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Title:

Continuous Glucose Monitoring: a review of the evidence, opportunities for future use and ongoing challenges

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Abstract

The advent of devices that can track interstitial glucose levels which are closely related to blood glucose levels on a near continuous basis has facilitated better insights into patterns of glycaemia. Continuous glucose monitoring (CGM) therefore allows for more intensive monitoring of blood glucose levels and potentially improved glycaemic control. In the context of the announcement on 1 April 2017 that the Australian Government will fund CGM monitoring for people with type 1 diabetes under the age of 21, this paper provides a review of the evidence for CGM and some of the ongoing challenges. The advent of devices that can track interstitial glucose levels which are closely related to blood glucose levels on a near continuous basis has facilitated better insights into patterns of glycaemia. Continuous glucose monitoring (CGM) therefore allows for more intensive monitoring of blood glucose levels and potentially improved glycaemic control. In the context of the announcement on 1 April 2017 that the Australian Government will fund CGM monitoring for people with type 1 diabetes under the age of 21, this paper provides a review of the evidence for CGM and some of the ongoing challenges. There is evidence that real-time CGM in type 1 diabetes improves HbA1c and hypoglycaemia, whilst in type 2 diabetes, the evidence is less robust. Initial barriers to widespread implementation of CGM included issues with accuracy and user friendliness, however, as the technology has evolved, these issues have largely improved. Ongoing barriers include cost, and weaker evidence for their benefit in certain populations such as those with type 2 diabetes and less glycaemic variability. CGM has the potential to reduce health care costs, although real world studies including cost-effectiveness analyses, are needed in this area.

Key words: Continuous Glucose Monitoring, Flash glucose monitoring, type 1 diabetes, type 2 diabetes

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Introduction

Use of continuous glucose monitoring (CGM) technology in the management of diabetes is gaining increasing interest. CGM is a means of measuring glucose levels continuously to gain insight into patterns and trends in glucose levels. A sensor is inserted subcutaneously by either the health professional or patient, and measures interstitial glucose concentrations (1). The sensor links to a transmitter which sends signals to a hand-held receiver or an insulin pump. The data gathered from CGM may be used in real-time by patients (real-time CGM) or retrospectively by clinicians (retrospective CGM).

The current standard of care in people with diabetes on insulin or oral agents, with potential to cause hypoglycaemia, is self-monitoring of blood glucose (SMBG) through finger prick testing of capillary blood glucose. Due to various factors, such as pain, inconvenience and perceived pointlessness, many people with diabetes do not perform frequent SMBG (2, 3). Furthermore, capillary glucose readings are initiated by the person with diabetes, only record one reading in time and do not provide information about patterns of blood glucose levels. This provides insufficient glucose data throughout the day and especially at night (4).

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With advances in technology, CGM has become more accurate, reliable and user friendly, with potential to improve glycaemic control, to avoid hypoglycaemia, and to inform and empower people with diabetes. There is strong evidence for the benefit of real-time CGM in type 1 diabetes and guidelines from professional bodies typically endorse the use of CGM for people with hypoglycaemia unawareness or frequent hypoglycaemic episodes (5, 6). These observed benefits are likely to have occurred because type 1 diabetes is characterised by greater unpredictably and variability in blood glucose levels requiring an immediate response on the part of the person with diabetes or their care-giver.

The Australian Government announced on 1 April 2017, significant funding for real-time CGM in young people with type 1 diabetes who are less than the age of 21 (7). This announcement has been welcomed by people with diabetes and clinicians alike. Initial anecdotal communication from paediatric centers suggests a major uptake which has stretched available resources. The ability to provide adequate resources to teach health professionals and patients to use and interpret CGM is likely to be an ongoing major challenge. Education of the person with diabetes and their behaviour adaptation following feedback from CGM will likely have a large influence on outcomes.

While the evidence is less robust, more recently, it has been argued that benefits of CGM may apply whenever insulin therapy is used, regardless of diabetes type, increasing interest in CGM use in type 2 diabetes. Before recommending widespread implementation, consideration needs to be given to the weaker evidence for CGM use in type 2 diabetes, high cost, and insufficient guidance from randomised clinical trials on the duration and frequency of CGM in this population. Furthermore, the primary mechanism of improved glycaemic control with CGM has not been delineated. It likely varies from patient to patient and may be due to lifestyle change, patient empowerment of the person with diabetes or changes in insulin dosing secondary to the person with diabetes learning from the CGM. In select people with long standing type 2 diabetes on insulin, whose glycaemic profile is characterised by recurring patterns, retrospective CGM may play a significant role, although those with recent

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onset type 2 diabetes and on oral agents have largely predictable glycaemic profiles and may be less likely to benefit.

