-continuously, and report data every 1–15 minutes. The most commonly used systems utilize an enzymatic reaction based on glucose oxidase, while other systems (such as Eversense from Senseonics, [Germantown, MA, USA]) use a fluorescence-sensing technology.[9] Data collected by these systems are sent to a transmitter, then displayed in various devices. CGM systems can display their data on a receiver (Dexcom G6 and G7 [Dexcom Inc, San Diego, CA, USA]), FreeStyle Libre 14 day and FreeStyle libre 2

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(Abbott Diabetes Care Inc, Alameda, CA, USA) or via mobile applications on smartphones and smartwatches (Apple/Android for DexcomG6 and G7 Mobile; Medtronic Guardian Connect Mobile, FreeStyle Libre 14 days, FreeStyle Libre 2 and 3 Librelink; Eversense Mobile app).[10–14]

There are two main categories of CGM: professional (diagnostic) and personal. Professional CGM systems are used to record and evaluate glycemic data over a period of 7–14 days. This procedure can be either blinded or unblinded. During the blinded procedure the patient does not have access to CGM data until evaluated by the provider and analysis is, therefore, retrospective.[1] On the contrary, during the unblinded CGM procedure, patients have access to CGM data and are able to make adjustments to the regimen in real-time or after evaluation of the data with the healthcare provider.[1]

Personal CGM systems are FDA-approved to be used in T1D and T2D age 2 and above (with brand-specific age approval). Sensor life can range from 7–180 days, depending on the brand. Currently US-FDA approved personal CGM systems are outlined in Table 1.

There are two different types of personal CGM systems: real-time CGM (rt-CGM) and intermittently scanned CGM (is-CGM). rt-CGM systems allow users to visualize glucose levels, determine the direction of change with trend arrows, and receive alerts for current or impending hypoglycemia or hyperglycemia. These can also have alerts that predict urgent low glucose levels or can alert the user with on-body transmitter vibrations. The newest rt-CGM systems in the USA are the Abbott FreeStyle Libre 3 and the Dexcom G7 (see Table 1). These new systems have updated, advanced features and even greater accuracy that will provide individuals with diabetes enhanced CGM use and experience overall. The Abbott FreeStyle Libre 3 is a rt-CGM with every minute data transmission to a smartphone application, 1 hour warm-up period and 14 days duration; at the size of two stacked pennies, it is the thinnest available rt-CGM in the market.[15] Dexcom G7 rt-CGM has the shortest warm-up period in the market of 30 minutes, predictive low alerts and alarms, 10 days sensor duration, and a 12 hours grace period to replace finished sensors for a more seamless transition between sessions.[16] Is-CGM systems measure glucose levels continuously and record readings every 15 minutes; however, in order to view glucose levels, the user needs to scan the sensor with a reader or a smartphone application. The US-FDA approved is-CGM system is the Abbott FreeStyle Libre system; the original system did not have audible alarms; however, the updated FreeStyle Libre 2 system does have optional alarms for hypoglycemia and hyperglycemia.[17]

According to the American Diabetes Association 2023 Standards of Care, rt-CGM or is-CGM should be offered to youth and adults with type 1 and type 2 diabetes on intensive insulin therapy or continuous subcutaneous insulin infusion who are able to use the devices safely. In addition, rt-CGM or is-CGM should be offered for diabetes management in adults with diabetes on less intensive insulin therapy (ie, basal insulin with oral medication or non-insulin injectables).[7]

More specifically, rt-CGM should be considered in people with diabetes who are at risk of hypoglycemia, in those who have hypoglycemia unawareness, as well as in people with frequent nocturnal hypoglycemia events.[18] Is-CGM may be considered for people with T2D, who are not on intensive insulin therapy or with intact hypoglycemia awareness who are unable or unwilling to monitor glucose by finger-sticks. Most CGM systems are approved for non-adjunctive use, in that the users do not have to confirm blood glucose by fingerstick prior to making insulin dose decisions. While some CGM systems still require calibrations, most of them are factory calibrated. Nevertheless, users should still confirm glucose level measurements with finger sticks whenever symptoms do not match sensor readings.

Users can view CGM reports using their smartphone applications, whereas healthcare providers can review these reports using several different platforms (Dexcom CLARITY, Glooko, Tidepool, Abbott LibreView, Medtronic CareLink and Senseonics Eversense Pro Data Management System).[1] In 2019 the International Consensus on Time in Range standardized the reporting of CGM metrics with the ambulatory glucose profile (AGP) becoming the standard CGM report. The AGP report includes a variety of glucometrics that can be analyzed and interpreted by providers in order to make important clinical management decisions. These are the time in ranges such as time in target range (TIR) (70–180 mg/dL or 3.9–10 mmol/L), time below range (TBR) (<70 mg/dL or <3.9 mmol/L), time above range (TAR) (>180 mg/dL or >10 mmol/L), glycemic variability, and glucose management indicator (GMI). The latter represents a linear-regression CGM-derived estimation of average glucose levels of at least 14 days expressed in percentages.[19–21]

