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FreeStyle Libre

THE sensor report

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WELCOME TO
THE SENSOR REPORT, ISSUE 3, 2024

For the third issue of the *Sensor Report* for 2024, we are able to highlight a number of important opinions and contributions on the wider use of the FreeStyle Libre systems, and other continuous glucose monitoring (CGM) devices, in people with T2DM. Importantly, there is a growing consensus that CGM systems should be adopted for the care of all people with T2DM, including those who are treated with non-insulin drugs. Certainly, the evidence supports this role for the FreeStyle Libre portfolio and other CGM devices that have been part of randomized controlled trials (RCTs) and other prospective studies.

In a very-recent consensus report published in *Nature Reviews Endocrinology*, an expert panel of diabetologists and endocrinologists have laid out the case for using CGM technology in individuals across the full natural history of T2DM, beginning as soon as possible after first diagnosis and continuing with periodic or continual use through treatment with non-insulin agents. Once insulin is added to the therapeutic management plan, then continuous application of CGM sensors is indicated as now established in joint ADA/EASD guidelines. This end-to-end approach is an evidence-based extension of the key learnings from the landmark UK Prospective Diabetes Study (UKPDS), which ran for 20 years from 1977 to 1997. This made it clear that early intervention to improve glucose control in newly-diagnosed adults with T2DM could significantly reduce the occurrence of microvascular and microvascular complications of diabetes over a median 10 year period. Moreover, this early control imprinted a legacy effect, such that long-term complications were significantly reduced even in individuals in whom early good control was not maintained over the full study period. The opinions expressed in the consensus report are further supported by recent meta-analysis and systematic reviews of the RCTs conducted to date in T2DM, comparing use of CGM versus SMBG in study cohorts on intensive insulin therapy, on basal-insulin therapy or on non-insulin treatment regimens. We have summarized these analyses for you in this edition of the *Sensor Report*.

Along with presenting these new insights and opinions for use of CGM in T2DM, we also look at the important impact of using the FreeStyle Libre systems on non-glycemic psychosocial factors for people with diabetes. Finally, we have summarized a number of presentations from the 17th ATTD International Conference that shine a spotlight on the benefits of CGM, including how the FreeStyle Libre portfolio can be used to augment therapy with glucagon-like peptide-1 receptor agonists (GLP-1 RA) in people with T2DM.

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featurestory

Expert opinion recommends use of CGM immediately after diagnosis in people with T2DM and as part of non-insulin therapy

The use of CGM for routine care of people with T2DM who are on intensive or non-intensive insulin regimens is now being incorporated into guidelines.[1,2] However, most people with T2DM are on non-insulin treatment regimens with oral or injectable non-insulin drugs. This consensus report[3] argues, with evidence, that expanding CGM use to this group of people with T2DM will minimize adverse hypoglycemia while allowing for escalation of non-insulin therapy in a timely manner. This can improve the quality of life for people with T2DM, while reducing the risk of acute and long-term complications of diabetes, and reduce the associated costs of hospital admissions.

Current guidelines for treating adults with T2DM[1] emphasize the importance of healthy behaviours regarding diet and lifestyle, and to optimize the outcomes of pharmacological treatment strategies.[4] Pharmacotherapy in T2DM typically starts with non-insulin medications, primarily as oral drugs, including metformin, sodium-glucose cotransporter-2 inhibitors (SGLT2i), dipeptidyl peptidase-4 inhibitors (DPP-4i) or injectable glucagon-like peptide 1 receptor agonists (GLP-1 RA). Using this selection of non-insulin agents, treatment can be intensified in a stepwise fashion to improve glycemia, as measured by a decrease in HbA1c, which can contribute to reducing the risk of microvascular complications and long-term macrovascular disease.[5]

Despite these strategies, the majority of people with T2DM do not achieve recommended HbA1c targets.[1,6] The landmark UK Prospective Diabetes Study (UKPDS) demonstrated that early intensive glycemic control, starting soon after diagnosis of T2DM, is associated with significant reductions in the risk of microvascular disease,[7] along with sustained reductions in risk of myocardial infarction and death from any cause. It is estimated that a one-year delay in treatment intensification for people newly diagnosed with T2DM and HbA1c >7.5% (58 mmol/mol) is associated with a 67% increased risk of myocardial infarction, a 51% increase in risk of stroke and a 64% increased risk of heart failure, compared to those who receive timely treatment intensification.[8] Early glycemic control is therefore critical for long-term prevention of complications for people with T2DM.