It is conceivable that CGM could reduce health care costs both in the short term by averting hospitalisation, and in the long-term, by decreasing complications through improved glycaemic control, although rigorous trials with economic evaluation are needed. Whilst there is an expanding body of evidence for the use of CGM in carefully regulated clinical trials, we are now moving to a phase of widespread use in the community, particularly with the reimbursement of sensors in people less than the age of 21 years with type 1 diabetes, and it remains to be determined which benefits or issues will emerge with real-world use of these devices.

The aim of this paper is to familiarise a wider medical audience with CGM and to explore the nuances around its use. This is based on a comprehensive review of existing studies investigating benefits of both real-time and retrospective CGM in patients with type 1 and type 2 diabetes.

The review author: AW performed Medline searches combining *Subject Headings* [continuous glucose monitoring or flash glucose monitoring/], with key words of type 1 diabetes, type 2 diabetes, pregnancy, with the applied limits: published from “1999 to current”.

<u>What is continuous glucose monitoring and what is flash glucose monitoring?</u>

The CGM devices can be grouped as:

1. Personal “real-time” use, whereby people with diabetes are presented with glucose information continuously independent of any action on their part. These devices can be divided into stand-alone units which link to a hand-held receiver and those integrated as part of an insulin pump.

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2. Professional or "retrospective" use, whereby glucose levels are recorded continuously but this information is only accessed retrospectively by the person with diabetes and health care professionals.
3. Flash glucose monitoring, utilises variant technology and unlike the traditional CGM devices described above, does not require calibration with capillary finger prick testing. Available devices are summarised in Table 1.

As CGM measures interstitial glucose, an ongoing issue is the delay due to the physiological lag as glucose moves from the vascular to the interstitial space, and has been estimated to be 5-6 minutes in healthy adults with type 1 diabetes (5). Rapid changes in circulating glucose levels can result in significant differences between measured interstitial and blood glucose levels.

The difference between CGM (figure 1) and flash glucose monitoring (figure 2)

The key difference between traditional CGM and flash glucose monitoring is that CGM needs calibration while flash glucose monitoring does not, and CGM has alarm capability if glucose data is provided in real-time while flash glucose monitoring does not (Table 2). Both technologies use an enzyme coated wire which - when inserted by the patient into subcutaneous tissue - measures interstitial glucose via generation of an electrical current when glucose reacts with the enzyme glucose oxidase. The current generated is proportional to the interstitial glucose level measurement which is converted to an estimated blood glucose level by an algorithm (and calibration by capillary blood glucose measurements for some devices) (1). The sensor links to a transmitter which sends signals to a hand-held receiver or an insulin pump. Traditional CGM requires a process of calibration to relate glucose to the electrical current upon which the continuous glucose measurements are based. A finger-prick glucose measurement is performed by the patient at least twice a day and the value entered into the CGM system (1). Flash glucose monitoring is calibrated in the factory, bypassing the regular calibration requirement.

When worn in association with an insulin pump, the traditional CGM systems can be programmed to alarm when a low glucose level is detected. Some devices e.g.

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Medtronic®Veo and 640G (Medtronic®, Northridge,CA), when used in conjunction with CGM can suspend insulin delivery by the pump in order to minimise hypoglycaemia. The Medtronic®Veo incorporates a low glucose suspend feature which automatically ceases insulin delivery when glucose levels are low and recommences after 2 hours. The Medtronic® 640G has predictive low glucose suspend, which automatically ceases insulin delivery in order to pre-empt hypoglycaemia when a computerised algorithm predicts (based on the recent CGM profile) that glucose levels will go low in the near future. Insulin delivery is suspended for at least 30 minutes and recommenced based on criteria related to the duration of insulin suspension and the resolution of hypoglycaemia. Hence, unlike flash glucose monitoring, in type 1 diabetes, traditional CGM systems can prevent impending hypoglycaemia, which is particularly important in people with impaired hypoglycaemia awareness. Recent advances in CGM and pump technology have enabled the development of hybrid closed loop systems such as the Medtronic®670G which now has FDA approval for use (8). Whilst the user must still initiate bolus doses of insulin for meals and correction of high glucose levels, the insulin pump automatically adjusts the delivery of basal insulin in response to sensor glucose readings.Clinical trials are underway, and this technology is likely to be a major step forward in the management of type 1 diabetes.

