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Review Article

Real-Time Continuous Glucose Monitoring in the Management of Type 1 Diabetes: A Review of the Progress over the Last Decade

Elena Toschi*

Staff Physician, Joslin Diabetes Center, One Joslin Place, Boston, Massachusetts, 02215, Harvard Medical School, USA

***Address for Correspondence:** Elena Toschi, One Joslin Place, Boston, Massachusetts 02215, USA, Tel: 617-309-1997; Fax: 617-309-2667; E-mail: elena.toschi@joslin.harvard.edu

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ABSTRACT

Aim: This a review article on the advancement of Continuous glucose monitoring (CGM) systems over the last decade and their impact on the management of Type 1 Diabetes (T1D).

Background: In the last 10 years, an increasing amount of evidence has been gathered showing efficacy and effectiveness of the use of CGM in the management of T1D.

Methods: In this article, a review of the literature on the advancement of this technology and its positive impact on the management of T1D as improving glycemic control along

Results: Over the last decade a wealth of data on the positive impact on the use of CGM to improve glucose control and reduce risk of hypoglycemia in people with T1D independent of the modality of insulin administration have been gathered. American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) jointly developed a consensus statement on how to report the new metrics gathered by CGM. Data generated by CGM has highlighted discrepancies between mean glucose average by CGM and A1c, therefore a new term was coined: Glucose management Indicator or GMI, which report the glucose control calculated from CGM data. Last but not least, glycemic control measured by CGM as time in range was shown, using retrospective data, a predictor of long-term complications similar to A1c.

Conclusions: The use of CGM over last decade has made a major impact on management of diabetes in people with T1D. This is revolutionizing the way of managing diabetes in persons with T1D not only improving glucose control but reducing hypoglycemia.

Keywords: Type 1 Diabetes, Continuous glucose monitoring, Glucose control

Type 1 Diabetes and Use of CGM: A Decade of Improvement

In 1981, use of in-home glucometer become available, this innovation changed the way of managing diabetes. Until then, glucose value was measured using urine sample once or less per day. The introduction of the glucometer made possible to check glucose values multiple time per day. This made possible to test the hypothesis to "keep the blood sugar constantly normal may be ideal in theory, but in practice it is very difficult to achieve" formulated by what RD Lawrence, a prominent dialectologist of the early 20th century. The Diabetes Control and Complications Trial (DCCT) tested this hypothesis of keeping blood glucose constantly near normal range would be beneficial in reducing the so called chronic complications of diabetes. The trial was made possible thank to the introduction of long and short acting insulins as well the glucometers [1]. In 1993, the results of DCCT were published and demonstrated that not only keeping blood glucose level near normal range was possible with the use of intensive insulin therapy and frequent blood glucose monitoring but this reduce risk of micro vascular complications of

diabetes [2]. However, along with improvement of glucose control – keeping them near normal range-- an increased risk of hypoglycemia and severe hypoglycemia events were also observed [2].

Over the last decade, advancement in technology has created new systems for monitoring glucose level. Continuous glucose monitoring (CGM) and flash glucose monitoring devices measure interstitial glucose concentration every 1-5 minutes intervals. The data generated are displayed either in real-time or on demands on smart devices, some has built-in alarm and alert to help with monitoring. The data can be can be used to make diabetes management decision by user and clinicians.

CGM and Impact on Glucose Control

In 2006 Garg et al. [3] evaluated for the first time the impact of the use of CGM in reducing glycemic excursion compared to SMBG in people on insulin therapy in the outpatient settings. Participants used CGM in blinded or displayed mode for 3 consecutive periods of 3-day each. Participants using the CGM on displayed mode spent 21% less time in hypoglycemia – defined as sensor glucose <55mg/dl- and 23% less time in hyperglycemic range – defined as sensor glucose ≥ 240 mg/dl. Therefore, time in near normal range - in this study defined as glucose level between 81-140mg/dl -increased. This short term study showed for the first time that use of CGM was effective and safe to improve glucose control [3]. Moreover, when participants were asked to wear CGM for 7 consecutive days on display mode the time spent near normal range improved independent of baseline glucose control [4].

