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FreeStyle Libre

THE sensor report

ISSUE 4/2024

WELCOME TO
THE SENSOR REPORT, ISSUE 4, 2024

For the fourth issue of the *Sensor Report* for 2024 you will see we are evolving our look, with additional infographics to accompany the articles and research updates in each issue. We believe these will add context to the important medical and scientific summaries. To make sure that you have rapid access to the discussions that have highest value to you, we are also introducing a contents list, with hypertext links embedded in the digital PDF structure. Clicking on these will get you straight to the research areas identified.

Celebrating a decade of FreeStyle Libre systems presence

We also take the opportunity in this issue to celebrate the ten-year anniversary of the launch of the FreeStyle Libre system as an accessible technology able to monitor interstitial glucose levels continuously, not possible using finger prick capillary blood glucose monitors§. Because the original FreeStyle Libre glucose monitoring sensors had to be scanned using a reader or a smartphone app in order for users to view their current glucose levels and see the trend arrows indicating whether their glucose was stable, or was rising or falling and how fast, these first sensors were termed 'flash glucose monitoring' or 'intermittently scanned CGM'. Importantly, the original FreeStyle Libre sensor had a 14-day wear time, with demonstrated accuracy across the full period, which was a significant increase over the 7 to 10 day performance periods of other CGM systems**.

Although launched in 2014, the IMPACT randomized controlled trial (RCT) using the FreeStyle Libre system was published in 2016, showing that the FreeStyle Libre system was highly effective in reducing the amount of time spent in hypoglycemia for adults with well-controlled T1DM.[1] The REPLACE RCT, published in 2017, demonstrated similar results in adults with T2DM on intensive insulin therapy.[2] In 2018 the prospective SELFY study in children and adolescents with T1DM, aged 4-17 years, showed a significant improvement in HbA1c over 8 weeks when using the FreeStyle Libre system, with no increase in hypoglycemia.[3] Thereafter, real-world studies confirmed that initiating flash glucose monitoring was associated with reduced HbA1c in people with suboptimally controlled T1DM or T2DM, less hypoglycemia, as well as reductions in diabetes distress and improved treatment satisfaction.[4,5]

In 2020 came the launch of the FreeStyle Libre 2 system, with improved accuracy performance across the full dynamic range of glucose. The FreeStyle Libre 2 system was also enabled with optional high and low glucose alarms, that allowed users to be alerted to adverse hypoglycemia or hyperglycemia, at any time of day or night†. Significantly, in June 2020, the FreeStyle Libre 2 system received approval from the US Federal Drug Administration (FDA) as an integrated continuous glucose monitoring (iCGM) device.[6] The FDA iCGM standard recognizes higher accuracy, reliability and performance requirements of CGM systems, making them suitable for safe and effective use with other digital health appliances, including insulin pumps and automated insulin delivery (AID) systems. To date, only three CGM manufacturers have achieved iCGM status with the FDA. In 2023, the FreeStyle Libre 2 system was also updated to include the option of real-time minute-by-minute glucose readings, streamed directly to the FreeStyle LibreLink smartphone app*,‡, without the need for intermittent scanning#.

Further technical innovation delivered in the FreeStyle Libre 3 system in 2022. With it's 21mm diameter and discreet 2.9mm profile, it is smaller than two stacked 5-cent Euro coins. This third-generation sensor has exceptional accuracy and Bluetooth integration that sends continuous, real-time glucose readings to users' smartphones over a 10-meter range.[7]

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§Finger prick blood glucose monitoring is required if glucose readings and alarms do not match symptoms or expectations.

†Alarm notifications will only be received when alarms are turned on and the sensor is within 6 metres unobstructed of the reading device.

*The FreeStyleLibreLink 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.

**Data on file, Abbott Diabetes Care.

‡Glucose readings are automatically displayed in the app only when the smartphone and sensor are connected and in range.

#For a complete glycemic picture with the FreeStyle Libre 2 system users can scan their sensors once every 8 hours during signal loss.

1. Bolinder J, *et al.* Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet.* 2016; 388(10057):2254–2263

2. 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(1):55–73

3. Campbell, FM, *et al.* Outcomes of using flash glucose monitoring technology by children and young people with type 1 diabetes in a single arm study. *Pediatr Diabetes.* 2018; 19(7): 1294–1301

4. Deshmukh H, *et al.* Effect of Flash Glucose Monitoring on Glycemic Control, Hypoglycemia, Diabetes-Related Distress, and Resource Utilization in the Association of British Clinical Diabetologists (ABCD) Nationwide Audit. *Diabetes Care* 2020; 43:2153–2160

5. 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; 42:1178–1184

6. Integrated continuous glucose monitoring system. US Food & Drug Administration regulation 862.1355. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm?id=SAF accessed August 18 2024

7. Alva, S, *et al.* Accuracy of the Third Generation of a 14-Day Continuous Glucose Monitoring System. *Diabetes Ther.* 2023; 14(4):767–776

Use of CGM in gestational diabetes mellitus

Using CGM in gestational diabetes mellitus (GDM) has not been extensively studied to date. Observational data show that daytime glycemic variability (GV) and elevated mean glucose overnight are both associated with increased risk of fetal complications, including large for gestational age (LGA) birthweight in women with GDM.[1–4]

American Diabetes Association (ADA) guidelines recommend screening for GDM at 24–28 weeks of gestation,[5] using a fasting 75-g oral glucose tolerance test (OGTT), whereas the International Association of Diabetes and Pregnancy Study Groups (IADPSG)[6] propose testing for overt diabetes, and diagnosing GDM if fasting plasma glucose (FPG) is 92–126 mg/dL (5.1–7.0 mmol/L) during the first 24 weeks of gestation. In support of this, the Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy (TOBOGM) trial[7] found fewer neonatal complications (25% vs 30%) associated with early treatment of GDM. Using CGM to screen for GDM as early as possible in pregnancy has been proposed, and using metrics of GV have been shown to have benefits over traditional OGTT in this context.[8]