Table 1 US-FDA Approved Personal CGM Systems

CGM Category	Rt-CGM					Is-CGM
	Dexcom G6	**Dexcom G7**	**Medtronic Guardian 3**	**Senseonics Eversense**	**Abbott FreeStyle Libre 3**	**Abbott Freestyle Flash Libre 14 Days and Libre 2**
Population age (years)	≥2	≥2	≥7	≥18	≥4	Libre 14 days 18 Libre 2 ≥4
Pregnancy approval	FDA - No CE - Yes	Yes	No	No	Yes	Yes (Libre 2)
Warm up time (hours)	2	0.5	2	24	1	1
Sensor wear (days)	10	10	7	90 and 180	14	14
Calibrations	None	None	2–4/day	1-2/day	None	None
Non-adjunctive Use	Yes	Yes	No	Yes	Yes	Yes
Audible alarms/alerts	Yes Predictive alerts	Yes Predictive alerts	Yes Predictive alerts	Yes Predictive alerts (vibrate)	Yes (optional)	Libre: No Libre 2: Yes (optional)
Trend arrows	Yes	Yes	Yes	Yes	Yes	Yes
Share features	Yes (Dexcom Share)	Yes (Dexcom Share)	Yes (Guardian Connect Mobile)	Yes	Yes (Librelink)	Yes (Librelink)
Pump integration	Tandem t:slimx2 w/Basal IQ Tandem t:slim x2 w/ Control IQ Insulet Omnipod 5	N/A	Medtronic 670G, 770G	None	None	None
Software compatibility	Dexcom Clarity Glooko, Tidepool	Dexcom Clarity	Medtronic CareLink, Tidepool	Glooko	LibreView	LibreView
Acetaminophen interference	No	No	Yes	No	No	No
MARD %	9	8.2	Abdomen: 10.6–9.6 Arm: 9.1–8.7	8.8	7.9	Libre: 9.4 Libre 2: 9.3
X-Ray/MRI compatible	No	No	No	Yes	No	No
Receiver	Yes	Yes	No	No	No	Yes
Use with Smartphone App	Yes	Yes	Yes	Yes	Yes	Yes

CGM systems provide trend arrows to reflect rates of glucose changes. These can be utilized to anticipate future glucose levels and make adjustments to insulin regimen as needed. Providers should keep in mind that current CGM systems have different trend arrows with different rates of changes, unique to each system. Clinicians should be aware of these nuances in order to accurately interpret the information provided by the specific CGM system.[1] Table 2 represents the trend arrow for various CGM systems.

Progress

Since the introduction of CGM, multiple studies have shown that CGM use significantly improves HbA1c levels, while simultaneously decreasing and even preventing hypoglycemia. A randomized controlled trial (RCT) of 158 subjects compared HbA1c levels in people with T1D randomized to MDI plus CGM vs MDI and BGM.[4] Results showed that

Table 2 Rate of Change Trend Arrows Based on US-FDA Approved CGM Brands

Arrow Direction	Medtronic Guardian 3	Dexcom G6, G7	Abbott FreeStyle Libre (14 Days, 2 and 3)	Senseonics Eversense (90 and 180 Days)
⇈	Glucose is rising at a rate of ≥3 mg/dL per minute	N/A	N/A	N/A
↑↑	Glucose is rising at a rate of ≥2 but <3 mg/dL per minute	Glucose is rapidly rising >3 mg/dL per minute	N/A	N/A
↑	Glucose is rising at a rate of ≥1 but <2 mg/dL per minute	Glucose is rising 2–3 mg/dL per minute	Glucose is rising quickly (>2 mg/dL per minute)	Very rapidly rising glucose levels, rising at a rate more than 2 mg/dL per minute
↗	N/A	Glucose is slowly rising 1–2 mg/dL per minute	Glucose is rising (1–2 mg/dL per minute)	Moderately rising glucose level, rising at a rate between 1 mg/dL and 2 mg/dL per minute
→	N/A	Steady; glucose is not increasing/decreasing >1 mg/dL per minute	Glucose is changing slowly (<1 mg/dL per minute)	Gradually rising or falling glucose levels, falling or rising at a rate between 0 and 1 mg/dL per minute
↘	N/A	Glucose is slowly falling 1–2 mg/dL per minute	Glucose is falling (1–2 mg/dL per minute)	Moderately falling glucose levels, falling at a rate between 1 mg/dL and 2 mg/dL per minute
↓	Glucose is falling at a rate of ≥1 but <2 mg/dL per minute	Glucose is falling 2–3 mg/dL per minute	Glucose is falling quickly (>2 mg/dL per minute)	Very rapidly falling glucose levels, falling at a rate more than 2 mg/dL per minute
↓↓	Glucose is falling at a rate of ≥2 but <3 mg/dL per minute	Glucose is rapidly falling >3 mg/dL per minute	N/A	N/A
⇊	Glucose is falling at a rate of ≥3 mg/dL per minute	N/A	N/A	N/A

