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DIABETIC Medicine

REVIEW

Continuous glucose monitoring: A review of the evidence in type 1 and 2 diabetes mellitus

Rose Lin[1,2] | **Fran Brown**[3] | **Steven James**[4] | **Jessica Jones**[2,5] | **Elif Ekinci**[1,2,5]

[1]Department of Endocrinology, Austin Health, Heidelberg, Vic., Australia

[2]Department of Medicine, Austin Health, Heidelberg, Vic., Australia

[3]Melbourne Diabetes Education and Support, Heidelberg Heights, Vic., Australia

[4]School of Nursing, Midwifery and Paramedicine, University of the Sunshine Coast, Petrie, Qld, Australia

[5]Melbourne Medical School, University of Melbourne (Austin Campus), Melbourne, Vic., Australia

Correspondence
Elif Ekinci, Department of Medicine, Austin Health, The University of Melbourne, Level 1 Centaur Building Repatriation Campus, Heidelberg, Australia.
Email: elif.ekinci@unimelb.edu.au

Abstract

Context and Aim: Continuous glucose monitoring (CGM) is becoming widely accepted as an adjunct to diabetes management. Compared to standard care, CGM can provide detailed information about glycaemic variability in an internationally standardised ambulatory glucose profile, enabling more informed user and clinician decision making. We aimed to review the evidence, user experience and cost-effectiveness of CGM.

Methods: A literature search was conducted by combining subject headings 'CGM' and 'flash glucose monitoring', with key words 'type 1 diabetes' and 'type 2 diabetes', limited to '1999 to current'. Further evidence was obtained from relevant references of retrieved articles.

Results: There is a strong evidence for CGM use in people with type 1 diabetes, with benefits of reduced glycated haemoglobin and hypoglycaemia, and increased time in range. While the evidence for CGM use in type 2 diabetes is less robust, similar benefits have been demonstrated. CGM can improve diabetes-related satisfaction in people with diabetes (PWD) and parents of children with diabetes, as well as the clinician experience. However, CGM does have limitations including cost, accuracy and perceived inconvenience. Cost-effectiveness analyses have indicated that CGM is a cost-effective adjunct to type 1 diabetes management that is associated with reduced diabetes-related complications and hospitalisation.

Conclusions: Continuous glucose monitoring is revolutionising diabetes management. It is a cost-effective adjunct to diabetes management that has the potential to improve glycaemic outcomes and quality of life in PWD, especially type 1 diabetes.

KEYWORDS

blood glucose self-monitoring, health technology, type 1 diabetes, type 2 diabetes

Abbreviations: DCCT, Diabetes Control and Complications Trial; GOLD, glycaemic control and optimisation of life quality in type 1 diabetes; DIAMOND, multiple daily injections and continuous glucose monitoring in diabetes; SWITCH, sensing with insulin pump therapy to control HbA_{1c}; JDRF, Juvenile Diabetes Research Foundation; CITY, CGM intervention in teens and young adults with type 1 diabetes; WISDM, wireless innovation for seniors with diabetes mellitus; HypoDE, real-time continuous glucose monitoring in patients with type 1 diabetes at high risk for low glucose values using multiple daily injections in Germany; IN CONTROL, continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia; IMPACT, novel glucose-sending technology and hypoglycaemia in type 1 diabetes; SELFY, FreeStyle libre glucose monitoring system paediatric study; REPLACE, an evaluation of a novel glucose sensing technology in type 2 diabetes; GP-OSMOTIC, general practice optimising structured monitoring to improve clinical outcomes in type 2 diabetes.

1 | INTRODUCTION

It has been three decades since the landmark Diabetes Control and Complications Trial trial demonstrated the importance of glycaemic management in the prevention or delay of microvascular complications.[1] HbA_{1c} has long been the gold standard for assessing long-term glycaemic management.[2] However, HbA_{1c} does not provide information about glucose trends and excursions; individuals with the same HbA_{1c} can have significantly different diurnal glucose variation.[3] Therefore, self-monitoring of blood glucose (SMBG) is also recommended in select individuals, such as those receiving insulin therapy.[2] Structured SMBG can distinguish between fasting and post-prandial hyperglycaemia, uncover glycaemic variability, and allow people with diabetes (PWD) to intervene promptly to minimise dysglycaemia.[3,4] In individuals receiving insulin, international guidelines recommend SMBG several times per day (e.g. before meals, at bedtime, before exercise, when hypoglycaemia is suspected),[2,5,6] although factors including pain, cost, inconvenience and fear of needles often lead to non-adherence. It has been estimated that only 44% of people with type 1 diabetes mellitus and 24% of people with type 2 diabetes mellitus routinely perform SMBG as per guidelines.[7]

Continuous glucose monitoring (CGM) is a minimally invasive modality of monitoring glucose levels. Unlike SMBG, which provides discrete snapshots of glucose levels, CGM records glucose levels continuously.[8] Despite first becoming available in 1999, CGM use has only really increased during recent years, due to wider availability, evidence and subsidised funding.[9-11] For example, recognising the increasing demand for CGM in PWD, the Australian Government recently announced an AUD$300 million CGM initiative. Since 1 March 2020, eligible Australians have been able to receive fully subsidised CGM products.[12] Global CGM usage is expected to further increase, with recent international guidelines recommending that CGM be considered in all children and adolescents with type 1 diabetes mellitus.[5]

This review aims to review the literature on CGM in terms of efficacy, user experience and cost-effectiveness. Medline and Embase searches were conducted by combining subject headings 'CGM' and 'flash glucose monitoring (FGM)', with key words 'type 1 diabetes' and 'type 2 diabetes', limited to '1999 to current'. Clinical trials and systematic reviews describing CGM use in type 1 diabetes mellitus and type 2 diabetes mellitus were included. Articles describing CGM use in gestational diabetes, use of CGM as a tool for assessing other diabetes interventions or comparing CGM with interventions other than standard care were excluded. Further evidence was obtained from relevant references of retrieved articles.

What is new?

What is already known?

- Currently, standard practice in diabetes management involves self-monitoring of blood glucose and measurement of glycated haemoglobin.

What has this study found?

- Continuous glucose monitoring can offer added benefits to standard care, especially in type 1 diabetes, including improvements in:
  a. Glycaemic management;
  b. Quality of life in people with diabetes and parents of children with diabetes and
  c. Clinician experience.

What are the clinical implications of this study?

- Continuous glucose monitoring is a clinically effective and cost-effective adjunct to diabetes management, and may improve diabetes outcomes.

2 | WHAT IS CGM?

Continuous glucose monitoring allows continuous monitoring of glucose levels via a tiny electrochemical sensor electrode inserted under the skin.[8] The sensor is connected to a transmitter, which sends this information to a detector, such as a smartphone, or a continuous subcutaneous insulin infusion (CSII) device. CGM devices are of two types: traditional CGM and FGM, also known as intermittently scanned CGM. Both systems provide information about current and previous glucose levels, glucose trends and anticipated future glycaemic status.[13] A main difference is that CGM passively transmits this information continuously to the reader without user engagement, whereas FGM only provides this information when the user scans the sensor.[14] A summary of available CGM devices is provided in Table 1.