However, additional studies are needed to examine the impact of using CGM on pregnancy outcomes and to determine the optimal CGM-derived glucose targets for women with GDM further studies will be required. A specific TIR pregnancy range (TIRp) of 63–140 mg/dL (3.5–7.8 mmol/L) is recommended for women with pregestational T1DM, with a daily TIRp of >70%.[9] However, studies using CGM in healthy and in GDM pregnancies suggest that a more-stringent target range may be appropriate in GDM, possibly in the range 63–120mg/dL (3.5–6.7 mmol/L).[11] In a prospective observational cohort, those with uncomplicated pregnancies, (defined as HbA1c <39 mmol/mol [5.7%], without GDM, LGA births or hypertensive disorders of pregnancy) demonstrated fairly stable glucose levels throughout pregnancy with an overall mean glucose of 98 mg/dL (5.4 mmol/L). The median percent time spent >120mg/dL (6.7 mmol/L) and >140 mg/dL (7.8 mmol/L) was low, 11% and 2.5%, respectively.[10]

In the GLAM prospective observational study in a cohort of low-risk pregnancies in women (n=768) without pregestational diabetes, those who went on to develop GDM as diagnosed by traditional OGTT presented with higher mean glucose, greater SD and a higher percent time spent >120mg/dL (6.7 mmol/L) (median 23% vs 12%, p<0.001), and higher percent time >140 mg/dL (7.8 mmol/L) (7.4% vs. 2.7%) throughout the gestational period prior to OGTT diagnosis.[11] Use of CGM confirmed that these glycemic trends were measurable as early as 13–14 weeks gestation, compared to pregnant women who did not develop GDM. These glycemic patterns and trends remained consistent throughout pregnancy from 13-weeks onwards for women ultimately diagnosed with GDM using OGTT, compared to those who did not develop GDM.[11] This suggests the potential utility of first-trimester CGM screening for early detection of GDM. Studies have also found that measures of GV correlated with fasting OGTT values predictive of GDM.[12] Even in cases where there was limited evidence of glycemic benefit, the FLAMINGO RCT showed that using CGM by women with GDM significantly reduced the incidence of fetal macrosomia, compared to women with GDM using SMBG.[13]

Data in T1DM pregnancies emphasize the benefits of meeting CGM-measured glucose targets from early pregnancy[14] and optimization of maternal glucose at the earliest opportunity would also likely be beneficial, both in pregestational T2DM and in GDM pregnancies. CGM could also be appropriate for screening for post-partum dysglycemia in women with GDM, who are known to have a seven-fold increased risk of developing T2DM after giving birth,[15] in particular if hyperglycemia is present from early gestation, which has been documented in a cohort of women with obesity.[16]

The use of CGM is revealing a more-complex early dysglycemia in women without pregestational diabetes who develop GDM. Given the impact of higher glucose on neonatal outcomes for women who develop GDM, it is clear that additional studies are needed to understand the application of CGM and CGM metrics for women with a risk of GDM, to optimize maternal and neonatal outcomes.

Key learning points

GDM is associated with increased risk of neonatal complications

Dysglycemia, detected by CGM, is evident as early as 10–13 weeks of pregnancy in women who develop GDM, which is not evident even when using OGTT ahead of the recommended test date

Studies are needed to better define CGM target ranges and targets for women with, or at risk of, GDM

1. Shen SY, *et al.* Identification of maternal continuous glucose monitoring metrics related to newborn birth weight in pregnant women with gestational diabetes. *Endocrine* 2021; 74: 290–299

2. Law GR, *et al.* Suboptimal Nocturnal Glucose Control Is Associated With Large for Gestational Age in Treated Gestational Diabetes Mellitus. *Diabetes Care* 2019; 42: 810–815

3. Gáborová M, *et al.* Glycaemic Variability and Risk Factors of Pregnant Women with and without Gestational Diabetes Mellitus Measured by Continuous Glucose Monitoring. *Int J Environ Res Pub Health* 2021; 18: 3402

4. Liang X, *et al.* Continuous glucose monitoring-derived glycemic metrics and adverse pregnancy outcomes among women with gestational diabetes: a prospective cohort study. *Lancet Reg. Health West Pac.* 2023; 39, 100823

5. ElSayed NA, *et al.* 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023. *Diabetes Care* 2022; 46, S19–S40

6. International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy. *Diabetes Care* 2010; 33, 676–682

7. Simmons D, *et al.* Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. *New Engl J Med.* 2023; 388: 2132–2144

8. Quah PL, *et al.* Glycemic Variability in Early Pregnancy May Predict a Subsequent Diagnosis of Gestational Diabetes. *Diabetes Metabolic Syndrome Obes.* 2022; 15: 4065–4074

9. 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

10. Carlson AL, *et al.* Glucose levels measured with continuous glucose monitoring in uncomplicated pregnancies. *BMJ Open Diabetes Res Care* 2024; 12, e003989

11. Durnwald, C. *et al.* Continuous Glucose Monitoring Profiles in Pregnancies With and Without Gestational Diabetes Mellitus. *Diabetes Care* 2024; doi:10.2337/dc23-2149

12. Filippo DD, *et al.* Continuous Glucose Monitoring for the Diagnosis of Gestational Diabetes Mellitus: A Pilot Study. *J Diabetes Res* 2022; 5142918

13. Majewska A, *et al.* Flash glucose monitoring in gestational diabetes mellitus (FLAMINGO): a randomised controlled trial. *Acta Diabetol.* 2023; 1171–1177

14. Scott EM, *et al.* Continuous Glucose Monitoring Metrics and Birth Weight: Informing Management of Type 1 Diabetes Throughout Pregnancy. *Diabetes Care* 2022; 45: 1724–1734

15. Bellamy L, *et al.* Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet* 2009; 373:1773–1779

16. Champion ML, *et al.* Postpartum glucose intolerance following early gestational diabetes mellitus. *Am J Obstetrics Gynecol MFM* 2022; 4:100609

Understanding the value of CGM as a diabetes intervention as well as a glucose monitoring tool

Since their introduction, CGM systems have been seen as alternative tools to self-monitored blood glucose (SMBG) testing, providing greater coverage and information on glucose levels. Accumulated evidence now indicates that CGM technologies can also be viewed as diabetes interventions, that constitute disease-modifying treatment.[1]

The value of CGM as tools is predicated on their comparison against SMBG devices in routine measurement of glucose levels. Finger prick SMBG meters provide only single 'point-in-time' glucose readings, that do not allow users with diabetes to see how their daily behavior influences their glucose levels, nor to predict impending hypoglycemia. Also, SMBG testing requires time-consuming and potentially painful finger prick tests. Multiple surveys report that regular SMBG testing is performed by fewer than 50% of people with T1DM,[2,3] and that approximately one-third of people with insulin-treated diabetes do not test their glucose routinely, rising to two-thirds for those on non-insulin therapies.[4]

