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Continuous Glucose Monitoring: Optimizing Type 1 Diabetes Management in Older Adults

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Abstract

Introduction: Type 1 diabetes (T1D) impacts many individuals around the world. Treatment goals of T1D include lowering hemoglobin A1c (HbA1c) values while minimizing the time spent in hypoglycemia. Frequent glucose monitoring is required to achieve optimal glycemic control.

Background: HbA1c has been used for many years to track glycemic control. When discussing care of older adults, hypoglycemia is a more important marker to track. The risks associated with hypoglycemia are higher among older adults with T1D than the general population. Multimorbidity, polypharmacy, and age-related mental decline increase the likelihood and danger of severe hypoglycemic episodes. Self-monitoring blood glucose (SMBG) provides point-in-time glucose measurements. Continuous glucose monitors (CGM) are wearable devices that transmit continuous glucose measurements throughout the day. Variations in glucose are viewed in real time, and users can be alerted when glucose levels are dangerously high or low.

Methods: A literature search was completed to assess the benefits of CGM use in older adults. The PubMed database was used to identify relevant articles.

Discussion: CGM devices show greater improvements in HbA1c and greater reductions in hypoglycemia over SMBG. Health-related quality of life is also seen to increase with use. Given the significant effects of CGM use on hypoglycemia, the devices should be recommended for use in all older adults with T1D.

Conclusion: Further research is needed to evaluate the benefits of CGM use in various subpopulations of older adults. Reasons for limited use in this population should also be explored with the goal of increasing accessibility and usability.

Introduction

Type 1 diabetes (T1D) is a multifactorial disease affecting 1.6 million Americans and many more, worldwide.[1] Over recent years, the landscape of the T1D population has been changing. For unidentified reasons, incidence and prevalence of the disease has been increasing worldwide.[2,3] Furthermore, as technology and treatment regimens undergo changes and progress, more patients with T1D are living longer and the proportion of older adults living with T1D is increasing.[2] While there is a large amount of research on T1D in younger populations, large-scale research focusing on management in older adults has previously been lacking. Age-related mental decline, multimorbidity, and more physical and social limitations differentiate this population from others. The unique needs of elderly individuals combined with the complicated management of T1D requires an intersectional approach to care.

T1D results in an absolute deficiency in endogenous insulin due to the autoimmune-mediated destruction of islet β-cells in the pancreas. Without insulin production, patients will develop hyperglycemia, leading to acute conditions such as diabetic ketoacidosis and long-term sequelae including nephropathy, neuropathy, retinopathy, atherosclerotic cardiovascular disease, and cerebrovascular disease.[4,5] Exogenous insulin administration is required for management and, unfortunately, introduces the risk of hypoglycemia. Effects of hypoglycemia can range from confusion and discomfort to life-threatening cardiac abnormalities and death.[6]

An integral component of T1D management from diagnosis through end of life is the monitoring of blood glucose levels throughout the day with an optimal glucose range between 70 and 180 mg/dL.[7] Frequent monitoring of blood glucose allows individuals to adjust carbohydrate intake and exogenous insulin administration appropriately.[8,9] For several decades the standard of care has been centered around self-monitoring blood glucose (SMBG) with a glucometer,

allowing individuals to obtain point-in-time plasma glucose concentrations. The advent of continuous glucose monitoring (CGM) has expanded patients' ability to understand their own glycemic patterns and has shown measurable improvement in care within the general T1D population.[10–12] Within the past 5 years, CGM has become more user friendly, gained important FDA clearances, and has been approved for use by patients on Medicare.[13,14] For older adults with T1D, limiting hypoglycemia has become as a priority.[7] As more patients with T1D age, the current available glucose monitoring systems must be evaluated for their impact on hypoglycemia in this age group.

Background: Literature Review

Hemoglobin A1c as a Marker for Control

Hemoglobin A1c (HbA1c) has long been used as a marker for glycemic control in T1D. The value represents the degree of glycation of hemoglobin, and thus gives an indirect measure of free glucose in the blood. HbA1c values are seen to be higher in patients who experience more glycemic variability, and studies have shown that HbA1c levels may also be used to estimate average blood glucose values in T1D and type 2 diabetes (T2D).[5,15] The American Diabetes Association (ADA) recommends routine monitoring of HbA1c two to four times per year for T1D and T2D patients and sets less than 7.0% as the target level for nonpregnant individuals with diabetes.[7] A retrospective observational study by Pettus et al.[5] in 2019 illustrated the predictive value of HbA1c on several serious complications associated with T1D. Increasing HbA1c values were consistently associated with higher rates of diabetic ketoacidosis (DKA), severe hypoglycemia, neuropathy, and nephropathy, with markedly higher rates occurring at HbA1c values greater than 9.0%.