HbA1c decreased 1.1% at 12 weeks and 1.0% at 24 weeks in the CGM group and 0.5% and 0.4%, respectively, in the usual care group ($p<0.001$) with a mean HbA1c difference of −0.6%. Median hypoglycemia (<70 mg/dL) duration was 80 min/day (IQR=36–111) in the usual care group, and 43 min/day (IQR=27–69) in the CGM group. The authors concluded that CGM use was associated with decreased HbA1c, decreased time in hypoglycemia, and high satisfaction in

adults with T1DM on MDI with HbA1c 7.5–9.9%.[4] Additionally, an RCT crossover trial of 52 subjects of 18–75 years of age with T1DM performing more than three BGM measurements per day with hypoglycemia unawareness were randomized to either 16 weeks of CGM followed by BGM or 16 weeks of BGM followed by CGM. Participants wore a blinded CGM during the BGM phase. CGM use led to improved TIR, with less TAR and TBR. TIR was 65.0% (95% CI=62.8–67.3) during CGM versus 55.4% (53.1–57.7; mean difference=9.6%, 95% CI=8.0–11.2; $p<0.0001$) while using BGM. Time spent in hypoglycemia was significantly reduced in the CGM group (6.8% vs 11.4%, mean difference=4.7%, 3.4–5.9; $p<0.000$). Time spent in hyperglycemia was also reduced in the CGM group compared to the BGM group (28.2% vs 33.2%, mean difference=5.0%, 3.1–6.9; $p<0.0001$). Significantly less severe hypoglycemia events in this high-risk population were also observed.[22]

Additionally, data from the WISDM trial suggests that use of CGM in older adults with T1D improves both glycemic control and reduces hypoglycemia events. This multi-center RCT carried out over 26 weeks compared CGM vs BGM in 203 subjects >60 years old with T1D who had an HbA1c <10% at baseline and no prior CGM use within 3 months of enrolling. They used a blinded CGM to generate baseline data. At baseline, elderly participants were spending 5% of time (72 min per day) at glucose <70 mg/dL and 1.6% of time (24 min per day) at glucose <54 mg/dL.[23] During the 12-month extension, the BGM group started CGM for an additional 26-week period. This analysis showed that CGM use in elderly subjects with T1D decreased hypoglycemia, improved TIR, and decreased HbA1c. In the CGM-CGM group, median time <70 mg/dL decreased from 5.0% to 2.6% at 26 weeks and a median of 2.8% at 52 weeks ($p<0.001$ baseline to 52 weeks). This group also spent more time in the target range (70–180 mg/dL or 3.9–10.0 mmol/L) (mean 56% vs 64%; $p<0.001$) and had lower HbA1c (mean 7.6% [59 mmol/mol] vs 7.4% [57 mmol/mol]; $p=0.01$) from baseline to 52 weeks. In the BGM-CGM group, from week 26 to week 52, median time <70 mg/dL decreased from 3.9% to 1.9% ($p<0.001$), TIR increased from 56% to 60% ($p=0.006$) and HbA1c decreased from 7.5% (58 mmol/mol) to 7.3% (57 mmol/mol) ($p=0.025$). The results of this study confirmed that use of CGM decreased hypoglycemia in the elderly without causing hyperglycemia.[24]

Another study demonstrated that CGM can unmask glucose excursions that may not be detected through BGM measurement and not captured by HbA1c levels. The authors gathered data from 61 subjects, 27 with T1D and 34 with T2D. The participants were already on insulin therapy. In the T1D group, nine participants were on insulin pumps, whereas there was one participant in the T2D group that used an insulin pump. The remainder were on MDI therapy. They compared the highest, lowest, and average blood glucose levels recorded by BGM with concurrent CGM readings. Results showed that the lowest values measured by BGM were 25 mg/dL higher than the lowest glucose level measured by CGM in both T1D ($p=0.0232$) and T2D ($p=0.0003$). The highest glucose level by BGM was 30 mg/dL lower than those recorded by CGM in T1D ($Pp=0.0005$) and 55 mg/dL in T2D ($p<0.0001$). HbA1c correlated with both BGM and CGM measurements.[25]

Interestingly, some studies have not only demonstrated that CGM use has positive effects on glucometrics, but also on quality-of-life. The DIAMOND study showed that participants who wore CGM experienced less diabetes distress and improved hypoglycemia confidence. The GOLD trial was a multi-center crossover RCT that enrolled 161 subjects over 69 weeks comparing CGM to BGM in adults with T1D on MDI. This study demonstrated that CGM use significantly reduced nocturnal as well as daytime hypoglycemia. Using a questionnaire, it also found that CGM improved hypoglycemia-related confidence in social situations, helped to avoid serious problems due to hypoglycemia, and overall improved conviction that they could freely live life despite the risk of hypoglycemia. This led to an overall improvement of quality-of-life as well.[4,5,26] Another study assessed elderly patients on MDI who started using CGM. Satisfaction with CGM was high; 95% of participants felt it improved their sense of security, 68% felt it improved sleep quality, and 82% wanted to continue using CGM at the end of study period. CGM also improved glycemic control (improved TIR (3.9–10.0 mmol/L) (66.3±2.6% vs 76.9±3.0%; $p<0.001$), reduced hypoglycemia (9.6±2.1% vs 5.2±1.1%; $p=0.041$), and decreased variability (%CV) (37.3±11.1 vs 32.9±6.3; $p<0.001$)).[27]

