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THE sensor report

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WELCOME TO
THE SENSOR REPORT, ISSUE 2, 2024

In this second issue of the *Sensor Report* for 2024, we look in detail at the emerging use of time in tight range (TITR) as a CGM-derived metric of glycemic management for people with diabetes, both for children and adults with T1DM on intensive insulin therapy, and for people with T2DM, particularly those on newer glucose-lowering non-insulin drugs. The definition of TITR is typically glucose values between 70-140 mg/dL (3.9-7.8 mmol/L), but can also include glucose levels 63-140 mg/dL (3.5-7.8 mmol/L) in women with diabetes during pregnancy or in gestational diabetes mellitus (GDM). For people with T1DM, the use of TITR has been developed as a target particularly for individuals who use automated insulin devices (AID). In T2DM, TITR is managed using CGM technology alongside diverse treatment regimens, to provide the person with T2DM important feedback on glycemic performance such that they can make appropriate changes to daily treatment, diet and lifestyle.

In this issue we are able to highlight further research that provides a clear association between CGM metrics of glycemic control and the long-term cardiovascular complications of diabetes. Increased glycemic variability and lower time in range are shown to correlate with coronary artery disease, which links CGM metrics to outcomes and underlines the importance of using these metrics to guide cardioprotective therapy in diabetes.

Other notable highlights in this issue of the *Sensor Report* are recent studies on the impact of the FreeStyle Libre 2 system with optional real-time alarms, the emerging insights into how application of CGM is helping to understand the glycemic challenges faced by frail and vulnerable older people with diabetes, and new data on the cost-effectiveness of the FreeStyle Libre systems compared to finger prick testing in a large healthcare economy. These are brief summaries of the many current research studies that we are able to report in this issue of the *Sensor Report.*

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Time in tight range: new treatment targets to accompany new diabetes treatment options

Widespread use of continuous glucose monitoring (CGM) technology by children, adolescents and adults with type 1 diabetes (T1DM) and by adults with type 2 diabetes (T2DM), has been accompanied by a paradigm shift in the way that glycemic control is assessed. As experience and confidence with new treatment options in conjunction with use of CGM increases, the value of using time in tight range (TITR) in monitoring people with diabetes is becoming clear.

HbA1c is still widely used as a measure of average glucose control over 2-3 months, but it's utility is restricted by infrequent testing schedules and the limited information that it provides in these periodic snapshots. More robust glycemic information is available for people using CGM systems, providing real-time insights into glucose levels and glucose variability throughout the course of each day. Among the available CGM metrics, time in range (TIR) is widely used to assess glycemic control, as it reports on the amount of time that the person with diabetes maintains their glucose levels between 70-180 mg/dL (3.9-10.0 mmol/L). International consensus recommends a target for TIR of >70% of each day, for children and adults (non pregnant) with T1DM or T2DM, and a target of >50% for frail or vulnerable individuals.[1] Importantly, evidence now indicates that increased TIR is associated with lowered risk of microvascular and macrovascular complications of diabetes.[2,3]

The benefits of maintaining a high %TIR are now being refined further to propose that an increased percentage of glucose values in the range 70-140 mg/dL (3.9-7.8 mmol/L), so-called time in tight range (TITR),[4,5] may be more-widely used, as a primary or secondary target, since it approximates normoglycemia more-closely than TIR,[4] and can be a realistic goal for some groups of people with diabetes. This would include people with T1DM using automated insulin delivery (AID) systems and people with T2DM on glucose-lowering agents, such as glucagon-like peptide 1 receptor agonists (GLP-1 RA), sodium glucose cotransporter 2 inhibitors (SGLT2i) and newer drugs such as tirzepatide, that combine glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 dual receptor agonist activity. The recommended target range for women during pregnancy is already 63-140 mg/dL (3.5-7.8 mmol/L).[1] The proposed value of TITR is based on studies in healthy children and adults, showing that the median time spent in the glucose range 70-140 mg/dL (3.9-7.8 mmol/L) was 96%.[6]

Several studies have established that women with pregestational T1D should aim for a specific glycemic target of >70% time in range for pregnancy (TIRp) of 63-140 mg/dL (3.3-7.8 mmol/L) during pregnancy.[7] However, the small number of studies using CGM during pregnancy in T2D or GDM have used TITR 70-140 mg/dL (3.9-7.8 mmol/L) rather than TIRp. Using percentage of TITR readings as a glucose management goal has been shown to have an impact for women with T2DM during pregnancy and women with gestational diabetes mellitus (GDM), when supported with CGM.[8] In this study, 57% of women were able to achieve >70% TITR and had reduced occurrence of large for gestational age (LGA) births or neonatal admissions to NICU, compared to women with <70% TITR.