2.1 | Traditional CGM

Continuous glucose monitoring can be further categorised into personal or 'real-time' use, and professional or 'retrospective' use.[15] Personal CGM allows PWD to access continuous glucose data and intervene as required in real time, whereas with the less commonly used professional CGM the data are blinded to PWD and only accessible retrospectively by clinicians. Some personal CGM devices, such as the Dexcom G5™ Mobile, Dexcom G6™ Mobile and Medtronic Guardian™ Connect, allow remote monitoring, where up to five individuals are able to view CGM readings and receive alerts in real time.[10,16] Most transcutaneous sensors have a wear life of 7–10 days. An alternative is

TABLE 1 List of continuous glucose monitoring devices available

	Accuracy (MARD %)	Sensor life (Days)	Calibrations required (times/day)	Attachment site	Alert capability	How CGM is used	Smart phone compatibility	Insulin pump compatibility	Automated Insulin Adjustment	Approved for insulin dosing
Continuous glucose monitoring										
Real time										
Dexcom G4 Platinum™	9	7	2	Abdomen	Yes	Standalone or insulin pump	No	Animas Vibe	No	No
Dexcom G5 Mobile™	9	7	2	Abdomen	Yes	Standalone or insulin pump	Yes	Tandem T-Slim X2™	No	Yes
Dexcom G6™	9.3	10	None	Arm[b] or Abdomen	Yes	Standalone or insulin pump	Yes	Tandem T-Slim X2™, Diabeloop™ DBLG1	Yes	Yes
Medtronic Enlite™ sensor and Guardian™ Link 2 transmitter	11	6	2	Abdomen	Yes	Insulin pump	No	MiniMed™ 640G	Yes	No
Medtronic Enlite™ Sensor and MiniLink™ Transmitter	14	6	2	Abdomen	Yes	Insulin pump	No	MiniMed™ Veo	No	No
Medtronic Guardian™ Sensor 3 and Guardian™ Connect transmitter	9.4	7	2	Arm or abdomen	Yes	Standalone	Yes	No	-	No
Medtronic Guardian™ Sensor 3 and Guardian™ Link 3 transmitter	9.6	7	3–4	Arm or Abdomen[c]	No	Insulin pump	No	MiniMed™ 630G, MiniMed™ 640G, MiniMed™ 670G, MiniMad™ 770G, MiniMed™ 780G[d]	Yes	No
Senseonics Eversense™	8.5	90–180[a]	2	Arm	Yes	Standalone	Yes	No	-	Yes
Retrospective										
Medtronic Enlite™ Sensor and iPro2™ Recorder	11	6	2	Abdomen	N/A	N/A	No	N/A	N/A	N/A
Flash glucose monitoring										
Real time										
Abbott™ FreeStyle Libre	9.3	14	None	Arm	No	Standalone or insulin pump	Yes	Omnipod Horizon™	Yes	Yes
Abbott™ FreeStyle Libre 2	9.3	14	None	Arm	Yes	Standalone or insulin pump	Yes[e]	Omnipod Horizon™	Yes	Yes

(Continues)

TABLE 1 (Continued)

	Accuracy (MARD %)	Sensor life (Days)	Calibrations required (times/day)	Attachment site	Alert capability	How CGM is used	Smart phone compatibility	Insulin pump compatibility	Automated Insulin Adjustment	Approved for insulin dosing
Retrospective										
Abbott™ FreeStyle Libre Pro	12.3	14	None	Arm	N/A	N/A	No	N/A	N/A	N/A

Abbreviations: FDA, Food and Drug Administration; MARD, mean absolute relative difference.

[a]Implantable sensor approved for 3 months use in America, and 6 months use in Europe.

[b]Upper arm approved for use in Europe only, not approved by the FDA.

[c]Abdomen only if used with MiniMed™ 670G.

[d]Smartguard feature which automatically gives insulin boluses and adjusts basal insulin rate, CE approved for use in Europe only.

[e]Designed for use with the FreeStyle Libre 2 app, which is currently under FDA review.

Eversense™, an implantable real-time CGM device which is approved for up to 6 months use in Europe and 3 months use in America.[10]

Continuous glucose monitoring devices measure interstitial glucose levels. Although generally comparable, blood and interstitial glucose readings can differ by 10%–20%.[8] To maintain accuracy of readings, older CGM devices require calibration multiple times per day. Calibration is not required with newer devices such as Dexcom G6™, unless the difference between CGM readings and blood sugar levels (BSL) is consistently >20%.[17] SMBG is also recommended before treating hypo- or hyperglycaemia.[15] Studies have shown that using CGM to guide insulin dosing without confirmatory SMBG is safe,[18] although currently only Dexcom G5™ Mobile and Dexcom G6™ are approved for insulin dosing by the Therapeutic Goods Administration (TGA) and Food and Drug Administration (FDA).[5,19] Eversense™ is also FDA approved for insulin dosing.[20] CGM devices can also provide alarms during times of actual or impending dysglycaemia, which can be particularly useful in PWD prone to hypoglycaemia, and those with hypoglycaemia unawareness.[11]

Most CGM devices are compatible with CSII pumps. Some devices can also lead to alteration of insulin administration. The Medtronic Guardian™ 2 Link system (Enlite™ sensor, Guardian™ Link 2 transmitter and MiniMed™ 640G pump) can suspend insulin delivery either when glucose levels reach a pre-specified low-glucose threshold, or when glucose trends predict hypoglycaemia beyond the threshold within the next 30 min.[21] The Medtronic MiniMed™ 670G system (Guardian™ Sensor 3, Guardian™ Link 3 transmitter and MiniMed™ 670G pump) utilises hybrid closed-loop technology to automatically increase, decrease or suspend insulin delivery to maintain a target glucose level of 6.7 mmol/L.[21] Real-world data indicate this technology results in increased time in range (TIR), reduced hypoglycaemia and increased user quality of life (QOL).[10,22]

2.2 | Flash glucose monitoring

Flash glucose monitoring is a relatively newer CGM technology, first becoming available in 2016. In contrast to traditional CGM, FGM information is only available when the user accesses it. PWD can flash a reader over the sensor to obtain glucose information including current glucose level (within the last minute), glucose trend and results from the past 8 h or up to the last scan, if scanned <8 h ago.[3] To maintain adequate data collection, PWD must scan the sensor at least every 8 h, otherwise data will be lost and the report will show data gaps.[13] The FreeStyle™ Libre Pro is a retrospective FGM device, which does not require any action by the user, including sensor scanning. The data provided for

retrospective analysis are similar to that provided by traditional CGM.