We now have considerable evidence that CGM can contribute significantly to optimizing glycemia for people with T1DM, compared to usual care with SMBG. The available evidence now clearly indicates that using CGM in people with T2DM on any insulin therapy can have a comparable impact.[9–11] Outcomes data from three randomized controlled trials (RCTs),[12–14] two of which used the FreeStyle Libre systems, have now demonstrated the glycemic benefits of using CGM technology for people with T2DM on non-insulin treatment. These studies showed significant reductions in HbA1c, increased time in range and reduced glycemic variability for CGM users compared to a control group using SMBG. RCTs are accepted as providing the highest level of evidence in making clinical recommendations. Separately, analysis of commercial health insurance databases in the US has shown that use of the FreeStyle Libre system in 6,298 people with T2DM on non-insulin therapy was associated with a 25% reduced risk of acute diabetes events requiring hospital attendance or admission in the 6 months after starting CGM, compared to the 6 months prior.[15]

These data support the use of CGM systems, such as the FreeStyle Libre 2 flash GM and FreeStyle Libre 3 Continuous GM systems, in management of people with T2DM who are not treated with insulin (**see Table**). Although the data on hospital admissions points to potential cost savings, there is an unmet need for cost-effectiveness analysis on use of CGM technology in people with T2DM on non-insulin therapies. A potential way to further manage costs is to use CGM technology only periodically in people who are not treated with insulin.

Adopting CGM in this way, for people with T2DM, is recommended in the most-recent ADA guidance for technology use in diabetes.[2] Using CGM systems only every 3 months can achieve a significant reduction in HbA1c compared with SMBG alone.[16] These outcomes are encouraging in this context but additional studies are necessary to further develop this proposition. A potential further benefit of periodic CGM assessment for people with T2DM is the opportunity to combine this with periodic HbA1c testing, in order to monitor the variability or stability of HbA1c values, since a coefficient of variation of HbA1c greater than 5% is indicative of an increased risk of microvascular and macrovascular complications of diabetes mellitus.[17] Combining periodic use of CGM with assessment of HbA1c stability for people with suboptimally controlled T2DM (HbA1c >7%) would be an effective check on the need for therapeutic adjustment.

Although the value of CGM in people with established T2DM on non-insulin therapies is clear, a very significant opportunity is presented by the use of CGM technology immediately after diagnosis of T2DM, given the heterogeneous nature of the condition. Adults with newly-diagnosed T2DM may have different disease progression and risk profiles for long-term complications.[18,19] Application of CGM at this critical moment can effectively establish a baseline glycemic profile for each person newly-diagnosed with T2DM, and contribute to the optimization of glycemic control during the period following diagnosis (**see Table**). Subsequent treatment decisions can be compared against these glycemic profiles and T2DM disease progression can be monitored against multiple glycemic measures, thus avoiding delays in therapy intensification. Just as important, this early period after diagnosis of T2DM is a critical

Proposed use of CGM throughout the natural history of T2DM

<table>
<tr><th></th><th>At diagnosis and early disease</th><th>Management of stable disease</th><th>Long duration of disease</th></tr>
<tr><td>All people with T2DM</td><td>• Utilize CGM for 14 days after T2DM diagnosis, to establish a baseline glycometric profile
• Provide education on the glycemic response to diet and exercise in T2DM</td><td>• Predict risk of microvascular complications
• Manage glycemic goals for TIR, TBR, TAR, GV, GMI</td><td rowspan="4">• Facilitate T2DM therapy de-escalation in older and/or frail people with T2DM
• Prevent hypoglycemia
• Reduce risk of cardio-renal complications (e.g. chronic kidney disease)
• Reduce incidence and progression of microvascular disease
• Allow care workers to more effectively manage the care of people with T2DM</td></tr>
<tr><td rowspan="2">People with T2DM on:
• Multiple daily injections
• Basal insulin
• Premixed insulin
• Insulinotropic drugs</td><td colspan="2">Continuous access to CGM for daily use</td></tr>
<tr><td>• Prevent hypoglycemia, manage hyperglycemia and support daily self-management by people with T2DM</td><td>• Prevent hypoglycemia, manage hyperglycemia and support daily self-management by people with T2DM
• Facilitate periods of therapy escalation or de-escalation</td></tr>
<tr><td rowspan="2">People with T2DM on non-insulin therapy</td><td colspan="2">Intermittent use of CGM at least every 3 months, with HCP review</td></tr>
<tr><td></td><td>• Can be combined with a coincident HbA1c test to make decisions on whether to change therapy or not
• Predict changes in risk of microvascular complications
• Education to re-establish the behaviours of good self-management.</td></tr>
</table>

For a full discussion of the elements in this summary table, please refer to Ajjan RA, et al. Continuous glucose monitoring for the routine care of type 2 diabetes mellitus. *Nature Reviews Endocrinology* (2024) doi: 10.1038/s41574-024-00973-1

CGM, continuous glucose monitoring; GV, glycemic variability; TIR, time in range; TAR; time above range; TBR, time below range; T2DM, type 2 diabetes mellitus.