For children and adolescents with T1DM, achievement of TITR goals is assisted by AID systems. In a study on 854 children and adolescents with T1DM, those on AID therapy achieved a TITR of 45%, compared to 36% on sensor-augmented pump (SAP) therapy and 34% on MDI with CGM.[9] Since a TITR of 50% corresponds to an HbA1c value of 6.5% (48 mmol/mol),[10] which is the HbA1c target suggested by current guidelines, the value of setting TITR targets is clear, however specific targets may need to be considered for different groups of people with diabetes.

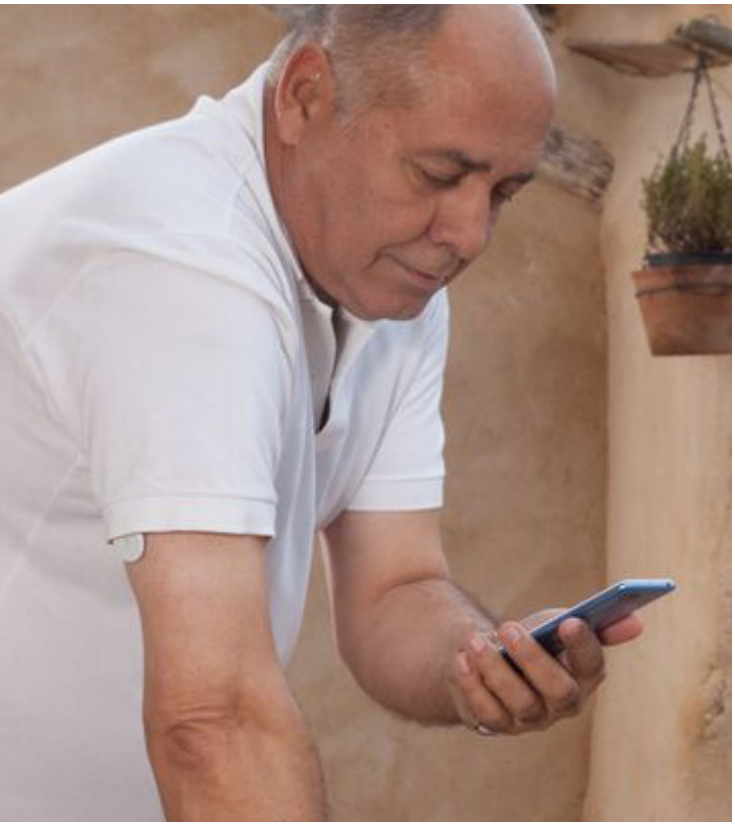

Image for illustrative purposes only. Not real patient.

The greatest clinical gains against setting TITR goals may be seen in people with T2DM on newer non-insulin therapies when used with CGM. The SURPASS-3 trial[11] included 243 persons with T2DM and a mean HbA1c of 8.2% (66 mmol/mol), treated with metformin alone or in combination with a SGLT2 inhibitor for at least 3 months. Baseline TITR was 23%. Study participants were assigned to therapy either with tirzepatide or long-acting basal insulin for 52 weeks. Those assigned to receive 10 mg or 15 mg tirzepatide increased their percentage TITR to 73% at 52 weeks compared to 48% achieved by those in the long-acting insulin arm, with significantly less hypoglycemia.

Use of GLP-1 RA drugs in T2DM has not been assessed against TITR, but changes in TIR from baseline are significant for these therapeutic options.[12] Since increased TIR is highly correlated to TITR, it can be predicted that TITR will be more-widely used as a target range for persons with T2DM as additional non-insulin therapies become available, with the goal of near-normal glycemia in T2DM becoming a realistic goal.[4] The use of TITR to monitor glucose and guide long-term therapy in T2DM may be possible with use of CGM on a periodic basis, as has been proposed in EASD and ADA guidelines for managing glycemia in T2DM,[13] for example in T2DM on non-insulin therapies. In such circumstances, the most-accurate assessment and comparison of glycemic metrics requires a 10-14 day period of CGM application and data collection.[14]

It is clear that TITR represents a more precise approach to glucose management in diabetes, focusing on maintaining glucose levels within a very specific, narrow range. The advent of newer treatment options make TITR a relevant option to guide and monitor glycemic control in conjunction with CGM, particularly in T2DM, with the potential to achieve near-normal glycemia for some individuals.

1. 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.

2. Beck RW, *et al.* Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials. *Diabetes Care* 2018; 42(3):400-405.

3. Malahi AE, *et al.* Relationship Between Time in Range, Glycemic Variability, HbA1c, and Complications in Adults With Type 1 Diabetes Mellitus. *J Clin Endocrinol Metab.* 2022; 107(2):e570-e581.

4. Beck RW, *et al.* A Comparison of Continuous Glucose Monitoring-Measured Time-in-Range 70-180 mg/dL Versus Time-in-Tight-Range 70-140 mg/dL. *Diabetes Technol Ther.* 2023; doi:10.1089/dia.2023.0380.

5. Danne T, *et al.* International Consensus on Use of Continuous Glucose Monitoring. *Diabetes Care* 2017; 40:1631-1640.