Several studies have also evaluated the efficacy and safety of CGM systems. One of these studies looked at the efficacy and safety of CGM systems initiated within 1 year of diagnosis of T1D. This retrospective study included 396 participants of all ages and found that early initiation of CGM, regardless of insulin delivery modality (MDI or insulin pump), resulted in lower HbA1c levels. Interestingly, they observed a reduction in emergency department visits related to

diabetes.[28] Long-term glycemic outcomes were also evaluated, and results showed that HbA1c levels were maintained up to 7 years after implementation of CGM systems (7.6% vs 9.8%; $p<0.001$) adjusting for age at diagnosis, sex, and insulin delivery method.[29]

Trials evaluating the use of CGM found similar results including such as the case for the REPLACE-BG and IMPACT studies. These studies did show improved hypoglycemia outcomes, but no difference was found in HbA1c levels or TIR. The REPLACE-BG study aimed to determine whether rt-CGM use without confirmatory SMBG measurements is as safe and effective as using rt-CGM in adjunctive fashion in adults with T1D. This multi-site randomized non-inferiority clinical trial enrolled 149 subjects with T1D diagnosis for at least 1 year, who were 18 years old or older with HbA1c <9%, using an insulin pump.[30] Mean TIR was 63±13% at both baseline and 26 weeks in the CGM only group and 65±13% and 65±11% in the CGM+BGM group (adjusted difference 0%; one-sided 95% CI −2%). No events of severe hypoglycemia were observed in the CGM only group, and one event was observed in the CGM+BGM group. This study concluded that CGM without BGM is as safe and effective as using CGM as an adjunct to BGM in adults with T1D who are considered to be at low risk for severe hypoglycemia.[30] Additionally, the IMPACT study enrolled 26 youth subjects with T1D from underserved communities and aimed to determine if a CGM trial improves uptake of CGM systems on this population. They were provided with rtCGM systems (Dexcom G6) and were followed at 3 and 6 months after wearing rtCGM. Seventeen participants completed a 3-month follow-up visit (14 of these also completed a 6-month follow-up), and seven participants only completed a 6-month follow-up. Results showed that, after trialing a CGM, 85% reported interest in personal CGM, 76% had obtained a CGM, and 43% were already using a CGM. No improvements in HbA1c or TIR were observed, but participants reported an increase in the perceived benefits of CGM usage (4.0 vs 4.3, $p=0.03$). However, the authors did report improved uptake of personal CGM, which may reduce disparities in CGM use among minorities and underserved communities.[31]

There has been an overwhelming amount of data published in recent years demonstrating the impact of CGM on the development of diabetes-related complications such as nephropathy, retinopathy, neuropathy, and cardiovascular events.[32,33] One study demonstrated that improved TIR over 1 year is associated with reduced albuminuria in patients with T1D who use a sensor augmented insulin pump. This RCT enrolled participants with T1D using multiple daily injections and started 26 of these participants on sensor-augmented insulin pumps for 1 year. Urine albumin-creatinine ratio (ACR) decreased by 19% per 10% increase in %TIR, 18% per 10 mmol/mol decrease in HbA1c ($p<0.07$), and 31% per 10-mmHg decrease in mean arterial pressure. Therefore, they concluded that increased %TIR is significantly associated with improved albuminuria in T1D and that %TIR complements HbA1c in predicting microvascular complications.[33] Similarly, a retrospective observational study evaluated subjects with T2D with a measured ACR that underwent CGM for 3 or 6 days. The prevalence of albuminuria was lower in subjects who met the targets for TIR 70–180 mg/dL, time above range (TAR) >180 mg/dL, and TAR >250 mg/dL ($p<0.001$), as recommended by international consensus. The odds ratio of having albuminuria was 0.94 (95% CI=0.88–0.99, $p=0.04$) per 10% increase in TIR. The results were similar for hyperglycemia metrics. These studies suggest that TIR may be a valuable surrogate metric to predict risk of albuminuria in T2D.[34]

Studies have also suggested an association between TIR with diabetic retinopathy (DR) in patients with T1D and T2D. One study evaluated the association of TIR in 1,440 participants from the Diabetes Control and Complications Trial (DCCT) data. Blood glucose was measured using seven fingerstick samples (before meals, 90-minutes post-meals, and at bedtime) collected during 1 day every 3 months, and progression of DR was assessed every 6 months. Mean TIR was 41 ±16%. The hazard ratio of DR progression increased by 64% (95% CI=51–78), for each 10% points lower TIR ($p<0.001$). Similar results were reported for mean glucose and hyperglycemia metrics. Hence, this study suggests that TIR is strongly associated with risk of DR and other microvascular complications.[35] Similar results have been found in other trials evaluating the association between DR and TIR in patients with T2D.[36]