Hypoglycemia

Hypoglycemia is most commonly defined as blood glucose less than 70 mg/dL, and it is a serious complication that occurs in T1D due to the patients' reliance on exogenous insulin. Asymptomatic and moderately symptomatic hypoglycemic episodes are common, whereas severe hypoglycemic episodes are less frequent. For the purposes of this paper and the studies described within, severe hypoglycemia is not tied to a specific glucose value, but is instead an individualized event in which the person loses consciousness or requires another person to assist them in resolving the hypoglycemia.[11,16,17] The condition has been associated with negative acute and chronic effects and greatly impacts the quality of life of individuals with T1D. Several acute symptoms can be attributed to the physiologic stress response triggered by low blood glucose.[6] The autoimmune destruction of pancreatic β-cells seen in T1D produces an associated defect in glucagon secretion by α-cells, causing the body to rely more on a response by the sympathetic nervous system and catecholamine release to raise blood glucose.[6,18] The sympathetic stress response produces tachycardia and widened arterial pulse pressure, and may lead to lengthening of the QTc interval and arrhythmias in cases of severe hypoglycemia.[2,6] The danger of the potential cardiac abnormalities due to hypoglycemia is compounded by a concurrent risk for acute coagulopathies and contributes to the risk of fatality with hypoglycemia. Acute hypoglycemia has been shown to contribute to 10% of deaths under 40 years of age in individuals with T1D.[6]

Given the acute dangers associated with hypoglycemia, awareness of hypoglycemia must be discussed. Impaired awareness of hypoglycemia is seen in 25% of those with T1D.[19] Individuals with severely reduced subjective awareness are described as having a syndrome of impaired awareness (SIA) and are at a 20-fold increased risk of a severe hypoglycemic episode.[18]

The most common etiology for SIA is a history of recurrent hypoglycemic episodes. Frequent exposure to hypoglycemia lowers the threshold concentration for plasma glucose at which autonomic counterregulatory processes are initiated. Additionally, those with SIA demonstrate changes in the brain in areas involved in interoception.[6] Whether a person exhibits SIA or not, they are at increased risk for hypoglycemia overnight because deep sleep also inhibits the counterregulatory autonomic response. Thus, overnight episodes may be asymptomatic and remain undetected. Without the physiologic response to wake them, people are unable to treat their hypoglycemia. As a result, they are at greater risk for a nocturnal severe hypoglycemic episode. More than 50% of severe hypoglycemic episodes in people with T1D occur overnight.[6] As a result, fear of hypoglycemia is a common finding in T1D. An analysis by Martyn-Nemeth[20] in 2018 showed that fear of hypoglycemia is significantly associated with a decrease in sleep quality. Those with SIA or frequent hypoglycemia may also be at risk for losing driving privileges and being restricted in their employment opportunities.[6]

The effect of hypoglycemia on cognition is multifactorial. Acute effects of confusion, irrational behaviors, and drowsiness are seen in hypoglycemic episodes. More serious complications including seizures and coma are possible in cases of severe hypoglycemia.[6] Multiple studies have shown it to affect memory. Immediate memory, working memory, and the consolidation of memory can be impaired acutely during hypoglycemic episodes. Decreases in global cognitive function, especially in regards to slowing of cerebration and performance have been associated with hypoglycemia and are seen more in cases of repeated episodes.[2,6] In 2014, Ryan et al.[21] conducted a follow-up study of the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) longitudinal cohort group to assess cognitive function in adults with T1D. The study revealed that an episode of severe hypoglycemia within the past 12 months was

associated with worse nonverbal memory and mental efficiency. Mental efficiency was also worsened by hyperglycemic complications including decreased retinal arteriolar and venular diameters and carotid artery plaques.[21]

Considerations for Older Adults

In regards to the older adult, the management of T1D is more specialized to limiting hypoglycemia, rather than preventing microvascular and macrovascular complications associated with high blood glucose. In terms of care guidelines, the ADA relaxes the goal HbA1c level to < 8.0% in older adults with impaired awareness of hypoglycemia and multiple comorbidities, in contrast to the goal of < 7.0% in healthy, nonpregnant adults.[7] This is done according to the assumption that lower HbA1c values are correlated with a lower mean plasma glucose, and is therefore associated with a greater risk of hypoglycemia.[22] However, more focused research in older adults with T1D has revealed that hypoglycemia and severe hypoglycemia occur more frequently with age, both in older adults with HbA1c less than 7.5% and less than 8.0%.[2]

The increased risks for hypoglycemia can be partially attributed to the effects of polypharmacy and multimorbidity seen in older adults. Age-related changes in metabolism lead to greater and more unpredictable drug effects. Pain medications cause confusion and coordination changes which could affect insulin self-management, and the use of non-selective β-blockers has been associated with higher rates of severe hypoglycemia.[2] With increased duration of T1D, higher incidences of microvascular complications are seen, and nephropathy and neuropathy have also been associated with increased rates of severe hypoglycemia.[2,5] In 2020, McCoy et al published a cohort study using claims data from 201,705 adults with T1D and T2D which investigated risks for hypoglycemia-related emergency department visits and hospitalizations. Risks identified as being significant included age greater than 75 years, T1D

diagnosis, patients with multiple comorbidities, and previous hypoglycemia-related ED visit or hospitalization.[23]

As impaired awareness of hypoglycemia has been shown to increase the risk of severe episodes in all adults with T1D, a further investigation in the older adult population is warranted. In 2021 Carlson et al.[13] conducted an analysis of baseline data from the Wireless Innovations for Seniors with Diabetes Mellitus (WISDM) study, which investigated the predictors of hypoglycemia in adults > 60 years with T1D. Blinded CGMs were worn for 14-21 days by 203 participants. Participants spent a median time of 5.0% in hypoglycemia which is greater than the recommended limit of 4.0%. Individuals that were rated as having reduced awareness of hypoglycemia spent more time in very low hypoglycemia (less than 54 mg/dL; 2.7% vs 1.3%). Nocturnal hypoglycemia was observed to be prevalent in all participants, regardless of hypoglycemia awareness.[13] Compounding the concern that older adults spend more time in hypoglycemia are the factors which may prevent older adults from appropriately self-managing their glucose levels, such as reduced psychomotor performance. Additionally, the counterregulatory responses including glucagon and catecholamine secretion are reduced in older adults.[24]

