Flash glucose monitoring in people with diabetes

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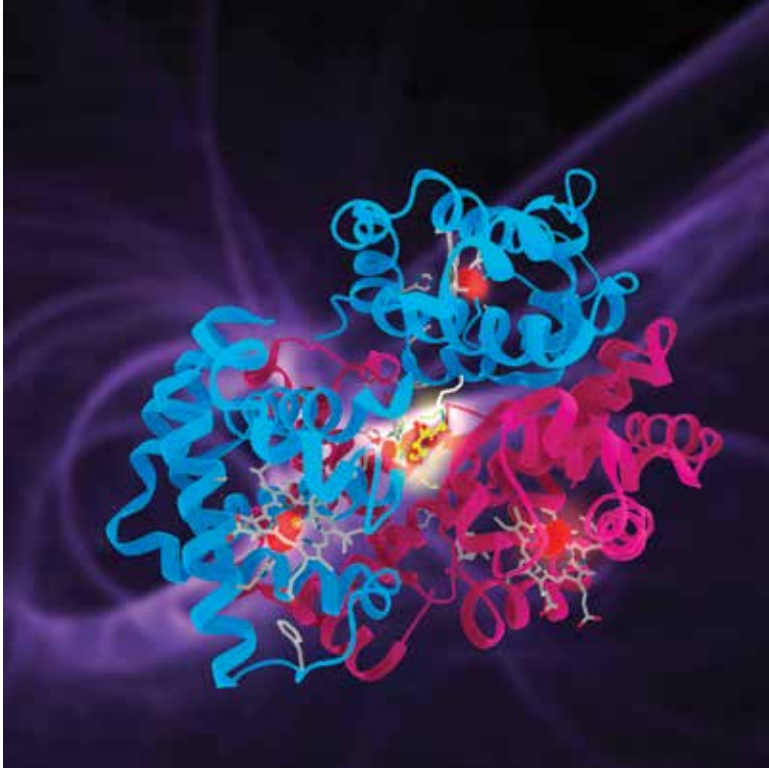
A flash glucose monitoring system has been approved for use in monitoring glucose levels in adults who have diabetes mellitus treated with insulin. This new technology has high potential for assisting people to optimise self-management of glycaemia.



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Self-monitoring of blood glucose (SMBG) is an integral component of diabetes care in people using intensive insulin regimens (multiple-dose insulin or insulin pump) and is useful for many people on less intensive insulin regimens or non-insulin diabetes therapy. People on intensive insulin regimens should consider SMBG prior to meals and snacks, occasionally postprandially, at bedtime, prior to exercise, when they suspect hypoglycaemia, after treating hypoglycaemia and prior to critical tasks such as driving.[1] There is a strong association between higher frequency of SMBG and lower glycosylated haemoglobin (HbA_{1c}) levels in people with type 1 diabetes, with the association levelling off at approximately 10 SMBG measurements/day.[2] Although the act of performing SMBG in itself does not improve HbA_{1c} levels, the use of SMBG data is vital to effectively managing glycaemia through adjustments in insulin dosing, meal intake and physical activity.[1] SMBG is also essential for preventing, detecting and treating asymptomatic hypoglycaemia and hyperglycaemia.[1]

Continuous glucose monitoring (CGM) measures interstitial glucose and can be a useful supplemental tool to SMBG, particularly for those who have impaired hypoglycaemia awareness or have frequent hypoglycaemia episodes.[1] Real-time CGM devices have alarms for hypo- and hyperglycaemia, and some devices can be used in sensor-augmented insulin pump therapy with low-glucose suspend settings to reduce hypoglycaemia. CGM still requires calibration with SMBG measurements, and the current CGM technology is not recommended as a replacement for self-monitoring.

The new FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care) is an interstitial glucose monitoring system

Key points

- **Fingerprick capillary blood glucose testing is a key component of management in many people with diabetes, but some people find it painful and inconvenient, which may be a barrier to optimal self-monitoring.**
- **The new FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care) is an interstitial glucose monitoring system that is TGA approved for detecting trends and tracking patterns in adults with diabetes treated with insulin.**
- **The sensor is worn on the arm, and interstitial glucose levels over the preceding eight hours can be viewed with a one-second 'flash' of the handheld reader over the sensor.**
- **Fingerprick glucose calibration is not required.**
- **Reports are generated in the freely available software, which summarises glucose data across the day.**
- **Flash glucose monitoring is relatively painless, convenient and discreet and the sensor lasts up to 14 days.**
- **Challenges in using flash glucose monitoring include the financial cost, which may be a barrier for many people.**

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Figures 1a and b. The Freestyle Libre Flash Glucose Monitoring System showing (a, left) the sensor in place on the patient's arm, and (b, right) the data provided on the reader with the past eight hours of glucose levels and the trend arrow.