Subsequently, in 2008 the Juvenile Diabetes Research Foundation (JDRF) CGM study group performed a randomized clinical trial to assess real-time CGM impact on glycemic control and quality of life in people with T1D 8 years old or older. In the 6-month, multicenter, randomized, parallel study participants with T1D on pump therapy or multiple daily injections (MDI) were assigned either to control group -- standard of care with Self-monitoring Blood Glucose (SMBG) ≥4/day - or use of any of the available CGM systems at the time. After the first 6 month, all the participants were offered to continue the study using CGM for additional six month [5]. In the first six month an improvement in A1c in adult age 25 yrs or older, as well in the children between age 8-14 yrs was observed, however no improvement was observed in the adolescent and young adult group (age between 15-24yrs). This age group wore the least amount of time CGM [6] highlighting the importance of daily use of the system to get benefit from it.

In the consecutive six months all participants that decided to continue to participate in the study extension used CGM as adjunctive therapy to SMBG. They were followed similarly to clinical practice with visit at 1 month to follow up on CGM training, 3 month and 6 month. An improvement in A1c along with reduction of hypoglycemia was noted in participants with a baseline A1c above 7%. Again, participants who benefit the most from CGM were the ones using it almost on daily basis [7]. A limitation of the JDRF CGM study group was that most of the participants enrolled were using insulin pumps as insulin delivery methods; however the majority of people with T1D administer insulin MDI [8].

The limited data gathered during this study suggested that MDIers benefited on glycemic control similarly to pump users, despite the less flexible, less accurate method of insulin delivery use.

In 2017, two studies, one held in Europe [9] – GOLD study -and one in United States [10] –DIAMOND study -addressed the question if people on MDI would be able to get similar benefit on glucose control as people using insulin pump.

The (Continuous Glucose Monitoring vs. Conventional Therapy for Glycemic) GOLD study [9], performed in Sweden, used a crossover design where half of the participants were randomized to use CGM for the first 6 months of the study in addition to SMBG, then a 4-month washout period preceded another 6 months of usual care with SMBG alone, whereas the other half of participants performed SMBG for the initial 6 months plus during the 4-month of washout followed by the final 6 months of CGM as adjunctive therapy to SMBG. During the time where participants wore CGM A1c an improvement of A1 – average 7.9% - *vs* when participants used SMBG – A1c average 8.35% - difference of 0.4% (p=0.01). During the time they used CGM time spent in hypoglycemia (defined as <54 mg/dl) was halved (0.79 vs. 1.89%). Interestingly, five participants in the conventional treatment group and only 1 participant in the CGM group had severe hypoglycemia during the study and 7 participants had severe hypoglycemia during the washout period – while using SMBG only. Notably, significant improvement in subjective wellbeing and treatment satisfaction, as well as hypoglycemia confidence was reported to be improved during the CGM treatment period [9].

The Diamond (Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes) study in T1D MDI [10] design aimed to mimic clinical practice with very minimal touch from study team. Participants after been randomized either to usual care – SMBG ≥4/day – or SMBG with adjunctive CGM therapy were seen at 1 month to follow up on CGM use and review technicality of using the system, and then at 3 and 6 months, with minimal feedback from study team on insulin therapy and diabetes management. Compared to current clinical care based on SMBG monitoring, use of adjunctive CGM therapy was superior as glycemic control with improvement in A1c at 3 and 6 months, with an adjusted A1c reduction of 0.6% ((-0.8% to -0.3%) from baseline at six month. Moreover, independent of age, education, baseline glycemic control, baseline hypoglycemia risk, and diabetes numeracy all participants benefit on use of glucose control. Interestingly, despite the study was not design to assess impact on hypoglycemia as primary endpoint, a reduction of time spent in hypoglycemia was observed, greater reduction was observed at night [10]. Severe hypoglycemia occurred similarly in the two arms (2 events per group). The amount of insulin used did not differ between baseline and end of study, suggesting that improvement in glucose control was due to how participants used the information provided by CGM rather than an increase of insulin dose. The impact of use of CGM on psychosocial factors showed a benefit in diabetes distress and hypoglycemia confidence, however did not improve overall well-being or healthy status [11].

