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FreeStyle Libre

THE sensor report

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WELCOME TO
THE SENSOR REPORT, ISSUE 2, 2023

In this second 2023 issue of *The Sensor Report*, we are taking you inside the fundamentals of flash glucose monitoring and other continuous glucose monitoring (CGM) technologies, to outline the key aspects of behind the FreeStyle Libre system that underpin its reputation for consistent glucose measurement for people with diabetes. At the heart of this is the system accuracy and its precision.

In this issue we also discuss the retrospective data that indicate how use of the FreeStyle Libre system may be helping to combat the phenomenon of treatment inertia in diabetes, which is characterized by poor attainment of glycemic targets and a reluctance of healthcare professionals to escalate therapy, often due to concerns regarding hypoglycemia. A study, including data from over 370,000 people with type 2 diabetes (T2DM), shows that progression to more-intensive glucose-lowering therapy is more likely once FreeStyle Libre is provided to people with T2DM in support of treatment escalation by their healthcare professionals.

As well as promoting reductions both in high and low glucose, use of CGM systems by people with diabetes is increasingly being shown to be associated with reductions in microvascular complications, including diabetic retinopathy, diabetic nephropathy and diabetic peripheral neuropathy. In this issue we will highlight the research behind these observations.

As always, this issue of *The Sensor Report* will also provide insights from many recent studies that further establish the benefits of using the FreeStyle Libre systems and other CGM sensors in people with diabetes.

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1. Alva S, et al, *Diabetes Ther.* 2023; 14: 767-776.

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featurestory

Understanding the accuracy and precision of the FreeStyle Libre glucose sensor in daily diabetes care

Continuous glucose monitoring (CGM) devices are now commonly used in the management of people with type 1 diabetes (T1DM) or type 2 diabetes (T2DM) who are receiving insulin therapy. CGM systems measure glucose in the subcutaneous interstitial fluid (ISF), in contrast to self-monitoring of blood glucose (SMBG) meters, which measure glucose in capillary blood. The application of CGM systems has led to significant improvements in glucose management for people with T1DM or T2DM, with reductions in HbA1c[1,2] and in hypoglycemia[3,4], increased time in range[3,4], decreased risk of diabetes complications[5,6] and acute diabetes events[7].

MARD and MAD: measuring accuracy at high and low glucose

The accuracy of CGM systems is critical because they must be reliable at different glucose levels, including at extremes of glucose concentration, and also during periods of rapid glucose change. The measure of accuracy most quoted is the mean absolute relative difference (MARD) of CGM sensor glucose readings when compared to a series of blood glucose reference samples taken at the same time.

Once calculated, MARD is expressed as a percentage number. A lower percentage MARD means better accuracy, as this indicates only a small difference from the reference samples. A common interpretation is that a MARD of 10% or below represents the level of accuracy required for safe use of CGM readings to make insulin dosing decisions, without the need for an adjunct SMBG blood glucose reading[8]. It is worth pointing out that SMBG fingerprick glucose meters are also evaluated using MARD calculations, and these can vary widely, from 5.6% to 20.8%, depending on the meter[9].

Ideally, MARD for CGM systems should be calculated in a diverse racial population, including individuals with T1DM or T2DM, and be based on a large set of paired readings with an adequate number of samples to assess accuracy in hypo-, hyper- and euglycemic ranges[10].

In calculating MARD, the reference blood glucose value is used as the denominator, meaning that MARD can be incorrect at low reference glucose values and may not closely reflect accuracy. Therefore, the mean absolute difference (MAD) is preferred as an accuracy metric for glucose levels <80 mg/dL (<4.4 mmol/L). Although lower MARD/MAD is regarded as better, to date, no prospective clinical studies have evaluated the clinical significance of lower MARD or MAD.

Alongside MARD, the number of CGM values that fall within ± 20 mg/dL or ± 20% of the paired reference values are also used for accuracy reporting. A CGM system with a MARD of 9-10% can be expected to have 90% or more readings within this range[11]. As CGM technology further develops, the requirement is increasingly for sensor glucose readings to fall substantially within ± 15 mg/dL or ± 15% of the paired reference values.

Precision is also an important measure

The concordance between CGM glucose readings and reference blood glucose readings is an assessment of how closely they match. This is dependent both on the accuracy and the precision of the CGM device **(Fig. 1)**.

Figure 1.