FGM is pre-calibrated in the factory, requiring no further calibration throughout use.[23] One FGM device is approved by the TGA, the FreeStyle™ Libre. The FreeStyle™ Libre 2 is currently approved for use in America and Europe.[24] Both devices are FDA approved for insulin dosing without SMBG.[21,25] The only situations where SMBG is recommended to make therapeutic decisions when using FGM include the following: when symptoms do not match the glucose level detected, hypoglycaemia needs to be confirmed and when glucose levels are changing rapidly.[13]

The FreeStyle Libre™ does not provide alarms.[3] The FreeStyle Libre™ 2 offers optional customisable alarms for hypo- and hyperglycaemia.[26] In contrast to traditional CGM which alarm every minute if dysglycaemia is sustained, the FreeStyle Libre™ 2 does not alarm again once the alarm is confirmed, until the system resets when euglycaemia is re-established. FGM may be more suited to PWD who find alarms intrusive, people who do not perform SMBG often and people who are unable or unwilling to perform regular SMBG for calibration. FGM is also cheaper than CGM, probably related to a longer wear life of 14 days.[14]

3 | AMBULATORY GLUCOSE PROFILE

Traditionally, different CGM devices have required use of unique software to report glycaemic control, rendering analysis and interpretation time-consuming and difficult. Nowadays, an internationally standardised report, called the ambulatory glucose profile (AGP), is commonly utilised (Figure 1). The AGP is a single-page report with statistical and graphic information organised into five major components: (1) data completeness captured by sensor; (2) glucose level statistics (e.g. hypoglycaemia, TIR); (3) glucose profile based on a 'model day' (also called the AGP); (4) glucose management indicator and (5) daily glucose profiles.[13,27,28] CGM data can be provided from the previous 5 days to 3 months. Data are collated to produce a glucose profile as if all the readings had occurred in a single 24-h period (the 'model day').[13] The AGP enables retrospective analysis of CGM data, allowing PWD and clinicians to characterise diurnal glucose patterns to inform management.[11,29]

International guidelines have been developed to aid interpretation of the AGP. The primary goal of diabetes management is to increase TIR while reducing hypoglycaemia.[5,11] Increased TIR is associated with slowed progression of complications such as diabetic retinopathy[30,31] and microalbuminuria,[31] and reductions in HbA_{1c}.[32] For individuals with type 1 diabetes mellitus and type 2 diabetes mellitus, targets of >70% TIR and <4% hypoglycaemia are recommended.[11] Guidelines also recommend a glycaemic variability target (% coefficient of variation [CV]) of ≤36%,[11] although studies have shown that a lower %CV target of <33% provides additional protection against hypoglycaemia for PWD on insulin or sulphonylureas.[33] The AGP facilitates easy identification of these parameters, allowing safe and effective glucose management.

There are several practical challenges associated with the AGP. Healthcare practices must be equipped with adequate technology systems, and be able to link these systems to the appropriate software at the time of the consultation to access CGM data.[27] Furthermore, data need to be near-complete to allow accurate interpretation. The timing of activities such as meals and exercise may vary between days, and glucose variability between days may be diluted in summary data, which combined with the time constraints in clinical settings, can make interpretation challenging.[28] However, with apt education on AGP interpretation, clinicians are able to make informed treatment decisions to improve diabetes management.[34]

4 | EVIDENCE FOR CGM

Recently, there has been an increasing number of trials demonstrating the efficacy of CGM and FGM in improving diabetes-related outcomes. Notably, many have demonstrated an HbA_{1c} reduction, increased TIR (3.9–10.0 mmol/L) and reduced hypoglycaemia (<3.9 mmol/L). Currently, the majority of the evidence supports CGM and FGM use in type 1 diabetes mellitus. Findings involving people with type 2 diabetes mellitus on insulin are also available in the literature, whereas studies involving people on oral hypoglycaemics are scarce. Tables 2 and 3 contain summaries of randomised controlled trials (RCTs) on CGM and FGM.

Maiorino et al conducted a meta-analysis of RCTs assessing the efficacy of CGM or FGM in people with type 1 diabetes mellitus or type 2 diabetes mellitus. They found an overall weighted mean reduction in HbA_{1c} of 2 mmol/mol (0.2%; $p = 0.003$), and an overall increase in TIR of 70.74 min/day (95% CI 46.73–94.76; $p < 0.001$) (S3). Time in level 1 hypoglycaemia (3.0–3.9 mmol/L) reduced by 27.16 min/day (95% CI −42.08 to −12.25; $p < 0.001$), whereas time in level 2 hypoglycaemia (<3.0 mmol/L) reduced by 13.58 min/day (95% CI −20.63 to −6.53; $p < 0.001$) (S3).

4.1 | Traditional CGM

4.1.1 | Type 1 diabetes

Glycated haemoglobin

There is a strong evidence for CGM use in people with type 1 diabetes mellitus. RCTs including the GOLD, DIAMOND, SWITCH, CITY and WISDM studies all reported significant

MRN: _____ PAGE: 1 / 1
DEVICE: FreeStyle Libre GENERATED: 04/05/2020

AGP Report

21 April 2020 - 4 May 2020 (14 Days)

LibreView

GLUCOSE STATISTICS AND TARGETS

21 April 2020 - 4 May 2020	14 Days
① % Time CGM is Active	75%

② Ranges And Targets For	Type 1 or Type 2 Diabetes
Glucose Ranges	**Targets** % of Readings (Time/Day)
Target Range 3.9-10.0 mmol/L	Greater than 70% (16h 48min)
Below 3.9 mmol/L	Less than 4% (58min)
Below 3.0 mmol/L	Less than 1% (14min)
Above 10.0 mmol/L	Less than 25% (6h)
Above 13.9 mmol/L	Less than 5% (1h 12min)
Each 5% increase in time in range (3.9-10.0 mmol/L) is clinically beneficial.	

Average Glucose	11.2 mmol/L
④ Glucose Management Indicator (GMI)	8.1% or 65 mmol/mol
Glucose Variability	38.4%

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

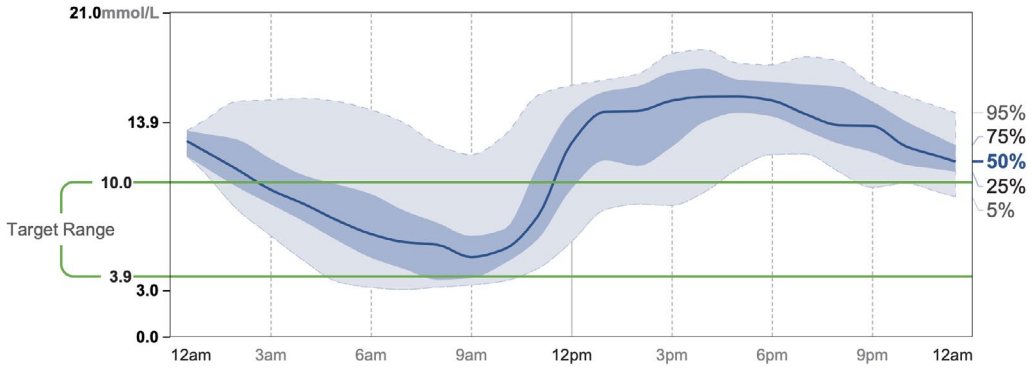
TIME IN RANGES

② 13.9 10.0 3.9 3.0

Very High	>13.9 mmol/L	35%	(8h 24min)
High	10.1 - 13.9 mmol/L	26%	(6h 14min)
Target Range	3.9 - 10.0 mmol/L	34%	(8h 10min)
Low	3.0 - 3.8 mmol/L	5%	(1h 12min)
Very Low	<3.0 mmol/L	0%	(0min)

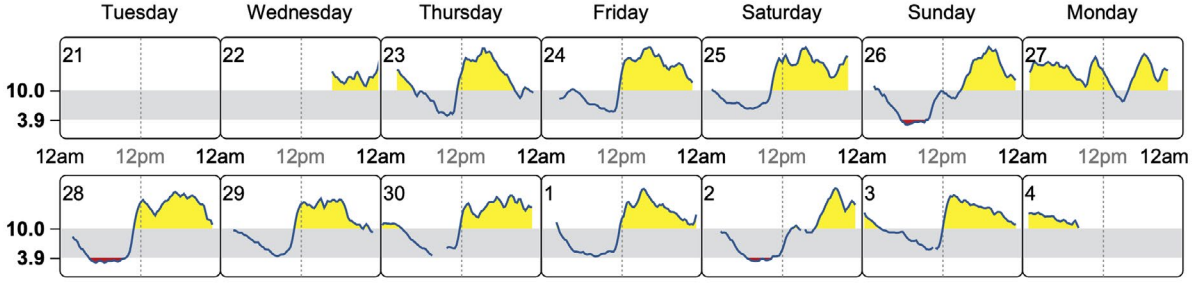
③ AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



⑤ DAILY GLUCOSE PROFILES

Each daily profile represents a midnight to midnight period with the date displayed in the upper left corner.