There are also available data suggesting an association between TIR and peripheral diabetic neuropathy (DPN) in patients with T2D. A cross-sectional study performed in participants with T2D used composite Z-scores of nerve conduction velocity (CV), latency, and amplitude to evaluate for peripheral neuropathy. Participants were divided into tertiles according to the TIR. Higher TIR was associated with a higher composite Z-score of CV ($\beta=0.230$, $p<0.001$), amplitude ($\beta=0.099$, $p=0.010$), and lower composite Z-score of latency ($\beta=-0.172$, $p<0.001$). Thus, higher TIR was

associated with better peripheral nerve function, and TIR may be applied as a means to screen patients for additional evaluation of possible DPN.[37]

CGM systems provide the information necessary to create individualized therapeutic plans. It also empowers people with DM with real-time information and data that allows them to take an active role in their diabetes management at home.[32] Ultimately, CGM systems are ideal for practicing individualized medicine as they provide a sustainable approach that can be readily available to all physicians interested in learning how to use and interpret these systems.[38]

Challenges

While CGM has a multitude of clear benefits both for people with T1D and the providers who take care of them, CGM use comes with its own unique challenges at a personal as well as population level. Whereas overall CGM accuracy used to be a great concern, currently available CGM systems have greatly improved and have achieved accuracy that is similar or even superior to the available blood glucose monitoring systems. One major concern is the accuracy and reliability of CGM readings in specific situations. A common source of error is the so-called "compression artifact" that can occur if patients are lying in a position that compresses the device, often during sleep. One study observed that aberrant CGM readings >25 mg/dL away from the median were noted in certain sleep positions which were thought to compress the local tissue around the CGM and decrease blood flow.[39] These falsely low values, when linked with a CGM alarm that alerts the patient about dangerous low blood sugars, can awaken and startle the patient and lead to overnight confusion about whether or not this low value would need to be corrected with carbohydrate intake. It has also been noted that the initiation of a new sensor comes with a warm-up period and that CGM readings may be less accurate on day 1 of a new sensor session, necessitating some patients to obtain capillary fingerstick measurements on this day for better assessment of glycemia.[40] The recent approval of the Dexcom G7 system with a warm-up time of 30 minutes and the new Abbott Libre 3 system with a 1 hour warm up time have substantially reduced some of the challenges associated to warm-up times. Nevertheless, as CGM provides monitoring of interstitial fluid rather than directly measuring the blood, there is a lag-time with CGM values reflecting a time-point slightly behind capillary blood glucose measurement.[41] One study noted that a drop in glucose during prolonged aerobic exercise was reflected on CGM 12±11 minutes behind direct blood measurement and additionally noted a slight decrease in accuracy during exercise; this suggests that hypoglycemia symptoms during exercise may be better assessed and more quickly addressed if checked with BGM rather than CGM.[42]

Additional factors that can complicate the accuracy of CGM are various interfering substances. A major concern was that acetaminophen was found to falsely elevate CGM sensing in the two FDA-approved CGMs of the mid 2010s which at the time would complicate the reliability of CGM for clinical decision-making and use in closed-loop systems given the pervasiveness of acetaminophen use in children and adults.[43] Thankfully, this interfering effect of acetaminophen has not been seen in the subsequent generations of CGM, including most of the devices currently available on the market. This does not, however, preclude other substances from interfering with CGM readings. Of note, ascorbic acid (Vitamin C) supplements have been found to falsely raise sensor glucose readings for the Freestyle Libre CGM, as noted on the device website.[14] Hydroxyurea is another substance that has been found to cause falsely elevated sensor readings, specifically in the Dexcom G5, G6, and G7 systems.[16,44] It is possible that other substances cause CGM sensing interference that have not yet been identified. It is imperative that patients and providers be aware of these known interferences and that clinical decisions be made accordingly to avoid the hypoglycemia which could result from treating a falsely elevated sensor glucose reading.

Some challenges with CGM use adherence relate to issues with device adhesion as well as body image. A 2014 survey of over 17,000 participants who had T1D and had used CGM at baseline noted that 41% had discontinued CGM within 1 year, and the top cited reasons were discomfort when wearing CGM, problems with inserting the CGM sensor, and problems with adhesive holding the sensor on the skin.[45] Adhesion can be improved with various supplemental products such as dressings, tapes, and wraps but these come at an additional cost and finding the right product can be difficult with consideration for temperature variation and activities such as swimming.[46] Additionally, sites must be rotated to prevent irritation and rashes. If the CGM does fall off earlier than scheduled removal, it may become expensive to replace devices early if supply has run out. Additionally, due to limited testing/data, it is recommended that the CGM be removed for CT or MRI which ultimately means replacing a new sensor after each imaging study.[47] For pediatric

patients, additional practical issues arise due to limited body surface area to place CGM, especially for patients that are on an insulin pump device that additionally needs space for safe pump placement.[48] Furthermore, some individuals still feel stigmatized by diabetes or have a fear of or simply dislike having devices on one's body and these body image concerns are sometimes a barrier to routine CGM use despite the known clinical benefits.[49]