High Precision, High Accuracy

Low Precision, High Accuracy

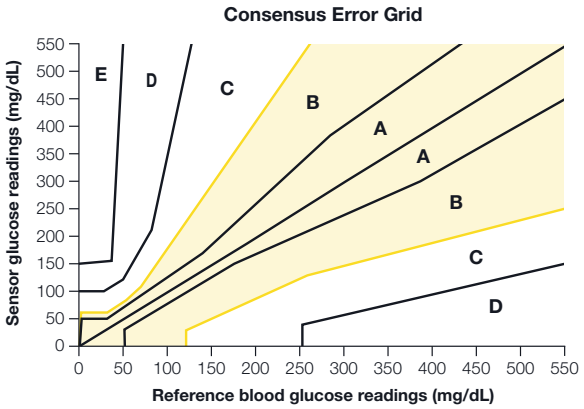
High Precision, Low Accuracy

Low Precision, Low Accuracy

MARD is a metric of average accuracy, but not of precision, which can be visualised together with MARD in a consensus error grid (CEG)[12].

The CEG evaluates the clinical significance of inaccuracies in CGM sensor glucose readings and assigns a specific level of risk to any errors within defined zones (A-E), based on whether these have an impact on clinical decision making **(Fig. 2)**. Readings that fall into zones A and B are acceptable for making clinical decisions, whereas those in zones C-E have questionable clinical accuracy[13]. The outcomes of CEG analysis are used alongside MARD to validate system accuracy and precision, on which regulatory decisions can be based to indicate the suitability and safety of each CGM device for use in glycemic self-management by people with T1DM or T2DM.

Figure 2.



The FreeStyle Libre systems are part of a small number of CGM devices that have been approved for making insulin-dosing decisions without the need for SMBG confirmation[14], based on viewing a current CGM glucose reading and the associated trend arrow that indicates the direction and rate of change of glucose. It has also met the stringent FDA accuracy criteria for integrated CGM systems, that can be used in future automated insulin delivery (AID) systems with fewer regulatory barriers. These conditions for safe and effective use are not met by all CGM devices currently available[15].

The accuracy and precision of CGM systems, such as the FreeStyle Libre portfolio, has helped them to become trusted and powerful components of daily diabetes care. The availability of glucose readings on demand, accompanied by clear information about the direction and rate of glucose changes has helped people with T1DM or T2DM to optimise their glucose control and to avoid the harmful consequences of hypoglycemia or hyperglycemia[16].

1. Leelarathna L, *et al.* Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes. *New Engl J Med.* 2022. 387(16): 1477–87. DOI:10.1056/nejmoa2205650.

2. Yaron M, *et al.* Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. *Diabetes Care* 2019; 42(7): 1178–84. dc180166.

3. Haak T, *et al.* Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes: a Multicenter, Open-Label Randomized Controlled Trial. *Diabetes Ther.* 2017; 8: 55–73.

4. Bolinder J, *et al.* Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet* 2016; 388: 2254–63.

5. Lu J, *et al.* Time in Range in Relation to All-Cause and Cardiovascular Mortality in Patients With Type 2 Diabetes: A Prospective Cohort Study. *Diabetes Care* 2021; 44: 549–55.

6. Yang J, *et al.* Association of time in range, as assessed by continuous glucose monitoring, with painful diabetic polyneuropathy. *J Diabetes Invest.* 2021; 12: 828–36.

7. Riveline J-P, *et al.* Reduced rate of acute diabetes events with flash glucose monitoring is sustained for two-years after initiation: extended outcomes from the RELIEF study. *Diabetes Technol Ther.* 2022; 24(9): 611–18. 0. DOI:10.1089/dia.2022.0085.

8. Kovatchev BP, *et al.* Assessing sensor accuracy for non-adjunct use of continuous glucose monitoring. *Diabetes Technol Ther.* 2014; 17: 177–86.

9. Ekhlaspour L, *et al.* Comparative Accuracy of 17 Point-of-Care Glucose Meters. *J Diabetes Sci Technol.* 2017; 11: 558–66.

10. Ajjan RA, *et al.* Accuracy of flash glucose monitoring and continuous glucose monitoring technologies: Implications for clinical practice. *Diabetes Vasc Dis Res.* 2018; 15: 175–84.

11. Alva S, *et al.* Accuracy of a 14-Day Factory-Calibrated Continuous Glucose Monitoring System With Advanced Algorithm in Pediatric and Adult Population With Diabetes. *J Diabetes Sci Technol.* 2022; 16(1): 70–7. 193229682095875.

12. Pfützner A, *et al.* Technical Aspects of the Parkes Error Grid. *J Diabetes Sci Technol.* 2013; 7: 1275–81.

13. Parkes JL, *et al.* A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. *Diabetes Care* 2000; 23:1143–1148.

14. Akturk HJ, *et al.* Technological advances shaping diabetes care. *Curr Opin Endocrinol Diabetes Obes.* 2019; 26:84-89.

15. Pemberton JS, *et al.* CGM accuracy: Contrasting CE marking with the governmental controls of the USA (FDA) and Australia (TGA): A narrative review. *Diabetes Obes Metab.* 2023; 25: 916–39.