opportunity to use CGM as an educational tool to illustrate, in real time, how glycemia is affected by changes in diet and exercise, and to reinforce initial education on the need for behavioural change. Thereafter, periodic use of CGM technology can assist with timely changes to treatment, to the point at which insulin may be indicated. The FreeStyle Libre system can support earlier treatment escalation and reduce therapeutic inertia in people with T2DM, including non-insulin users. People with T2DM using the FreeStyle Libre system do experience a shorter time to treatment intensification compared with those using SMBG.[20]

This proposed use of CGM technology as soon as possible after diagnosis of T2DM is an evidence-based extension of the learnings from the landmark UKPDS Study, which ran for 20 years and made it clear that early intensive glycemic control, starting soon after diagnosis of T2DM, is associated with significant reductions in the risk of microvascular disease,[7] along with sustained reductions in risk of myocardial infarction and death from any cause. Early glycemic control, using CGM systems such as the FreeStyle Libre 2 flash GM and FreeStyle Libre 3 Continuous GM systems, is therefore critical for long-term prevention of complications for people with T2DM, and to reduce the associated long-term costs of care.

1. Davies MJ, *et al.* Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 2022; doi:10.1007/s00125-022-05787-2.

2. American Diabetes Association Professional Practice Committee. 7. Diabetes Technology: Standards of Care in Diabetes—2024. *Diabetes Care* 2023; 47: S126–S144.

3. Ajjan RA, *et al.* Continuous glucose monitoring for the routine care of type 2 diabetes mellitus. *Nature Reviews Endocrinology* 2024; doi: 10.1038/s41574-024-00973-1.

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11. 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.

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15. Miller E, *et al.* Flash CGM associated with event reduction in nonintensive diabetes therapy. *Am J Managed Care* 2021; 27: e372–e377.

16. Moon SJ, *et al.* Efficacy of intermittent short-term use of a real-time continuous glucose monitoring system in non-insulin–treated patients with type 2 diabetes: A randomized controlled trial. *Diabetes Obes Metab.* 2022; doi:10.1111/dom.14852.

17. Monnier L, *et al.* HbA1c variability and diabetes complications: assessment and implications. *Diabetes Metab.* 2023; doi:10.1016/j.diabet.2022.101399.

18. Hall H, *et al.* Glucotypes reveal new patterns of glucose dysregulation. *Plos Biol* 2018; 16: e2005143 (2018).

19. Nair BG, *et al.* A Pilot Study of the Feasibility and Accuracy of Inpatient Continuous Glucose Monitoring. *Diabetes Care* 2020; 43: e168–e169.

20. Harris S and Levrat-Guillen F. Use of the FreeStyle Libre system and diabetes treatment progression in T2DM: Results from a retrospective cohort study using a Canadian private payer claims database *Diabetes Obes Metab.* 2023: 25:1704-1713.

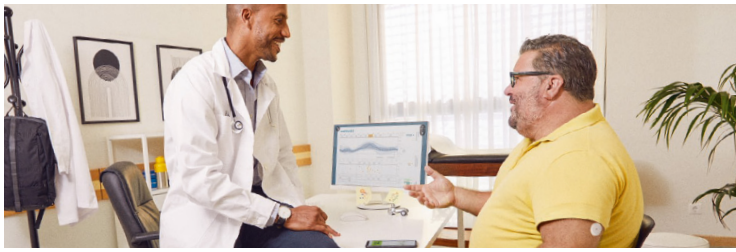

Image for illustrative purposes only. Not real patient or healthcare professional.

In a meta-analysis of RCTs in T2DM, flash glucose monitoring is associated with lower HbA1c and better user satisfaction compared to traditional CGM

The study assessed the outcomes of all available randomized controlled trials (RCTs) that evaluated use of available continuous glucose monitoring (CGM) systems compared with usual care or self-monitoring of blood glucose (SMBG) in individuals with T2DM.

The researchers reviewed 26 RCTs involving 2,783 people with T2DM, comparing usual care with SMBG versus either flash glucose monitoring or traditional CGM devices. Overall, use of traditional CGM sensors in RCTs reduced HbA1c levels by -0.19% (95% confidence interval [CI] -0.34, -0.04) and use of flash glucose monitoring by -0.31% (95% CI -0.46, -0.17).

Notably, use of traditional CGM in RCTs was associated with decreased user satisfaction (-0.54, 95% CI -0.98, -0.11), whereas flash glucose monitoring in RCTs was associated with improved user satisfaction (0.44, 95% CI 0.29, 0.59). Neither device significantly impacted body composition, blood pressure, or lipid levels. Limitations included small sample sizes and variability in populations.

This meta-analysis was centered only on RCT data, but concluded that traditional CGM devices and flash glucose monitoring both reduced HbA1c levels in people with T2DM, whereas only flash glucose monitoring was associated with improved user satisfaction.