The editorial piece written by Davidson to comment these two studies summarized the findings well: "the clinical trials Diamond and GOLD involving people with type 1 diabetes who receive insulin via multiple daily injections demonstrate that compared with SMBG, CGM limits hyperglycemia and hypoglycemia, improves diabetes control, and reduces glucose variability" [12].

Interestingly, while CGM was prescribed as adjunctive therapy, in the DIAMNOD study use of SMBG declined throughout the six month among the CGM users, suggesting that participants used CGM to take self- diabetes management decision.

In December 2016, the Food and Drug Administration (FDA) approved the use of Dexcom G5 CGM system independent of SMBG. Meanwhile, the REPLACE-BG study demonstrated the safety and efficacy of CGM without confirmatory SMBG in adult with T1D to make diabetes management decision. The study was a non-inferiority study where participants were asked either to use standalone CGM or CGM along with confirmatory SMBG to make diabetes management decision. The results did show NO difference between the two groups in time in range, time spent in hypoglycemia or in time spent in hyperglycemia. All participants using CGM were asked to perform SMBG during warm period of the sensor, during sick days, while having symptoms suggestive of hypoglycemia, after treating hypoglycemia if CGM sensor reading did not rise after 20 minutes, before administering insulin if sensor read was >250 mg/dl, or fasting sensor glucose was >300 mg/dl or at any time of the day of SG >300 mg/dl for longer than one hour. These recommendations are still currently valid since sensor reading may be off at very low or very high glucose reading and this could impact dramatically diabetes management decision [13].

The approval of CGM as non-adjunctive therapy to SMBG overcome several challenges: first the lack data overnight when person with T1D does not check glucose values, unless awaken, frequency of SMBG during the day that can varies widely for several different reason, moreover SMBG are time consuming, can draw unwanted attention when performed in public area, can be painful.

It has been discussion if taking diabetes management decision based only on CGM can be harmful, of note many of glucometer devices on the market do not meet gold standard criteria (ISO 15197), and in US monitors that met standard criteria when released on the market meet standard may not meet the current standards, manufacturer are not asked to release updated information on quality of production over time [13-15].

Use of CGM and Impact on Hypoglycemia

The GOLD and DIAMOND studies suggested that use of CGM reduced time spent in hypoglycemia, however they were not power or design to evaluate impact of CGM use on hypoglycemia. The HYpoDE (Hypoglycemia in Deutschland) study was specifically designed to address impact of use of CGM on hypoglycemia [16]. Participants with T1D on MDI with history of impaired hypoglycemia awareness and/or events of severe hypoglycemia during the previous year were enrolled for 6 month to use CGM. A reduction of incidence of episode of hypoglycemia (glucose level <55mg/dl for ≥20 min) by 72% was seen along with a reduction in the number of hypoglycemic events compared to the control group [16].

Similarly, the impact of reduction of hypoglycemia was evaluated using intermittent scanned (is) CGM. The isCGM system, or Free Style Libre Flash Glucose Monitoring System produced by Abbott Diabetes Care, Alameda, CA) differs from Real Time-CGM (RT-CGM) in the sense that the user needs to actively scan over the sensor with a reader to gather information on glucose level, trend and pattern rather than having those values on display at all time. See below for more in details information on isCGM versus RT-CGM.

This system was used in the Randomized Controlled Study to Evaluate the Impact of Novel Glucose Sensing Technology on Hypoglycemia in T1D, IMPACT study [17] in which well controlled people with T1D, baseline A1c 6.7%, use this systems for 6-month. A reduction of time spent in hypoglycemia (<70 mg/dl) by 38% was observed in the intervention group. Similar results were described when is CGM was used by people with T2D on insulin therapy [18] with a reduction of 43% of time spent in hypoglycemia. Of note, the time measured to be spent in hypoglycemia was greater than in other studies using different types of CGMs, suggesting that isCGM readings at the upper and lower glucose value may not as accurate [19].