16. Evans M, *et al.* Reductions in HbA1c with Flash Glucose Monitoring Are Sustained for up to 24 Months: A Meta-Analysis of 75 Real-World Observational Studies. *Diabetes Ther.* 2022; 13:1175–1185.

Accuracy of CGM devices, the unmet need for internationally agreed accuracy measures

There is substantial evidence showing that CGM devices can improve glycemic outcomes and quality of life for people with diabetes, when compared to self-monitored blood glucose (SMBG) finger prick testing. Accuracy of CGM devices, as measured by mean absolute relative difference (MARD, see previous article), has improved such that current devices can achieve a MARD <10%. However, accuracy of CGM devices is assessed and certified on a regional basis, rather than to internationally agreed standards[1].

Point accuracy, which is the headline measure of CGM system accuracy, is the closeness of agreement between a CGM glucose test reading and an accepted reference value at a single point in time. MARD, MAD and consensus error grid analysis (see previous item) are the most common point accuracy metrics reported in CGM accuracy studies. Across the full glucose range, point accuracy metrics can fail to identify inaccuracy in the hypoglycemic range, and thus increase the risk of hypoglycemia.

Overall, CGM devices with respectable averages but erratic overall performance can be viewed as safe. Therefore, point accuracy glucose metrics using a specified target range with reference agreement rates are the most informative and straightforward to understand. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has established a working group to address the challenges of setting standards for CGM accuracy. Currently, the integrated CGM (iCGM) metrics and performance standards from the FDA are the only published regulatory standards with minimum accuracy requirements using a specified target range with agreement rates[2].

In Europe the most common medical device certification procedure is the Conformité Européenne (CE) marking, in which the manufacturer must choose and implement a conformity assessment procedure before placing them on the market. CGM systems are Class IIb devices which are 'medium risk'. However, there is no published guidance that specifies the minimum level of clinical evidence that must be provided to support the CE mark. Prior to May 2021, the clinical data submitted by a device manufacturer was through a Notified Body accredited by the European Commission, and the submission could include published or unpublished studies using the device, with a representative sample of clinical data provided. From May 2021 onwards, there is greater emphasis on the oversight of Notified Bodies by national authorities (where the device will be marketed), requiring a submission dossier that includes clinical data on device performance and safety, as well as enhanced post-market surveillance. This adds to the available information that clinicians, payers and people with diabetes can verify that CE-marked CGM devices are accurate and effective.

The FreeStyle LibreLink app works with FreeStyle Libre and FreeStyle Libre 2 sensor. The FreeStyle LibreLink app is only compatible with certain mobile devices and operating systems. Please check the website for more information about device compatibility before using the app. Use of FreeStyle LibreLink may require registration with LibreView.

The US Food and Drug Administration (FDA) has a significantly different approval process. Until February 2018, CGM systems were indicated as Class III, high-risk devices requiring a complete set of device-specific clinical data to be submitted prior to premarketing approval. After February 2018, CGM devices were given a Class II indication, requiring 'special controls' that provide reasonable assurance of safety and effectiveness. In response to the increasing interoperability of CGM systems with insulin pumps and other digitally connected medical devices, the FDA created the Class II iCGM premarketing approval pathway[2]. This specifically details the CGM-specific clinical data requirements that should be included in study design and accuracy measures. These include rigorous minimum percentage agreement rates with reference blood-glucose analyzer readings, at all glucose ranges identified by International Consensus Guidelines[3], with minimum error rates when used with known interfering substances such as paracetamol or vitamin C. To date, the FreeStyle Libre 2, FreeStyle Libre 3, Dexcom G6 and Dexcom G7 are the only CGM sensors to be approved through the FDA Class II iCGM pathway.

The growing number of CGM devices being marketed with medical device certification means that payers, healthcare professionals and people with diabetes should understand the strengths and limitations of each certification process, such that the accuracy, efficacy and safety of each system is a key part of the decision to select between available systems[1].

1. Pemberton JS, *et al.* CGM accuracy: Contrasting CE marking with the governmental controls of the USA (FDA) and Australia (TGA): A narrative review. *Diabetes Obes Metab.* 2023; 25: 916–939.

2. Garg SK and Akturk HK. A New Era in Continuous Glucose Monitoring: Food and Drug Administration Creates a New Category of Factory-Calibrated Nonadjunctive, Interoperable Class II Medical Devices. *Diabetes Technol Ther.* 2018; 20: 391–394.

3. Battelino T, *et al.* Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. *Diabetes Care* 2019; 42: 1593–1603.

Flash glucose monitoring can support escalation of diabetes therapy to improve treatment inertia in T2DM

Use of the FreeStyle Libre portfolio is associated with significant improvements in glycemic control for people living with T1DM or T2DM, including lowered HbA1c[1,2], reductions in hypoglycemia[3,4] and a fall in hospital admissions for acute diabetes events (ADEs) such as diabetic ketoacidosis (DKA) or severe hypoglycemia[5]. However, studies to date have not investigated treatment progression to more-intensive glucose lowering regimens in T2DM when using the FreeStyle Libre portfolio, compared to those using self-monitored blood glucose (SMBG) finger prick testing.