Source: Battelino, Tadej, et al. "Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range." Diabetes Care, American Diabetes Association, 7 June 2019. https://doi.org/10.2337/dci19-0028.

FIGURE 1 The ambulatory glucose profile is an internationally standardised report of continuous glucose monitoring information. The report is organised into five major components: ① Sensor capture data completeness; ② Glucose level statistics including hypoglycaemic events and time in range; ③ Glucose profile based on a 'model day'; ④ Glucose management indicator and ⑤ Daily glucose profiles

TABLE 2 Summary of continuous glucose monitoring studies in people with type 1 or type 2 diabetes

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in Range (3.9–10 mmol/L)
Type 1 diabetes						
Heinemann et al [35] (HypoDE Study)	2018	Adults Hypoglycaemia unawareness	6 months	No significant difference	Reduction in mean number of hypoglycaemia events per 28 days by 0.28 events (95% CI −0.39 to −0.20; $p < 0.0001$) in CGM group compared to control Median time in hypoglycaemia in the CGM group was reduced from 70.9 min/day (95% CI 38.8–130.2) to 23.9 min/day (95% CI 12.9–54.5), compared to a reduction from 99.5 min/day (95% CI 52.3–178.1) to 92.2 min/day (95% CI 51.8–172.6) in the control group, $p < 0.0001$.	No significant difference
Van Beers et al [36] (IN CONTROL study)	2016	Adults Hypoglycaemia unawareness CSII or MDI	44 weeks	No significant difference	Reduction in mean time in hypoglycaemia by 1.1 h/day (95% CI −1.4 to −0.8; $p < 0.0001$) in CGM group compared to control	Increase in mean time in range by 2.3 h/day (95% CI 1.9 to 2.7; $p < 0.0001$) in CGM group compared to control
Lind et al [37] (GOLD Study)	2017	Adults MDI HbA_{1c} ≥59 mmol/mol (7.5%)	26 weeks	Reduction in mean HbA_{1c} by 5 mmol/mol (0.4%) (95% CI −6 to −3 mmol/mol [−0.6 to −0.3%]; $p < 0.001$) in CGM group compared to control	Mean percentage of time in hypoglycaemia was 2.97% (95% CI −2.85% to 8.79%) in the CGM group compared to 4.79% (95% CI −3.11% to 12.69%) in the control group	—
Beck et al [38] (DIAMOND Study)	2016	Adults MDI HbA_{1c} 59–85 mmol/mol (7.5–9.9%)	24 weeks	Reduction in mean HbA_{1c} by 7 mmol/mol (0.6%) (95% CI −9 to −3 mmol/mol [−0.8 to −0.3%]; $p < 0.001$) in CGM group compared to control	Median time in hypoglycaemia was 43 min/day (IQR 27–69) in the CGM group compared to 80 min/day (IQR 36–111) in the control group ($p = 0.002$)	Increase in mean time in range by 77 min/day (99% CI 6–147; $p = 0.005$) in CGM group compared to control
Battelino et al[39] (SWITCH Study)	2012	Children and adults CSII HbA_{1c} 59–80 mmol/mol (7.5–9.5%)	6 months	Reduction in mean HbA_{1c} by 5 mmol/mol (0.4%) (95% CI −6 to −3 mmol/mol [−0.6 to −0.3%]; $p < 0.001$) during sensor on (CGM) compared to sensor off (control)	Median time in hypoglycaemia was 19 min/day (IQR 7.9–38) during sensor on (CGM) compared to 31 min/day (IQR 10–57) during sensor off (control; $p = 0.009$)	Mean time in range was 774 min/day (95% CI 737–812) during sensor on (CGM) compared to 669 min/day (95% CI 635–703) during sensor off (control; $p < 0.001$)

(Continues)

TABLE 2 (Continued)

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in Range (3.9–10 mmol/L)
Tamborlane et al [40] (JDRF CGM Study)	2008	Children and adults HbA_{1c} 53–86 mmol/mol (7.0–10.0%)	26 weeks	Age ≥25 years: Reduction in mean HbA_{1c} by 6 mmol/mol (0.5%) (95% CI −8 to −4 mmol/mol [−0.7 to −0.4%]; $p > 0.001$) in CGM group compared to control. Age 15–24 years: No significant difference Age 8–14 years: No significant difference	No significant difference	Age ≥25 years: Mean time in range was 986 min/day in the CGM group compared to 840 min/day in the control group ($p < 0.001$) Age 15–24 years: No significant difference Age 8–14 years: No significant difference
Laffel et al [41] (CITY Study)	2020	Young adults 14–24 years CSII or MDI HbA_{1c} 59–96 mmol/mol (7.5–10.9%)	17 months	Reduction in mean HbA_{1c} by 4 mmol/mol (0.37%) (95% CI −7 to −1 mmol/mol [−0.7 to −0.1%]; $p = 0.01$) in CGM group compared to control	Reduction in median percentage time in hypoglycaemia by 0.7% (95% CI −1.5 to −0.1; $p = 0.02$) in CGM group compared to control	Increase in mean percentage time in range by 6.9% (95% CI 3.1–10.7; $p < 0.001$) in CGM group compared to control
Pratley et al [42] (WISDM Study)	2020	Adults (≥60 years) CSII or MDI HbA_{1c} <86 mmol/mol (10.0%)	26 weeks	Reduction in mean HbA_{1c} by 3 mmol/mol (0.3%) (95% CI −4 to −1 mmol/mol [−0.4 to −0.1%]; $p < 0.001$) in the CGM group compared to control	Reduction in median percentage time in hypoglycaemia by 1.9% (95% CI −2.8 to −1.1; $p < 0.001$) in the CGM group compared to control	Increase in mean percentage time in range by 8.8% (95% CI 6.0–11.5; $p < 0.001$) in the CGM group compared to control
Type 2 diabetes						
Beck et al [43]	2017	Adults MDI HbA_{1c} 59–85 mmol/mol (7.5–9.9%)	24 weeks	Reduction in mean HbA_{1c} by 3 mmol/mol (0.3%) (95% CI −5 to 0 mmol/mol [−0.5 to 0.0%]; $p = 0.022$) in the CGM group compared to control	No significant difference	Median time in range increased from 802 min/day to 882 min/day in the CGM group compared to an increase from 794 min/day to 836 min/day in the control group
Ehrhardt et al [44]	2011	Adults HbA_{1c} 53–108 mmol/mol (7.0–12.0%) Not on prandial insulin	12 weeks	Mean reduction in HbA_{1c} was 11 mmol/mol (1.0%) (95% CI −14.2 to −8 mmol/mol [−1.3 to −0.7%]) in the CGM group compared to 5 mmol/mol (0.5%) (95% CI −8 to −3 mmol/mol [−0.7 to −0.3%]) in the control group ($p = 0.006$)	—	—

(Continues)

TABLE 2 (Continued)

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in Range (3.9–10 mmol/L)
Type 1 and type 2 diabetes						
Cosson et al [45]	2009	Adults HbA_{1c} 64–91 mmol/mol (8.0–10.5%) type 1 diabetes mellitus: CSII or MDI Type 2 diabetes mellitus: MDI or oral hypoglycaemics	48 h	Overall: Reduction in mean HbA_{1c} by 7 mmol/mol (0.6%) (95% CI −8 to −5 mmol/mol [−0.8 to −0.5%]; $p = 0.023$) in the CGM group, compared to no significant HbA_{1c} reduction in the control group Type 2 diabetes mellitus: Reduction in mean HbA_{1c} by 7 mmol/mol (0.6%) (95% CI −8 to −5 mmol/mol [−0.8 to −0.5%]; $p = 0.05$) in the CGM group compared to no significant HbA_{1c} reduction in the control group Type 1 diabetes mellitus: No significant difference	No significant difference	No significant difference

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; CSII, continuous subcutaneous insulin infusion; IQR, interquartile range; MDI, multiple daily injections.