Seidu S *et al.* Efficacy and Safety of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring in Patients With Type 2 Diabetes: A Systematic Review and Meta-analysis of Interventional Evidence. *Diabetes Care.* 2024;47(1):169-79. doi:10.2337/dc23-1520.

Scan the QR code below to listen to Professor Sam Seidu's podcast on *The use of CGM in optimizing type 2 diabetes management with non-intensive insulin treatment in the primary care setting*

In this podcast Professor Seidu highlights the considerable potential of using CGM in people with T2DM to transform their diabetes care. It encourages people living with T2DM and healthcare providers to consider CGM technology as an integral part of treatment plans, ultimately improving daily living with T2DM.

https://link.springer.com/article/10.1007/s13300-023-01524-z

Systematic review confirms using CGM versus SMBG is associated with improved glycemic control in adults with T2DM

This systematic review and associated meta-analysis undertook a comprehensive overview of the impact of using continuous glucose monitoring systems on glycemic control in adults with T2DM.

Twelve open-label trials with a total of 1,248 participants investigated use of CGM systems compared with self-monitoring of blood glucose (SMBG) in people with T2DM. Use of CGM systems resulted in a significant reduction in HbA1c: mean difference of –3.43 mmol/mol (–0.31%; 95% CI –4.75, –2.11, p<0.00001); this effect was comparable in studies that included individuals who were using insulin with or without oral agents.

Furthermore, CGM use was associated with a significant increase in time in range (+6.36%; 95% CI 2.48, 10.24, p=0.001) and significant reduction in: time below range (–0.66%; 95% CI –1.21, –0.12, p=0.02), time above range (–5.86%; 95% CI –10.88, –0.84, p=0.02), and glycemic variability (–1.47%; 95% CI –2.94, –0.01). There were no significant differences between CGM and SMBG for the incidence of severe hypoglycemia events or macrovascular complications, although only three studies reported these outcomes.

Overall, this systematic review and meta-analysis further supports the role of using CGM systems versus SMBG to drive reductions in HbA1c and improvements in other parameters of glycemic control in adults with T2DM.

Jancev M, *et al.* Continuous glucose monitoring in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabetologia.* 2024. doi: 10.1007/s00125-024-06107-6. Online ahead of print.

Using the FreeStyle Libre 2 system improves overall glycemic control in people with T2DM on basal insulin or non-insulin therapy

This observational, retrospective, real-world study assessed the efficacy and safety of flash glucose monitoring with the FreeStyle Libre 2 system use in people with T2DM treated with basal insulin or oral antihyperglycemic agents in Italy.

A total of 132 people with T2DM (69.5% men) with a mean age 68.2 years, mean disease duration of 19.0 years, and mean baseline HbA1c of 8.1% were included in the study. The majority of participants (79.7%) were on basal insulin therapy, with the remainder (20.3%) on non-insulin therapies.

Following the introduction of the FreeStyle Libre 2 system, the estimated mean change from baseline in HbA1c was –0.4% at 3 months (p=0.003) and –0.6% after 6 months (p<0.0001), independently from any changes in therapy. The improved glycemia was associated with reductions in hypoglycemia, with significant reductions in time below range (TBR) with glucose 55-70 mg/dL (3.1-3.9 mmol/L) and <55 mg/dL (<3.1 mmol/L) after 6-months (p=0.001 in each case). No episode of severe hypoglycemia was reported throughout the follow-up period.

For this cohort of people with T2DM in Italy, on non-intensive therapies, use of the FreeStyle Libre 2 system was an effective strategy for improving glycemic control, as measured by HbA1c, with reductions in hypoglycemia.

Conti M, *et al.* Effectiveness and safety of the intermittently scanned continuous glucose monitoring system FreeStyle Libre 2 in patients with type 2 diabetes treated with basal insulin or oral antidiabetic drugs: an observational, retrospective real-world study. *J Clin Med.* 2024; 13(3): 642, doi: 10.3390/jcm13030642.

FreeStyle Libre 3 system has greater accuracy than Dexcom G7 in all glycemic ranges for all days of sensor wear

A multicenter, prospective study assessed the accuracy of the FreeStyle Libre 3 system and the Dexcom G7 system against laboratory reference capillary blood glucose samples.

This study included adults ≥18 years with T1DM (n=33) or T2DM (n=23) treated with insulin. All participants wore one FreeStyle Libre 3 sensor for 14 days and one Dexcom G7 sensor for 10 days on the back of the upper arm. Sensors were placed on opposite arms, where possible. Participants also performed at least 8 SMBG tests per day, including on waking, before and after each meal, and before bedtime. Outcome measures were the percentage of sensor-glucose values within ±20 mg/dL of reference glucose values and the mean absolute relative difference (MARD) between sensor glucose values and reference laboratory venous blood values using the YSI analyzer.