This study[6], using a Canadian private insurance drug-claims database, investigated whether use of flash glucose monitoring among people with T2DM in Canada can be associated with changes in treatment intensification, when compared to people with T2DM using SMBG alone. In total, 373,871 people with T2DM using the FreeStyle Libre systems were included in the study, 37% of whom were naïve to diabetes therapy at the point of starting flash glucose monitoring and 63% who were established on glucose-lowering regimens. The diabetes treatment progression of these groups was tracked retrospectively over a 24-month period against 8 escalating treatment categories (see insert) and compared to a matched cohort of people with T2DM using SMBG alone.

Treatment progression followed in the study

1. No diabetes drug therapy (diet and exercise)
2. Monotherapy with non-insulin OADs
3. Dual therapy with non-insulin OADs
4. Triple therapy with non-insulin oral OADs
5. >3 non-insulin OADs
6. Injectable GLP1-RA (± OADs)
7. Basal insulin therapy (± OADs)
8. MDI therapy (± OADs)

OAD, oral antidiabetic drugs; GLP-1 RA, glucagon-like peptide 1 receptor agonist; MDI, multiple daily injections with insulin.

People with T2DM who were treatment-naïve when starting flash glucose monitoring (the index date) were 86% more likely to have their non-insulin treatment intensified after starting, compared to the SMBG cohort. Patients already on diabetes therapy at the index date were 103% more likely to have their non-insulin treatment intensified, compared to the SMBG cohort. Those already on basal insulin therapy at the index date were 181% more likely to progress to MDI therapy compared to the SMBG cohort ($p<0.0001$ in all cases).

People with T2DM starting with non-insulin treatment category 2, 3 or 4 at the index date had a higher probability of treatment escalation than those who were at more-advanced treatment categories 5, 6, or 7. A higher probability of treatment progression was independent of the diabetes treatment at the index date, and independent of whether patients were treatment naïve or on established diabetes therapy. Assessment of the ending treatment relative to the starting therapy indicated that dynamic treatment changes were most evident for patients using the FreeStyle Libre systems. This cohort also had a much greater portion who ended with insulin treatment (category 6 or 7) compared to the cohort using SMBG alone.

This retrospective analysis of a large payer claims database indicates that the FreeStyle Libre systems can be used to support more-timely escalation of diabetes therapy to improve therapeutic inertia in T2DM.

1. Leelarathna L, *et al.* Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes. *New Engl J Med.* 2022; 387(16): 1477–87. DOI:10.1056/nejmoa2205650.

2. Yaron M, *et al.* Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. *Diabetes Care* 2019; 42(7): 1178–84. dc180166.

3. Bolinder J, *et al.* Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet* 2016; 388: 2254–63.

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5. Riveline J-P, *et al.* Reduced rate of acute diabetes events with flash glucose monitoring is sustained for two-years after initiation: extended outcomes from the RELIEF study. *Diabetes Technology Ther.* 2022; 24(9): 611–18. DOI:10.1089/dia.2022.0085.

6. Harris SB and Levrat-Guillen F. Use of the FreeStyle Libre system and diabetes treatment progression in T2DM: Results from a retrospective cohort study using a Canadian private payer claims database. *Diabetes Obes Metab.* 2023; Feb 21. doi: 10.1111/dom.15025.

The FreeStyle Libre 2 system, with optional alarms, extends the attributes of flash glucose monitoring

A number of recent studies have now investigated the impact of using the FreeStyle Libre 2 system, with optional high and low glucose alarms, on metabolic outcomes and healthcare-related quality of life for people with T1DM previously using the FreeStyle Libre flash glucose monitoring system without optional alarms.

When children and adolescents with T1DM (n=47), with experience of using the FreeStyle Libre system without alarms, started to use the FreeStyle Libre 2 system with alarms for 14 days[1], they experienced a significant increase in time in range (TIR) 3.9-10.0 mmol/L (70-180 mg/dL), a reduction in time below range (TBR) <3.9 mmol/L (70 mg/dL), reduced frequency of hypoglycemic events, and lower glycemic variation. A series of psychosocial and sleep-related questionnaires, including amongst caregivers, found that the optional alarms did not adversely affect sleep duration or quality, either for the FreeStyle Libre 2 system users or their parents, who also reported improved quality of life.

Image for illustrative purposes only. Not real patient.