HbA_{1c} reductions with CGM use in children and adults with type 1 diabetes mellitus.[37-39,41,42] A meta-analysis reported that CGM was associated with a significantly lower HbA_{1c} at end point compared to SMBG, with a between-group difference of −2 mmol/mol (−0.2%) (S4). The JDRF study stratified the study population according to age and reported a mean between-group difference in HbA_{1c} of −6 mmol/mol (−0.5%; $p < 0.001$) in adults (≥25 years), but no significant change in children 8-14y or adolescents 15-24y.[40] In another meta-analysis, CGM was associated with an HbA_{1c} reduction of 3 mmol/mol (0.3%; $p = 0.004$), although these changes were only significant in people aged >15 years (S5). The benefits of CGM are primarily seen in PWD with near daily use ([39],S6). This age-related phenomenon could potentially be explained by reduced sensor use in children and adolescents, as observed in the JDRF study.[40] An RCT by Cosson et al which involved two discrete 48-h CGM wears 3 months apart, reported no significant difference in HbA_{1c} change between the CGM and control groups,[45] which further emphasises the importance of daily CGM use.

TIR and hypoglycaemia

The DIAMOND, SWITCH, CITY and WISDM RCTs all reported an increased mean TIR of 1.3–2.4 h/day.[38,39,41,42] When stratified according to age, the JDRF study demonstrated a significant increase in TIR in adults, but no significant difference in children and adolescents.[40] Reduced time in hypoglycaemia and reduced incidence of severe hypoglycaemic events were reported in the GOLD, DIAMOND, SWITCH, CITY and WISDM studies.[37-39,41,42] The DIAMOND study specifically noted reduced nocturnal hypoglycaemia in the CGM group.[38]

Continuous glucose monitoring is beneficial in people with hypoglycaemia unawareness. The HypoDE and IN CONTROL studies involved people with type 1 diabetes mellitus and hypoglycaemia unawareness, with the primary outcome of time spent in hypoglycaemia. The HypoDE RCT reported a median hypoglycaemia duration of 23.9 min/day (95% CI 12.9–54.5) in the CGM group, compared to 92.2 min/day (95% CI 51.8–172.6) in the control group ($p < 0.0001$).[35] The IN CONTROL crossover study showed a reduction in mean time in hypoglycaemia of 1.1 h/day (95% CI −1.4 to −0.8; $p < 0.0001$) in the CGM phase, compared to the SMBG phase.[36] The study also reported a between-group difference in mean TIR of 2.3 h/day (95% CI 1.9–2.7; $p < 0.0001$), favouring the CGM group.[36] No significant difference in TIR was reported in the HypoDE study.[35] No significant HbA_{1c} change was reported in either of these studies.[35,36]

4.1.2 | Type 2 diabetes

There are a handful of RCTs involving CGM use in type 2 diabetes mellitus, all of which have demonstrated an HbA_{1c}

TABLE 3 Summary of Flash glucose monitoring studies in people with type 1 or type 2 diabetes

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in range (3.9–10 mmol/L)
Type 1 diabetes						
Bolinder et al [46] (IMPACT Study)	2016	Adults HbA_{1c} ≤59 mmol/mol (7.5%) CSII or MDI Exclusion: Hypoglycaemia unawareness	6 months	No significant difference	Reduction in mean time in hypoglycaemia by 1.24 h/day (95% CI −1.71 to −0.77; $p < 0.0001$) in the FGM group compared to control (38.0% reduction). Reduction in mean time in nocturnal hypoglycaemia (11 pm to 6am) by 0.47 h (95% CI −0.70 to −0.24; $p < 0.0001$) in the FGM group compared to control (39.8% reduction).	Increase in mean time in range by 1.0 h/day (95% CI 0.41–1.59; $p = 0.0006$) in FGM group compared to control.
Campbell et al [47] (SELFY Single-Arm Study)	2018	Children and Teenagers (4–17 years) CSII or MDI	8 weeks	Mean HbA_{1c} reduced by 4 mmol/mol (0.4%) (95% CI −6 to −3 mmol/mol [−0.5 to −0.3%]) from 63 mmol/mol (7.9%) (95% CI 60 to 65 mmol/mol [7.7 to 8.1%]) at baseline to 59 mmol/mol (7.5%) (95% CI 56 to 61 mmol/mol [7.3–7.7%]) at study end ($p < 0.0001$).	No significant difference	Mean time in range increased by 0.9 h/day (95% CI 0.27–1.53) from 10.1 h/day (95% CI 9.42–10.8) at baseline to 11.1 h/day (95% CI 10.4–11.8) at study end ($p = 0.005$).
Tyndall et al [48] (Prospective observational Study)	2019	Adults CSII or MDI	—	Median reduction in HbA_{1c} by 4 mmol/mol (0.4%) (IQR −10 to 0 mmol/mol [−0.9 to 0.0%]); $p < 0.001$) between the last value prior to FGM use and the most recent value.	Frequency of symptomatic hypoglycaemia (<3.5 mmol/L) increased, with those reporting more than 2–3 episodes per week increasing from 25.8% to 48.8% ($p < 0.001$) following commencement of FGM. The proportion of people experiencing any asymptomatic hypoglycaemia (<3.5 mmol/L) increased from 20.4% to 29.5% ($p < 0.001$) following commencement of FGM.	—

(Continues)

TABLE 3 (Continued)