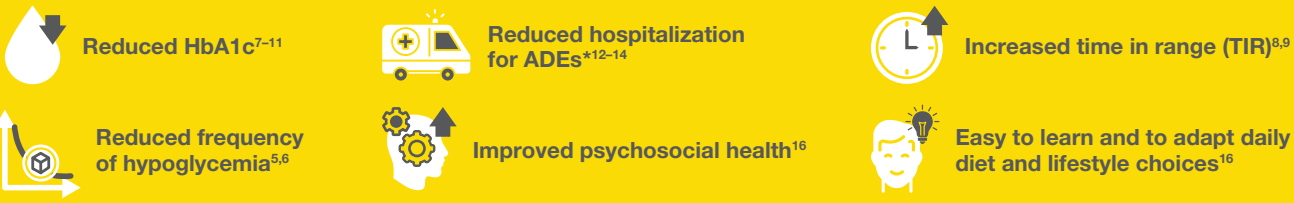
In contrast, CGM removes the need for time consuming or painful testing, and provides immediate and continuous feedback on glucose levels, including both the direction and speed of glycemic changes. Audible alerts can also be provided to warn the user of impending hypoglycemia and to take immediate action. The safety and efficacy of CGM devices has been validated in numerous clinical trials and real-world studies, in individuals with T1DM and T2DM on intensive insulin therapy,[5–8] and for people with T2DM on basal insulin or non-insulin therapies.[9–11] More notably, using CGM technology is associated with significant reductions in acute diabetes events (ADEs) requiring hospitalization, including diabetic ketoacidosis (DKA) and severe hypoglycemia, for people with T1DM or T2DM on intensive insulin therapy,[12] with similar reductions in admissions for ADEs for people with T2DM on basal insulin or non-insulin treatments.[13,14] The use of CGM technology has consequently been associated with improvements in psychosocial measures of diabetes-related fear and distress, and improved overall quality of life.[15]

An important observation in many prospective studies is that the impact of using CGM devices on measures of diabetes health, such as HbA1c and frequency of hypoglycemia, is achieved without changes in antihyperglycemic therapy. In the MOBILE study cohort with T2DM on basal insulin,[9] using CGM compared to SMBG significantly reduced mean HbA1c and increased time in range (TIR), without significant changes in insulin doses or non-insulin medications between CGM and SMBG groups. Similarly, in the IMPACT[5] and REPLACE[6] studies in T1DM and T2DM treated with multiple daily injections (MDI) with insulin, significant reductions in hypoglycemia were achieved in the CGM treatment groups compared to SMBG controls, without differences in total daily dose of insulin. These outcomes indicate that CGM on its own has a treatment effect on glycemia, potentially through changes to meal planning and lifestyle.

This has been tested using the FreeStyle Libre system in the AH-HA! Project,[16] which found that adults with recently diagnosed T2DM were able to self-learn how to use the continuous feedback provided by the FreeStyle Libre system to adapt their behaviours to improve their glucose control. During the study, participants were successfully encouraged to conduct 'personal experiments' to investigate how their own behaviors affect glucose levels, resulting in significant increases in TIR (p=0.01), with reported increases in healthy eating (p<0.001) and wellbeing (p=0.04).

The concept that CGM is a disease-modifying intervention for people with diabetes is supported by significant outcomes data, with demonstrated benefits in many aspects of diabetes care (see infographic). This is evident whether treatment is managed with insulin or non-insulin regimens. This should guide the use of CGM technology in all individuals with diabetes.

Demonstrated benefits of application of CGM technology for people with T1DM or T2DM, including those treated with insulin or non-insulin therapies.



*ADEs, acute diabetes events (such as diabetic ketoacidosis or severe hypoglycemia)

1. Wright EE, *et al.* Is Continuous Glucose Monitoring a Tool, an Intervention, or Both? *Diabetes Technol. Ther.* 2023; 25: S-48-S-55.

2. Karter AJ, *et al.* Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes registry*. *Am. J. Med.* 2001; 111: 1–9.

3. Moström P, *et al.* Adherence of self-monitoring of blood glucose in persons with type 1 diabetes in Sweden. *BMJ Open Diabetes Res Care* 2017; 5: e000342. doi: 10.1136/bmjdrc-2016-000342

4. Siddiqui MH, *et al.* Identifying Barriers to Therapeutic Adherence in Type 2-Diabetes: A Complex and Multidimensional Clinical Issue. *Asploro J. Biomed. Clin. Case Rep.* 2019; 2: 22–28.

5. Bolinder J, *et al.* Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet* 2016; 388: 2254–2263.

6. Haak T, *et al.* Use of Flash Glucose-Sensing Technology for 12 months as a Replacement for Blood Glucose Monitoring in Insulin-treated Type 2 Diabetes. *Diabetes Ther* 2017; 8: 573–586.

7. 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; 42:1178–1184

8. Leelarathna L, *et al.* Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes. *New Engl J Med* 2022; 387(16):1477–1487

9. Martens T, *et al.* Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin. *JAMA* 2021; 325: 2262–2272.

10. Carlson AL, *et al.* Flash glucose monitoring in type 2 diabetes managed with basal insulin in the USA: a retrospective real-world chart review study and meta-analysis. *BMJ Open Diabetes Res Care* 2022; 10, e002590 doi: 10.1136/bmjdrc-2021-002590

11. Wright EE, *et al.* Use of Flash Continuous Glucose Monitoring Is Associated With A1C Reduction in People With Type 2 Diabetes Treated With Basal Insulin or Noninsulin Therapy. *Diabetes Spectr* 2021; 34: 184–189.

12. Roussel R, *et al.* Important Drop in the Rate of Acute Diabetes Complications in People With Type 1 or Type 2 Diabetes After Initiation of Flash Glucose Monitoring in France: The RELIEF Study. *Diabetes Care* 2021; 44: 1368–1376.

13. Riveline J-P, *et al.* Reduced rate of hospitalizations for acute diabetes events before and after FreeStyle Libre® system initiation in some people with type 2 diabetes on insulin-secretagogue oral drug therapy without insulin in France. *Diabetes Technol. Ther.* 2024; doi: 10.1089/dia.2024.0171

14. Guerci B, *et al.* Important decrease in hospitalizations for acute diabetes events following FreeStyle Libre® system initiation in people with type 2 diabetes on basal insulin therapy in France. *Diabetes Technology Ther.* 2023; 25: 20–30.