Image courtesy of Abbott Diabetes Care Australia.

that does not require calibration with fingerprick capillary blood glucose measurement. The FreeStyle Libre Flash Glucose Monitoring System (real-time device) was approved by the Australian TGA on 5 February 2016 for use as a glucose monitoring device for detecting trends and tracking patterns in people aged 18 years and over with 'insulin-dependent diabetes mellitus'. This product is now available for purchase online. Another device, the FreeStyle Libre Pro Flash Glucose Monitoring System, collects glucose data over 14 days, to which the patient remains blinded and which is intended for retrospective review by the diabetes care team to subsequently guide changes in diabetes management, according to the identified glucose trend patterns. This article describes the flash glucose monitoring system (real-time device) and the differences between flash glucose monitoring, SMBG and CGM.

Diabetes care using the flash glucose monitor

Fingerprick capillary blood glucose testing is a key component of diabetes self-management in people with type 1 diabetes and many people who have type 2 diabetes. Some people find fingerprick glucose testing with lancets and test strips painful and inconvenient, and this may act as a barrier to optimal testing for self-monitoring. The new flash glucose monitoring system offers a convenient, relatively painless and discreet option for glucose monitoring, as an adjunct to fingerprick SMBG testing, providing people with diabetes and their diabetes care teams with accurate glucose data for managing their diabetes treatment. The flash glucose monitoring technology consists of a small sensor, applied to the arm with an applicator, and a handheld reader (Figures 1a and b). Glucose data can be downloaded and viewed as a summary in the ambulatory glucose profile (AGP) computer software.

Sensor

The single-use sensor unit is a 35 mm diameter disc with a height of 5 mm.[3] The sensor is applied to the back of the upper arm using an applicator that inserts a 5 mm thin, flexible filament into the subcutaneous tissue. The sensor is held in place by an adhesive pad. It uses osmium-based wired enzyme sensor technology that is factory calibrated.[4] One hour after being activated by scanning with the reader device, the sensor will start to record interstitial glucose levels every 15 minutes. The sensor lasts for up to 14 days. It is water resistant to one metre of water immersion for up to 30 minutes, and thus can be worn during showering, bathing and swimming.[3]

Reader

Interstitial glucose levels measured by the sensor can be viewed by a one-second scan (or 'flash') of the reader over the sensor while worn on the arm, over a clothing thickness of up to 4 mm.[3] The reader will provide the current glucose reading, in addition to a graphical view of the preceding eight hours of glucose recordings and a trend arrow to indicate the direction of glucose change (Figure 1b). Up to 90 days of glucose data can be stored in the reader memory; however, to capture the full glycaemic history over this time, the sensor must be replaced every 14 days and must be scanned by the reader at least every eight hours. The rechargeable reader features a backlit colour touchscreen. The reader also has a separate strip port for blood glucose and ketone testing. The blood glucose testing results do not affect the glucose results from the sensor.

Software

Data from the reader can be downloaded to a computer using a USB connection.[3] Reports are generated in the freely available FreeStyle Libre software, which summarises glucose data across the day in an AGP. This can help the patient and their diabetes care team identify overall glucose patterns and subsequently alter insulin administration or make behavioural changes to stabilise glycaemia. The report provides an estimated HbA_{1c} level, and specific summary data on low glucose levels, median glucose level and glucose variability. Glucose pattern insights are displayed in a pictorial colour-coded 'traffic light' format to indicate glucose trends across time periods in the 24-hour day (see AGP, Figure 2).