Another compounded concern of T1D in older adults is that of the risk of falls during an episode of hypoglycemia. A survey of patients with T1D and greater than 55 years of age was conducted by Shah et al.[25] in 2017 and revealed that the presence of severe hypoglycemic episodes within the past 12 months was associated with significantly increased risk of falls. One quarter of participants required medical attention for falls within the past 12 months, and 10% of participants experienced a fracture.[25] Diabetes-associated factors besides hypoglycemia which increase fall risk include peripheral neuropathy, vision loss, and depression.[2,25] Multiple studies

have also demonstrated that old age and longer duration of T1D increases the risk of fractures.[26,27] A 6-fold higher relative risk for hip fracture and 3-fold higher relative risk for fracture at any site has been shown in T1D. The increased fracture risk has been attributed to impaired bone formation due to T1D in adolescence, and is seen in deficits in bone density, size and structure.[27]

Cognitive function as it relates to hypoglycemia in T1D is also compounded by age-related decline in older adults. In regards to dementia, a bidirectional relationship between hypoglycemia and dementia has been seen in older adults, demonstrating that memory impairment can lead to increased hypoglycemia.[6] A small-cohort longitudinal study was completed by van Duinkerken et al in 2011 to investigate cognition over time in older T1D patients. An initial assessment was completed 4 years prior with 36 participants with T1D and 29 controls and demonstrated decreased information processing speed in the T1D group. The follow-up testing after 4 years showed that further decreased overall cognitive function and information processing speed only occurred in T1D participants that had experienced severe hypoglycemia in the time between assessments or had a history of emergency department visits or hospitalization for hypoglycemia in their lifetimes. [28] The Study of Longevity in Diabetes (SOLID), published in 2020 by Lacy et al.[16], investigated the relationship of severe hypoglycemia and brain health in 718 adults greater than 60 years of age with T1D. One third of participants had experienced a severe hypoglycemic episode within the past 12 months that required assistance from another person to resolve. Half of the participants had experienced a severe hypoglycemic episode that resulted in an ED visit or hospitalization within their lifetimes. A series of neurocognitive assessments in various fields were administered to assess brain health. Recent episodes of severe hypoglycemia were linked to lower performance in global cognition,

language, executive function and episodic memory. Lifetime episodes requiring were linked with lower executive function scores. Analyses showed that the effect of recent severe hypoglycemia was significant and independent of the effect of lifetime severe hypoglycemia.[16] This study supports the hypothesis that the brain is more susceptible to hypoglycemic insults during late adulthood, compared to middle age.[29] Age-related changes thought to contribute to this susceptibility include reduced brain volume and white matter integrity.[21]

Mental Health Concerns in Diabetes Management

A chronic disease such as T1D has many social, emotional, and physical burdens that can also affect the mental health of individuals. The relationship between mental health and glycemic control must also be considered. Adults with T1D have two- to three-fold higher rates of depression than the general population.[30] Given the complex self-care requirements of those with T1D, there is a greater psychological burden on these individuals. This has been considered as a possible contribution to the higher rates of depression in this population.[31] In a survey of adults with T1D, elevated diabetes-related distress, elevated depressive symptoms, and high HbA1c levels were all strongly correlated.[32] In those without a diagnosis of depression, the stress associated with maintaining adequate glucose control can still greatly affect quality of life. A cross-sectional study in Norway including 319 adults with T1D used a series of standardized questionnaires to assess stress, emotion, and diabetes management. Responses were analyzed in combination with HbA1c levels of participants. Diabetes-related distress was associated with an increase in HbA1c of 0.2% to 0.3%. When specifically evaluating regimen-related distress, an increase of 0.6% was seen.[33] Responses to scales for depression and anxiety were not significantly associated with changes in HbA1c in this study,[33] showing that the negative effects of diabetes-related distress were independent of other existing mental health disorders.

Regardless of the presence of microvascular and macrovascular complications of diabetes, high HbA1c levels are associated with poorer quality of life. In Sweden, a survey of adults with T1D and T2D was done to measure health-related quality of life (HRQOL). When controlling for demographics and diabetes complications, significant decreases in multiple domains of HRQOL were seen in those with HbA1c greater than 8.6%.[34] In addition to high HbA1c levels, longer duration of T1D is significantly associated with worse HRQOL.[35] A study by Hessler et al.[36] differed from others in that it included assessments both at baseline and at nine months. At both time points, high diabetes-related distress was associated with higher HbA1c among adults with T1D. However, if there was a decrease in diabetes-related distress at the nine-month follow-up, then this was significantly associated with a simultaneous decrease in HbA1c.[36]