Recently FDA approved the use of implantable CGM – Eversense – the data on this system are limited so far. In the PRECISE II study that evaluated accuracy and safety of this system in people with T1D and T2D showed excellent accuracy with ability to detect episode of hypoglycemia 81% of the time within 30 minutes, and no device related adverse events occurred over the 180 days of wear. Implantable CGM can be a good alternative to transcutaneous CGM, giving more flexibility of wear and fewer nuisances on changing it every few weeks. [20].

Overall these data show that the use of CGM improves not only glucose control as A1c, but reduce the risk of hypoglycemia. Since the publication of DCCT trial that showed that tighter control reduce risk of complication, clinician as and persons with T1D have been challenged in achieving tight glucose control along with avoidance of hypoglycemia. The continuous glucose monitoring provides information on glucose pattern throughout the 24 hours helping clinicians and person with T1D to identify area of hypoglycemia and hyperglycemia and address them.

Some of the studies also reported an improvement in well-being, diabetes distress and hypoglycemia confidence among study participants.

Differences and similarities between Real-Time CGM and intermittent CGM

Currently available CGM devices measure interstitial glucose concentrations subcutaneously at 1–5-minute intervals using enzyme-tipped electrodes or fluorescence technology. The most common CGM systems are worn trans-cutaneous, although a subcutaneous implantable CGM has recently become available.

Table 1: Glycemic variability was defined as the coefficient of variation (SD/glucose average), a cut off of>37% has been set to identify individuals with higher risk of hypoglycemia [23].

Severe hypoglycemia	Low glucose level associated with altered mental status and/or physical disability requiring assistance from other
Hypoglycemia Level 2	Glucose level <54 mg/dl independent of presence of symptoms
Hypoglycemia Level 1	Glucose level <70 but ≥54 mg/dl
Time in Range (70-180)	Measured as % of readings between 70-180 mg/dl
Hyperglycemia Level 1	Glucose level >180 but less than ≤250 mg/dl
Hyperglycemia Level 2	Glucose level >250 mg/dl
DKA	Elevated ketones level (blood and/or urine) and low bicarbonate level <15 mmol/L or pH <7.30
Coefficient of Variation (SD/Glucose average)	≤36%

The data gathered from CGM are collected by readers. Readers can be either stand- alone devices or integrated into insulin pumps or mobile phones, display transmitted interstitial glucose readings are either in real- time (real- time CGM) or on demand when scanning (isCGM) or simply collect data for retrospective readout and analysis (professional, masked or blinded CGM).

Real- time CGM systems automatically display glucose readings at regular intervals and utilize real- time data to generate alarms and alerts.

Alarms are generated when sensor glucose levels reach predefined thresholds set by users along with clinician. The alarm can help detect hypoglycemia and hyperglycemia, as well as rate- of-change – a rapid rise or drop of glycemic level. Flash glucose monitoring systems or is CGM (FreeStyle Libre, Abbott Diabetes Care), introduced on the market in Europe in 2014 and In US in 2017, reports glucose levels only when the user scans the sensor by holding a reader close to the sensor. This system currently does not have alarm and alert that go off independent of scanning by users.

Blinded CGMs are applied intermittently over a short period of time to provide information on glycemic patterns, hypoglycemic episodes, that especially overnight can be missed by lack of SMBG fatal and help health care professional to monitor and adjust therapy. Review of collected CGM data with user, especially if along with exercise and meals information, can be helpful educational tool.

Blinded CGM and flash glucose monitoring systems do not provide alarms.