The evidence for continuous blood glucose monitoring in type 1 diabetes

Real-time use

There is strong evidence to support the use of real-time CGM in children and adults with type 1 diabetes. Randomised, controlled trials such as the DIAMOND Randomised Clinical Trial (9), the Juvenile Diabetes Research Foundation (JDRF) CGM Study (10), the Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3 study) (11), and the Automation to Simulate Pancreatic Insulin Response (ASPIRE) study) (12), as well as observational data from the Type 1 Diabetes Exchange (T1D Exchange) clinic registry (5) all found that real-time CGM reduced HbA1c and either reduced hypoglycaemia or showed no change in hypoglycaemia rates in the setting of a reduction in HbA1c. Benefit was directly proportional to frequency of use and, importantly, no studies found increased risk of hypoglycaemia with improvement in HbA1c (1, 11). Both the DIAMOND and JDRF studies assessed glycaemic

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variability as a secondary outcome and demonstrated that real-time CGM decreased variability in type 1 diabetes (9, 13). In the DIAMOND study, adults with type 1 diabetes were randomised to real-time CGM (n=105) or usual care (n=53) for 24 weeks. Variability was assessed as the coefficient of variation, and after 24 weeks, the coefficient of variation in the CGM group was higher than in the control group, although this was unlikely to be clinically significant 38% (SD 7%) in the CGM group and 42% (SD 7%) in the control group (p=<0.01). The mean minutes/day spent in range (3.9-10 mmol/L) was 736 (SD 206) with CGM compared to 650 (SD 194) in the control group (p = 0.005). Median minutes/day spent with BGL > 10 mmol/L was 638 (IQR 503-807) in the CGM group and 740 (IQR 625-854) in the control group (p = 0.03). Median minutes/day spent with BGL <3.9 mmol/L was 43 (IQR 27-69) and 80 (IQR 36-111) for CGM and controls respectively (p=0.002) (9). The JDRF study randomly assigned 322 adults and children with type 1 diabetes to receive CGM or standard of care for a total of 26 weeks. The study evaluated 13 measures of glycaemic variability including coefficient of variation, mean amplitude of glycaemic excursions, lability index and mean absolute glucose change per unit time (MAG). A significant reduction in all glycaemic variability indices, except lability index and MAG, was demonstrated in the CGM group at 26 weeks compared with the control group (13).

In the SWITCH crossover study, individuals with type 1 diabetes were randomised to CGM 'on' or CGM 'off' for 6 months, and after a washout period, participants crossed over to the other arm for 6 months. The mean difference in HbA1c was -0.43% (-4.74 mmol/mol) in favour of the Sensor On arm (8.04% (64.34 mmol/mol) vs 8.47% (69.08 mmol/mol), 95% CI -0.32%, -0.55% (-3.5, -6.01 mmol/mol); p<0.001) and less time was spent in hypoglycaemia with CGM (19 vs 31 min/day; p=0.009). Interestingly, total insulin doses did not change but there was behavioural modification with more frequent insulin bolus administration along with more frequent use of temporary basal rates. Furthermore, the reduction in HbA1c largely dissipated when CGM was blinded, and returned when CGM data were again unblinded indicating that the efficacy of CGM depends upon its ongoing use (1, 14).

In the DIAMOND study, CGM contributed to significant improvement in diabetes-specific

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quality of life (QOL) measures (i.e., diabetes distress, hypoglycaemic confidence), but not with QOL measures that were not specific to diabetes (i.e., well-being, health status) (15). The STAR 3 study demonstrated an improvement in QOL after a year with the use of sensor-augmented insulin-pump therapy as compared with multiple daily insulin-injection therapy (11), consistent with previous evidence (16). Although the shorter 3-month ASPIRE study showed no benefit in QOL measures with CGM (12).

Flash Glucose monitoring (real-time)

Real-time flash glucose monitoring was compared with SMBG in type 1 diabetes (17). Mean sensor glucose levels and HbA1c levels did not change but mean time in hypoglycaemia changed from 3.38 h/day at baseline to 2.03 h/day at 6 months in the flash glucose monitoring group, and from 3.44 h/day to 3.27 h/day in the control group; with the between-group difference of -1.24 (SE 0.239; $p<0.001$) (17). Real-time glucose trend data, rather than retrospective analysis of the recordings, were predominantly used for self-adjustments of glycaemic control in this study (17). Participants were likely highly motivated with well controlled diabetes - HbA1c <7.5% (58 mmol/mol) - which may impact generalizability of these results.