Challenges associated with mental health are also seen to impact older adults with diabetes. Chronic physical illness is a risk factor for developing depression in those over the age of 65. Prevalence of depression is 5-10% in older adults, and this rises to 12-18% in those with diabetes.[37] As part of the Diabetes and Aging Study of Health, telephone interviews were done to assess factors affecting depressive symptoms in older adults with diabetes. Participants over 65 years of age were interviewed, and lower cognitive function and higher levels of diabetes-related distress were both significantly associated with an increase in depressive symptoms.[38] Another longitudinal study followed adults over 50 years of age with T1D over a 20-year period to assess complications over the lifespan. Twenty percent of participants were diagnosed with depression at baseline, and rates increased over the span of the study. Severe hyperglycemic and hypoglycemic events resulting in hospital admission or emergency care occurred twice as often in those with depression. Conversely, an episode of severe hyperglycemia was associated with a doubled risk of developing depression, and an episode of severe hypoglycemia was associated

with a 75% increased risk of a new depression diagnosis.[30] This bidirectional relationship between severe glycemic events and depression highlights the importance of optimizing glucose control.

Glucose Monitoring Modalities

Self-monitoring of blood glucose (SMBG) with a glucometer and finger-sticks has been the standard of care for several decades. The method involves sticking the finger with a disposable lancet and placing the resultant drop of blood onto a one-time use test strip that has been inserted into the glucometer. The glucometer then displays the plasma glucose concentration. It is a well-studied system and has been evaluated for accuracy. Studies have shown that if it is used between 6 and 10 times per day, then significant reduction in HbA1c can be achieved.[8,9] While this frequent use would be more ideal, the reality is that many T1D are unable to perform checks that often. Checking blood glucose with the finger-stick method produces a potential for biohazards that may not be welcome in all settings. Users are also limited by the need to access multiple supplies. Some older adults have also reported specific limitations in their ability to obtain enough finger-stick blood to use SMBG due to comorbidities including circulatory disorders, neuropathy, and arthritis.[39] SMBG also has the negative effect of causing pain. In Japan, a cross-sectional study was completed to assess patient attitudes surrounding blood glucose monitoring. Participants included 517 adults with T1D and 1648 with T2D that used SMBG for at least three months. Multiple questionnaires were included to assess mood status, diabetes therapy related quality of life, and perceptions of SMBG. A large fraction of participants reported pain associated with SMBG, 46.4% of T1D and 37.5% of T2D. Those that reported pain were then more likely to exhibit additional negative characteristics. Mood and HRQOL were rated more poorly, and HbA1c was higher in this group. Additionally, blood

glucose monitoring was seen as less important by those with pain than those without pain.[40] Due to the inconvenience and negative associations with SMBG, alternative glucose monitoring methods have been developed.

Continuous glucose monitoring (CGM) differs from SMBG in that it doesn't directly measure blood glucose and allows the reading of glucose concentration and trends as it continuously changes throughout the day. A sensor device is placed on the body, and a filament inserted in the skin measures glucose concentration in the interstitial fluid. Readings are available to view on a receiver or smartphone. Two types of CGM are available for use in T1D: real-time CGM (rtCGM) and flash glucose monitoring (FGM).

rtCGM uses a sensor that is placed on the abdomen or back of the upper arm and must be replaced every 10 days. The sensor measures the interstitial glucose concentration every 5 minutes and automatically transmits the reading to the receiver or smartphone. Because measurements are sent continuously, individuals can set their own high and low glucose thresholds, and an alarm will sound if the thresholds are crossed.[41] FGM sensors may only be placed on the back of the upper arm and differ from rtCGM in that a manual scan of the sensor with a receiver or smartphone is required to display the data. For this reason, the alarm functions are not available on FGM. Scans only take 1 second to complete and should be done at least once every 8 hours to ensure complete storage and transmission of data points.[42] Transmitters may be scanned more often than every 8 hours, and increased frequency of scans has been associated with lower HbA1c levels.[43] Despite the lack of alarm feature on FGM, the devices are still used commonly because they are a lower cost alternative to rtCGM.[44] Regarding accessibility, Medicare began covering both types of CGM in 2017 for eligible persons.[13]

Shared characteristics include the accuracy and types of data that can be obtained from the device. Studies have shown that CGM devices have equivalent or greater accuracy in tracking hyperglycemia and hypoglycemia compared to SMBG, and duration of hypoglycemic episodes decrease in both.[14,45] Earlier iterations required the use of SMBG for dosing insulin and calibrating the devices. As of 2016, Dexcom G5, a rtCGM, was approved by the FDA to use without adjunctive SMBG. The Abbott Freestyle Libre, a FGM, was approved to use independently in 2014.[14] Both devices also provide predictive indicator arrows based on the trends in previous readings to inform the user if they are approaching hypoglycemic or hyperglycemic thresholds.[8] Users can then adjust carbohydrate intake or insulin bolus doses to remain in a euglycemic range. Long-term trend data is available with FGM and rtCGM. Up to 90 days of data can be stored on the receiver, or more if using a smartphone application. Extended trends over time can then be downloaded and assessed by an endocrinologist to inform treatment decisions as an adjunct to HbA1c. Available data includes the fraction of time in range (TIR, greater than 70 mg/dL and less than 180 mg/dL), time below range (TBR, less than 70 mg/dL), and time above range (TAR, greater than 180 mg/dL). Increased fractions of TIR has been linked to improvements in microvascular and macrovascular complications of diabetes.[46–48] CGMs can also calculate a coefficient of variation (CV) to measure glycemic variability, something that cannot be assessed by HbA1c alone. A study including 130 adults greater than 65 years of age with T1D showed that those with high (greater than 36%) or low (less than 36%) CV could have the same HbA1c, but those with a high CV spent more time in hypoglycemia.[49]