6. Shah VN, *et al.* Continuous Glucose Monitoring Profiles in Healthy Nondiabetic Participants: A Multicenter Prospective Study. *J Clin Endocrinol Metab.* 2019; 104:4356-4364.

7. Murphy HR. Roadmap to the Effective Use of Continuous Glucose Monitoring in Pregnancy. *Diabetes Spectr.* 2023; 36:315-319.

8. Bitar G, *et al.* Continuous Glucose Monitoring and Time in Range: Association with Adverse Outcomes among People with Type 2 or Gestational Diabetes Mellitus. *Am J Perinatol.* 2023; doi:10.1055/s-0043-1764208.

9. Passanisi S, *et al.* Aiming for the Best Glycemic Control Beyond Time in Range: Time in Tight Range as a new CGM Metric in Children and Adolescents with Type 1 Diabetes using Different Treatment Modalities. *Diabetes Technol Ther.* 2023; doi:10.1089/dia.2023.0373.

10. Petersson J, *et al.* Translating glycated hemoglobin A1c into time spent in glucose target range: A multicenter study. *Pediatr Diabetes* 2019; 20: 339-344.

11. Battelino T, *et al.* Efficacy of once-weekly tirzepatide versus once-daily insulin degludec on glycaemic control measured by continuous glucose monitoring in adults with type 2 diabetes (SURPASS-3 CGM): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial. *Lancet Diabetes Endocrinol.* 2022; 10(6):407-417.

12. Frías JP, *et al.* Exenatide once weekly improved 24-hour glucose control and reduced glycaemic variability in metformin-treated participants with type 2 diabetes: a randomized, placebo-controlled trial. *Diabetes Obes Metab.* 2017; 19: 40-48.

13. Davies MJ, *et al.* Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2022; 45:2753-2786.

14. Riddlesworth TD, *et al.* Optimal Sampling Duration for Continuous Glucose Monitoring to Determine Long-Term Glycemic Control. *Diabetes Technol Ther.* 2018; 20:314-316.

Likelihood of achieving 50% time in tight range varies with age, glycemic variation, disease duration and treatment modality in children and adolescents with T1DM

This real-world, cross-sectional study conducted at two Italian pediatric diabetes centres aimed to evaluate time-in-tight-range (TITR) 70-140 mg/dL (3.9-7.8 mmol/L) and its correlation with key CGM metrics and clinical variables in a cohort of children with T1DM using different treatment strategies.

A total of 854 children and adolescents with T1DM were categorized into four treatment groups: multiple daily injections (MDI) + real-time CGM; multiple daily injections + FreeStyle Libre system; sensor augmented pump (SAP) or hybrid closed loop (HCL) system.

The average TITR for the overall population was 36.4%, highlighting the need for tailored interventions and strategies to increase TITR in children and adolescent with T1DM. The HCL group showed a significantly higher TITR level compared with the other treatment groups ($p<0.001$). The authors also reported a strong positive correlation ($r=0.95$, $p<0.001$) between participants who achieved a time in range (TIR) cut-off value of 72% and those who achieved a TITR target ≥50%. Other significant predictors of achieving higher %TITR were shorter disease duration, lower glycemic variability, and lower HbA1c.

Passanisi S, *et al.* Aiming for the best glycemic control beyond time in range: time in tight range as a new CGM metric in children and adolescents with type 1 diabetes using different treatment modalities. *Diabetes Technol Ther.* 2023; doi: 10.1089/dia.2023.0373. Online ahead of print.

GlucoMOMS trial in women with insulin-treated diabetes in pregnancy shows that CGM metrics are associated with perinatal outcomes

This post-hoc analysis of the GlucoMOMS RCT in the Netherlands evaluated the association between glycemic metrics, HbA1c, and perinatal outcomes per trimester in T1DM, T2DM and gestational diabetes mellitus (GDM).

A total of 115 out of 147 women randomized to the blinded CGM group in the GlucoMOMS trial were included in the analysis. The glucose target range was defined as 3.5-7.8 mmol/L (63-140 mg/dL). The authors found differences in perinatal outcomes that were dependent on the type of diabetes, with a higher second-trimester mean glucose being associated with large for gestational age (LGA) outcome (odds ratio 2.6 [95%CI, 1.1, 6.2]) in T1DM pregnancies, and an increased area under the curve above glucose levels of 7.8 mmol/L (140 mg/dL) being associated with LGA (odds ratio 10.0 [95%CI 1.4, 72.8]) in T2DM and insulin-treated GDM pregnancies.

There were no associations between CGM metrics and neonatal hypoglycemia, pre-eclampsia, shoulder dystocia, pre-term birth, or Neonatal Intensive Care Unit admission rates for pregnancies complicated by any type of diabetes. The novel finding of this analysis was that CGM metrics in T2DM and insulin-treated GDM might be able to indicate LGA.