Retrospective use

Most of the evidence showing benefit from retrospective CGM in type 1 diabetes comes from observational and non-randomised prospective trials (18, 19). The evidence from randomised controlled trials to support retrospective CGM in type 1 diabetes is varied. One trial found retrospective CGM improved HbA1c compared to SMBG (20) whilst another found a non-significant improvement in HbA1c (21), and others found no difference (22-28). Some randomised controlled trials also found improvement in hypoglycaemia detection (23, 25). More recently the majority of studies have focused on real-time CGM.

<u>The evidence for continuous blood glucose monitoring in type 2 diabetes</u>

The evidence for CGM in type 2 diabetes is not as well studied and the data from those studies that have been conducted is less compelling. The value of regular SMBG in patients

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on oral hyperglycaemic agents, not likely to cause hypoglycaemia, is questionable, and hence the value added by CGM may be limited. It is likely that the greatest benefit of CGM in type 2 diabetes would be in patients on insulin with long-standing disease.

Real-time use

A 2008 study assessed real-time CGM as a tool for behavioural change (29). Participants with type 2 diabetes with HbA1c levels of 8–10% (64-86 mmol/mol) on oral agents or insulin were randomised to real-time CGM 3 days per month versus SMBG for a total of 12 weeks. Both the CGM and the SMBG groups had significant reductions in HbA1c at 12-weeks but the difference in reduction in HbA1c was greater in the CGM group. In the CGM group, there was also a significant reduction in total daily calorie intake, weight, and postprandial glucose level, and a significant increase in total exercise time per week (30).

A study that included people with type 2 diabetes (n= 19) as well as type 1 diabetes (n= 126) found no difference in HbA1c reduction after 100 days of real-time CGM (31). A trial published in 2011 randomised 100 adults with type 2 diabetes who were not on prandial insulin to either real-time CGM versus four-times-daily finger prick monitoring. They demonstrated that 3 months of intermittent real-time CGM (two weeks on/ one week off) led to reductions in HbA1c. (32). Unlike the SWITCH cross over study in type 1 diabetes, they found this benefit was sustained during an additional 40 week follow-up period (33). The improvement in the real-time CGM group occurred without a greater intensification of medication suggesting that people made informed lifestyle choices leading to improved outcomes (33). This is consistent with another study which found continuous CGM increased physical activity (34). This sustained benefit and learned behaviour suggests that learning can be generalized and continued without ongoing use of real-time CGM, although the important question of what is the optimal duration and frequency of CGM remains unanswered.

Flash glucose monitoring (real-time use)

A 2016 study randomised patients with type 2 diabetes on intensive insulin therapy to real-time flash glucose monitoring versus SMBG for 6 months. They found a similar reduction in

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HbA1c between the two groups at six months, however, when stratified by age, there was greater improvement in HbA1c in those less than 65 years in the flash glucose monitoring group. The flash glucose monitoring group also had reductions in time spent in hypoglycaemia which was particularly pronounced during nighttime. A number of glucose variability measures including coefficient of variation and mean amplitude of glycemic excursions (MAGE), were analysed and an improvement in the flash glucose monitoring group was observed in three of these nine measures: coefficient of variation, low blood glucose index (LBGI) and continuous overall net glycaemic action x hours (CONGA) at 6 h, (but not at 2 h and 4 h time intervals) (35).

The study assessed patient satisfaction and QOL, and found improvements in the flash glucose monitoring group (35). The finding of improved QOL is in keeping with Polonsky's study of CGM users who completed an online questionnaire investigating perceived QOL benefits/losses since CGM initiation. Polonsky found improved QOL measures were attributed to various factors including reduced fear of hypoglycaemia, greater confidence and perceived control over diabetes (36).

Retrospective use

Several studies have been conducted to determine whether retrospective CGM can reduce HbA1c. Some studies, most of which were prospective, showed improved HbA1c with short term retrospective CGM compared to SMBG (23, 28), whilst another study showed no improvement (22). In the primary care setting, in patients commencing insulin, one study found no differences in major hypoglycaemia between retrospective CGM and SMBG, but did find enhanced post-prandial hyperglycaemia recognition and a trend towards improved HbA1c at 6 months with CGM, suggesting possible benefits (37).