15. Polonsky WH, *et al.* Psychosocial and Glycemic Benefits for Insulin-Using Adults With Type 2 Diabetes After Six Months of Pump Therapy: A Quasi-Experimental Approach. *J. Diabetes Sci. Technol.* 2023; doi:10.1177/19322968231198533.

16. Polonsky WH, *et al.* The AH-HA! Project: Transforming Group Diabetes Self-Management Education Through the Addition of Flash Glucose Monitoring. *Diabetes Technol Ther.* 2022; 25:194–200

insights from ADA 84th Scientific Sessions in Orlando

Using the FreeStyle Libre system to guide meal planning can reduce HbA1c and lead to weight loss in T2DM not treated with insulin

A prospective randomized study evaluated the effect of using CGM to reduce hyperglycemia in people with T2DM not taking insulin, by focusing on food and lifestyle choices.

A total of 72 adults with T2DM treated with non-insulin medications and not using sulfonylureas were randomized to use either the FreeStyle Libre system alone (n=31) or in conjunction with a food-logging smartphone app (n=41), for 6 months. All study participants had an HbA1c ≥7.5% (58 mmol/mol) but ≤12% (108 mmol/mol).

After 3 months, participants in the FreeStyle Libre only cohort had reduced their time above range (TAR) >180 mg/dL (>10.0 mmol/L) by -28% (p<0.001) and those in the FreeStyle Libre + app cohort had reduced their TAR by -23% (p<0.001), and both subgroups had reduced their HbA1c by 1.1% (12 mmol/mol; p<0.001). Mean glucose for all participants was decreased by -33 mg/dL (p<0.001) and time in range 70-180 mg/dL (3.9-10.0 mmol/L) was increased by 25% (p<0.001).

Mean weight loss across all participants was -4.0lbs (-1.81kg; p<0.001) after 3 months. Those using the food app logged reported increased exercise and meal-portion control.

Overall, use of the FreeStyle Libre system showed to improve glycemic control for people with T2DM on non-insulin therapy, and can be combined with food-logging apps to document dietary behaviors.

Martens TW, *et al.* A randomized controlled trial using continuous glucose monitoring to guide food choices and diabetes self-care in people with type 2 diabetes not taking insulin. American Diabetes Association 84th Scientific Sessions 2024. Oral presentation 356-OR.

People with T2DM on oral therapies with higher risk of hypoglycemia have fewer acute events when using the FreeStyle Libre system

A retrospective study using healthcare claims data compared rates of acute diabetes events (ADEs), as well as rates of hospitalizations and emergency department (ED) visits among people with T2DM treated with sulfonylurea or meglitinide agents, in the 6 months before and after starting the FreeStyle Libre system.

Claims data for 4,871 adults with T2DM were included in the study, including 2,976 aged <65 years old and 1,895 aged ≥65 years. Hyperglycemic and hypoglycemic ADEs were assessed, as well as all-cause hospitalization and all-cause ED visits.

For the <65 year age group, all ADEs were reduced by -49% in the 6 months after starting the FreeStyle Libre system, compared to the 6 months prior, and by -40.4% for the ≥65 year age group (p<0.05 in both cases). All cause hospitalizations were reduced by -21.2% for the <65 year age group and by -9.5% for those aged ≥65 years (p<0.05 in both cases). ED visits for any cause were reduced by -26.3% for the <65 year age group and by -10.4% for those aged ≥65 years (p<0.05 in both cases).

This study revealed that healthcare resource utilization for adults with T2DM on oral medications with a higher risk for hypoglycemia was significantly reduced in the 6 months after starting the FreeStyle Libre system, compared to the 6 months before.

Galindo RJ, *et al.* Use of Continuous Glucose Monitoring and Healthcare Resource Utilization in Patients with Diabetes treated with sulfonylureas/Meglitinides. American Diabetes Association 84th Scientific Sessions 2024. Poster presentation 1926-LB.

Healthcare resource utilization over 2 years is reduced for DKA and hypoglycemia with use of the FreeStyle Libre system in Canada

A longitudinal retrospective cohort study investigated healthcare resource utilization (HCRU) before and after adoption of FreeStyle Libre in people with diabetes using any therapy in Ontario.

A total of 45,523 people with T1DM (21%) or T2DM (79%) were included, having a first recorded use of the FreeStyle Libre system in the Ontario administrative health system between 16th September 2019 and 31st August 2020. Frequency of emergency department (ED) visits or hospital admission for diabetic ketoacidosis (DKA) or severe hypoglycemia (SH) were calculated for the 12 months prior to the FreeStyle Libre system index date and the final 12 months of the 24-month follow-up period.

Hospitalization and ED visits for DKA and SH were both significantly reduced in the 24 months after the FreeStyle Libre index date, compared to the 12 months before. For adults with diabetes aged <66 years (n=15,058) hospitalizations for DKA were reduced by -26% and for SH by -19%, whereas for adults aged ≥66 years (n=30,465), admissions for DKA were reduced by -40% and for SH by 26%. ED room visits were similarly reduced for DKA, by -27% for people with diabetes aged <66 years and by =50% for those aged ≥66 years. For SH, people with diabetes aged <66 years had a -22% reduction in ED visits, and those aged ≥66 years had -30% fewer ED visits.

The reduced HCRU after initiation of the FreeStyle Libre system provide strong clinical and economic support for Canadian payers to reimburse FreeStyle Libre technology for all people with diabetes.

Harris SB, *et al.* FRONTIER – Flash glucose monitoring system use in Ontario among patients with DM in the ICES database – evidence from real-world practice. American Diabetes Association 84th Scientific Sessions 2024. Poster presentation 1923-LB.

FreeStyle Libre technology lowers costs and improves quality of life for people with diabetes in Canada

This study assessed the cost-effectiveness of FreeStyle Libre systems, compared to SMBG, from the perspective of Canadian private payers, using the Determination of Diabetes Utilities, Costs and Effects (DEDUCE) microsimulation model.