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in range (3.9–10 mmol/L)
Type 2 diabetes						
Haak et al [49] (REPLACE Study)	2017	Adults HbA_{1c} 59–108 mmol/mol (7.5–12.0%) CSII or MDI	6 months	Overall: No significant difference Age <65 years: Mean HbA_{1c} reduced by 6 mmol/mol (0.5%) (95% CI −8 to −4 mmol/mol [−0.7 to −0.4%]) in the FGM group, compared to a reduction of 2 mmol/mol (0.2%) (95% CI −5 to 0.4 mmol/mol [−0.4 to 0.04%]) in the control group ($p = 0.03$). Age ≥65 years: Mean HbA_{1c} reduced by 5 mmol/mol (0.5%) (95% CI −8 to −3 mmol/mol [−0.7 to −0.2%]) in the control group, compared to a reduction of 1 mmol/mol (0.1%) (95% CI −3 to 2 mmol/mol [−0.3 to 0.2%]) in the FGM group ($p = 0.008$).	Reduction in mean time in hypoglycaemia by 0.47 h/day (95% CI −0.72 to −0.22; $p = 0.0006$) in the FGM group compared to control (43.1% reduction). Reduction in mean time in nocturnal hypoglycaemia (11 pm to 6am) by 0.29 h (95% CI −0.45 to −0.13; $p = 0.0001$) in the FGM group compared to control (54.3% reduction).	No significant difference
Haak et al [50]	2017	Adults HbA_{1c} 59–108 mmol/mol (7.5–12.0%) CSII or MDI	12 months	—	Mean time in hypoglycaemia reduced by 0.70 h/day (95% CI −1.01 to −0.39; $p = 0.0002$) in the FGM group from baseline to study end (49.4% reduction). Mean time in nocturnal hypoglycaemia (11 pm to 6am) reduced by 0.31 h (95% CI −0.45 to −0.17; $p = 0.0002$) in the FGM group from baseline to study end (52.3% reduction).	No significant difference
Yaron et al (S1)	2019	Adults HbA_{1c} 59–86 mmol/mol (7.5–10.0%) MDI	10 weeks	Mean HbA_{1c} reduced by 9 mmol/mol (0.9%) (95% CI −10 to −8 mmol/mol [−0.9 to −0.8%]) in the FGM group, compared to a reduction of 3 mmol/mol (0.3%) (95% CI −4 to −3 mmol/mol [−0.4 to −0.2%]) in the control group ($p = 0.005$).	No significant difference	—

(Continues)

TABLE 3 (Continued)

	Year	Inclusion criteria	Duration	Change in HbA_{1c}	Hypoglycaemia (<3.9 mmol/L)	Time in range (3.9–10 mmol/L)
Wada et al (S2)	2020	Adults HbA_{1c} 59–69 mmol/mol (7.5–8.5%) Non-insulin treated	24 weeks	At 12 weeks: No significant difference At 24 weeks: Reduction in mean HbA_{1c} by 3 mmol/mol (0.3%) (95% CI −6 to −1 mmol/mol [−0.5 to −0.1%]; $p = 0.022$) in the FGM group compared to control.	No significant difference	Increase in mean time in range by 2.36 h/day (95% CI 1.21 to 3.51; $p < 0.001$) in the FGM group compared to control.

Abbreviations: CI, confidence interval; CSII, continuous subcutaneous insulin infusion; FGM, Flash glucose monitoring; IQR, interquartile range; MDI, multiple daily injections.

reduction.[43-45] A meta-analysis comparing CGM to SMBG found a pooled mean HbA_{1c} reduction of 3 mmol/mol (0.3%; $p = 0.01$) (S7). Similarly, another meta-analysis reported an HbA_{1c} reduction of 2 mmol/mol (0.2%) (S8). Ehrhardt et al observed that a high baseline HbA_{1c} was associated with a greater HbA_{1c} reduction.[44] When considering glycaemic variability, Beck et al reported an increase in median TIR from 802 to 882 min/day in the CGM group, compared to an increase from 794 to 836 min/day in the control group.[43] Cosson et al. reported no significant difference.[45] No significant effect on hypoglycaemia was observed in any of these studies (43,45,S7), probably due to low levels of hypoglycaemia at baseline in people with type 2 diabetes mellitus.[43]

4.2 | Flash glucose monitoring

4.2.1 | Type 1 diabetes

Glycated haemoglobin

The efficacy of FGM in type 1 diabetes mellitus has been assessed in three studies: IMPACT, SELFY and Tyndall et al, all of which compared FGM to SMBG. The IMPACT RCT recruited adults with type 1 diabetes mellitus and HbA_{1c} ≤59 mmol/mol (7.5%), who reported SMBG ≥3 times/day. The investigators found that FGM had no significant effect on HbA_{1c}, although it is important to note that this study was designed for the effect of FGM on hypoglycaemia as the primary end point.[46] In contrast, the SELFY single-arm pre–post study in children and adolescents (mean baseline HbA_{1c} 63 mmol/mol [7.9%]) reported an HbA_{1c} reduction of 4 mmol/mol (0.4%; $p < 0.0001$) from baseline to study end,[47] with similar results seen in Tyndall et al, a real-world prospective observational study.[48] Tyndall et al. noted that individuals with a higher baseline HbA_{1c} were more likely to achieve HbA_{1c} reductions following FGM commencement,[48] which could explain why no HbA_{1c} reduction was seen in the IMPACT trial.

TIR and hypoglycaemia

The IMPACT and SELFY studies reported increased TIR of 1.0 h/day (95% CI 0.41–1.59; $p = 0.0006$) and 0.9 h/day (95% CI 0.27–1.53; $p = 0.005$), respectively, in the FGM group compared to control.[46,47] The impact of FGM on hypoglycaemia was variable. The IMPACT trial reported reduced mean time in hypoglycaemia by 1.24 h/day (95% CI −1.71 to −0.77; $p < 0.0001$), as well as a 39.8% reduction in nocturnal hypoglycaemia ($p < 0.0001$) in the FGM group.[46] The SELFY study observed that FGM had no impact on hypoglycaemia, although baseline time in hypoglycaemia was low in this population.[47] In contrast, based on questionnaire data, Tyndall et al found that hypoglycaemia (<3.5 mmol/L) was increased in individuals following FGM commencement.[48]

This was attributed to the revealing of previously unrecognised hypoglycaemia by FGM data, rather than the development of increased hypoglycaemia.[48]

4.2.2 | Type 2 diabetes

Glycated haemoglobin

Several studies have assessed FGM use in people with type 2 diabetes mellitus on insulin therapy. The REPLACE RCT analysed the effect of FGM compared to SMBG for 6 months in people with type 2 diabetes mellitus on intensive insulin therapy, and found no between-group difference in HbA_{1c} change.[49] However, subgroup analysis found that in people <65 years, FGM led to a greater HbA_{1c} reduction compared to controls ($p = 0.03$), whereas in people ≥65 years, the HbA_{1c} reduction was greater in controls compared to the FGM group ($p = 0.008$).[49] They hypothesised that the convenience of sensor scanning resulted in more frequent glucose readings in younger participants,[49] a population which is often less adherent to SMBG (S9). Yaron et al analysed the effect of FGM compared to SMBG for 10 weeks in people with type 2 diabetes mellitus on MDI, and reported a significant HbA_{1c} reduction in the FGM group (S1). In the REPLACE trial, the mean self-reported SMBG frequency was 3.6 times/day in the intervention group and 3.9 times/day in the control group, whereas this was not specified in Yaron et al. These contrasting findings may indicate that FGM is most effective in PWD who do not perform SMBG regularly.

Wada et al compared FGM with SMBG in people with non-insulin-treated type 2 diabetes mellitus over 24 weeks in an RCT. They reported an HbA_{1c} reduction of 3 mmol/mol (0.3%; $p = 0.022$) favouring the FGM group at study end, although there was no significant change in HbA_{1c} at 12 weeks (S2). This suggests that the benefits of FGM are less obvious in people with non-insulin-treated type 2 diabetes mellitus, and are only realised with a prolonged period of regular use.