Rademaker D, *et al.* Continuous glucose monitoring metrics and pregnancy outcomes in insulin-treated diabetes: A post-hoc analysis of the GlucoMOMS trial. *Diabetes Obes Metab.* 2023;25:3798-3806.

Women with T2DM and high risk of complications during pregnancy have improved sensor glycemic metrics with greater FreeStyle Libre sensor use

This prospective, single-center, observational pilot study in Australia investigated glucose metrics in a high-risk population of women with T2DM during pregnancy and explored the associations with neonatal outcomes.

Fifty-seven women were included and metrics from early and late gestation using the first and last two (mean 16 and 35) weeks of FreeStyle Libre sensor data were used to determine the continuous glucose monitoring trajectories. Of these, 41 women (mean age 33 years, 73% Aboriginal or Torres Strait Islander, 32% living remotely) used sensor technology for 15 weeks.

The authors observed only a limited change in average metrics from early to late pregnancy. However, for women with greater sensor use (>50%: n=29), the mean time in range (TIR) increased by 9%, time above range reduced by 12%, average glucose reduced by 1 mmol/L (18 mg/dL), and time below range increased by 3% which may have been related to treatment intensification and overall improved glycemic control during the study.

Logistic regression revealed that most sensor glucose metrics were associated with neonatal hypoglycemia throughout and large for gestational age (LGA) outcomes were associated with hyperglycemic metrics from early pregnancy. Notably, for each 1% increase in TIR there was a 4-5% reduction in risk of neonatal complications.

McLean A, *et al.* Continuous glucose monitoring metrics in high-risk pregnant women with type 2 diabetes. *Diabetes Technol Ther.* 2023. doi: 10.1089/dia.2023.0300. Online ahead of print.

FLASH-UK study indicates that FreeStyle Libre 2 system, with optional real-time alarms, is effective across a range of baseline characteristics in adults with T1DM

The FLASH-UK study was an independent multicenter, parallel-design RCT investigating use of the FreeStyle Libre 2 system* versus self-monitoring of blood glucose (SMBG) in people with T1DM[1] (see *Sensor Report* Issue 1, 2023). This pre-specified subgroup analysis[2] evaluated treatment effects between subgroups with different baseline characteristics, including baseline HbA1c, treatment modality, age, educational level, and ethnic group.

A total of 156 participants (44% women) with a mean baseline HbA1c of 71 mmol/mol (8.6%) and a mean age of 44 years were randomly allocated to the FreeStyle Libre 2 system (n=78) or SMBG (n=78). The study found a significantly lower HbA1c with FreeStyle Libre 2 system versus SMBG at 24 weeks (7.9% versus 8.3%; p<0.001)[1] but there was no impact of treatment modality, prior participation in structured education, deprivation index quintile, sex, or baseline depression category.

However, the between-group difference in HbA1c was significantly greater for younger people (reduction of 2.7 mmol/mol [0.25%] for every additional 15 years of age). Younger participants also showed a greater reduction in time above range (TAR) and mean glucose when using the FreeStyle Libre 2 system, compared to older participants, who had a larger benefit in hypoglycemia reduction. Educational level did correlate with a higher TIR (driven by lower TAR) and lower mean glucose being more pronounced for participants with a college-level education than those without.

1. Leelarathna L, *et al.* Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes. *New Engl J Med.* 2022; 387(16):1477-1487;
2. Leelarathna L, *et al.* Intermittently scanned continuous glucose monitoring in adults with type 1 diabetes: A subgroup analysis from the FLASH-UK study. *Diabetic Medicine.* 2023; 00:e15249. doi: 10.1111/dme.15249

*Also known as intermittently-scanned continuous glucose monitoring (isCGM, commonly referred to as 'Flash'). Both terms used in NICE NG17, www.nice.org.uk/guidance/ng17.

Image for illustrative purposes only. Not real patient.

Flash glucose monitoring over 24 weeks is associated with glycemic improvements for adults with T1DM or T2DM with suboptimal glycemic control

This real-world study investigated changes in glycemic parameters among Europeans with diabetes not meeting glycemic targets who started the FreeStyle Libre system.

De-identified data were obtained between 2014 and 2021 from 1,909 adults with T1DM and 1,813 with T2DM. Treatment regimens were basal-bolus insulin (n=1,499); basal insulin (n=189), or; non-insulin therapy (n=125). All included adults had used flash glucose monitoring uninterrupted for a 24-week period. Within each treatment group, subgroup analyses were performed in individuals with initial suboptimal glycemic control, as indicated by <70% time in range (TIR, 3.9-10 mmol/L [70-180 mg/dL]), >25% time above range (TAR, >10 mmol/L [>180 mg/dL]), or >4% time below range (TBR, <3.9 mmol/L [<70 mg/dL]).