The implantable sensor require a minor surgical procedure to insert and removal the sensor by a trained health- care professional, unlike for short- term CGM systems, which are self- inserted by the user. [20]

The differences between ISCGM, RT-CGM and implantable CGM should be discussed with users to best select system. Many people would like to have alarm and alerts, especially if they have developed hypoglycemia unawareness; however some people may find those nuisance and at times increasing anxiety around glucose control and diabetes management [21]

New Metrics Derived from CGM – A Consensus Statement

In December 2017 a joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Group was published on how to best use data gathered from CGM in clinical and research settings.

A steering Committee—comprising representatives from the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endocrine Society, JDRF International, The Leona M. and Harry B. Helmsley Charitable Trust, the Pediatric Endocrine Society, and the T1D Exchange— along with input from researchers, industry, and people with diabetes through Advisory Committees representing each stakeholder group met several times over the prior year to discuss how to best use the data derived from CGM use for clinical settings and clinical research. [22]

First, the consensus report on standardized the clinically meaningful outcome measures from CGM decided that at least a minimum of 2 weeks of CGM data, of which 70-80% of possible readings available should be used to derive any metrics. [23]

Then, Time in range, time spent in hypoglycemia (level 1-3), hyperglycemia (level 1-2, and DKA), metrics to derive A1c and glucose variability as coefficient of variation were defined.

Time in range was defined as time spent between 70 and 180 mg/dl. This may seems quite a wide range however, the use of CGM in healthy individuals has shown that glucose values over 140 mg/dL (7.8 mmol/L) may occur daily (average 26 min/day; range 0 min to 6 h 52 min/day) [24] and in about 10% of healthy individuals glucose level may get as high as 200 mg/dl for several hours per day and (11.1 mool/L) [24,25].

Hypoglycemia, which is an acute complication of diabetes, was classified as level 1 to 3.

Level 1: glucose between ≥54 mg/dl and 70 mg/dl, level 2 glucose level <54 mg/dl independent of presence of symptoms of hypoglycemia and, level 3 episode of severe hypoglycemia (SH). SH episode is defined as hypoglycemic event characterized by altered mental and/or physical status requiring assistance from third party independent of glucose value.

Ideally a person with T1D should not spend more than 3% of the time in level 1 of hypoglycemia (54-70 mg/dl) per day, equivalent to ~ 40 minutes per day.

Level 2: glucose level <54mg/dl or clinically significant hypoglycemia. This can occur in patients that have developed hypoglycemia unawareness, independent of presence of symptoms. At these glucose levels is well known that neuro-glycopenic and neurogenic symptoms begin to occur. Ideally less than 1% of time of the day (~15 min/day) should be spent at this range. When level 2 is identified on review of CGM metrics understandings causes and discussing with CGM users possible way to reduce it, it is a must, however thus far there are not clear guidelines how to instruct person with T1D to mitigate/avoid it.

Level 3 is any degree of hypoglycemia along with "altered mental and/or physical status requiring assistance".

Person with SH requires assistance from others to resolve the episode. When gathering information about episode of SH the term "assistance" may need to be clarified: assistance from a person may be varies from just providing some form of oral glucose up to administering intramuscular glucagon or IV glucose.

Moreover, time spent in hypoglycemia can impact quality of life, quality of sleep [26], and driving abilities, work efficiency among others factors [27]. Moreover, even when hypoglycemia events are asymptomatic, they can increase risk of subsequent episode of severe hypoglycemia, increased risk of developing hypoglycemia unawares [28] overtime and impact cognitive function. [28].

Therefore, clinicians should give particular attention to level and time spent in hypoglycemia and should address it carefully at every single visit.

Hyperglycemia was defined as level 1 >180mg/dl; level 2d >250 mg/dl and DKA. It is well established since DCCT that chronic hyperglycemia results n elevated A1c and relates with risk of micro-vascular complications.

In the follow up Epidemiology of Diabetes Interventions and Complications (EDIC) study it was shown that chronic hyperglycemia not only impact microvascular complications but also increase risk of nonfatal myocardial infarction, stroke, and death form cardiovascular disease [29].