Overall accuracy was substantially higher for the FreeStyle Libre 3 sensor, with 91.4% of readings within 20 mg/dL of reference glucose values, compared to only 78.6% for the Dexcom G7 sensor, giving a MARD of 8.9% for the FreeStyle Libre sensor and 13.6% for the Dexcom G7. This superior accuracy was also evident across all glucose ranges, with 88.6% of readings <70 mg/dL (3.9 mmol/L) within ±20 mg/dL of the YSI reference values for the FreeStyle Libre system compared to 65.7% for the Dexcom G7. Concordance within ±20 mg/dL of YSI reference values 70-180 mg/dL (3.9-10.0 mmol/L) was 90.4% for the FreeStyle Libre 3 sensor and 74.4% for Dexcom G7 sensor. Comparisons with capillary glucose reference samples gave an overall MARD of 11.4% for the FreeStyle Libre 3 system versus 18.5% for the Dexcom G7 sensor. Comparative accuracy was also higher for the FreeStyle Libre 3 system on all 10 days that the sensors were worn in parallel.

The greater accuracy of the FreeStyle Libre 3 system, on all days of sensor wear in all glycemic ranges, is important in the context of the many decisions that people with diabetes have to make every day when using a CGM system.

Hanson K, *et al.* Comparison of Point Accuracy Between Two Widely Used Continuous Glucose Monitoring Systems. *J Diabetes Sci Technol.* 2024; Jan 8: doi 10.1177/19322968231225676.

Multicenter study evaluating sensor data from FreeStyle Libre 3 and Dexcom G7 compared to blood plasma glucose under real world conditions. Study limitations: Study subjects followed their daily routines and were not exposed to risks of hyperglycemia or hypoglycemia manipulations, nor was either sensor evaluated for accuracy during times of rapidly changing glucose. Outcome measures: differences in MARD, number and percentage of matched glucose pairs within ±20 mg/dL/±20% of reference values. Results from 55 subjects (minimum required sample size: 42). Registration in clinicaltrials.gov is not required as the study does not meet the definition of ACT (Applicable Clinical Trial). Study funding provided by Abbott.

focus on psychosocial outcomes

FLARE-NL7 confirms use of the FreeStyle Libre system decreases rates of depressive disorders among persons with diabetes

This post-hoc analysis assessed the effects of commencing the FreeStyle Libre flash glucose monitoring system on the mental health of individuals with diabetes, considering the known association between glucose management burden and depressive symptoms.

Data from a 1-year nationwide registry of FreeStyle Libre system users examined participants who had used the system for 12 months and completed the validated Short Form Health Survey version 2 (SF-12v2) questionnaire at baseline, and after 6 and 12 months. An SF-12v2 Mental Component Score (MCS) ≤45 indicated a depressive disorder.

Among 674 patients (mean age 48.2 years; 51.2% men; 78.2% T1DM; mean baseline HbA1c 62.8 mmol/mol), 34.9% had an SF-12 MCS ≤45 at baseline, decreasing to 30.0% after 6 months ($p<0.01$) and 25.7% after 12 months of FreeStyle Libre use ($p<0.01$). Overall, MCS improved from 48.5 at baseline to 50.7 after 6 months and 51.3 after 12 months of FreeStyle Libre system use. Age and baseline MCS were associated with 12-month MCS improvement in multivariable regression analysis.

These outcomes make a clear connection between flash glucose monitoring with the FreeStyle Libre system and improved symptoms of depression.

Bakker JJ *et al*. Commencement of flash glucose monitoring is associated with a decreased rate of depressive disorders among persons with diabetes (FLARE-NL7). *BMJ Open Diabetes Res Care* 2022; 10(3):e002769. doi:10.1136/bmj drc-2022-002769.

Image for illustrative purposes only. Not real patient.

CGM use in adolescents with T1DM is associated with lower HbA1c and reduced diabetes distress

Using data from a multi-site RCT, collected between 2019 and 2022 in the US, this study examined the association of continuous glucose monitoring (CGM) use with HbA1c and a range of psychosocial aspects of living with T1DM in adolescents experiencing moderate to severe diabetes distress.

A total of 198 participants were included, 81% of which were 'current CGM users', 10% were 'past users', and 9% were 'never users'. Using analysis of variance (ANOVA), the study showed significant differences in HbA1c were reported between user groups ($p=0.04$), with post-hoc analyses showing that this difference was due to significantly lower HbA1c in 'current users' versus 'never users' ($p=0.02$). 'Current users,' also demonstrated significantly lower distress, as assessed by the Problem Areas in Diabetes-Teen (PAID-T) scale, compared with 'past users' ($p=0.04$).

The authors concluded that CGM use was associated with lower HbA1c and diabetes distress in adolescents with T1DM but not with improvements in other quality of life outcomes in this group, and postulated that longitudinal data on specific barriers might explain the latter findings, including the use of so-called 'follow' apps that allowed parental access to the data of adolescents with T1DM, who may not appreciate this aspect of CGM functionality.