Issues unfortunately persist in equity and disparities as it relates to access to CGM technology.[50] It has been demonstrated that part of the problem is rooted in biases at the prescriber level.[51] Providers serve as the "gatekeepers" to diabetes technologies such as CGM and an assessment of biases amongst multidisciplinary diabetes providers revealed evidence of bias to recommend or offer diabetes technology based on whether the patient was on private or public insurance.[52] As a result, people with diabetes who take insulin and are on Medicaid in the United States are 2–5 times less likely to use a CGM, which likely also reflects limited access by public insurance.[53] Beyond insurance status, there are overwhelming disparities in racial and ethnic distribution of diabetes technology use including CGM.[50] Despite minority young adults representing the largest growing population with Type 1 diabetes, a study of 300 young adults stratified by race and ethnicity showed less minorities (Hispanic, non-Hispanic Black) had ever used CGM compared to non-Hispanic White peers.[54] In assessing outcomes of these patients, the non-Hispanic Black patients in this cohort had a significantly higher HbA1c than peers, even after accounting for socioeconomic status, suggesting that diabetes technology prescribing practice based on implicit racial biases affected patient outcomes.

The American Diabetes Association's 2021 Executive Summary on access to CGM by payer and race noted that not only were people with diabetes on public insurance less likely to have access to CGM, but this was even less likely for patients of color on public insurance.[53] In fact, Black individuals had lower rates of CGM access and utilization, regardless of health insurance status or age. As a longstanding unfortunate trend in medicine, those who would benefit the most from advances in medicine, in this case CGM technology, are the ones that appear to be the least likely to have access. From a global perspective, access is even further limited in lower-income countries without public-funding that covers the technology – this has subsequently led to a "Grey Market" as a way for technology to flow from higher-income countries to lower-income countries via resale in a way that was not intended by the manufacturers.[55] Even after an individual is prescribed and obtains a CGM, the technology needs do not simply stop there. In order for fully integrated access, an individual will need a smartphone with Bluetooth capabilities as well as ongoing internet access with consistent signal and speed for remote upload of CGM. Additionally, if a patient has an insulin pump, these same tools are generally required in order to link the pump to the CGM for automated insulin delivery (AID) and the associated benefits of this combined technology. While most Americans do have access to the internet in today's digitally connected age, there are many individuals with diabetes who still do not, and this broad network of access to the internet certainly does not extend globally to less-wealthy countries.

The advanced technology of CGM comes with its own pitfalls as well. The huge amount of glucose data generated by these devices can feel overwhelming to some patients and lead to "information overload" and the inability to effectively use the data generated.[51] Furthermore, there are baseline technical skills that are needed to utilize CGM and understand how to react appropriately to avoid insulin stacking or overcorrection. Some patients may additionally feel fatigue from the alarms that can be in place to alert a person of a measured real-time or impending hypo- or hyperglycemia event; while these alarms are well-intentioned, many CGM users have reported frustration by the frequent interruptions in their life.[51] On the other hand, some individuals have reported sleeping through the alarms and not benefiting from them. Even with alarms in place, the CGM devices can only alert a user of a low or impending low, but cannot effectively treat a low glucose on their own; some individuals have unrealistic expectations of hypoglycemia protection from CGM, which can then lead to limited CGM uptake when confronted with the realities of the technology.[56] Lastly, there will always remain a theoretical risk for cybersecurity and confidentiality issues with medical technologies, and it is prudent that these devices are secure and inaccessible by others, especially when it comes to connected devices such as CGM and pumps.[57]

Despite the evidence pointing towards benefits of CGM use, high device cost, and limited insurance coverage have proven to be major barriers to routine CGM use for many patients.[58] In a survey of 411 adolescents with T1D, the most commonly endorsed barrier to device uptake was cost/insurance-related concerns which were cited by 61% of respondents, higher than barriers related to physical device wear.[55] Those adolescents who did report barriers had significantly higher diabetes distress and family conflict compared to those who did not. When it comes to public and private

insurance in the US, CGM coverage remains varied. The Medicaid eligibility requirements vary from state to state from one state not requiring any BGM for coverage to multiple states requiring documentation of 4 times per day minimum BGM to be eligible.[59] Medicare also had required the 4 times per day minimum BGM for CGM eligibility until the summer of 2021.[60] On the private insurance side, for many large insurers there is a lack of transparency of eligibility criteria for CGM coverage and this information is often not readily available for people with diabetes and their providers.[59] At this time, there remains a lack of studies that effectively evaluate the long-term economic benefits of CGM, and that remains a factor in assessing coverage by insurance provider[61] When device coverage is rejected by insurance, the appeal process can be burdensome and may take away from time that could be spent with patients. Beyond the cost of these devices, clinics too must find ways to integrate sensor data upload and utilization into the workflow, and this oftentimes means training ancillary staff on how to upload CGM devices for clinician review.