Hyperglycemia was divided in level 1 to 3.

Level 1: sensor glucose >180 mg/dl. The current guidelines recommend not exceeding peak >80 mg/dl post meals, however recent data on healthy individuals has reported that about 10% of healthy individuals glucose level may get as high as 200 mg/dl for several hours per day [25].

Level 2 is defined as very elevated >250 mg/dl. Level of blood glucose >250 mg/l increase risk of acute complications as DKA and elevated A1c.

Clinicians should consult on causes of hyperglycemia as missed insulin doses, delayed insulin bolus post-meals and food options with lower glycemic index to avoid rapid spikes in glucose level among possible factors.

DKA is an acute complication of T1D. See table for definitions. [23]

The data gathered by CGM informs clinicians on glucose pattern and glucose variability: wide excursion in timing and/or amplitude of glucose level increase the risk of hypoglycemia and hyperglycemia. A similar glucose average or similar A1c can be achieved by many different glucose patterns, with different amount of time spent in hypoglycemia and hyperglycemia. Therefore, glycemic variability has been proposed as a metric to evaluate glucose stability and risk of hypoglycemia.

Discrepancy between A1c and CGM Metrics

CGM data has highlighted further the limitations of A1c as metrics for diabetes management.

It is known that discrepancies between glucose average and A1c exist and these have been attributed to presence of a hemoglobinopathy, hemolytic anemia, or other diseases affecting red blood cell turnover. However CGM data has highlighted 1) similar glucose average and A1c can be derived from very different glycemic patterns; 2) a wide range of mean glucose concentrations and glucose profiles can be associated with a given HbA1c level; 3) racial differences may impact relationship between glucose average and A1c [30]. On average HbA1c levels in African-American people run ~ 0.4% (4.4mmol/mol) higher than those of Caucasian for any given mean glucose concentration determined by CGM.

At this time the causes that determines of such discrepancy are not fully understood. In particular some subjects may run A1C higher than CGM metrics; in this case intensifying the insulin regimen may put subjects at risk of hypoglycemia. On the other hands some subjects may run A1c lower than CGM metrics, in this case clinicians has to work with subjects to make achieve control despite good A1c.

Clinicians should not solely based diabetes therapeutic decision on A1c goal but also on CGM metrics. If A1c overestimates glucose control clinicians and person with T1D may take action to improve glucose control and potentially increase risk of hypoglycemia, while if A1c is underestimating glucose average clinicians may not advice person with T1D to make meaningful diabetes decision to improve glucose control and increase risk of long term risk of micro and macro vascular complications [31].

A change in mind set of clinicians and persons with diabetes that have been used to reason as A1c goal since the DCCT trial results in early 1990' must change. To reconcile A1c and CGM metrics, a new metrics that defines glucose control derived from CGM metrics has been recently proposed: Glucose management indicator or GMI. [32]

Glucose Management Indicator (GMI) and A1c

Over the last few years data from CGM has been used to generated an estimated A1c (eA1c) however as mentioned above the A1c data derived from CGM not always concord with laboratory-measured A1c.

The similarity in the name of CGM derived A1c or eA1c and laboratory-measured A1c may create confusion, in the clinical settings when the 2 values do not concord. Therefore, to highlight the differences between data derived from CGM metrics, eA1c and laboratory A1c a new name for estimated A1c Glucose management indicator (GMI) has been recently proposed [32].

While A1c is still an important population health metric closely associated with micro-vascular complications, its use in clinical practice and management decision may be limited at times.

In a the recent publication defining GMI, it was shown that GMI and A1c can differ more up to 0.5% in 28% of people with diabetes and >1% in about 3% of people with diabetes. When GMI and A1c differ, GMI can help clinicians and person with diabetes to create a more personalized diabetes management approach.

For example, a person with A1C of 7.0% but with GMI that is always lower (i.e. 6.6%); it would be advisable to ensure that the time spent in hypoglycemia is not excessive. If time spent in hypoglycemia is above goal (>1% <54 mg/dl or >3% <70 mg/dl) then a personalized plan to mitigate hypoglycemia should be implemented and consideration of increasing A1c goal may need to be considered.