Sensor accuracy

A clinical study assessing the accuracy of the FreeStyle Libre Flash Glucose Monitoring System in people with type 1 and type 2 diabetes over 14 days of home use found the overall mean absolute relative difference (MARD) was 11.4% for sensor results compared with a capillary blood glucose reference measurement.[5] A smaller MARD indicates a more accurate result. A different study of continuous glucose monitoring compared the Dexcom G4 Platinum and Medtronic Paradigm Veo Enlite systems in people with type 1 diabetes over six days of home use and found MARD to be 12.2% and 19.9%, respectively.[6] In these studies, all

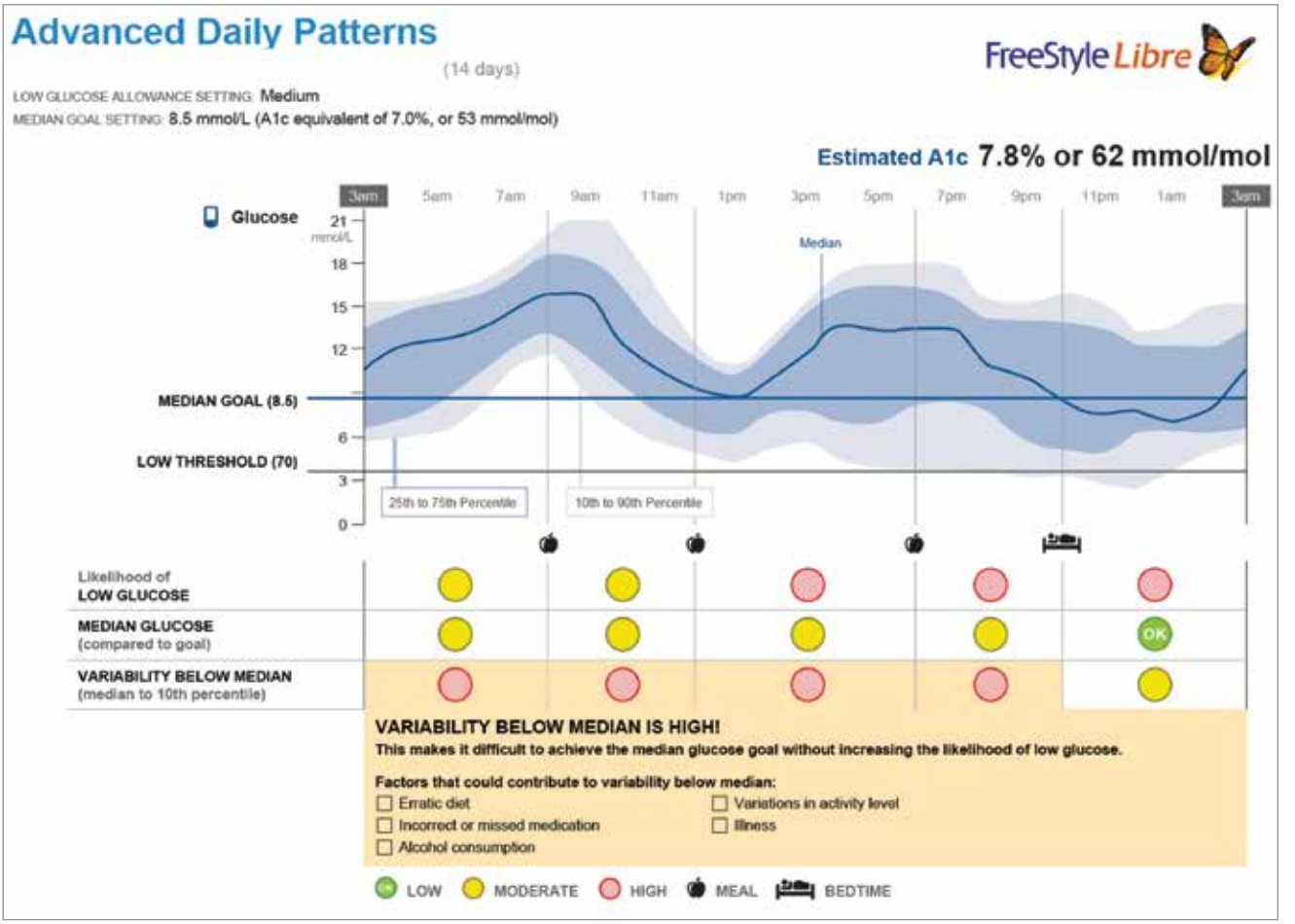

Figure 2. An example of an ambulatory glucose profile summary page of 14 days of data derived from the Freestyle Libre Flash Glucose Monitoring System. The user-friendly 'traffic light' signals help to identify where desirable outcomes in glucose levels are being realised and also areas for concern and improvement (red lights). In this example, some low glucose readings at certain time points later in the day, and also variability between days in blood glucose levels, are the main issues identified to be addressed.