Additional challenges of CGM use are issues related to provider comfort with utilization and prescribing. A notable barrier that prevents CGM from getting to patients who would benefit is that providers are resistant to change and stuck in a pattern of clinical inertia. This led to some providers in the mid-2010s expressing negative attitudes toward CGMs, although this has likely improved with better awareness of the benefits of the technology.[62] For providers, there are certainly time-constraints to effectively utilizing CGM to derive treatment decisions during a clinical visit, especially for providers who have a lack of experience with reviewing CGM reports.[63] While HbA1c is the well-understood "gold-standard" for diabetes monitoring and diagnosis, CGM metrics such as TIR or GMI do not perfectly correlate with HbA1c, and all measures of glycemia should be evaluated in the context of one another when taking care of a patient with diabetes.[64] Additionally, while the COVID-19 pandemic allowed for FDA enforcement discretion on temporary use of CGM on the inpatient setting, there is a lack of clear guidance or protocols for optimal CGM use in the hospital setting.[65] The reliability of CGM data in patients in an ICU setting remains unclear, with the various fluid shifts, hemodynamic changes, and vasoconstricting medications that may alter the accuracy of interstitial fluid glucose measurements. Also, in considering CGM use in the inpatient setting, it is worth noting that CGM data does not directly integrate with electronic health records at this time (providers often rely on screenshots of downloaded reports for documentation purposes). Despite the likely benefits, many issues must be addressed systematically before CGM can be regularly utilized as a tool in the inpatient care of people with diabetes.

Recommendations

CGM Initiation Considerations

Several professional societies have emphasized the role of CGM in type 1 and type 2 diabetes.[6] They also recognize the value of integrating CGM to guide therapy especially in patients with wide glycemic variability. Additional recommendations include using CGM to guide nutrition, physical activity, preventing hypoglycemia, and medication adjustments.[6]

The Standardized Ambulatory Glucose Profile (AGP) should be considered the standard for all CGM data interpretation.

The selection of a specific device should be tailored according to the patient's personal preference, specific needs, education/skill level, and device availability. Once these devices are prescribed, the provider should make sure that persons with diabetes, as well as any family members or caregivers who will be assisting with diabetes management, undergo initial training and receive continued education in use and interpretation, even after initiation.[6]

More importantly, clinicians initiating CGM technologies should be trained, committed, and experienced in order to prescribe and manage these tools. They should also make sure that they have access to the infrastructure required to support the people with diabetes initiating CGM. Providers should be aware of interfering substances, medications, and situations (hypoglycemia recovery, pressure induced sensor attenuation) that can alter CGM accuracy.[8]

rtCGM or isCGM should be offered to 1) people with diabetes on MDI or insulin pump therapy, 2) people with diabetes on basal insulin, 3) youth with T1D on MDI or insulin pump therapy, 4) youth with T2D on MDI or insulin pump therapy, 5) all individuals with problematic hypoglycemia, 6) pregnant women with T1D and T2D treated with intensive insulin therapy, 7) women with gestational diabetes mellitus (GDM) on insulin therapy, or 8) women with GDM who are not on insulin therapy.[6,8] The provider must always ensure that the user can operate the device safely.

rtCGM should be ideally used daily by people with diabetes on MDI or insulin pump therapy to achieve maximum benefits.[6] People using isCGM should scan at least every 8 hours. Additionally, people who could be considered for isCGM include being: 1) newly diagnosed T2D, 2) treated with non-hypoglycemic agents, 3) able to scan several times a day, or 4) at low risk for hypoglycemia.[8]

CGM systems can also be considered as an adjunct to pre- and post-prandial glucose monitoring for diabetes in pregnancy to achieve HbA1c goals.[6]

Professional CGM or periodic use of CGM can be incorporated for management of diabetes in individuals who are unable to use CGM continuously. This can be helpful in situations when the device cannot be worn continuously, if the person is unable to scan with sufficient frequency (for some CGM systems), or due to availability/access issues.[6,8] Additionally, professional CGM could be considered for newly diagnosed diabetes, for people with problematic hypoglycemia that have no access to personal CGM, as an educational tool for people with T2D on non-insulin therapies, or as an introduction to CGM.[8] CGM can also be used as a tool to assess glucose levels in response to exercise, and to guide therapy adjustments and carbohydrate consumption.[8]

Clinically validated smartphone applications can be recommended to teach self-management skills, improve engagement, and support healthy lifestyle habits. Such applications include those that support healthy eating, and physical activity tracking.[8]

Wherever possible, people with diabetes wearing a CGM should be allowed to continue its use in an inpatient setting or during outpatient procedures if they are able to safely manage the device or have proper supervision.[6]

Occasionally, some people may develop skin irritation or allergic reactions, in which case the provider should evaluate and treat the symptoms to prevent CGM cessation.[6]