The study revealed significant improvements in TIR, TAR, TBR and glycemic variability, both for adults with T1DM and those with T2DM. Adults with T1DM and initially with TIR <70% concurrently improved their TIR, TAR and TBR metrics after 24 weeks of flash glucose monitoring. This was also true for the adults with T2DM on basal-bolus insulin therapy. Adults with T2DM on basal insulin therapy or not on insulin therapy saw improvements in TIR, TAR and measures of average glucose. Overall, these real-world data show that adults with T1DM or T2DM, who have suboptimal glycemic control on any therapy, can achieve improved glycemic control following 24 weeks of flash glucose monitoring use.

Lameijer A, *et al.* Real-life 24-week changes in glycemic parameters among European users of flash glucose monitoring with type 1 and 2 diabetes and different levels of glycemic control. *Diabetes Res Clin Pract.* 2023;201:110735. doi:10.1016/j.diabres.2023.110735.

Use of alert functions with FreeStyle Libre 2 system is associated with improvements in time in hypoglycemia

This prospective observational study, using data from NHS Lothian (Scotland) prescribing analytical services assessed changes in sensor glucose metrics in adults with T1DM when switching from the FreeStyle Libre system to the FreeStyle Libre 2 system with optional real-time alarms.

In the 12 months after a change from FreeStyle Libre to FreeStyle Libre 2 percentage time below range (TBR) had significantly decreased, by a median of 1.0% (p=0.004). The average duration of low glucose events (<3.9 mmoL/L: 70 mg/dL) also significantly fell by 10 minutes (–46 to 18, p<0.001). Further, at 12 months use of low-glucose alarms was independently associated with a decrease in TBR of ≥0.5% (p=0.009). Use of high-glucose alarms was associated with improvements in TIR (p=0.029) and time above range (TAR) >13.9 mmol/L (>250 mg/dL; p=0.002) and independently associated with an increase in TIR of ≥5% (p=0.04).

Overall, the study demonstrated that conversion to the FreeStyle Libre 2 system with optional real-time alarms was associated with significant improvements in low glucose metrics and that patients who used alarms function were more likely to see improvements across all sensor glucose metrics.

Stimson RH, *et al.* Changes in continuous glucose monitoring metrics and predictors of improvement 12 months after conversion from Freestyle Libre to Freestyle Libre 2. *Diabetic Med.* 2023;40:e15130.

Increased time above range and reduced time in range are closely associated with cognitive decline over one year in older adults with T2DM

This analysis from an ongoing 2-year longitudinal study investigated the association between derived metrics and cognitive decline and brain structural alterations in older adults with T2DM in Japan.

Of 100 total participants, 70 and 68 individuals with T1DM were included in the analyses investigating the association of CGM-derived metrics at baseline and longitudinal mean CGM-derived metrics, with changes in cognitive function at 1-year follow-up, respectively.

There was no significant association between HbA1c levels and changes in the Japanese version of the Montreal Cognitive Assessment (MoCA-J) scores, which increase with greater cognitive function on a scale of 0-30. In contrast, a high mean glucose and time above range (TAR) at baseline were associated with negative changes in MoCA-J scores after 12 months, whereas a high time-in-range (TIR) was associated with a reduced risk of a decline in MoCA-J scores (p<0.05, in all cases). These findings remained significant after adjustment for demographic factors and potential confounders (p<0.05).

Multiple logistic regression analyses after adjustment for confounding factors also revealed that a high mean glucose and higher TAR at baseline were significantly associated with a decrease in the MoCA-J score by ≥2. These findings show a close association between higher TAR and reduced TIR with cognitive decline at 1-year follow-up in older patients with T2DM.

Sugimoto T, *et al.* Longitudinal association of continuous glucose monitoring-derived metrics with cognitive decline in older adults with type 2 diabetes: a 1-yearprospective observational study. *Diabetes Obes Metab.* 2023;25:3831-3836.

Using CGM reveals that nocturnal hypoglycemia is both common and underdiagnosed in older people with T2DM on insulin

The HYPOAGE prospective, observational, multicentre study was conducted at six diabetes centres in France to determine the frequency and predictors of hypoglycemia in older patients with insulin-treated T2DM.

The study population included 141 people with T2DM, who were treated with insulin and had a mean age >80 years. Participants used the blinded FreeStyle Libre Pro system for 28 consecutive days, with >70% sensor active time, and a mean HbA1c of 7.9% at baseline. Of the included participants, 72.3% were considered to have complex diabetes, with complications or life-limiting comorbid illness, and 27.7% were assessed as healthy following geriatric assessment.

Confirmed hypoglycemia <70 mg/dL (3.9 mmol/L), as measured by self-monitoring of blood glucose (SMBG) when awake, was recorded in 37.6% participants and was significantly associated with a longer duration of diabetes (p=0.04) and with glycemic variability, as assessed by CGM (p=<0.001). However, when using blinded CGM, 65.2% of the study group were shown to experience nocturnal hypoglycemia <54 mg/dL (3.0 mmol/L) for periods ≥15 consecutive minutes between midnight and 6 am. Cognitive impairment, heart failure, and depressive disorder were all risk factors for nocturnal hypoglycemia.