By assigning costs and utilities to long-term and acute complications of diabetes, the study evaluated the cost-effectiveness of using the FreeStyle Libre systems versus SMBG for people living with diabetes in Canada, including those not treated with insulin. Population characteristics, treatment outcomes, and utilities were based on randomized controlled trials (RCTs) and real-world studies.

Mean age at model entry was 23 years for people with T1DM and 40 years for people with T2DM. Costs were taken from Canadian sources, including acquisition costs for the FreeStyle Libre systems and for SMBG, as well as costs of treating diabetes complications and the cost of workplace absenteeism. In both T1DM and T2DM, use of the FreeStyle Libre system provided more quality-adjusted life years (QALYs) than SMBG (+1.25 in T1DM, +0.48 in T2DM), at a lower cost per person (-$32,287 in T1DM, -$8,091 in T2DM). From a Canadian private payer perspective, the modelled treatment impact of using the FreeStyle Libre systems makes it cost effective compared with SMBG for all people living with diabetes.

Harris SB, *et al.* Cost-effectiveness of Flash CGM compared with SMBG – a Canadian private payer perspective. American Diabetes Association 84th Scientific Sessions 2024. Poster presentation 1051-P.

TITR outperforms TIR for assessing glycemic status and progress toward stringent HbA1c

This real-life study evaluated the relationship between average glucose, time in range (TIR), and time in tight range (TITR) in a large cohort of CGM users, and considered the impact of glycemic variability (GV) across different diabetes types and treatment modalities.

In this real-life study, a large cohort of CGM users (n=22,006) were categorized into four groups: T1DM on multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) pump therapy; T2DM on MDI or CSII therapy; T2DM on basal insulin only, and; T2DM not on insulin therapy.

Results showed that the T2DM groups had the highest TIR and TITR with the lowest coefficient of variation (CV; 23-30%), while the T1DM group had the lowest TIR and TITR with the highest CV (36-38%). Higher CV was linked to lower TIR and TITR for average glucose levels below 180 and 140 mg/dL, respectively, and the opposite was true for average above these levels. TITR proved advantageous over TIR for assessing glycemic status and progress toward stringent HbA1c, especially as average glucose neared normoglycemia.

These findings highlight the impact of GV, as measured by CV, on the relationship between average glucose with TIR/TITR, suggesting that TITR may be a preferable metric to monitor when average is below 140 mg/dL.

Dunn, TC *et al.* Is It Time to Move Beyond TIR to TITR? Real-World Data from Over 20,000 Users of Continuous Glucose Monitoring in Patients with Type 1 and Type 2 Diabetes. *Diabetes Technol Ther.* 2024; 26(3):203-210. doi:10.1089/dia.2023.0565.

CGM is more-effective than SMBG in improving glycemia and health-related quality of life in people with T2DM treated with insulin

This single-center, open-label, randomized controlled trial (RCT) assessed the impact on glucose control and other person-reported outcomes (PROs) of using CGM versus SMBG over 12 months in adults with insulin-treated T2DM and suboptimal glycemia.

Conducted at Steno Diabetes Center Copenhagen, this study included 76 adults with T2DM and above target HbA1c ≥7.5% (58 mmol/mol), who were randomly assigned to use CGM or SMBG for 12 months. Baseline, 6-month and 12-month glucometrics were assessed using blinded CGM in both cohorts. The primary outcome was change in time in range (TIR) 3.9-10.0 mmol/L. Secondary outcomes included changes in HbA1c, daily insulin dose, weight, BMI, and self-rated health.

After 12 months, results showed that using CGM was associated with improvements in glycemic parameters, including increased TIR by 15.2%, HbA1c reduction by 0.9% (9.4 mmol/mol), decreased total daily dose of insulin by 10.6 units/day, mean 3.3 kg weight loss with a lowered BMI by 1.1 kg/m^2. CGM also significantly improved PROs for general health (p<0.001), diabetes treatment satisfaction (p=0.002), diabetes-related distress (p=0.011), as well as overall general well-being (p=0.041).

For adults with insulin-treated T2DM and suboptimal glycemia, use of CGM vs SMBG resulted in improved glycemic control over 12 months, along with significantly improved health-related quality of life measures.

Lind, N *et al.* Comparing Continuous Glucose Monitoring and Blood Glucose Monitoring in Adults With Inadequately Controlled, Insulin-Treated Type 2 Diabetes (Steno2tech Study): A 12-Month, Single-Center, Randomized Controlled Trial. *Diabetes Care.* 2024; 47(5):881-889. doi:10.2337/dc23-2194.

Satisfaction with CGM in youth with T1DM is associated with quality of life, independent of treatment regimen

This cross-sectional study of children and adolescents with T1DM and their parents or carers in Italy aimed to investigate the relationship between quality of life (QoL) and satisfaction with CGM, as well as the impact of different treatment regimens on QoL.

A total of 210 consecutively enrolled youths with T1DM and their parents or carers completed the 24-question KINDL health-related quality of life (HRQoL) survey, specific to children aged 3 years and older, and the 42-item CGM-SAT questionnaire, validated for assessing satisfaction with CGM. The mean total KINDL score was associated with improved QoL, both in youths with T1DM (3.99, range 1–5) and their parents or carers (4.06, range 1–5).

The highest score was reported in the disease dimension aspect of QoL in both groups, and the lowest score reported was in the self-esteem and QoL at school scales (youths) and the school and self-esteem scale (parents/carers), respectively. Lower overall CGM-SAT scores (i.e., higher satisfaction) both in children and parents/carers were significantly associated with higher QoL on all six KINDL subscales (p<0.05), independent of insulin-delivery method of glycemic control.

These findings indicate that CGM improves the well-being of youths with T1DM and that of their parents/carers. Therefore, perceived satisfaction with CGM should be incorporated within clinical practice to improv e person-reported outcomes.

Franceschi R *et al.* Satisfaction with continuous glucose monitoring is associated with quality of life in young people with type 1 diabetes regardless of metabolic control and treatment type. *Diabet Med.* 2024; 41(6): e15307.

Using flash glucose monitoring with alarms improves glycemic control in adults with T1DM in Spain

A longitudinal observational study of a single cohort of adults with T1DM in Valencia evaluated the effect of switching from the FreeStyle Libre system to the FreeStyle Libre 2 system with optional real-time alarms.

A total of 100 adults with T1DM (mean age 43.8 years) were included in the analysis, comparing their glycemic trends when using the original FreeStyle Libre system, with their metrics 3-months after switching to the FreeStyle Libre 2 system with optional alarms, as part of routine clinical practice.