Straton E, *et al*. Glycemic and psychosocial correlates of continuous glucose monitor use among adolescents with type 1 diabetes. *J Diabetes Sci Technol*. 2023; doi: 10.1177/19322968231186428. Online ahead of print.

Use of the FreeStyle Libre system further improves HbA1c in adults with T2DM receiving GLP-1 RA therapy

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and CGM sensors both improve glycemia for people with T2DM. A number of studies presented at the 17th International Conference on Advanced Technologies and Treatments for Diabetes (ATTD) in 2024 assessed whether using CGM in conjunction with GLP-1 therapy for people with T2DM could further improve HbA1c.

This real-world study used a database of linked electronic health records (EHR) and insurance claims from providers in the US. The analysis was focused on adults with T2DM and suboptimally-controlled glycemia, with HbA1c ≥8%. Changes in glycemic control for 478 adults with T2DM who initiated a flash glucose monitoring system within 30 days of starting GLP-1 RA therapy were compared to a group of 2,390 adults, matched for age, sex, baseline HbA1c and insulin therapy, who initiated GLP-1 RA treatment in the absence of the FreeStyle Libre system.[1]

The group who initiated GLP-1 RA and FreeStyle Libre system together had a significantly greater reduction in HbA1c after 6 months compared to the matched group who initiated GLP-1 RA only (-2.43% vs -2.06%, p<0.001). This differential in 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% at 6 months (62.1% vs. 55.6%, p=0.01).

A second investigation examined whether initiating the FreeStyle Libre system for adults already established on GLP-1 RA therapy and with HbA1c ≥8% could improve glycemic control.[2] In this before-and-after analysis, paired changes in HbA1c were assessed 6 months after starting the FreeStyle Libre system. After acquisiton of the FreeStyle Libre system a group of 1,781 adults with T2DM on GLP-1 RA therapy recorded an HbA1c decrease of -1.5%, p<0.001. Significant improvements were observed in those using bolus insulin (-1.3%) and those who did not (-1.6%).

Using a Determination of Diabetes Utilities Costs and Effects (DEDUCE) model, the cost-effectiveness of using GLP-1 RA therapy in conjunction with the FreeStyle Libre system in T2DM was compared to using GLP-1 RA treatment alone in a third study, from a US taxpayer perspective and using available US real-world evidence.[3] In the base-case analysis, using GLP-1 RA therapy in conjunction with the FreeStyle Libre system was cost effective compared to GLP-1 RA treatment alone, with an incremental cost-effectiveness ratio (ICER) of $78,550, which is well below the US willingness-to-pay threshold of $100,000 per quality-adjusted life-year (QALY). Results were similar for adults with T2DM on insulin therapy or on non-insulin therapies.

Together, these real-world retrospective studies show that using the FreeStyle Libre system together with GLP-1 RA therapy in people with T2DM, who have suboptimal glycemic control, is more-effective in reducing HbA1c than using GLP-1 RA in the absence of the FreeStyle Libre system. This conclusion is clear, whether GLP-1 RA and FreeStyle Libre are initiated at the same time, or if the FreeStyle Libre system is added to therapy at a later timepoint. Importantly, from a US payer perspective, the combined use is cost-effective over a lifetime treatment horizon, compared to GLP-1 RA therapy alone.

1. Wright E, *et al.* Initiating GLP-1 therapy in combination with Freestyle Libre provides greater benefit compared to GLP-1 therapy alone. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #1314.

2. Miller E, *et al.* FreeStyle Libre improves HbA1c in people receiving GLP-1 therapy for type 2 diabetes. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #1311.

3. Wright E, *et al.* Using FreeStyle Libre CGM with GLP-1 treatment is a cost-effective combination for people living with type 2 diabetes. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #1249.

Switching to flash glucose monitoring from traditional CGM can reduce HbA1c in people with T1DM

This retrospective analysis of adults with T1DM used the Swedish National Diabetes Register (NDR) to investigate the impact of switching from traditional real-time CGM devices to the FreeStyle Libre system on changes in HbA1c.

The study identified 773 adults aged ≥18 yrs with T1DM in the Swedish NDR (50.3% female; mean age 40.7 yrs; baseline HbA1c 8.0% [64 ± 14 mmol/mol]), who had an index date for FreeStyle Libre system reimbursement after 01/06/2017, and had previously used traditional CGM devices. HbA1c values recorded 3-8 months before the FreeStyle Libre index date were compared to HbA1c at 6, 12 and 24 months after switching.