<u>The evidence for continuous blood glucose monitoring in pregnancy</u>

Over the last ten years, there has been significant literature on CGM use in pregnancy in individuals with pre-gestational diabetes. Murphy et al evaluated the effectiveness of retrospective CGM during pregnancy on HbA1c, infant birth weight and macrosomia in

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women with type 1 and type 2 diabetes (65% type 1 diabetes). Women randomised to CGM wore the device for up to 7 days at intervals of 4-6 weeks between 8 and 32 weeks' gestation. The CGM group had lower HbA1c levels in the third trimester, 5.8% (40 mmol/mol) (SD 0.6) v 6.4% (46 mmol/mol) (SD 0.7), lower birth weight and lower risk of macrosomia (38). In contrast, a study looking at real-time CGM in pregnant women with pre-gestational diabetes (80% type 1 and 20% type 2 diabetes) found no improvement in glycaemic control or pregnancy outcomes (39). In this study, women were randomized to use real-time CGM for 6 days at 8, 12, 21, 27, and 33 weeks in addition to routine care, including self-monitored plasma glucose seven times daily, or routine care only. This study utilised older technology and compliance was suboptimal with only 64% women using CGM as per the study protocol. Hence, the negative result of this study may be due to poor compliance, or may be due to the need for continuous not intermittent CGM to see positive results, as evidenced in the non-pregnant population (1, 14).The CONCEPTT study randomised women who were pregnant or planning pregnancy with type 1 diabetes to capillary glucose monitoring with CGM or without. The primary outcome was change in HbA1c from randomisation to 34 weeks' gestation in pregnant women and change in HbA1c from randomisation to 24 weeks or conception in women planning pregnancy (40).In pregnant women using CGM, there was a small improvement in HbA1c (mean difference −0·19%; 95% CI −0·34 to −0·03; p=0·0207), and women randomised to CGM spent more time in target with less glycaemic variability. Neonatal health outcomes such as large for gestational age, neonatal intensive care admissions lasting more than 24 h and neonatal hypoglycaemia), were significantly improved, and this was postulated to be due to less exposure to maternal hyperglycaemia. There was no apparent benefit of CGM in reducing HbA1c in women planning pregnancy (40).

Barriers to implementation of CGM

Price

Certainly, an important consideration in any assessment of CGM is cost. A major barrier for people with diabetes is that frequent use is required, with most studies – particularly in type 1 diabetes – showing that people only benefit significantly if CGM is worn for the majority of

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the time. In Australia, the cost of real-time CGM can be prohibitive since it is not reimbursed for people over the age of 21 or with type 2 diabetes. On 1 April 2017, the Australian Government announced that it would direct $54 million towards fully subsidising CGM products for children and young people aged under 21 years with type 1 diabetes who face significant challenges in managing blood glucose levels. Implementation of this program is via the National Diabetes Services Scheme (NDSS). A patient's health professional needs to complete and sign the Continuous Glucose Monitoring Eligibility Assessment form, which is then submitted to their state or territory diabetes organisation for processing (7).

Not necessarily suitable for all

The expectations of benefit and choice of patient for CGM are factors requiring careful consideration. Polonsky pointed to three major types of self-monitoring obstacles: the desire to avoid thinking about blood glucose values and, more broadly, diabetes itself (Avoidance); the belief that self-monitoring is unlikely to be of value (Pointlessness); and the sense of self-monitoring of blood glucose as an unpleasant, costly task (Burden) (41). Whilst CGM may be less burdensome, it is unlikely to benefit people who do not check their blood glucose levels due to 'avoidance' or 'pointlessness'. Real-time CGM requires patient interaction and realistic expectations need to be set and health professionals need to consider what patient ideas, concerns and expectations are.

Accuracy reliability and wearability

Historically, the reluctance to adopt widespread use of CGM was due to concern over accuracy. Initially, there were problems with calibration error, sensor delay due to the physiological lag between interstitial glucose and blood glucose concentrations and interfering substances (42). These problems have decreased as technology has improved, with processes to reduce delay, filter out noise and eliminate the effects of interfering compounds (43). The delay as glucose is transported from blood to interstitial fluid is not important for retrospective CGM but may still be an important limitation for real-time CGM. If glucose levels are changing rapidly and if glucose level is low, this may delay warning of actual or impending hypoglycaemia (44, 45). Importantly, accuracy decreases at low glucose levels

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and when CGM devices record high or low readings all manufacturers recommend patients check their capillary blood glucose levels and take action based on the capillary blood glucose level. People with diabetes sometimes report frustration with CGM about lack of point accuracy, compared to a fingerstick reading. When using CGM, it is important to consider trends and the direction of glucose levels rather than glucose levels at one point and this requires education about how CGM values are best used and interpreted. Currently, for most devices used in Australia, CGM readings cannot be used as the only means of testing blood glucose levels and we recommend that regardless patients should be educated on the importance of fingerpick testing when glucose levels are unstable.