After starting to use the FreeStyle Libre 2 system with optional real-time alarms, significant improvements were evident during follow-up in: time below range (TBR) Level 2 (<54 mg/dL [<3.0 mmol/L] reduced by mean -0.9%: p<0.001); time in range (TIR) (70-180 mg/dL [3.9-10.0 mmol/L] increased by 5.2%: p<0.001); time above range (TAR) Level 1 (180-250 mg/dL[10.0-13.9 mmol/L] decreased by -2.4%: p=0.002); and there was significant improvement in glucose management indicator (p=0.04) and mean glucose (p=0.04). Glycemic variability as measured by coefficient of variation (CV) was also significantly lower after switching (p=0.004). Moreover, there was a significant association between the age of participants and their change in TIR such that, for every additional year in age, there was a mean increase of 0.23% in TIR. Similarly, there was a significant inverse association between participants age and change in TAR level 1, with a mean decrease of -0.11% for every additional year of age.

These findings show that the FreeStyle Libre 2 system with optional real-time alarms helped older adults with T1DM to achieve better glucose control in line with international consensus guidelines.

Gutierrez-Pastor A *et al.* Effect of switch from flash glucose monitoring to flash glucose monitoring with real-time alarms on hypoglycaemia in people with type 1 diabetes mellitus. *Prim Care Diabetes.* 2024; 18(3): 333–339.

Treatment cost analysis indicates that people with diabetes on insulin therapy can benefit from access to the FreeStyle Libre system in Italy

Using data from two local health authority administrative databases in Italy, this retrospective study examined the distribution of direct healthcare costs for people with diabetes, based on number of comorbidities, diabetes type and treatment regimen treated with multiple daily injections with insulin (MDI), T2DM on basal insulin only [T2DM-Basal], or T2DM not on insulin therapy [T2DM-Oral]).

The analysis included 288,097 participants (out of 304,779 people with diabetes identified during the period for which data were obtained [2014–2018]) who had been treated with glucose-lowering drugs (13% T1DM/T2DM-MDI, 13% T2DM-Basal, 74% T2DM-Oral).

On average, annual costs per patient for the year 2018 across the total cohort were similar between the T1DM/T2DM-MDI (€2,580) and T2DM-Basal groups (€2,254) and substantially lower for the T2DM-Oral group (€1,145).

Cost of hospitalisation was the main driver in all groups, representing 47% (T1DM/T2DM-MDI) or 45% (T2DM-Basal and T2DM-Oral) of total direct healthcare costs. This was followed by costs for drugs/devices (35% [T1DM/T2DM-MDI], 39% [T2D-Basal], 43% [T2D-Oral]) and outpatient services (18% [T1DM/T2DM-MDI], 16% [T2DM-Basal], 12% [T2DM-Oral]). Average per-patient costs of diabetes treatment increased incrementally with each additional comorbidity, from €459 for a patient with diabetes only to €7,464 for a patient with four comorbidities.

Because using the FreeStyle Libre systems is associated with significantly reduced hospitalisation rates for acute diabetes events, the authors concluded that the use of this CGM technology could positively impact the most significant treatment costs for people with diabetes in Italy, treated with MDI or basal insulin therapies.

Mennini FS *et al.* An analysis of the distribution of direct cost of diabetes care in selected districts in Italy. *Diabetes Ther.* 2024; 15(6): 1417–1434.

Initiating the FreeStyle Libre system further improves HbA1c in adults with T2DM on GLP-1 receptor agonist therapy

Flash glucose monitoring and glucagon-like peptide-1 receptor agonists (GLP-1 RA) are both known to improve glycemia for people with T2DM when used alone. In three real-world studies, changes in HbA1c were assessed when the FreeStyle Libre system was initiated for people with T2DM in combination with GLP-1 RA therapy.

In the first study,[1] linked analysis of electronic health records (EHR) and insurance claims from US providers, was used to review a cohort of 478 adults with T2DM and suboptimally-controlled glycemia, with HbA1c ≥8.0% (64 mmol/mol). Changes in glycemia were assessed for this group of adults with T2DM who initiated the FreeStyle Libre system within 30 days of starting GLP-1 RA therapy and compared to a group of 2,390 adults, matched for age, sex, baseline HbA1c and insulin therapy, who initiated GLP-1 RA treatment but were not users of the FreeStyle Libre system or other CGM devices.[1]

The group who initiated GLP-1 RA within 30 days of starting the FreeStyle Libre system had a significantly greater reduction in HbA1c after 6 months. compared to the matched group who initiated GLP-1 RA only (-2.43% [-26.5 mmol/mol] vs -2.06% [-22.5 mmol/mol], p<0.001). This differential HbA1c improvement was consistant for adults with T2DM, independently of whether they used bolus insulin or not. Additionally, a significantly higher proportion of the group who initiated GLP-1 RA with the FreeStyle Libre system achieved an HbA1c level <8% (64 mmol/mol) at 6 months (59.8% vs. 53.8%, p=0.02).

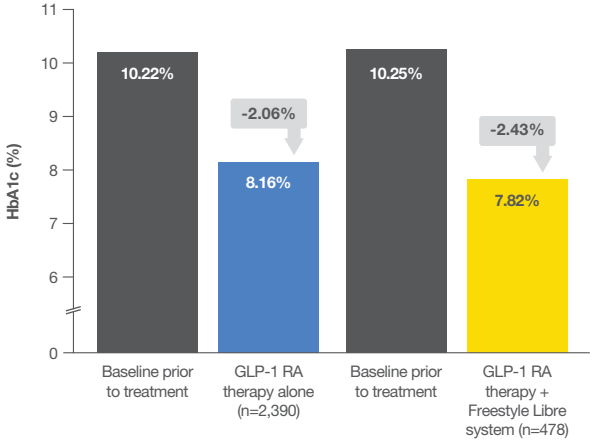
In a second retrospective observational study,[2] researchers used Optum's de-identified Market Clarity Data to assess changes in HbA1c following initiation of the FreeStyle Libre system in adults with T2DM already on GLP-1 RA therapy. Participants (n=1,454) were aged 18 years or older, had a baseline HbA1c of ≥8.0% (64 mmol/mol), with at least one GLP-1 RA prescription within 90 days of starting the FreeStyle libre system. The cohort had a mean age of 55 years, 52% were male and 38% were on intensive insulin therapy. The baseline HbA1c of the study cohort was 9.8% (84 mmol/mol) and the median time from GLP-1 RA initiation to starting the FreeStyle Libre system was 471 days.