Mean change in HbA1c after switching to the FreeStyle Libre system was -0.18% (-1.97 mmol/mol) at 6 months, -0.15% (-1.64 mmol/mol) at 12 months, and -0.28% (-3.06 mmol/mol) at 24 months (p<0.0001 at all time-points). Reductions in HbA1c were greatest for 454 individuals with suboptimal HbA1c >7.5% (>58 mmol/mol) following the switch, falling by -0.41% (-4.44 mmol/mol) at 6 months and by -0.41% (-4.52 mmol/mol) at 12 months, and by -0.52% (-5.63 mmol/mol) after 24 months. Switching to the FreeStyle Libre system did not result in reductions in HbA1c for individuals with baseline HbA1c <7.5% (<58 mmol/mol).

This real-world study indicates that, for adults with T1DM and suboptimal HbA1c control, significant reductions in HbA1c may be achieved when traditional CGM is replaced with the FreeStyle Libre system.

Bolinder J, *et al.* Glucose control in people with type 1 diabetes in Sweden after switching from real-time CGM to intermittently-scanned CGM. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #73.

Frequency of scanning the FreeStyle Libre sensor is better associated with improved time in range than insulin bolus frequency

Understanding the real-world frequency of insulin-bolus dosing for people with T1DM is possible using data from insulin smartpens, but has not been reported on a large scale. This study examined the smartpen-recorded insulin bolus frequency by FreeStyle LibreLink app* users in Europe and how it relates to their glucose control.

Sensor glucose and integrated insulin smartpen data were aggregated for users of the LibreView system^ between March and June 2023. Users' most-recent FreeStyle Libre sensor with glucose readings and rapid-acting insulin doses logged on at least 10 wear days were analyzed. A total of 277,197 boluses, spanning 152.2 patient years of data (13.6 average days/user), were analyzed for 4,082 FreeStyle LibreLink users.

Users were stratified both by average daily scan frequency (<8 scans, 8-15 scans or >15 scans per day) and average daily insulin bolus frequency (<3 boluses, 3-7 boluses or >7 boluses per day). Mean time in range (TIR) 70-180 mg/dL (3.9-10.0 mmol/L) per day was analyzed for the stratified scanning and bolus segments (**see Table**).

When daily sensor scanning and insulin bolus events are compared, improvements in daily TIR were greater as daily scan frequency increased compared with increased daily insulin-bolus frequency. This suggests that glucose monitoring behaviour is more predictive of overall glucose control than insulin dosing behaviour.

*FreeStyle LibreLink works with FreeStyle Libre or FreeStyle Libre 2 sensors and is only compatible with NovoPen® 6 and NovoPen Echo® Plus. 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. Sharing of glucose data requires registration with LibreView.

^The LibreView website is only compatible with certain operating systems and browsers.

Please check www.libreview.com for additional information.

Image for illustrative purposes only. Not real patient.

Mean TIR for defined bolus and scanning frequencies

	Daily scan frequency		
Daily bolus frequency	**<8 Scans/day**	**8-15 Scans/day**	**>15 Scans/day**
<3 Boluses/day	**45.9%**	**59.6%**	**69.8%**
3-7 Boluses/day	**47.9%**	**57.6%**	**68.6%**
>7 Boluses/day	**49.6%**	**58.6%**	**67.9%**

Choudhary P, *et al.* Contributions of scan frequency and bolus frequency to time in range; Data from CGM and connected pens. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #733.

Hospital admissions and emergency department visits are reduced for people with T2DM on insulin therapy after starting to use CGM

The association between initiating continuous glucose monitoring (CGM) and the prevalence of hospital admissions and emergency department visits for adults with T2DM on any insulin therapy was examined in a real-world setting in the United States.

This retrospective before-and-after study used a healthcare claims database Medicaid beneficiaries (aged <65 years) with T2DM, either on multiple daily injections (MDI) with insulin (n=35,367) or on basal insulin (n=9,574). Claims for hospital admission or emergency attendance were analyzed for at-least 6 months before and after initiation of CGM in the period from January 2017 and September 2022.

For people with T2DM on MDI, significant reductions were observed in the mean number of hospital admissions (0.70 vs. 0.50), emergency department visits (1.33 vs. 1.10) and outpatient visits (10.96 vs. 10.20) in the 6 months following CGM acquisition (p<0.001 in each case), compared to the 6 month period prior. Subgroup analyses showed that people with T2DM on MDI who had a high frequency of hospital attendance (≥3 visits in 6 months) had the greatest decrease in hospital admission (-58%, p<0.001) or emergency care (-43%, p<0.001).

Medicaid recipients with T2DM on basal-insulin therapy also had a significant reduction in hospital admissions (0.37 vs. 0.31), emergency department visits (9.11 vs. 8.60) in the 6 months following CGM acquisition (p<0.001 in both cases), compared to the 6 month period prior. As with the cohort with T2DM on MDI, those treated with basal insulin who had a high frequency of hospital attendance (≥3 visits in 6 months) had the greatest decrease in hospital admission (-68%, p<0.001) or emergency care (-44%, p<0.001).