Nevertheless, CGM devices now have an accuracy approaching 10% mean absolute relative difference (MARD) between CGM readings and the values measured at the same time using capillary blood glucose measurements, which is considered safe for insulin dosing (46). Due to its increased accuracy, in December 2016 the Dexcom G5®, with a MARD of 9% (47), was approved by the FDA to make diabetes treatment decisions without confirmation with a traditional fingerstick test (48). In September 2017, the FreeStyle® Libre™, with a MARD of 11.4% (49) was similarly approved to make treatment decisions (50) (Table 1). At present, for other systems with a lower level of accuracy it is recommended that finger-prick glucose measurements should be performed to confirm CGM levels prior to management decisions aimed at addressing acute changes in glucose levels.

Cost effectiveness of continuous glucose monitoring and flash glucose monitoring

It is possible that CGM could reduce health care costs:

- In the short-term, by averting hypoglycaemia and diabetic ketoacidosis requiring hospitalisation;
- In the long-term, by decreasing complications through better glycaemic control (although evidence to support this statement is limited); and
- Through more efficient use of health professional time.

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An American study examined the potential cost implications of real-time CGM as a tool for reducing rates of severe hypoglycemia requiring hospitalisation in adult patients with type 1 diabetes who have hypoglycemia unawareness. In a hypothetical scenario the investigators found that real-time CGM reduced the cost of annual hypoglycemia-related hospitalisations by $54,369,000, yielding an estimated net cost savings of $8,799,000 to $12,519,000, which equates to savings of $946 to $1,346 (US dollars) per patient per year (51). An Australian study compared sensor-augmented insulin pump therapy with "Low Glucose Suspend" functionality versus standard pump therapy with self-monitoring of blood glucose, in patients with type 1 diabetes who had impaired awareness of hypoglycemia. The investigators demonstrated an incremental cost-effectiveness ratio of $18,257 (AUS dollars) per severe hypoglycemic event avoided in those with hypoglycaemia unawareness (52). A UK study in a similar patient population also found the addition of CGM to pump therapy to be cost effective (53).

In terms of cost effectiveness in type 2 diabetes, in a previously mentioned study where Vigersky et al (52) demonstrated various glycemic benefits of a 3-month course of real- time CGM in people with type 2 diabetes not taking prandial insulin, they went on to examine the impact on economic outcomes. The investigators used the IMS Core Diabetes Model for analyses and modelled life expectancy and quality-adjusted life expectancy from real-time CGM. Due to its low cost and improvement in HbA1c, the investigators found it to be a cost-effective disease management adjunct (52).

Studies looking at cost effectiveness are important as reimbursement by government and insurance companies is largely decided on cost-effectiveness. Even if CGM effectively reduces HbA1c and hypoglycemia, it will not be reimbursed if the incremental cost-effectiveness ratio is above the "willingness-to-pay" threshold for that country and its healthcare scheme (54). Based on the above studies that use cost modelling, it seems likely that CGM will reduce healthcare resource utilisation for acute and chronic complications, but such studies based on economic modelling can only be used as estimations of costs. As

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recommended by international bodies, we need more real-world analyses to confirm potential cost savings (5).

Conclusions

Advances in technology have improved the accuracy and reliability of CGM performance and reduced cost and the physical burden imposed on the patient. There is now a significant body of evidence for real-time CGM benefiting glycaemia in type 1 diabetes. The Australian Government has recognised this and is supporting funding of real-time CGM for people less than 21 years old. The benefit of retrospective CGM in type 1 diabetes is less apparent. This observation may be explained by the greater unpredictably in people with type 1 diabetes requiring an immediate response by the patient. In select people with type 2 diabetes characterised by recurring patterns of glycaemia, retrospective CGM may play a significant role. Whilst further research into cost analysis is needed, CGM may reduce the overall cost of diabetes management and improve QOL and long-term complications, particularly in type 1 diabetes.