These real-world data highlighted that nocturnal hypoglycemia is very common and largely underdiagnosed by self-monitored blood-glucose (SMBG) testing in older adults with insulin-treated T2DM, underlining the importance of CGM technologies for diabetes care in this population.

Boureau AS, *et al.* Nocturnal hypoglycemia is underdiagnosed in older people with insulin-treated type 2 diabetes: The HYPOAGE observational study. *J Am Geriatr Soc.* 2023;71(7):2107-2119. doi: 10.1111/jgs.18341.

*FreeStyle Libre Pro system availability may vary by country. If you require product information please refer to your local Abbott representative.

Time in range and glycemic variability are significantly associated with atherosclerotic changes in the carotid artery wall in people with T2DM

This exploratory analysis used sensor glucose monitoring data collected with the FreeStyle Libre Pro system*, over 14 days at baseline and after 104 weeks, from an ongoing prospective, multicenter, observational study in Japan. This study aimed to investigate the association between sensor derived metrics and atherosclerosis progression in people with T2DM and no history of symptomatic cardiovascular disease.

Six hundred participants underwent sensor glucose monitoring and ultrasonographic atherosclerosis measurements of the carotid arteries, including the intima-media thickness (IMT) and grey-scale median (GSM). Over 104 weeks, there were significant increases in mean IMT (from 0.759 to 0.773 mm; p<0.001) and thickened-lesion GSM (from 43.5 to 53.9 units; p<0.001), but there were no significant changes in common carotid artery maximum-IMT or mean GSM. Linear regression revealed that TIR and glycemic variability, as measured by coefficient of variation (CV) at baseline were significantly associated with both the annual change in mean GSM and with the annual change in thickened-lesion GSM (p=0.04, in both cases).

The authors also noted that those who achieved on-target glucose metrics as provided by the sensor at baseline showed significant annual changes in mean GSM compared with those who did not (0.94 versus −0.21 units/year; p=0.007), indicating more-stable vascular-wall composition for individuals with better glycemic control.

Mita T, *et al.* Continuous glucose monitoring-derived time in range and CV are associated with altered tissue characteristics of the carotid artery wall in people with type 2 diabetes. *Diabetologia.* 2023; 66:2356-2367.

*FreeStyle Libre Pro system availability may vary by country. If you require product information please refer to your local Abbott representative.

Beyond glycemic control: the OPTIMAL trial and the importance of CGM data in predicting coronary atherosclerosis

This study investigated the association between CGM-derived measures of glycemic control and the progression of coronary atherosclerosis in people with T2DM.

In the OPTIMAL trial, 94 adults with T2DM and diagnosed coronary artery disease (CAD) were randomised to CGM-guided or HbA1c-guided glycemic control over 48 weeks. The primary endpoint was a change in total atheroma volume (TAV) as measured by intravascular ultrasound (IVUS). The secondary outcome measure was a change in histological lipid content of plaques as measured by maxLCBI4mm (maximum lipid-core burden index at 4-mm segment) on near-infrared spectroscopy imaging.

Compared to HbA1c-guided control, use of CGM achieved a greater reduction in glycemic variability, as measured by % coefficient of variation (-3.3% vs -0.1%; p = 0.01), and increased time in range (TIR) (6.7% vs -1.5%; p = 0.02). TAV decreased by -3.29 mm^3 in the CGM-guided group compared to an increase of 0.11 ± 1.9 mm^3 in the HbA1c-guided group. Post-hoc analysis also revealed a significantly greater regression of maxLCBI4mm in the CGM-guided group (20.4%; p = 0.03). Although CAD progression was not slowed over the 48-week study period, these data warrant further investigation of CGM-guided management of glycemic control in long-term management of coronary atherosclerosis.

Kataoka Y, *et al.* The effect of continuous glucose monitoring-guided glycemic control on progression of coronary atherosclerosis in type 2 diabetic patients with coronary artery disease: The OPTIMAL randomized clinical trial. *J Diabetes Complications.* 2023: 108592. doi:10.1016/j.jdiacomp.2023.108592

Increased glycemic variability is associated with diastolic dysfunction in people with T2DM without a diagnosis of coronary artery disease

This study aimed to investigate the association between glycemic variability (GV) and signs of diastolic dysfunction in patients with T2DM without coronary artery disease in Ukraine.

There were 78 participants with T2DM, who underwent CGM to evaluate glycemic variability, and echocardiography to assess diastolic dysfunction. Patients were divided into two groups, according to GV: Group 1 (n=40): standard deviation (SD) >2 (high GV); Group 2 (n=38): SD ≤1.9 (normal GV).

Adults with T2DM and high GV were significantly older (mean 49 vs 46 yrs; p<0.05) and had a significantly longer duration of disease (mean 10 vs 6 yrs; p<0.01) than those with normal GV. They also had more severe diastolic dysfunction, as evidenced by increased myocardial stiffness index, speed of early transmitral flow, and peak rate of tricuspid regurgitation. The only significant independent predictors of diastolic dysfunction identified by multivariate regression analysis were high GV and older age.