Comparative Effects of Glucose Monitoring Technology

rtCGM vs SMBG

Many studies have been done to analyze the difference between T1D management with rtCGM and SMBG. An early meta-analysis done in 2012 by Floyd et al.[50] included 14 randomized control trials (RCT) comparing the two modalities. The analysis revealed that across all studies, if rtCGM was used for at least 8 weeks, significantly greater reductions in HbA1c and time spent in hypoglycemia from baseline in the rtCGM groups were observed, though no significant changes were seen in hypoglycemia frequency.[50] Later studies were done over longer durations to evaluate for long-term effects of rtCGM use. The Comparison of Sensory Augmented Insulin Regimens (COMISAIR) study by Šoupal et al.[17] in 2016 was conducted with adult participants with T1D to evaluate the effects of sensor-augmented insulin regimens (SAIR). Though not randomized, participants were divided into 4 groups utilizing different treatment modalities for glucose monitoring and insulin administration. The SAIR groups included rtCGM used with multiple daily injection (MDI) and continuous subcutaneous insulin infusion (CSII, insulin pump). The other groups used SMBG with MDI and SMBG with CSII.[17,51] Results after 1 year support the findings of the earlier meta-analysis in that the rtCGM groups showed significantly lower HbA1c levels than SMBG with MDI group after only 3 months of treatment. As the study continued, the difference in HbA1c between the rtCGM groups and SMBG with CSII group became significant after 9 months. After 1 year, rtCGM groups also showed decreased average glucose values, time spent in hypoglycemia, and glycemic variability when compared to their baseline.[17] After 3 years, the improvements in glycemic control were still apparent, and decreases in TBR was only seen in the rtCGM groups.[51]

In 2017 Beck et al.[11] published results from the Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes (DIAMOND) RCT. This trial included 158 participants with T1D from the United States and was conducted over a span of 6 months. Participants were

divided to rtCGM and SMBG groups, all using MDI insulin regimens. Significant differences in HbA1c were seen after 12 weeks and were maintained at the end of the 6 months. Mean HbA1c reduction was 1.0% in the rtCGM group, and 0.4% in the SMBG group. The rtCGM group also spent less time in hypoglycemia than the SMBG group (43 min/d vs 80 min/d). According to qualitative surveys administered in the study, participants who used the CGM rated it highly on user satisfaction.[11] Ruedy et al.[52] expanded on the DIAMOND trial results by including data from participants in Canada and focusing on subjects greater than 60 years of age. The subgroup again showed greater decrease in HbA1c and high rates of user satisfaction.[52] A later analysis of the DIAMOND study data by Oliver et al.[10] in 2020 revealed that rtCGM use altered the historical inverse relationship between HbA1c and time spent in hypoglycemia. Findings from earlier studies showed that lower mean glucose levels or HbA1c were associated with more time spent in hypoglycemia.[22] The new data showed that rtCGM users were able to achieve a lower HbA1c while still spending less time in hypoglycemia when compared to SMBG users.[10]

The Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections (GOLD) RCT conducted in Sweden in 2018 was designed similarly to the DIAMOND study but also included a 17-week washout period where users in the rtCGM group were returned to SMBG. Like the DIAMOND trial, adults with T1D were shown to have reduced time in hypoglycemia, both in daytime and nocturnal hours, when using rtCGM.[22] However, during the washout period, time in hypoglycemia returned to pre-rtCGM levels, reinforcing the association between rtCGM use and a reduction in duration of hypoglycemia. Users also rated their hypoglycemia management confidence at the end of the treatment arm. Confidence after using rtCGM was higher than after SMBG treatment.[53,54]

Additional studies were done to evaluate time spent in hypoglycemia. The data analysis by Avari et al.[55] for the Randomized Trial Comparing Continuous Glucose Monitoring With and Without Routine Blood Glucose Monitoring in Adults With Type 1 Diabetes (REPLACE-BG)[56] used rtCGM and SMBG data from 226 participants with T1D. rtCGM users were calculated to spend a significantly greater percentage of time in range (TIR) and lower percentage of time below range (TBR) when compared to SMBG users.[55] A much smaller prospective cohort study containing only 11 participants with T1D and impaired hypoglycemia awareness was published by Rickels et al.[18] in 2018. The results were in line with previous studies and participants showed a reduction in time in hypoglycemia compared to their baseline.[18]

The Reimbursement Study of Continuous Glucose Monitoring in Belgium (RESCUE) trial assessed both clinical and qualitative outcomes after one year of CGM use in patients using an insulin pump. Similar to studies using MDI regimens,[11,18,22,55] HbA1c and time spent in hypoglycemia were seen to decrease significantly from baseline. Hypoglycemia-related hospitalizations and days of missed work due to diabetes-related issues also decreased between the year prior and the duration of the study.[57] Quality of life assessments showed improvements in diabetes-related worry, general health, and social functioning. The greatest improvements were noted in individuals that had poorly managed hypoglycemia at the start of the study.[57]