An adult group with T1DM (n=38, mean age 34 yrs) with at least 6 months use of the FreeStyle Libre system were introduced to the FreeStyle Libre 2 system for 8 weeks[2]. In the first 4-weeks after starting to use the FreeStyle Libre 2 system, TIR increased from 52.8 to 57.0% (p=0.001), TBR <3.9 mmol/L (70 mg/dL) decreased from 6.2 to 3.4% (p<0.0001) and TBR <3.0 mmol/L (54 mg/dL) fell from 1.4% to 0.3% (p<0.0001). These changes were maintained at 8 weeks and subjects who had >4% TBR at baseline showed the greatest improvements in glucose control and treatment satisfaction.

A group of older adults with T1DM (n=108, mean age 58 yrs) who reported fear of hypoglycemia or impaired awareness of hypoglycemia (IAH) while using the FreeStyle Libre system without alarms were provided with the FreeStyle Libre 2 system and followed for 12 weeks[3]. During this period, TBR <3.9 mmol/L (70 mg/dL) decreased from 4.5% to 2.3% (p<0.001) and TBR <3.0 mmol/L (54 mg/dL) decreased from 1.4% to 0.3% (p<0.001). The participants (n=48) who were most at risk for hypoglycemia reduced their TBR <3.9 mmol/L (70 mg/dL) from 8.1% to 3.9% (p<0.0001) and their TBR <3.0 mmol/L (54 mg/dL) from 3.1% to 0.75% (p<0.0001). Notably, all study subjects opted to keep using the FreeStyle Libre 2 system beyond the study period.

Together, these outcomes show that the FreeStyle Libre 2 system with optional alarms can significantly reduce the incidence of hypoglycemic events in children, adolescents and adults with T1DM. Importantly, for people with T1DM with fear of hypoglycemia or IAH, use of the FreeStyle Libre 2 system significantly lowered their risk of severe hypoglycemia.

1. Franceschi R, *et al.* Impact of intermittently scanned continuous glucose monitoring with alarms on sleep and metabolic outcomes in children and adolescents with type 1 diabetes. *Acta Diabetol.* 2022; 59: 911–9.

2. Boscari F, *et al.* Effectiveness of adding alarms to flash glucose monitoring in adults with type 1 diabetes under routine care. *Acta Diabetol.* 2022; 59(7): 921–928.

3. Oriot P and Hermans MP. Intermittent-scanned continuous glucose monitoring with low glucose alarms decreases hypoglycemia incidence in middle-aged adults with type 1 diabetes in real-life setting. J *Diabetes Complications.* 2023; 37(2): 108385.

Reductions in impaired awareness of hypoglycemia and severe hypoglycemia are associated with FreeStyle Libre systems use

Impaired awareness of hypoglycemia (IAH) affects up to a third of people with T1DM, which puts them at a 6-fold increased risk of severe hypoglycemia. Data from the UK Association of British Clinical Diabetologists (ABCD) audit of FreeStyle Libre system users has allowed this aspect of living with T1DM to be investigated[1,2].

The presence of IAH amongst people with T1DM is confirmed by a Gold score of ≥4 and a Gold score ≥7 indicates complete loss of awareness. Baseline and follow-up Gold scores were available for 4,391 people included in the ABCD audit, the majority (98.2%) of whom had T1DM. At baseline, 28.1% of the audit population had IAH, and 37.2% of this group reported experiencing at least one episode of severe hypoglycemia, compared to 11.1% of those without IAH (p<0.001). After a mean 7.6 months using the FreeStyle Libre system, the prevalence of IAH had fallen to 18.1% of people. The proportion of those with complete loss of awareness fell from 3.7% at baseline to 3.2% after use of the FreeStyle Libre system.

Restored awareness of hypoglycemia was associated with increased time in range 3.9-10.0 mmol/L (70-180mg/dL) of 48.6%, compared to 44.9% for people who continued to have IAH (p=0.002). People with longer duration of diabetes and higher baseline Gold scores were less likely to regain hypoglycemia awareness after using the FreeStyle Libre system. Restored awareness of hypoglycemia was also correlated with less diabetes distress in the ABCD audit population and these benefits were sustained over a 2-year follow-up period[2].

These real-world study outcomes show that the prevalence of IAH and associated episodes of severe hypoglycemia are significantly reduced after initiation of the FreeStyle Libre system in a large population of people predominantly living with T1DM.

1. Pieri B, *et al.* Impaired awareness of hypoglycaemia: Prevalence and associated factors before and after FreeStyle Libre use in the Association of British Clinical Diabetologists audit. *Diabetes Obes Metabolism* 2023; 25: 302–5.

2. Shah N, *et al.* The long-term impact of glucose monitoring with the FreeStyle Libre on glycaemic control and hypoglycaemia awareness in people with type 1 diabetes: Insights from the Association of British Clinical Diabetologists national audit *Diabet Med* 2023; Feb 16: e15070.