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Table 1: Characteristics of CMG devices available in Australia

Sensor Device	*Accuracy (MARDS %)**	*TGA approved for dosing*	*Duration of wear*	*Calibration requirement*	*Connect to smart phone*	*Connect to insulin pump*	*Remote monitoring*	*Alarm capacity*	*Low glucose suspend*
RETROSPECTIVE									
Medtronic iPro® 2 *Enlite™ Sensor & iPro recorder*	9	No	6 days	2/day	No	No	No	No	No
REAL-TIME									
Medtronic									
*Enlite™ Sensor & Guardian™ 2 link transmitter***	11	No	6 days	2/ day	No	Yes MiniMed® 640G	No	Yes	Yes
Enlite™ Sensor & MiniLink®	14	No	6 days	2/day	No	Yes MiniMed®	No	Yes	Yes

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*transmitter****						Veo			
Enlite™ Sensor & Guardian™ connect transmitter	11	No	6 days	2/day	Yes	No	Yes	Yes	No
Dexcom									
Dexcom G4®	13	No	7 days	2/day	No	Yes Animas	No	Yes	No
Dexcom G5®	9	Yes	7 days	2/day	Yes	Yes Animas	Yes	Yes	No
Abbott									
FreeStyle® Libre™	11.4	Yes	14 days	None	No	No	No	No	No

*%MARD=percentage mean absolute relative difference. Values should be interpreted with caution as few direct comparative studies within or between device manufacturers are available (47, 49, 55-57).

**Can only be worn with insulin pump Mini MiniMed® 640G, does not connect to other receiver

***Can only be worn with insulin pump Mini MiniMed® Veo, does not connect to other receiver

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Table 2: Comparison between self-monitoring of blood glucose, CGM and flash glucose monitoring technology.

	Self-monitoring of blood glucose	**Continuous glucose monitoring**	**Flash glucose monitoring**
Glucose measurement	Capillary	Interstitial	Interstitial
Calibration	NA	Twice daily	Not required
Finger-prick required	Yes	Yes	If rapidly changing glucose levels, hypoglycaemia or symptoms do not match sensor
Duration of sensor use	NA	7 days	14 days
Data updated	NA	Every 5 minutes	When the sensor is scanned with the reader
Hypoglycaemic alarm	No	Yes	No
Connection to insulin PUMP	No	Yes	No
Connection device	NA	Disposable sensor worn on the abdomen	Disposable sensor worn on the back of the arm

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Figure 1: Visual depiction of Dexcom G4® continuous glucose monitoring system.
The sensor is worn on the abdomen and continuously records blood glucose levels which is displaced on the handheld receiver.

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Figure 2: Visual depiction of flash glucose monitoring system.

The sensor is worn on the back of the arm and a real-time glucose level is obtained by scanning the sensor with the reader.