More focused qualitative studies were done to assess the patient satisfaction when transitioning from SMBG to CGM in patients using insulin pumps. A study by Rubin and Peyrot[58] in 2009 consisted of a survey given to 311 adults with T1D that used either a rtCGM/CSII system or SMBG with CSII. Participants using rtCGM rated it higher in overall satisfaction and glucose control and were more likely to recommend their monitoring system than those using SMBG.[58] HRQOL and convenience were not significantly different between

groups in this study. [58] In 2014, Hommel et al.[59] analyzed data from the SWITCH (sensing with insulin pump therapy to control HbA1c) study. All participants in this study went through phases with and without linking the CGM to their insulin pumps. Treatment satisfaction was again significantly higher when using the CGM, though HRQOL was not significantly impacted.[59] In contrast to the earlier study,[58] convenience was rated higher following CGM use.[59]

In a more recent study, interviews were conducted among 24 adults and parents of children with T1D that had been using a CGM for at least four weeks. Participants stated several benefits to the device. Using a CGM made it easier and faster to check glucose levels and was compared to checking the time on a watch. Users found the trending arrows to be accurate predictors of their glucose patterns and to be the most helpful feature in making decisions surrounding food intake, insulin administration, and activities such as exercise or driving. The alarm function for severe high or low glucose levels also gave users a sense of security and reduced anxiety.[60]

In 2020 the first large RCT involving only older adults with T1D was published by Pratley et al.[61] The WISDM study included 203 adults greater than 60 years of age using either MDI or CSII insulin regimens. The study focused on the effect of rtCGM on time in hypoglycemia, and results showed the difference between rtCGM and SMBG groups to be significant, with effects seen after one month and remaining through the six months of the trial. The rtCGM group reduced TBR from 5.1% to 2.7%, while the SMBG TBR remained constant (4.7% to 4.9%). The average decrease in HbA1c was also greater in the rtCGM group.[61] Based on the results of the WISDM trial, the ADA adopted a new recommendation in 2021 that providers should consider CGM use in older adults with T1D.[62]

Litchman et al.[24] and Polonsky et al.[63] conducted additional qualitative studies with individuals with T1D or insulin dependent T2D greater than 65 years of age. Current rtCGM users and SMBG users were both included.[24,63] Respondents noted that they were better able to self-treat hypoglycemia using the visible trends and alarms found on the rtCGM, and felt they could effectively avoid severe hypoglycemia. rtCGM users in both studies experienced fewer severe hypoglycemic episodes and related falls.[24,63] An improved sense of safety allowed individuals to drive, exercise, and travel with less worry.[24] Assessments of hypoglycemia fear and diabetes-related distress were scored lower in rtCGM users.[63]

FGM vs SMBG

The Novel Glucose-Sensing Technology and Hypoglycemia in Type 1 Diabetes: a Multicentre, Non-masked, Randomized Controlled Trial (IMPACT) by Oskarsson et al.[64] was done to compare FGM with SMBG across Europe over a 6-month period. 167 participants with well-controlled (HbA1c < 7.5%) T1D were included in the study, as the primary goal was to assess change in hypoglycemia rates. After a 2-week blinded run-in stage to establish baseline hypoglycemia rates, participants were divided randomly into FGM and SMBG groups. As with rtCGM, FGM users rated their satisfaction with the device highly. Time in hypoglycemia decreased by 46% in the FGM group over the 6-month trial, from 3.44 hr/d to 1.86 hr/d. No change in HbA1c was seen in this study.[64]

Tyndall et al.[43] produced a prospective observational study with HbA1c change as the primary investigation. 900 participants were given FGM devices, and 518 participants used SMBG for the control group. In contrast to the IMPACT trial, participants of all HbA1c ranges were included in the study, and reductions > 0.5% were seen in 48.1% of FGM users. The greatest change from baseline was seen in users with a HbA1c >9.0%. No significant change in

HbA1c was seen in the control group. A secondary finding was a significant decrease in the rate of DKA admissions in the FGM group.[43]

In 2021, Nathanson et al.[44] published the results of a 2-year observational cohort study of FGM and SMBG users with T1D. Data was obtained from the Swedish National Diabetes Registry. The FGM group consisted on individuals that were newly started on FGM and remained on the system for 2 consecutive years. SMBG users from the same date range were used as controls. The study showed that HbA1c decreased gradually in both FGM and SMBG groups, but the decrease was significantly greater in the FGM group. Like the Tyndall et al.[43] study, the greatest change in HbA1c occurred in those who started with higher baseline values (> 8.5%). Unlike the previous studies in FGM, a decreased risk of severe hypoglycemia was seen with FGM use. The treatment group had a 21% lower risk of experiencing 1 or more severe hypoglycemic episodes when compared to the control group.[44]