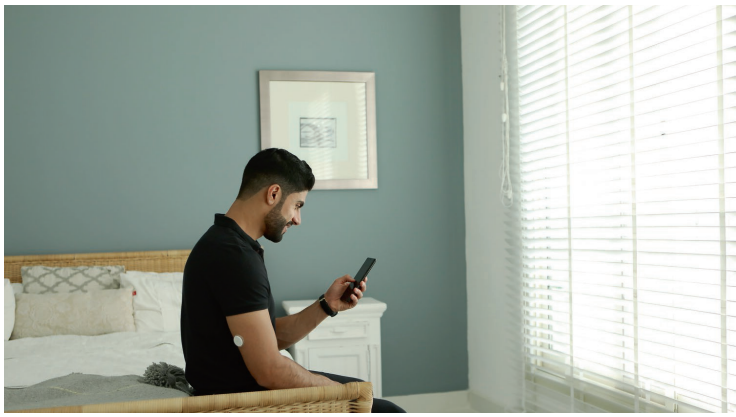

Image for illustrative purposes only. Not real patient.

CGM-derived time in range is a predictor of microvascular complications in T2DM

Since the landmark UK Prospective Diabetes Study (UKPDS), the primary measure for predicting the risk of diabetes-related microvascular complications in T2DM has been HbA1c[1,2]. However, HbA1c has several limitations and is affected by factors such as age, ethnicity, hematological conditions, chronic kidney disease, and pregnancy. CGM devices, including the FreeStyle Libre portfolio, provide more-comprehensive glucometric data beyond HbA1c and are more convenient for people with T2DM.

This systematic review by Raj and colleagues[3] identified eleven studies on a total of 13,987 people with T2DM that evaluated the relationship between CGM-derived time in range (TIR) and diabetic retinopathy, diabetic nephropathy and diabetic neuropathy. Four studies investigated the relationship between TIR and diabetic retinopathy or diabetic nephropathy, and seven studies evaluated the relationship between TIR and diabetic neuropathy.

The authors concluded that a 10% increase in TIR is associated with reduction in severity of diabetic retinopathy. Overall, CGM-derived TIR was found to be equivalent to HbA1c in predicting diabetic retinopathy among people with T2DM. For diabetic nephropathy, two studies showed a decrease in severity of albuminuria with a 10% increase in TIR and one study showed that an increased TIR was associated with a lower risk of macroalbuminuria and diabetic kidney disease. A further study provided evidence that increased TIR was associated with a decrease in urinary albumin to creatinine ratio (UACR) but not with estimated glomerular filtration rate (eGFR). In limited studies evaluating the relationship between TIR and diabetic nephropathy, it was found to be similar to HbA1c in predicting diabetic nephropathy among patients with T2DM.

Of the seven studies investigating the relationship between TIR and diabetic neuropathy, four evaluated the association of TIR with diabetic painful neuropathy, two examined the association of TIR with cardiovascular autonomic neuropathy and one study looked at the association of TIR with peripheral nerve function.

Increases in TIR were associated with reduced prevalence and severity both of diabetic painful neuropathy and cardiovascular autonomic neuropathy. In line with international consensus recommendations[4], TIR >70% was associated with significantly lower prevalence of diabetic painful neuropathy compared with TIR <70%. Notably, TIR was found to more closely correlate with diabetic painful neuropathy and cardiovascular autonomic neuropathy, when compared with HbA1c. However, it must be emphasized that this observation is based on limited outcomes.

It must also be noted that ten out of eleven of the studies reported were conducted in Asia, restricting their generalizability, and it will be important to support these observations with studies in a wider selection of ethnic groups. However, the outcomes support the application of CGM metrics alongside HbA1c in predicting microvascular complications for people with T2DM.

1. Stratton IM, *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321: 405.

2. Laiteerapong N, *et al.* The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study). *Diabetes Care* 2019; 42: 416–26.

3. Raj R, *et al.* Time in range, as measured by continuous glucose monitor, as a predictor of microvascular complications in type 2 diabetes: a systematic review. *BMJ Open Diabetes Res Care* 2022; 10: e002573. doi: 10.1136/bmjdrc-2021-002573.

4. Battelino T, *et al.* Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. *Diabetes Care* 2019; 42(8): 1593–1603.

Reduced hospital admissions for acute diabetes events among older people with T2DM using the FreeStyle Libre system

Older people with T2DM on insulin are at increased risk of hypoglycemia and management of this group must optimize glycemic control while minimizing risks for hypoglycemia and diabetic ketoacidosis (DKA). This report assessed the impact of starting the FreeStyle Libre system on hospitalizations for acute diabetes events (ADEs) in people ≥65 years old with T2DM on intensive insulin therapy.

This retrospective study on the French Système National des Données de Santé (SNDS) claims database was part of the RELIEF study outcomes and centred on 38,312 people ≥65 years old with T2DM on intensive insulin therapy. The analysis covered claims data for the 12 months before, and up to 24 months after starting the FreeStyle Libre system.