TIR and hypoglycaemia

The REPLACE RCT found that time in hypoglycaemia reduced by 0.47 h/day (95% CI 0.21–0.72; $p = 0.0006$) in the FGM group compared to control, where nocturnal hypoglycaemia reduced by 0.29 h (95% CI −0.45 to −0.13; $p = 0.0001$), although there was no significant difference in TIR.[49] Haak et al. analysed the effects of FGM in the intervention group from the REPLACE trial for further 6 months, and yielded similar results.[50] In contrast, Wada et al reported increased TIR of 2.36 h/day (95% CI 1.21–3.51; $p < 0.001$) in the FGM group compared to SMBG, with no significant difference in time in hypoglycaemia (S2). Yaron et al. found that there was no difference in frequency of hypoglycaemic events in the FGM group compared to control (S1).

Retrospective FGM

Ajjan et al. involved people on insulin therapy, and the GP-OSMOTIC RCT involved people on insulin therapy or ≥2 oral hypoglycaemic agents (S10,S11). Both studies reported HbA_{1c} reductions. Ajjan et al. reported a between-group difference in HbA_{1c} change of −5 mmol/mol (−0.5%; $p = 0.004$) favouring FGM, with no significant effect of professional FGM on hypoglycaemia (S10). In contrast, the GP-OSMOTIC trial found a between-group difference in HbA_{1c} change of −5 mmol/mol (−0.5%; $p = 0.0001$) at 6 months, although these observations were not sustained at 12 months, with no significant between-group difference (S11). In terms of glucose variability, the GP-OSMOTIC trial reported that the mean percentage TIR at 12 months was 7.9% (95% CI 2.3–13.5; $p = 0.006$) higher in the FGM group compared to control, whereas Ajjan et al. reported no significant difference (S10,S11).

5 | USER EXPERIENCE

5.1 | People with diabetes

Many studies have demonstrated that CGM user satisfaction is high, and that CGM contributed to improved diabetes-related QOL compared to SMBG (35–38,43,46,S1,S10,S12,S13). In a systematic review of FGM, all RCTs found improvements in diabetes treatment satisfaction, diabetes QOL and diabetes-related stress (S12). Reduced fear of hypoglycaemia was reported in multiple studies (36,37,S14,S15), perhaps because CGM allows PWD to easily and quickly identify and respond to dysglycaemia, thereby allowing individuals to regain a sense of empowerment over glucose management, and more broadly, their diabetes (S16). CGM can also allow PWD to better understand the impact of food and exercise on glucose management, enabling short-term lifestyle planning such as changing the timing of a meal or reducing the length of a run to avoid dysglycaemia (S7,S15,S17). A recent position statement recommended specific target glucose levels and corrective actions before, during and after exercise for PWD using CGM, depending on their risk of hypoglycaemia (S18). CGM readings and BSL may differ during exercise; therefore, the CGM reading needs to be interpreted together with the trend arrow (S18). Lawton et al. reported that while participants expressed confidence in adjusting insulin and lifestyle to address impending dysglycaemia, most needed clinicians to interpret retrospective CGM data and determine changes to diabetes treatment (S15).

5.1.1 | Driving

Continuous glucose monitoring can potentially increase safety when driving for PWD. Driving simulator studies

have demonstrated that driving performance deteriorates during hypoglycaemia (S19). In Australia and Europe, guidelines require that glucose level is checked ≤2 h before driving to ensure glucose level >5 mmol/L, then every 2 h thereafter to ensure levels remain >5 mmol/L (S20–S22). Similarly, American guidelines recommend that an extended drive not be initiated with low-normal glucose level (3.9–5.0 mmol/L) without prophylactic carbohydrate consumption, and that glucose levels be checked at regular intervals when driving for >1 h (S23). CGM allows PWD to effortlessly determine current glucose level and predictive trends, to ensure normoglycaemia is maintained. Glucose data can even be shared to the car dashboard via Apple CarPlay or Android Auto, although there are no studies evaluating this technology. The alarm capacity for current or impending hypoglycaemia can add another layer of safety.

5.2 | Parents

Interviews with parents of children with diabetes revealed that CGM with remote monitoring has enabled parents to pre-empt and prevent dysglycaemia in a timely manner (S15). Some parents noted the capacity to examine night-time readings and readings when children were at school offered peace of mind (S15). One study reported that parental hypoglycaemia fear scores were lower when their children were using CGM with remote monitoring, and that parental health-related QOL, family functioning, anxiety and parental sleep measures also improved significantly.[16]

5.3 | Clinicians

Healthcare professionals are vital in helping PWD adopt new technology (S24). Clinicians have reported that CGM data supported effective communication with PWD (29,S10), and that the AGPs were easy to read and understand, enabling them to make informed decisions on therapy adjustments (S10,S17). However, some clinicians find CGM adoption difficult. Barriers include limited time in clinic to download data and explain glycaemic trends to PWD, and limited time to learn about different CGM devices and new developments in CGM, with inconsistent resources for training (3,13,S25). Moreover, guidelines dictate that PWD using CGM must receive adequate education, training and support to ensure adherence and help achieve glycaemic goals (5,S26). Tanenbaum et al found that clinicians who had more time with PWD, were younger and found it easy to keep up with technological advances were more likely to recommend CGM to PWD (S25).

5.3.1 | CGM in telemedicine

Following the outbreak of COVID-19, telemedicine has replaced majority of face-to-face appointments. There is an evidence that supports the use of telemedicine in diabetes with benefits in glycaemic management (S27,S28) and satisfaction in PWD (S29) compared to conventional practice. CGM can potentially further improve this experience for clinicians and PWD, by remotely providing a wealth of data. However, studies in this area are lacking.

6 | DISADVANTAGES

6.1 | Cost

Continuous glucose monitoring devices are costly, with inconsistent reimbursement across government bodies.[3,8,14] Many countries, including Australia and America, offer reimbursement for people with type 1 diabetes mellitus, with limited subsidisation for people with type 2 diabetes mellitus (S30,S31). Germany reimburses real-time CGM for all types of diabetes, whereas Spain offers no reimbursement at all (S30). CGM systems require sensor changes every 6–14 days, which costs AU$3000–$6000 per year without subsidisation.[21] Table 4 shows the summary of the cost of CGM devices in Australia.

6.2 | Accuracy

Multiple factors affect CGM device accuracy. CGM measures interstitial glucose levels, which compared to BSLs have a mean absolute relative difference of 10%–20%. Accuracy reduces at the extremes of glycaemia and during times of rapid glucose change, especially during exercise (8,14,S32–S34). Therefore, many CGM devices require calibrations to maintain reliable correlation between CGM readings and BSL, and infrequent or incorrect calibration could potentially reduce the accuracy of CGM.[13] FGM and newer CGM devices are factory calibrated so do not have the same issue. There is also a physiological lag of 5–10 min between blood and interstitial glucose concentrations, which could result in inappropriate or excessive correction of dysglycaemia.[8,13]

Certain chemicals can interfere with the accuracy of readings, including medications such as paracetamol, ibuprofen, lisinopril and vitamin C; and endogenous substances such as bilirubin, cholesterol and creatinine (8,S35,S36). Paracetamol in particular is known to falsely elevate interstitial glucose readings, due to interference with the electrochemical reaction that occurs during CGM sensing (S37,S38). One study reported that, following oral administration of 1 g paracetamol, glucose reading increased by 1.6 mmol/L with the Dexcom G4™ Platinum compared to BSL. In comparison,