These studies highlight the association between starting CGM and reduced hospital attendance or admission for people with T2DM on any insulin therapy, which emphasizes the need for a shift towards proactive outpatient care that may translate into real-world cost savings.

Hirsch IB, *et al.* Impact of continuous glucose monitoring on healthcare resource utilization among Medicaid beneficiaries with type 2 diabetes treated with multiple daily injection therapy: real-world insights from the US. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #789.

Hirsch IB, *et al.* Impact of continuous glucose monitoring on healthcare resource utilization among Medicaid beneficiaries with type 2 diabetes treated with basal insulin. Advanced Technologies and treatments for diabetes (ATTD) 17th international congress 2024. Poster #633.

Understanding GMI and HbA1c: measures of average glucose

Laboratory measured glycated hemoglobin A1c (HbA1c) has been the gold standard for assessing glycemic control in people with T1DM or T2DM. The HbA1c assay is a convenient assessment of average blood-glucose levels over the previous 2-4 months and is correlated with risk of diabetes-related complications, such as retinopathy, chronic kidney disease, clinical neuropathy, as well as myocardial infarction and risk of death from any diabetes-related cause. However, widespread use of CGM technology has confirmed the limitations of HbA1c as a marker of glycemic control for people with diabetes **(see Box right).**

Although HbA1c is perceived to reflect the weighted average of blood-glucose levels during the lifetime of red blood cells (RBCs) in a person with diabetes, only 19% of measured HbA1c values will be within ±0.1% (±1.2 mmol/mol) of what is predicted, based on CGM-measured average glucose.

The development and use of the glucose management indicator (GMI)

The need for consistent measure of short-term glucose control based on CGM-derived data led to the establishment of the glucose management indicator (GMI), a metric that could be compared against long-term HbA1c but without implying that the two measures should be identical in value. GMI is a measure of average glucose, but is based on a calculation derived from a regression analysis of mean glucose and contemporaneously measured HbA1c using data from 4 randomized controlled trials, each of which exclusively used CGM data from people with T1DM or T2DM. GMI uses the same scale (% or mmol/mol) as HbA1c, but is based on short-term average glucose values, rather than long-term glucose exposure. HbA1c and GMI values differ in up to 81% of individuals by more than ±0.1% (and by more than ±0.3% in 51% of cases).

Clinical implications of using GMI and HbA1c readings together

Since GMI can be expected to be noticeably different from laboratory HbA1c, individuals with identical HbA1c levels may have different levels of hypoglycemia risk based on their GMI values. Those with lower GMI levels (i.e., with lower average glucose) would be at greater risk for hypoglycemia than those with higher GMI levels. This difference is an important factor to take into account when setting HbA1c goals and intensifying therapy, as detailed below:

- If HbA1c is consistently higher than GMI, HbA1c itself should not be a factor in intensifying therapy, especially for people at increased risk of hypoglycemia.
- When GMI is higher than HbA1c, more-intensive glucose control may be targeted based on the HbA1c reading, with less risk of adverse hypoglycemia.
- Always review other CGM-derived components of the AGP alongside GMI, such as % time in range, % time below range and % coefficient of variation.

Limitations of HbA1c as a measure of glucose control

- Does not measure glucose levels directly and neglects other influencing factors.
- HbA1c levels can only reflect changes in average glucose levels over three months.
- Conveys no information about short-term glycemic control, hypoglycemia or glycemic variability.
- Older age, comorbid disease and ethnic and racial differences, can also influence glycation rates.

Physiological factors that influence HbA1c values

- Glycation rates can vary significantly between individuals and between different ethnic and racial populations, even if glucose levels are the same.
- The average production rate and half-life of RBCs can vary significantly between individuals.
- Hemoglobinopathies, chronic kidney disease, cirrhosis and other conditions can all modify HbA1c, independently of glucose levels.

HbA1c can vary widely between people with diabetes and the same average glucose levels

HbA1c	**6.9%** (51.8 mmol/mol)	**5.9%** (33.4 mmol/mol)	**6.5%** (49.4 mmol/mol)	**7.8%** (55.2 mmol/mol)
GMI	**6.9%** (51.8 mmol/mol)	**6.9%** (51.8 mmol/mol)	**6.9%** (51.8 mmol/mol)	**6.9%** (51.8 mmol/mol)
Average glucose	**150 mg/dL** (8.3 mmol/mol)	**150 mg/dL** (8.3 mmol/mol)	**150 mg/dL** (8.3 mmol/mol)	**150 mg/dL** (8.3 mmol/mol)

Each column indicates how HbA1c can vary for a person with diabetes despite identical CGM-detected GMI and average glucose values.

Gomez-Peralta F, *et al.* Understanding the clinical implications of differences between glucose management indicator and glycated haemoglobin. *Diabetes Obes Metab.* 2022; 24:599-608.