Hospitalizations for ADEs were observed in 1.60% of subjects in the 12 months before FSL initiation, compared to 1.05% after 12 months and 0.96% after 24 months, a 34% and 40% reduction, driven by fewer DKA admissions after 12 months and by fewer admissions for hypoglycemia at 24 months.

These results indicate that using the FreeStyle Libre system can reduce hospitalization for ADEs in this vulnerable older population of adults aged 65 years and older with T2DM on intensive insulin therapy.

Guerci B, *et al.* Reduced acute diabetes events after FreeStyle Libre® system initiation in people 65 years or older with type 2 diabetes on intensive insulin therapy in France. *Diabetes Technol Ther.* 2023; 0. DOI: 10.1089/dia.2023.0034.

Image for illustrative purposes only. Not real patient or healthcare professional.

Reductions in HbA1c in adults with T2DM are associated with flash glucose monitoring in a large cohort of users in Sweden

The Swedish National Diabetes Register (NDR) initiated registration of the FreeStyle Libre system in June 2016. This study investigated change in HbA1c for 711 adults with T2DM using the FreeStyle Libre system in Sweden.

This study reports a before/after comparison of laboratory measured HbA1c in the 6 months before starting the FreeStyle Libre system (the index date) and up to 12 months after the index date for adults with T2DM, 79% of whom were treated with insulin. The NDR data reveal a significant association between FreeStyle Libre system use after the index date and reductions in HbA1c. Across the whole cohort there was a 0.5% reduction in HbA1c at 6 months after starting flash glucose monitoring, which was maintained at 12 months. Significant reductions in HbA1c were evident for all adults with T2DM aged 25–74 years.

Within the adults with T2DM in the study cohort, those truly naïve to prior use of CGM experienced reductions in HbA1c of 0.67% at 6 months, maintained at 12 months. People with unknown prior use of CGM also achieved reductions in HbA1c of 0.49% at 12 months. When stratified based on baseline HbA1c status, the largest reductions were evident amongst adults with T2DM and HbA1c 9.0-11.9% (-1.10% at 6 months) and HbA1c ≥12% (-3.6% at 6 months).

Eeg-Olofsson K, *et al.* Real-world study of flash glucose monitoring among adults with type 2 diabetes within the Swedish National Diabetes Register. *Diabetes Vasc Dis Res.* 2022; 20(1): 14791641211067418. doi: 10.1177/14791641211067418.

What do adults with T1DM think about using ambulatory glucose profile reports?

Continuous glucose monitoring (CGM) devices summarize data in ambulatory glucose profile (AGP) reports that are used by healthcare professionals (HCPs) to evaluate dynamic glycemic control for people with T1DM or T2DM. An important question is how these AGP reports are perceived and used by people with diabetes using CGM or flash glucose monitoring devices.

This study reported on the results of an online survey amongst 291 adults with T1DM in Canada who used CGM devices, in order to understand their attitudes toward the AGP report format. The results showed that approximately 80% of respondents reviewed their AGP report, with 50% reporting that they often discussed it with their HCP. There was a positive relationship between motivation and better understanding of the AGP report, linked to support from family members and their HCP.

A significant majority (92%) of respondents indicated that the AGP report is important for their diabetes management. However, free-text responses suggested some concern with the complexity of information contained in the AGP report and most respondents indicated dissatisfaction with the cost of CGM devices.

Although the cost of CGM devices was identified as a barrier, this online survey revealed few other barriers to the use of the AGP report by adults with T1DM. With support from family members, discussions between HCPs and people with diabetes centred on AGP reports can bring a benefit to people with T1DM.

Mackett K, *et al.* Patient Perspectives on the Ambulatory Glucose Profile (AGP) Report for Type 1 Diabetes Management: A National Online Survey. *Can J Diabetes* 2023. DOI:10.1016/j.jcjd.2023.01.001.

Flash glucose monitoring is cost-effective for people with T2DM receiving intensive insulin treatment compared to SMBG

The high risk of many complications associated with T2DM has led to a large and growing economic burden for healthcare systems. This study assessed the cost-effectiveness of flash monitoring versus self-monitored blood glucose (SMBG) testing in people with T2DM on intensive insulin therapy in the UK.

Using the IQVIA CORE Diabetes Model, the impact of flash glucose monitoring versus SMBG was analysed over a 40-year horizon from the perspective of payers in the UK. The model included costs for intervention effects, resource utilization and utilities, based on recently published literature and national databases.

In the base-case analysis, flash glucose monitoring compared to SMBG resulted in an incremental cost of £5,781 and an additional 0.47 quality-adjusted life years (QALY), at an incremental cost-effectiveness ratio (ICER) of £12,309/QALY. The key drivers of differentiation were change in HbA1c and costs for intervention-related health utilities. All scenario analyses, including different discount rates, time horizons, effects on HbA1c and on the intervention-related health utility, as well as glycemic emergencies, generated ICERs of less than £20,000 per QALY.