TABLE 4 Cost of continuous glucose monitoring devices available in Australia

	Sensor wear life (days)	Cost per sensor	Transmitter wear life	Cost per transmitter	Cost per receiver/reader	Annual cost	Annual cost with subscription
Continuous glucose monitoring							
Real time							
Dexcom G4 Platinum™	7	$92.50	12 months	$580	$810	$6,195	—
Dexcom G5 Mobile™	7	$92.50	3 months	$540	$650 (Optional)	$6,970[a]	—
Dexcom G6™	10	$110	3 months	$400	$650 (Optional)	$5,560[a]	$3,960
Medtronic Enlite™ sensor and Guardian™ Link 2 transmitter	6	$75	12 months	$699	N/A	$5,199	$3,000
Medtronic Enlite™ Sensor and MiniLink™ Transmitter	6	$75	12 months	$699	N/A	$5,199	$3,000
Medtronic™ Guardian Sensor 3 and Guardian™ Connect transmitter	7	$75	12 months	$699	N/A	$5,199	$3,300
Medtronic Guardian™ Sensor 3 and Guardian™ Link 3 transmitter	7	$75	12 months	$699	N/A	$5,199	$3,000
Retrospective							
Medtronic Enlite™ Sensor and iPro2™ Recorder	6	$75	12 months	$995	N/A	$5,495	N/A
Flash glucose monitoring							
Abbott™ FreeStyle Libre	14	$92.50	N/A	N/A	$95 (Optional)	$2,405[a]	N/A

[a] Annual cost without receiver.

the Dexcom Seven Plus™, an older sensor no longer available, saw a 10.0 mmol/L increase (S39). With technological improvements, the issue of chemical interference has improved dramatically, with a recent study showing no significant paracetamol interference with the Dexcom G6™ (S40). FGM devices also avoid paracetamol interference (S39).

6.3 | Inconvenience

PWD are prone to 'alarm fatigue'. Alarms can result in interrupted sleep and/or unwelcomed distractions at school or work, which can lead to silencing of the alarm function and disengagement with CGM (13,S15). Allergic reactions to adhesive materials used to keep CGM sensors in place can also occur. In the IMPACT trial, 10 out of 328 participants reported local allergic reactions or insertion site symptoms.[46] Furthermore, CGM devices are not compatible with magnetic resonance imaging and need to be removed prior.

7 | COST-EFFECTIVENESS

Continuous glucose monitoring systems are expensive, although with the potential benefits of improved glycaemic management and reduced diabetes-related complications, CGM may be a cost-effective adjunct to diabetes management. Studies have demonstrated that CGM use is associated with reduced hospitalisation for hypoglycaemia and diabetic ketoacidosis (DKA), as well as reduced diabetes-related work absenteeism (48,S14,S41,S42). In a study by Charleer et al, initiation of reimbursed CGM in 515 adults with type 1 diabetes mellitus resulted in a 12% reduction in hospitalisation with reduced admission days compared to the year prior, equating to a nationwide saving of EUR€345,509 (AU$563,460) over the study period of 27 months (S14). Although cost-effectiveness analyses of CGM have yielded varying results, studies have commented that the incremental cost-effectiveness ratio (ICER) of CGM can be significantly improved with reduced CGM cost, increased HbA_{1c} reduction and increased adherence to CGM use (S31,S43).

7.1 | Type 1 diabetes

Wan et al performed cost-effectiveness analysis on the DIAMOND trial population, and found that during the 6-month trial, compared to SMBG, CGM increased costs (US$11,032 [AU$15,882] vs. US$7,236 [AU$10,417]) without immediately improving QOL (S43). However, in

predictive lifetime analysis, CGM emerged as a cost-effective intervention with PWD gaining 0.54 quality-adjusted life years (QALYs) and an ICER of US$98,108 (AU$141,242) per QALY compared to SMBG, assuming a willingness-to-pay of US$100,000 per QALY (S43). Similarly, the JDRF study, comparing usual care to CGM in PWD with HbA_{1c} ≥53 mmol/mol (7.0%), reported a reduction in projected lifetime risk of microvascular complications, with a gain of 0.60 QALYs and an ICER of US$98,679 (AU$142,064) per QALY (S44). The cost-effectiveness of CGM was even greater in the HbA_{1c} <53 mmol/mol (7.0%) cohort, with an average gain in 1.11 QALYs and an ICER of US$78,943 (AU$113,651) per QALY (S44). Another study comparing CGM versus SMBG in people on intensive insulin therapy reported an improvement in cost-effectiveness of 0.52 QALYs and an ICER of US$45,033 (AU$64,832) per QALY (S45). However, a Spanish study by Garcia-Lorenzo et al comparing CGM to SMBG in a model population showed that CGM was not cost-effective, with a gain of 0.05 QALYs and an ICER of EUR€2,554,723 (AU$4,166,268) per QALY, assuming a willingness-to-pay of EUR€25,000. However, this study did not include costs such as emergency visits and diabetes-related hospital admissions in their economic evaluation (S31). Overall, CGM seems to be a cost-effective intervention in the management of type 1 diabetes mellitus, especially with long-term regular use.

7.2 | Type 2 diabetes

An American study of people with type 2 diabetes mellitus not on prandial insulin, using CGM as a tool to inform behavioural choices without clinician guidance, reported a gain of 0.07 QALYs and an ICER of US$8898 (AU$12,810) per QALY with CGM compared to SMBG, deeming it a cost-effective intervention (S46). However, Garcia-Lorenzo et al reported that CGM was not cost-effective, with a gain of 0.27 QALYs and an ICER of EUR€180,533 (AU$294,415) per QALY (S31). These findings suggest that CGM may be cost-effective in people with type 2 diabetes mellitus on insulin treatment.

8 | CONCLUSION

As CGM continues to evolve, a new era of diabetes management has come. CGM offers added benefits compared to traditional HbA_{1c} measurement and SMBG, including detailed information on glycaemic trends and excursions. CGM can improve glycaemic outcomes including HbA_{1c}, TIR and reduced hypoglycaemia, with study findings consistently proving either non-inferiority or superiority compared to SMBG, except for one study. Many studies have also shown high user satisfaction with CGM. CGM can significantly improve long-term diabetes management and QOL in PWD. Further studies around the impact of CGM on driving and telemedicine are required.

There is a strong evidence for CGM use in type 1 diabetes mellitus management. Studies suggest that CGM is most beneficial in adults with poorly managed type 1 diabetes mellitus, with a high HbA_{1c} and/or hypoglycaemia unawareness. Studies have also demonstrated that CGM is a cost-effective intervention in the management of type 1 diabetes mellitus. Long-term, regular daily use of CGM is required to maximise its benefits and value. Further study is required to assess the efficacy and cost-effectiveness of CGM in people with well-managed type 1 diabetes mellitus.

The evidence for CGM use in type 2 diabetes mellitus management is less robust. There is more evidence for FGM rather than traditional CGM use in type 2 diabetes mellitus, especially in people <65 years on insulin therapy with a high HbA_{1c}, and those who seldom perform SMBG. The main benefit of FGM in this population is HbA_{1c} reduction without increased hypoglycaemia. Further study around the cost-effectiveness of CGM in type 2 diabetes mellitus management is required.

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CONFLICT OF INTEREST

The authors SJ and JJ have type 1 diabetes and have used CGM technology. The other authors have no conflicting interests to declare.

ORCID

Rose Lin https://orcid.org/0000-0003-4331-0706
Fran Brown https://orcid.org/0000-0002-0332-5121
Steven James https://orcid.org/0000-0002-3928-9206
Elif Ekinci https://orcid.org/0000-0003-2372-395X

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