The authors concluded that, in the absence of coronary artery disease, increased GV was associated with diastolic dysfunction and could predispose to development and progression of heart failure in patients with T2DM.

Dzhun Y, *et al.* Glycemic variability is associated with diastolic dysfunction in patients with type 2 diabetes. *J Diabetes Complications.* 2023; 37: 108519 doi: 10.1016/j.jdiacomp.2023.108519.

Flash glucose monitoring improves hypoglycemia confidence in T1DM compared to SMBG testing

This longitudinal observational study investigated the impact of using the FreeStyle Libre system on hypoglycemic confidence in 121 adults with T1DM.

Adults transitioning from self-monitored blood glucose (SMBG) finger-prick testing to using the FreeStyle Libre system were assessed at baseline and after 12 months using the four-point (1 to 4) hypoglycemic confidence scale (HCS), the diabetes treatment satisfaction questionnaire (DTSQ), as well as for change in HbA1c. The primary endpoint was changes in hypoglycemic confidence attributed to use of the FreeStyle Libre system.

After using the FreeStyle Libre system, HCS scores significantly improved from 2.89 to 3.00 ($p < 0.001$). At baseline, participants who had experienced level 3 hypoglycemia in the past 6 months reported enhanced confidence during sleep, in social situations, and in avoiding serious hypoglycemia-related problems ($p < 0.05$ in all cases). Despite hypoglycemia risk, individuals could maintain daily activities using the FreeStyle Libre system ($p < 0.05$), with 69% effectively utilizing trend arrows.

The findings suggest that using the FreeStyle Libre system enhances hypoglycemic confidence in adults with T1DM, enabling a more flexible lifestyle and improved management of hypoglycemia.

Takaike H, *et al.* Recovery of hypoglycemic confidence using intermittently scanned continuous glucose monitoring among adults with type 1 diabetes with level 3 hypoglycemia: A prospective, single-center, single-arm study. *Diabetes Res Clin Pract.* 2023; 204: doi:10.1016/j.diabres.2023.110890

Risks for microvascular complications are associated with <40% time in range in T2DM

The relationship between time in range (TIR) and risk of microvascular complications was assessed using the FreeStyle Libre system, providing further evidence for the association of sensor glucose metrics in outcomes for people with T2DM.

This study focused on people with T2DM using the FreeStyle Libre system continuously for 12 months (n=545), with monitoring for relevant glycemic indexes for diabetic vascular complications. Lower percentages of TIR were associated with higher HbA1C, higher glycemic variability and mean amplitude of glycemic excursion (MAGE).

TIR was significantly lower in adults with T2DM changes predictive of diabetic microvascular complications, compared to those without evidence of complications. Specifically, TIR <40% was identified as a risk factor for diabetic nephropathy (DN), diabetic peripheral neuropathy (DPN), and diabetic retinopathy (DR). Increased time above range (TAR), CV, SD, MAGE, and HbA1C were associated with specific complications, such as a higher TAR in DN, elevated TAR, CV, SD, MAGE, and HbA1C in DR, and increased TAR, CV, SD, MAGE, HbA1C and arterial blood glucose (ABG) in DPN.

Overall, the evidence presented here indicates that integrating sensor glucose derived data into glycemic control strategies can assist in predicting and managing the risk of microvascular complications of T2DM.

Sheng X, *et al.* Correlation Between Blood Glucose Indexes Generated by the Flash Glucose Monitoring System and Diabetic Vascular Complications. *Diabetes Metab Syndr Obes.* 2023; doi:10.2147/DMSO.S418224.

*FreeStyle Libre Pro system availability may vary by country. If you require product information please refer to your local Abbott representative.

Beyond insulin therapy: intermittent use of sensor glucose technology in T2DM can be clinically beneficial and cost saving

A review of available studies suggests that periodic rather than continuous application of CGM can be a cost-effective part of glycemic management in several situations in individuals with T2DM not on insulin.

Intermittent use of CGM, defined as the 'use of CGM once in 2 or 3 months or a fixed frequency', is infrequently applied in clinical studies but this review has identified several situations where this strategy may be useful in people with T2DM not on insulin, for example: in individuals with newly diagnosed diabetes during the period when treatment is being initiated; in suboptimally controlled diabetes where treatment is being adjusted; starting intensive life style modification; infections; perioperative control; gestational diabetes mellitus and diabetes complicating pregnancy; children and adolescents with T2DM; as a motivational tool to improve behavioural modification; after metabolic surgery; and for patients receiving steroids (e.g., during COVID-19).

Furthermore, given that an important barrier to the use of CGM is cost, the authors pointed out that intermittent use of CGM allows for considerable cost savings (around 75% reduction) versus continuous use, which would make it particularly useful in resource-constrained regions of the world.