The results across the base case and other scenario analyses indicate that using flash glucose monitoring is cost-effective compared to SMBG in a UK population for managing people with T2DM on intensive insulin therapy, based on clinical efficacy and a cost-effectiveness threshold of £20,000-30,000 per QALY.

Ajjan RA, *et al.* Cost-Effectiveness Analysis of Flash Glucose Monitoring System for People with Type 2 Diabetes Receiving Intensive Insulin Treatment. *Diabetes Ther.* 2022; 13:1933-1945.

Using CGM reveals that nocturnal hypoglycemia is common and undetected in older people with T2DM

Nocturnal hypoglycemia is a common and often underdiagnosed problem in older people with insulin-treated T2DM. The multicenter HYPOAGE study examined the frequency and predictors of hypoglycemia in this growing population in France.

This prospective study included 141 people with T2DM on insulin therapy, aged ≥75 yrs (mean age 81.5 yrs) who received blinded ambulatory CGM for 28 days using the FreeStyle Libre Pro system and who also undertook ≥2 self-monitoring of blood glucose (SMBG) daily tests. The study population reported >70% CGM data capture.

Based on SMBG alone, 37.6% of subjects experienced hypoglycemia <3.9 mmol/L (70 mg/dL) during the study, whereas CGM data confirmed that 65% of the study cohort experienced nocturnal Level 2 hypoglycemia <3.0 mmol/L (54 mg/dL) events lasting ≥15 consecutive minutes. In multivariable analyses, cognitive impairment, heart failure and depressive disorder were each risk factors for nocturnal hypoglycemic events.

The HYPOAGE data confirm that nocturnal hypoglycemia is frequent in older people with T2DM and undetected by SMBG because these episodes often do not waken the affected person. The use of CGM is a powerful tool to detect a nocturnal hypoglycemia and to personalize T2DM management, especially for those with cognitive impairment.

Boureau A, *et al.* Nocturnal hypoglycemia is underdiagnosed in older people with insulin-treated type 2 diabetes: The HYPOAGE observational study. *J Am Geriatr Soc.* 2023. DOI:10.1111/jgs.18341.

Flash glucose monitoring can empower young people with T1DM to understand adherence with diabetes care more completely

Flash glucose monitoring allows people with T1DM to avoid frequent painful fingerprick glucose testing and improve their frequency of glucose self-monitoring. This qualitative study explored the experiences of young people using the Freestyle Libre system and their parents.

Semi-structured interviews were conducted online with 10 young people with T1DM (aged 8-17 years) and 10 parents, as well as with 14 healthcare professionals. All interviewees were recruited via social media and through NHS diabetes clinic staff. Young people reported that life was much easier after starting flash glucose monitoring, increasing their confidence and giving them independence to manage their diabetes. Parents reported improved quality of life and they appreciated access to real-time data. The study authors conclude that flash glucose monitoring empowers young people and their parents to understand diabetes management better, including adjusting their own self-care.

Healthcare professional (HSP) interview responses were mapped onto normalisation process theory (NPT) constructs and showed how flash glucose monitoring technology was positively integrated into routine care, with HCPs adapting well to the extra glycemic data which enabled them to provide more-tailored support within and between clinic visits.

Beasant L, *et al.* Flash glucose monitoring in young people with type 1 diabetes-a qualitative study of young people, parents and health professionals: ' It makes life much easier'. *BMJ Open* 2023; 13(4):e070477. doi: 10.1136/bmjopen-2022-070477

Flash glucose monitoring is accurate and safe when used in women with gestational diabetes

Glucose control in women with gestational diabetes mellitus (GDM) requires close surveillance to prevent perinatal morbidity, yet CGM systems are not well validated in this population. This study examined the accuracy and concordance of the Freestyle Libre system compared to reference blood glucose tests in women with GDM.

The study investigated glucose levels when fasting and in the 2-hour postprandial window for 14 days, using the Consensus Error Grid (see feature article on page 3) to evaluate the CGM data in Zone A (clinically accurate measurements with no effect on clinical action) or Zone B (values that would have benign or no clinical impact). MAD and MARD were 15.9 mg/dL and 12.5%, respectively and 99.8% of the readings were in Zone A or Zone B of the Error Grid, indicating the clinical utility.

In women with GDM, glucose monitoring with the FreeStyle Libre system is accurate and safe from a clinical perspective, indicating that it can be used for glycemic control in this important group.

Hussain FN, *et al.* Comparison of an Intermittently Scanned (Flash) Continuous Glucose Monitoring System to Standard Self-Monitoring of Capillary Blood Glucose in Gestational Diabetes Mellitus. *Am J Perinatol*. 2023. DOI: 10.1055/a-2053-7650.

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