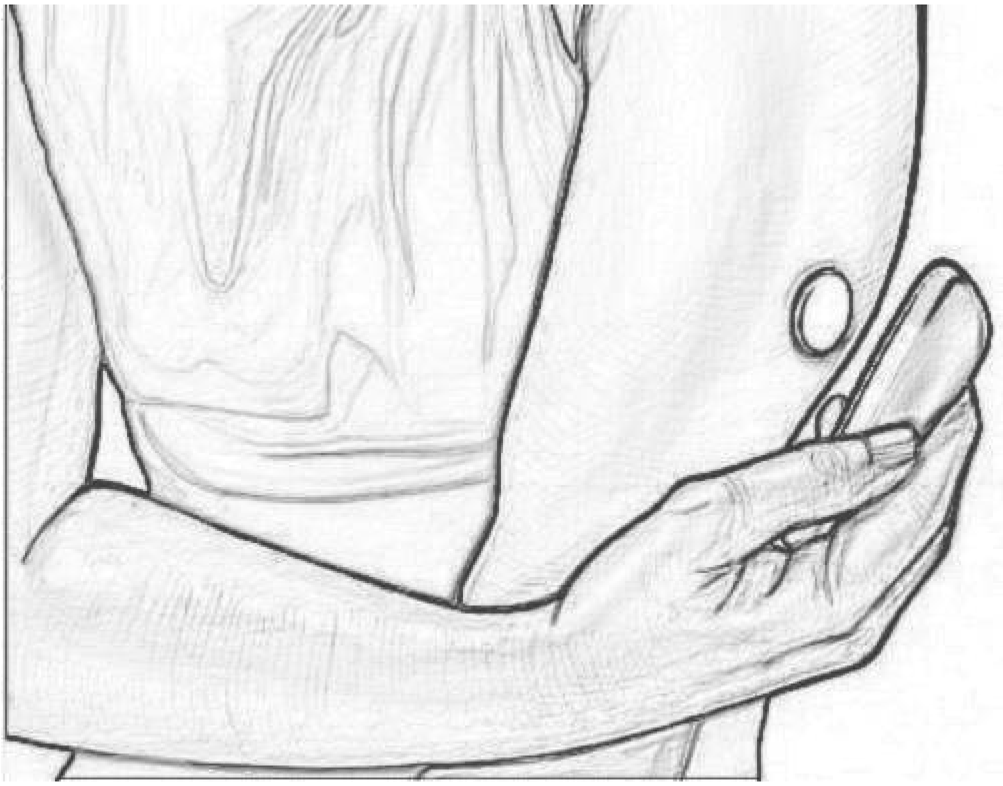

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Figure 1.jpg

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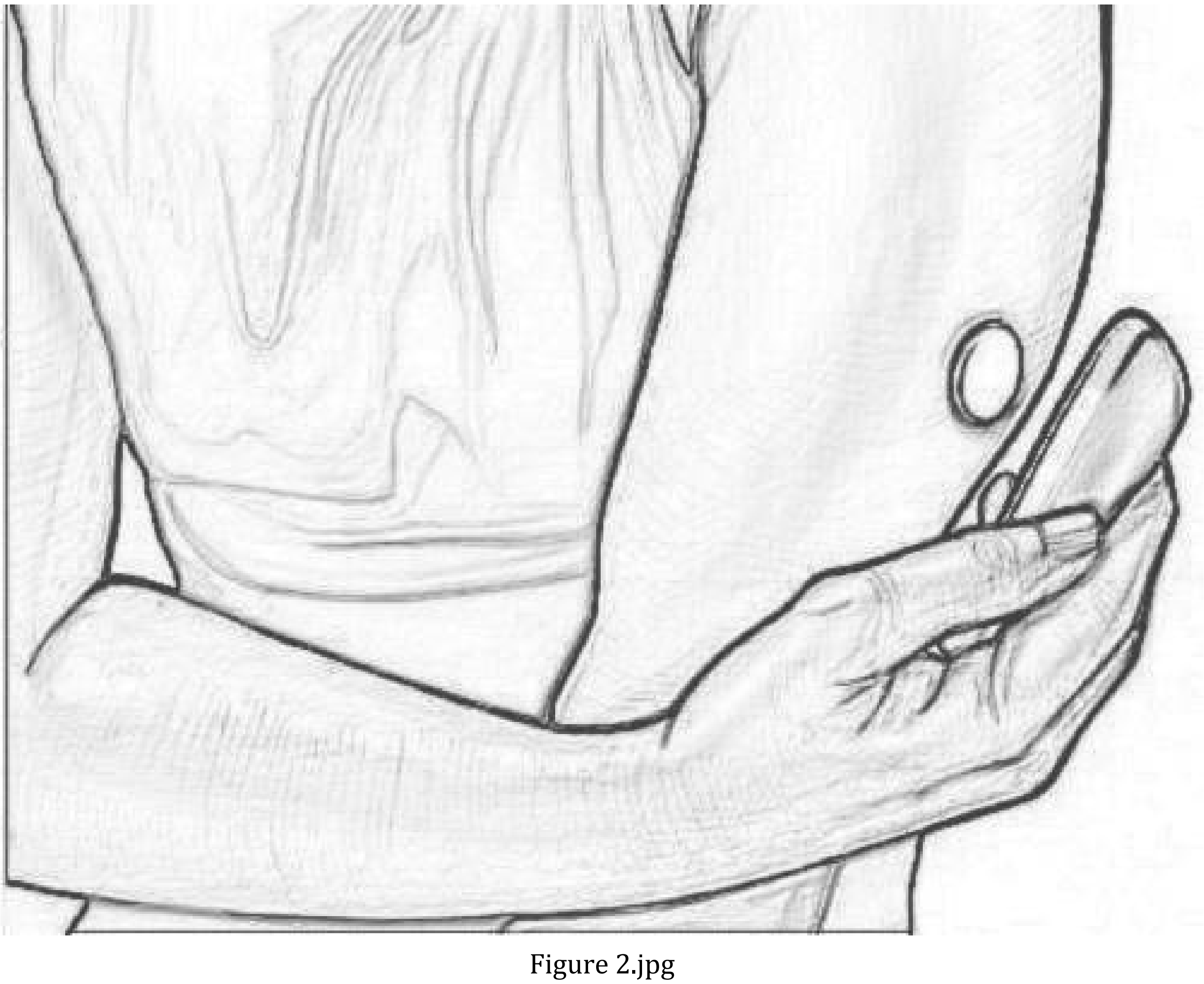

Figure 2.jpg

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