Another prospective observational study was completed by Fokkert et al.[65] to assess glycemic and qualitative outcomes after one year of FGM use. The flash monitor registry in the Netherlands (FLARE-NL) included 1365 adults with T1D or T2D that relied on insulin administration. Baseline data from the prior year was compared with values measured after using FGM. The study again revealed a decrease in HbA1c and hypoglycemic events with FGM use. Additionally, diabetes-related hospital admissions and work-absenteeism decreased significantly. Qualitative observations included decreased perception of disease burden and improved HRQOL. Participants reported better understanding of their glucose variations and greater confidence in self-treating glucose fluctuations. Family and housemates of participants also worried less about the participants' diabetes following FGM use.[65]

rtCGM vs FGM

As rtCGM and FGM have both shown to reduce hypoglycemia duration, a direct comparison study was done to assess which CGM type is optimal for adults with T1D that have an impaired awareness of hypoglycemia. The Randomized Controlled Pilot Study of CGM and FGM in People with T1D and Impaired Awareness of Hypoglycemia (I-HART CGM) by Reddy et al.[12] was a shorter trial at only 16 weeks in length. The first phase included 40 adults with T1D and impaired awareness of hypoglycemia, as rated by a self-report questionnaire or a history of a recent severe hypoglycemia episode. Participants were randomly divided into rtCGM or FGM groups for 8 weeks. Both groups saw an increased TIR from their baseline, but only the rtCGM group showed significant decrease in time in hypoglycemia (4.5% to 2.4%). Fear of hypoglycemia was also rated lower in the rtCGM group.[12] An extension phase continued the study for another 8 weeks, this time assessing if improvements in glycemic outcomes were seen when switching from FGM to rtCGM. All participants used rtCGM for the next 8 weeks, and the participants previously using FGM showed significantly reduced time in hypoglycemia and increased TIR after switching to rtCGM. No significant changes were seen in HbA1c in either the initial or extension phases of the study.[66]

Methods

The articles used in this review were found in a literature search of the PubMed database and Google Scholar between June 1 and July 1, 2021. The search was filtered to include peer-reviewed articles with subjects “middle aged +, age 45+ years” and publication date within the last 10 years, with the majority being published within the past 5 years. Search terms included “type 1 diabetes”, “older adult”, “continuous glucose monitoring”, “hemoglobin A1c”, “hypoglycemia”, “risks”, “polypharmacy”, “mental health”, “quality of life” and “falls”. Reference lists of articles were further reviewed to identify additional relevant studies.

Discussion

The complex nature of T1D necessitates a thorough evaluation of optimal treatment strategies, especially regarding the additional needs of older adults. In all individuals, the clinical goals of care include lowering HbA1c and minimizing the time spent in hypoglycemia.[7] With close control of blood glucose, HbA1c can be lowered to ideal levels of less than 7.0%.[9,11,51] Without control, rates of long-term diabetic complications including neuropathy and nephropathy are higher, as well as rates of DKA and severe hypoglycemia.[5] Frequent or severe hypoglycemia has additional negative effects. Cardiac effects include tachycardia, lengthening of the QTc interval, and possible arrhythmias, which may be fatal. Hypoglycemia impacts cognition through impaired memory and decreased global cognitive function, and repeated events can lead to worsening mental efficiency.[2,6] Older adults have more risk associated with the cognitive deficits. In addition to these acute effects, the risk for dementia is higher in this population. The combination of poor coordination and higher rates of osteoporosis increases the likelihood of a dangerous fall and serious fracture occurring during an episode of hypoglycemia.[6,31] Not only do older adults with T1D have more risk associated with severe hypoglycemia, but they are more likely to experience it than younger individuals. As prevalence of dementia and depression increase in this age group, so do the rates of severe hypoglycemic episodes.[6,31] Altered nutritional intake may also couple with the decreased rates of insulin clearance to increase the chances of becoming hypoglycemic.[6] With increased prevalence of hypoglycemia and its associated dangers, controlling glycemic variability is of great importance among older adults with T1D.

Blood glucose monitoring is essential to lower HbA1c and protect against hypoglycemia. For many years, SMBG has been the standard of care for those with T1D. If it is done frequently

enough and individuals are able to recognize and interpret trends appropriately, then good outcomes may be achieved.[8,9] However, proper and frequent use of SMBG is limited by several factors, several of which disproportionately affect older adults. Poor circulation, dehydration, and anemia caused by poor nutrition or chronic disease can impair an individual's ability to obtain enough blood with finger sticks for accurate readings. Higher rates of neuropathy and arthritis[39] add to the pain that is already experienced by many that use SMBG, further disincentivizing the practice.[40] Arthritis and vision decline also increase the difficulty of using SMBG, as fine motor skills are required for the multistep process.[39] Given these limitations, it is not surprising that this is no longer the best option for monitoring glucose levels.

Within the past decade, studies have shown that CGM technology consistently outperforms SMBG in several categories. The foremost metric for monitoring treatment efficacy in diabetes is HbA1c. Those using SMBG must do six to ten checks every day to achieve and maintain modest reduction in HbA1c, but most individuals with T1D do an average of four to five checks daily.[8,9] Those that use CGM are more likely to reduce their HbA1c levels, and in direct comparison trials, greater reductions are seen with CGM.[10–12,17,43,44,50,51,65] Given the relationship between HbA1c and complications of diabetes, the overwhelming amount of evidence favoring CGM makes it clear that the recommendation for all persons with T1D should be to use a CGM. Even for older adults, any efforts that can be made to slow the progression of cardiovascular, cerebrovascular, or renal disease should be considered.