On the other hands a person with A1c of 7.0% but GMI always higher (i.e. 7.8%), then would be advisable to evaluate time spent in hyperglycemia, and a more aggressive diabetes management decision along with a lower A1c target should be set.

Moreover, someone who has an A1C of 8.0% and who spends 10% of the day in hypoglycemia would benefit from a diabetes management plan different than someone who has an A1C of 8.0% and who only spends 1% of the day in hypoglycemia. The first one would benefit for education and evaluation of use of insulin, compared to the second one that may just need intensification of insulin therapy to better cover hyperglycemia.

More data and studies are needed to implement use of GMI in clinical practice.

CGM metrics and Relationship with Long Term Complication

A1c has been used by clinicians and in clinical research to assess glycemic control since the DCCT results were published in 1992 showing correlation between glucose control and long-term micro vascular complications. The goal of A1c ≤7% has been ingrained in clinicians and people with diabetes as definition of excellent

glucose control and low risk of long-term complications. However, as discussed A1C measures hyperglycemia, and does not give any information on hypoglycemia, glucose variability, and daily glucose patterns.

A similar A1c of 7% may be the result of two completely different glucose pattern that results in an overall similar average. While, this difference may not be that relevant when used for comparison of groups in clinical trials or evaluating outcomes in a large cohort, this is of relevance in the management of a person. The discrepancy between A1c and CGM metrics has raised the question among clinicians and persons with diabetes if CGM metrics can predict also risk of long-term complications. Currently, the FDA does not consider CGM metrics good enough to claim approval for a new medication or device, since no proof of correlation with reduction of long-term complications. Long-term data on use of CGM are not yet available; however a short cut was taken using the data from the DCCT trial data. Participants of the DCCT trial were asked to collect a "seven point testing" (before and 90-minutes after a meal and before bedtime) once every 3 months. This data were used to calculate time in range. The same statistical analysis used in the DCCT to show relationship between A1c and micro-albuminuria and retinopathy was used and it showed that Time in range of ≥50% was equivalent of A1c of 7% in predicting risk of retinopathy, while an TIR<30 was equivalent to an A1c of 9% or greater [33].

While FDA has not changed decision on use of CGM metrics, this data are a positive reinforcement for clinicians and people with diabetes that made diabetes management decision is effective and efficacious not only for short term well-being but very likely also for long-term outcomes.

Guidelines and Recommendations

The American Diabetes Association guidelines for 2019 recently published recommend use of CGM in all adults with T1D on intensive insulin regimens to lower A1C, not meeting glycemic targets, with hypoglycemia unawareness, or frequent episodes of hypoglycemia.

Real-time continuous glucose monitoring should be used as close to daily as possible for maximal benefit.

While isCGM may be considered as a substitute for self-monitoring of blood glucose in adults with diabetes requiring frequent glucose testing. This is also an affordable alternative to RT-CGM systems for individuals with diabetes who are on intensive insulin therapy and cost is a barrier [15].

Medicare is now covering CGM in people with T1D that are using multiple daily injections or on pump therapy.

Conclusion

Over last decade, clinical evidence of use of CGM on glucose management, impact on glucose control and risk of hypoglycemia in T1D has continued to grow. ADA and EASD has jointly created guidelines for use of CGM derived metrics. Moreover, the 2019 ADA standards of medical care in diabetes guidelines recommend the use of CGM for all people with T1D. The new metrics derived from CGM are helpful for clinicians to develop a more personalized diabetes management plan that addresses specific challenges to reach excellent glycemic control and reduce risk of hypoglycemia. Recently, data suggestive that time in range can predict long-term outcomes similar to A1c have been published. More studies are needed to confirm this association.

Use of CGM is revolutionizing the way of managing T1D improving not only glucose control, but also reducing hypoglycemia along with personalized diabetes management.

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