Education and Training

Several professional societies, including American Diabetes Association (ADA), The Endocrine Society, and the American Association of Clinical Endocrinology outline in their guidelines in-depth guidance to make sure optimal education and training is provided to people with diabetes on a CGM to ensure success. Overall, they recommend education and training at the time of CGM initiation, while also emphasizing the importance of continued education and assessment of the user's ability to use the glucose data collected to guide therapy.[6–8]

The individual with diabetes should collaborate with the health care provider and a multidisciplinary diabetes team by maintaining regular follow-up. The clinician should provide education when upgrading a CGM system or when otherwise indicated. The clinician should evaluate if a patient is using the CGM properly overtime and needs to be aware of any changes in cognition, physical fitness, insurance coverage, or any other age-related changes that may be compromising the ability to use CGM properly at each visit. The clinician should assess the individual's understanding of CGM system components, how CGM data differs from BGM, interpretation of glucose trend information to adjust insulin doses, site selection and care, and alarms.[7]

Clinicians should create an educational plan for initiation of insulin pump systems and rtCGM, especially if integrated in automated insulin delivery systems. They should work with a diabetes multidisciplinary team to evaluate candidates, provide education, and initiate therapy. The team should also provide long-term support to people using insulin pumps and rtCGM. If a diabetes team is not available, the clinician can provide education and support with the help of other providers and industry consultants.[7]

Future

As the technology further advances over time, the role of CGM in diabetes care will continue to evolve. CGM has already changed the way that providers and people with diabetes think about glycemic control and glucose goals, and one should expect that evolution to continue as CGM becomes more commonplace in diabetes care. While CGM glucometrics do not have the same robust, long-term outcomes data as HbA1c, a number of studies have already linked CGM-measured TIR to various surrogate measures for diabetes complications, including albuminuria, peripheral nerve function, retinopathy, and carotid intima media thickness (a possible marker for CVD/macrovascular risk) and more studies looking at these long-term relationships are underway.[34,35,66] TIR has been

strongly associated with risk of microvascular complications, leading some leaders in the field to comfortably declare that TIR is an acceptable endpoint for clinical trials.[34,35] Most importantly, CGM creates a fuller profile of glycemic data and trends as compared to the limited information gleaned from an HbA1c, as it relates to glycemic variability. In addition, clinical use of CGM provides for a more personalized and targeted approach to diabetes care. Given the clear benefits of CGM in people with T1D, it will not be surprising to see CGM used in more and more people with type 2 diabetes as well, especially those on insulin or at risk for hypoglycemia. With over 30 million people with type 2 diabetes in the US and a majority of care taking place in the primary care setting, CGM will likely become a part of the internist's diabetes care toolbox as well, and internists should adopt a systematic yet efficient approach to CGM interpretation.[38]

One of the most rapidly advancing technologies associated with CGM is integration with insulin pumps and one should expect that technology to continue to evolve. It has been demonstrated that adding CGM use in a patient already on an insulin pump improved TIR and that was without direct integration between the CGM and pump.[67] In the years since that observation was first noted we now have fully integrated hybrid closed-loop systems available using CGM as part of an algorithmic automated insulin delivery (AID) system. These AID systems have helped in achieving clinical targets by minimizing hypoglycemia.[68] In the future, CGM will likely be a key component in a closed-loop or perhaps even dual-hormone artificial pancreas system with minimal user input required and even further improved quality-of-life.

The future of CGM appears bright, as it has been demonstrated to improve care in both the inpatient and outpatient settings. The COVID-19 pandemic has allowed for inpatient usage of CGM and performance data collection which could pave the way for future full FDA approval.[65] With the Endocrine Society's most recent Clinical Practice Guidelines on hyperglycemia management for hospitalized patients in non-Critical Care settings now outright recommending real-time CGM for inpatient care for adults with insulin-treated diabetes with POC blood glucose measurements only as a confirmatory measure, we should expect to see in time more CGM use as part of the routine inpatient care of diabetes.[69] Outpatient care has been optimized by CGM as well as with the expansion of telehealth since the COVID pandemic and the ability for providers to view to-the-minute glycemic trends from afar and to make adjustments. Additionally, with proper education, training, and experience people with diabetes themselves can feel empowered to make their own insulin adjustments and monitor response which can lessen the burden on providers.[70] While the future of telehealth expansion is unclear, it is clear that CGM has enhanced the quality of delivery of remote diabetes care at the convenience of both individuals and providers.

A major hurdle to providing this improved diabetes care afforded by CGM is ensuring access to this technology in a way that is equitable and just. While huge strides must be made in this realm, it is promising to see that public insurance programs such as Medicare have increased access by eliminating barriers such as the 4-times a day minimum blood glucose testing rule in 2021.[60] Additionally, we have seen a US state legislature now take action to improve access by mandating private insurance coverage for CGM.[71] The largest efforts need to be focused on providing access to this technology to those on publicly-funded insurance programs for low-income individuals as well as the uninsured. We remain hopeful that, with the abundance of benefits that CGM provides and the clear recommendations in clinical practice guidelines from various specialty organizations, access for CGM will continue to expand with time, working towards eliminating disparities in diabetes outcomes.

Disclosure

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