A more immediate concern for older adults with T1D is time spent in hypoglycemia. Again, studies have demonstrated that CGM is more effective than SMBG at reducing frequency of hypoglycemic events and total time below range.[10,11,17,18,22,51,53,55] A large disadvantage of SMBG is that it only provides point-in-time glucose values. If a person does not check their

glucose, they may not realize that they are in hypoglycemia. Mild to moderate hypoglycemia may be asymptomatic for many, including older adults that are less likely to mount the compensatory catecholamine response. As the frequency of hypoglycemic events increases, the symptomatic threshold can also shift, creating impaired awareness of hypoglycemia which only serves to further this cycle.[6,18,19] Because CGM provides the user with glucose levels at regular intervals throughout the day, both the patient and their provider are made aware of any hypoglycemic episodes that occur, whether symptoms are present or not. The CGM devices also display arrows to show which direction glucose levels are currently trending, so users are able to predict and prevent hypoglycemic episodes before they occur.[60]

Though the predictive trend arrows are available on all CGM devices, the rtCGM holds a major advantage over FGM. Whereas FGM requires the individual to scan the sensor with receiver every eight hours, rtCGM automatically sends all data to the receiver.[41,42] Real-time CGM also has the added function of alarms to signal departure from optimal glucose ranges. For those at risk for frequent or severe hypoglycemia, users may set their rtCGM to alert them if their glucose goes below a self-determined threshold. Many individuals with T1D have found that this function causes the greatest reduction in diabetes-related anxiety.[60] From a clinical standpoint, the rtCGM is shown to reduce time in hypoglycemia and hyperglycemia more than FGM. Both serve to reduce HbA1c, though comparative studies have not shown the difference in reduction between the two systems to be significant. However, the increased TIR with rtCGM is statistically significant.[66] Further, this factor is of more importance to older adults with T1D, in whom hypoglycemia is the greatest concern. The rtCGM is preferrable for older adults in other ways, beyond clinical endpoints. The automatic transfer of data without the need to scan the

sensor is easier for those that may have impaired memory function. For those that have impaired awareness of hypoglycemia, the alarm functions can prevent critically low glucose levels.

Several benefits to quality of life are possible with CGM use. Diabetes-related distress is associated with poorer HRQOL and higher HbA1c.[36] Many factors can be causes of distress including the presence of complications, frequency of severe hypoglycemic events, anxiety surrounding the disease, impacts on occupational and social activities, and the time and effort required to maintain adequate glucose levels. Specifically, regimen-related stress was demonstrated to have a greatest impact.[33] Maintenance regimens for those with T1D include appropriate insulin administration, dietary choices, and blood glucose monitoring. By switching individuals from SMBG to CGM, the stress associated with glucose monitoring may be reduced. Users report CGM to be easier and faster than SMBG, with less disruption to their daily lives.[60] Because the CGM is used continuously for 10 to 14 days, patients do not have a need to bring glucose testing supplies with them at all times. Considering this and the improvements in glycemic control, it is understandable that qualitative studies of CGM users have demonstrated high treatment satisfaction and improved HRQOL.[57–60] For those with T1D and a concurrent depressive disorder, this reduction in regimen-related stress would also possibly result in fewer depressive symptoms. Importantly for older adults, this would further reduce risks of severe hyperglycemic and severe hypoglycemic episodes.[30]

Conclusion

In light of the advantages of CGM, it is no surprise that the ADA updated recommendations in 2021 to include CGM as the preferred method of glucose monitoring for older adults.[62] However, this recommendation was based primarily on the publication of the WISDM study, which demonstrated the ability of daily CGM use to reduce hypoglycemia in this

population.[61] While this endpoint has the greatest immediate impact on the health of many older adults with T1D, there is potential for further study in other areas. Quality of life assessments were completed for CGM users of all ages, but no specific studies were done among older adults, and the broad range of lifestyle differences in those over 65 years of age was not explored. All studies were done among community-dwelling older adults, excluding those residing in assisted living or skilled nursing facilities. Further studies should be done to explore CGM use in these settings. For parents and caregivers of children with T1D, CGM use was associated with decreased diabetes-related distress and improved HRQOL.[60] At this time, no similar study has been done with caregivers of older adults with either T1D or T2D.

Despite the many known advantages of CGM, SMBG continues to be the standard of care for those with T1D. The use of CGM is increasing among all individuals with T1D, but the slowest increase is among adults over 50 years of age. SMBG use is more than twice as common as CGM use in this age group.[67] It's possible that many older adults are simply resistant to change after having the same treatment method for many years. Though treatment satisfaction is high among CGM users,[58,59] there may be apprehension due to the learning curve associated with all new technologies. Usability among older adults should be studied to evaluate how to optimize CGM systems for use by this population. In the past, cost was a large factor in decreasing use. However, in 2017 Medicare began covering CGMs, improving access for many older adults with T1D. As access has increased and many benefits are possible, including reducing hypoglycemia, CGM use should be standard of care in all older adults with T1D, and providers should advocate for their use in all who are willing.

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Author(s) of Work(s): Alyssa Clements

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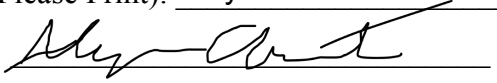
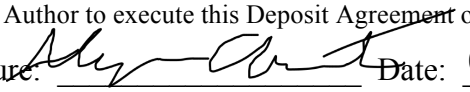
Author's Signature:  Date: 08/12/21

If the Deposit Agreement is executed by the Author's Representative, the Representative shall separately execute the Following representation.

I represent that I am authorized by the Author to execute this Deposit Agreement on the behalf of the Author.

Author's Representative Signature:  Date: 08/12/21