Saboo B, *et al.* Intermittent use of continuous glucose monitoring: a new paradigm in treatment of Type 2 diabetes. *J Assoc Physicians* India 2023;71(6):51-56 doi: 10.5005/japi-11001-0274.

Image for illustrative purposes only. Not real patients.

Cost-efficacy of using the FreeStyle Libre 2 system compared to SMBG is supported in adults with T1DM in England

Cost-effectiveness data is examined in this economic impact study of the use of the FreeStyle Libre 2 system compared with self-monitoring of blood glucose (SMBG).

Participant-level baseline and follow-up health status data, using the EuroQol-five-dimensional questionnaire (EQ-5D-5L), were collected, as well as the within-trial healthcare resource-use data. The EQ-5D-5L is a patient-reported questionnaire that measures quality of life on a 5-component scale including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Quality-adjusted life-years (QALYs) at 24 weeks were derived, adjusting for baseline EQ-5D-5L responses. Within the evaluation, use of the FreeStyle Libre 2 system showed an adjusted incremental QALY gain of 0.006 and an adjusted cost increase of £548 per participant compared to SMBG.

The lifetime projected incremental cost of the FreeStyle Libre 2 sensor was £1,954, resulting in an incremental QALY gain of 0.436 and an incremental cost-per-QALY of £4,477. In all subgroups, isCGM demonstrated an incremental cost-per-QALY better than £20,000 compared with SMBG; for those with baseline HbA1c >75 mmol/mol (9.0%), it was also cost-saving. Sensitivity analysis suggested that use of the FreeStyle Libre 2 system remains cost-effective if its effectiveness lasts at least seven years.

Despite initial short-term costs, the long-term benefits of the FreeStyle Libre 2 system in lowering HbA1c make it cost-effective within a medium term timeframe.

Elliott RA, *et al.* Estimating the cost-effectiveness of intermittently scanned continuous glucose monitoring in adults with type 1 diabetes in England. *Diabetic Med.* 2023, doi:10.1111/dme.15232

Use of CGM reveals high incidence of hypoglycemia in elderly people receiving home-care visits

This study assessed hypoglycemic episodes using blinded CGM in older people receiving home care for their diabetes. It also compared episode frequency and duration across different demographic and clinical subgroups.

This observational study investigated the occurrence of hypoglycemia in individuals aged ≥65 years with diabetes, with no previous suspicion of hypoglycemia, using blinded CGM for five days. Data from 56 participants (median age 82, 52% men) also included HbA1c and eGFR measurements.

Of 36 insulin users, 33% experienced hypoglycemia; among 18 non-insulin, non-sulfonylurea users, 44% had episodes of hypoglycemia. 86% of those experiencing hypoglycemia were living alone. Median hypoglycemia duration was 1 hr 25 min (15 min to 8 hr 50 min). This high incidence of undetected hypoglycemic episodes among older home-dwelling individuals with diabetes, not treated with insulinotropic drugs, was previously unknown using capillary glucose testing.

The findings underscore the need for comprehensive glucose monitoring routines and preventive measures and highlight the importance of improving care for this vulnerable population.

Fløde M, *et al.* High number of hypoglycaemic episodes identified by CGM among home-dwelling older people with diabetes: an observational study in Norway. *BMC Endocr Disord.* 2023, doi:10.1186/s12902-023-01472-6.

Image for illustrative purposes only. Not real patient or data.

Use of CGM by ethnically diverse populations with T2DM significantly reduces HbA1c within 6 months

This study examined the clinical impact of initiating CGM systems, including FreeStyle Libre systems, in diverse populations with T2DM.

Researchers analyzed data from the electronic health records from an urban family medicine clinic, with >80% of patients coming from racial or ethnic minorities. The study included adults with T2DM who initiated a CGM device between January 1, 2019, and February 23, 2022. The HbA1c test values closest to the index date and after 6 months were used to assess the impact of CGM use. The primary outcome was comparing the percentage of individuals meeting the Minnesota Community Measure (MNCM) D5 HbA1c goal (<8%) at follow-up versus the index date.

After applying exclusion criteria, 72 patients were identified, one-third of whom required interpreters and 76% were documented as of racial or ethnic minorities. Mean HbA1c was 9.8% prior to the CGM index date, and only 16.7% of individuals met the MNCM D5 HbA1c goal. At 6-month follow-up mean HbA1c was 8.4% (mean difference -1.4%; $p < 0.001$) and 41.7% met the goal (mean difference +25%; $p < 0.001$). Subgroup analyses indicated sustained results, irrespective of insulin use.

These outcomes show that a population of racially and ethnically diverse adults with T2DM achieved a significant HbA1c reduction and a greater likelihood of meeting the MNCM D5 HbA1c goal after approximately six months following initiation of CGM.

Larson RJ, *et al.* Evaluating the clinical effect of personal continuous glucose monitoring in a diverse population with type 2 diabetes. *J Pharm Technol.* 2023; doi:10.1177/87551225231194027.