After starting the FreeStyle Libre system, HbA1c decreased by -1.5% (-16.4 mmol/mol; p<0.001), with the largest reduction (-2.7% [-29.5 mmol/mol]; p<0.001) in those with baseline HbA1c >10% (86 mmol/mol). Significant improvements in HbA1c were observed after starting the FreeStyle Libre system, irrespective of GLP-1 RA treatment duration, GLP-1 RA formulation, or insulin therapy type.

A third retrospective study[3] found that treatment with GLP-1 RA was more impactful in adults with T2DM on basal insulin if they were using the FreeStyle Libre system for at least 80% of days during the 12-month study period.

These real-world studies clearly show that using the FreeStyle Libre system with GLP-1 RA therapy in people with T2DM and suboptimal glycemic control, is more-effective in reducing HbA1c than using GLP-1 RA alone.

Addition of the FreeStyle Libre system resulted in a -0.37% greater reduction in HbA1c compared to GLP-1 RA alone (p<0.001).



GLP-1 RA, glucagon-like peptide 1 receptor antagonist

Matched cohorts of adults with poorly controlled T2DM were treated with GLP-1 RA alone or in conjunction with the FreeStyle Libre system. Follow up was 6 months after the treatment intervention.[1]

1. Wright EE, *et al.* Initiating GLP-1 therapy in combination with FreeStyle Libre provides greater benefit compared to GLP-1 therapy alone. *Diabetes Technol Ther.* 2024; doi: 10.1089/dia.2024.0015

2. Miller E, *et al.* Association of Changes in A1C Following Continuous Glucose Monitoring Acquisition in People with Sub-Optimally Treated Type 2 Diabetes Taking GLP-1 RA Therapy. *Diabetes Ther.* 2024;doi:10.1007/s13300-024-01619-1

3. Huang E, *et al.* Association of FreeStyle Libre utilization and glycemic outcomes among people with type 2 diabetes treated with basal insulin and glucagon-like peptide 1 receptor agonists. American Diabetes Association 84th Scientific Sessions 2024. Poster presentation 1917-LB.

Tell us what you think!

The team at the *Sensor Report* is always keen to hear your feedback and suggestions. Please send any comments and ideas that you have regarding how research on diabetes technologies is covered in the *Sensor Report* to **Wiebke Jessen at** wiebke.jessen@abbott.com.

We look forward to hearing from you!

Flash glucose monitoring is associated with reduced HbA1c in adults with T2DM on intensive insulin therapy

This retrospective observational study evaluated the effect of initiating FreeStyle Libre technology on HbA1c after 3–6 months in adults living with T2DM treated with multiple daily injections (MDI) of insulin.

In total, 87 adults with T2DM and baseline HbA1c 8.0-12.0% (64-108 mmol/mol) were included from 10 UK clinical centres. Mean age was 60.0 years, mean BMI was 31.6 kg/m^2 and mean duration of insulin use was 8.1 years. All individuals had been using the FreeStyle Libre or FreeStyle Libre 2 system for at least 3 months. There was a high prevalence of long-term complications, including cardiovascular disease (28.7%) and retinopathy (43.7%).

Mean baseline HbA1c was reduced from 9.5% (80 mmol/mol) to 8.5% (69.0 mmol/mol), a fall of -1.0% (-11.0 mmol/mol) after 3-6 months using FreeStyle Libre technology ($p < 0.0001$). The reduction in HbA1c was greatest for those with baseline HbA1c ≥9.0% (≥75.0 mmol/mol), with mean -1.4% (15.3 mmol/mol) change after 3-6 months. Obese adults with a body-mass index (BMI) ≥30 kg/m^2 experienced more substantial falls in HbA1c compared to those with BMI <30 kg/m^2, as did adults aged <65 years compared to those ≥ 65 years.

This study further reinforces the conclusion that using FreeStyle Libre technology is an effective component of reducing glycemic exposure, as measured by HbA1c, for adults living with T2DM and managed using intensive insulin therapy.

Adamson KA, *et al*. Flash glucose monitoring is associated with HbA1c improvement in type 2 diabetes managed with multiple daily injections of insulin in the UK: a retrospective observational study. *Diabetes Ther*. 2024; 15:2109-2118

Using the FreeStyle Libre system reduces both HbA1c and total daily basal-insulin dose in adults with T2DM

An observational cohort study evaluated the impact of starting the FreeStyle Libre system on suboptimal HbA1c levels in adults with T2DM managed with basal insulin.

This study, involving 79 adults with T2DM aged 18 years or older and an HbA1c of 8.0-12.0% (64-108 mmol/mol), was conducted across nine clinical centers in Canada to evaluate the impact of initiating FreeStyle Libre technology on HbA1c in adults with T2DM managed with basal insulin-only for at least 1 year. Data were collected at baseline and at 3-6 months for follow-up of HbA1c levels and medication changes.

Baseline HbA1c was 8.9% (74 mmol/mol), reducing by -0.6% (-6.6 mmol/mol) at follow-up ($p < 0.0001$). The reduction was significant across all baseline levels of HbA1c, but was greater for those with baseline HbA1c ≥9.0% (≥75.0 mmol/mol), with mean -1.1% (13.0 mmol/mol) falls in HbA1c versus -0.3% (-3.3 mmol/mol) for individuals with baseline HbA1c <9.0% (<75 mmol/mol). Significantly, the mean total daily dose of basal insulin decreased by -3.4 units ($p = 0.03$) after 3-6 months.

The reductions in HbA1c and total daily dose of basal insulin indicate that using the FreeStyle Libre system is supportive of changes to lifestyle and diet that result in improved glycaemic control for people with T2DM not on intensive insulin therapy.

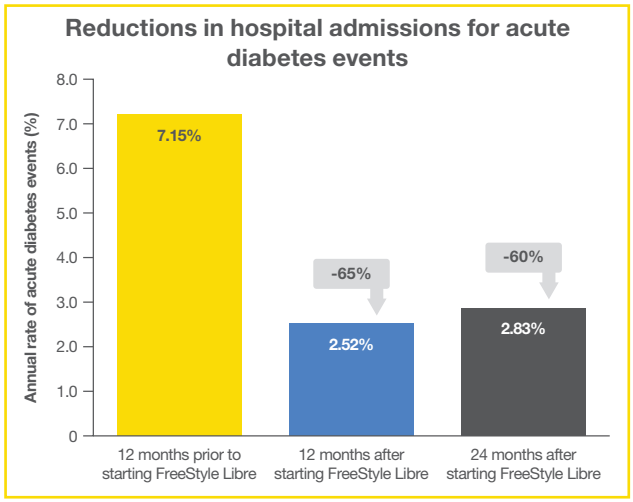
Abitbol A, *et al*. Use of flash glucose monitoring is associated with HbA1c reduction in type 2 diabetes managed with basal insulin in Canada: A real-world prospective observational study. *Diab Vasc Dis Res*. 2024; 21(3): doi:10.1177/14791641241253967

Flash glucose monitoring is associated with reduced hospitalizations for acute diabetes events for people with T2DM on oral non-insulin therapies in France

This study investigated the change in hospitalization rates for acute diabetes events (ADEs) following initiation of the FreeStyle Libre system in people with T2DM in France, treated with oral insulin-secretagogue drugs without insulin.

Retrospective study of the French national SNDS claims database identified 1,272 people with T2DM treated with oral insulin-secretagogue agents only and a FreeStyle Libre initiation date between 1st August 2017 and 31st December 2018. Data for the 12 months before and the 12 and 24 months after starting the FreeStyle Libre system were included. Hospitalizations were assessed for ADEs, including diabetic ketoacidosis (DKA), hyperglycemia-related admissions, hypoglycemic events and comas.

Of the 1,272 individuals with T2DM on oral glucose-lowering drugs who started to use the FreeStyle Libre system during the selection period, 7.15% had at least one hospitalization for any ADE in the year before FSL initiation, compared with 2.52% at 12 months and 2.83% at 24 months following FSL initiation. These represent 65% and 60% fewer hospital admissions, respectively (see Figure). Reductions in ADEs were driven by -73%



fewer admissions for ADEs related to diabetic ketoacidosis (DKA) or other hyperglycemia-related events. These patterns of reduced ADEs persisted after 2 years.

Riveline JP, *et al*. Reduced rate of hospitalizations for acute diabetes events before and after FreeStyle Libre system initiation in some people with type 2 diabetes on insulin-secretagogue oral drug therapy without insulin in France. *Diabetes Technol Ther*. 2024 Jul 4. doi: 10.1089/dia.2024.0171.

Copy as text: a highly useful feature of the AGP report in the LibreView for Professionals platform*

The ambulatory glucose pattern (AGP) reports that are available in LibreView display a significant number of important glycemic metrics that are collected by the FreeStyle Libre systems. Many, but not all of these metrics are valuable to also have included in the electronic health record (EHR) for a person with diabetes. Ideally, this data would be directly harvested from the AGP report and integrated into the EHR for each LibreView user. However, relatively few healthcare organisations have systems that can automatically harvest CGM data from the AGP in LibreView and have it logged in the EHR. Consequently, valuable metrics such as TIR, TBR, TAR, glucose management indicator (GMI) and glycemic variability, may need to be transcribed into the EHR by the healthcare professional (HCP).

We must therefore bring to your attention an important feature of the LibreView for Professionals platform*, that is used by HCP to view FreeStyle Libre sensors data shared with them by a person using the LibreView for Patients platform. This is the **Copy as text** icon, which sits immediately on right-hand side of the **AGP Report** title. When you mouse-over the blue roundel, the icon lets you know that it is ready to copy as text. When you click the Copy as text icon, the LibreView system generates a basic text file that summarizes the key glycemic metrics for easy inclusion in an EHR, saving time.

AGP Report

11 March 2024 - 8 June 2024 (90 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

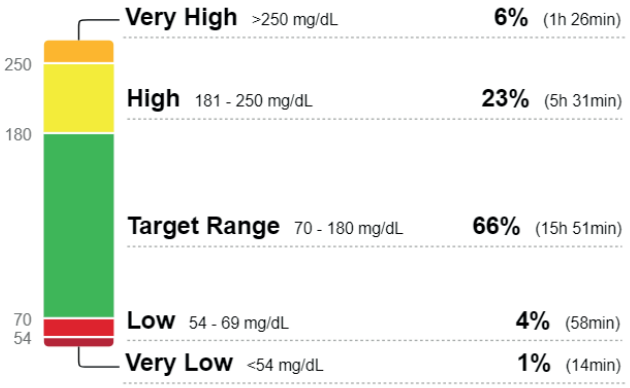
11 March 2024 - 8 June 2024	**90 Days**
Time Sensor Active:	**99%**

Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	**Targets** % of Readings (Time/Day)
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 180 mg/dL	Less than 25% (6h)
Above 250 mg/dL	Less than 5% (1h 12min)
Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.	

Average Glucose	**155** mg/dL
Glucose Management Indicator (GMI)	**7.0% or 53 mmol/mol**
Glucose Variability	**37.5%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



Copy as text report

```
**********
Name: John Smith
Date of Birth: 19/12/1973
Report Period: 11/03/2024 – 08/06/2024 (90 days)
Generated: 23/07/2024
% Time Sensor Active: 99%
**********

**********
Glucose Statistics and Targets
Average Glucose: 155 mg/dL
Glucose Management Indicator (GMI): 7.0% or
53 mmol/mol
Glucose Variability (%CV): 37.5%
Target Range: 70 – 180 mg/dL
**********

**********
Time in Ranges
Very High: >250 mg/dL --- 6%
High: 181 – 250 mg/dL --- 23%
Target Range: 70 – 180 mg/dL --- 66%
Low: 54 – 69 mmol/L --- 4%
Very Low: <54 mg/dL --- 1%
**********
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Image for illustrative purposes only. Not real data.

*The LibreView website is only compatible with certain operating systems and browsers. Please check with www.libreview.com for additional information. The LibreView data management software is intended for use both by patients and healthcare professionals to assist people with diabetes and their healthcare professionals in the review, analysis, and evaluation of historical glucose device data to support effective diabetes management. The LibreView software is not intended to provide treatment decisions or to be used as a substitute for professional healthcare advice.

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FreeStyle Libre

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life. to the fullest.®