Image courtesy of Abbott Diabetes Care Australia.

three types of sensors showed a higher MARD (and thus reduced accuracy) when in the hypoglycaemia range compared with the MARD in the normoglycaemia range.[5,6] It is difficult to make clear comparisons between studies because of the different methodologies used. The quoted MARD in the product information is 9% for the Dexcom G5 Mobile CGM System,[7] and 13.6% for the Medtronic Enlite sensor used in the MiniMed 530G System.[8]

The accuracy of the FreeStyle Libre Flash Glucose Monitoring System remained reasonably stable over 14 days of wear during a clinical study, and sensor accuracy was not affected by patient factors such as body mass index, age, type of diabetes, left and right arm insertion sites, insulin administration or HbA_{1c} level.[5] The mean lag time between sensor- and laboratory-measured venous glucose results was reported as 4.5 minutes.[5]

Clinical trials of flash glucose monitoring

Recently completed randomised controlled trials in 2016 (REPLACE study in type 2 diabetes and IMPACT study in type 1 diabetes) have, in abstract form, reported the effects on glycaemic control and the patient experience of using flash glucose monitoring compared with SMBG. The IMPACT study in people with type 1 diabetes comparing six months of SMBG with flash glucose monitoring was presented at the recent American Diabetes Association meeting.[9] This study showed a 38% reduction in time in hypoglycaemia (<3.9 mmol/L), with reductions in hypoglycaemia occurring both during the day and overnight. There were no differences in mean glucose or HbA_{1c}. Scanning frequency averaged 15.1 per day when using the FreeStyle Libre Flash device, and SMBG tests dropped from a baseline median of 5.4 to 0.1 times per day. In the control group, the SMBG frequency remained unchanged at 5.6 times per day. Those using flash glucose monitoring reported a significant improvement in treatment satisfaction and quality of life.

Results of the REPLACE study were presented as an abstract in early 2016 at the 9th International Conference on Advanced Technologies & Treatments for Diabetes in Milan.[10] In this study, patients with type 2 diabetes on intensive insulin regimens were randomised to either six months SMBG or use of flash glucose monitoring for diabetes self-management. Although the reduction in the level of HbA_{1c} was similar overall in the two groups, there was a significantly greater reduction of HbA_{1c} level in patients less than 65 years of age in the flash glucose monitoring group compared with SMBG. In the total cohort there was a significant reduction in overall hypoglycaemia during daytime and night-time in the flash glucose monitoring group compared with the SMBG group.

Use of the flash glucose monitoring system in the real-world is very limited to date in Australia, and in time the clinical utility of this new type of glucose monitoring will become clearer, and can then increasingly be compared with the experience being reported in other countries,[4] and in Europe.

Reported benefits of flash glucose monitoring

The reported benefits of using the flash glucose monitor are as follows.

- Easy to apply sensor with no or minimal discomfort in the process.
- No fingerprick glucose calibration is required, and people may be more willing to monitor glucose levels using this painless sensor.
- The sensor lasts up to 14 days (longer than currently available continuous glucose monitoring sensors).
- The sensor is water resistant.
- The relatively discreet sensor is worn on the upper arm and can be scanned through clothing.
- The current glucose reading is obtained by a one-second 'flash' of the sensor by the reader.
- Trends in glucose readings across the preceding eight hours are displayed.
- Downloading reader data to the free, user-friendly AGP software is straightforward.

Challenges in using flash glucose monitoring

Some barriers and challenges to using the flash system include the following.

- The flash glucose monitoring system is not a continuous glucose monitor, and thus requires scanning at least once every eight hours to capture the full glucose profile.
- The financial cost may be a barrier for many patients, with the FreeStyle Libre sensor which lasts up to 14 days, currently priced in Australia at A$95), and the reusable FreeStyle Libre reader also at A$95.
- There are no real-time alarms for hypoglycaemia or hyperglycaemia.
- It cannot be linked directly to insulin pumps in sensor-augmented insulin pump therapy with low-glucose suspend settings.
- The sensor worn on the upper arm may accidentally fall off if subjected to trauma in some people, despite the sensor adhesive.
- A fingerprick test with a blood glucose meter is still recommended during times of:
  - rapidly changing glucose levels, as the interstitial glucose levels during this time may not accurately reflect blood glucose levels
  - during hypoglycaemia or impending hypoglycaemia
  - symptoms that do not match the flash glucose monitor readings.

Conclusion

The new flash glucose monitoring system is a glucose sensor technology that can potentially replace most fingerstick capillary blood glucose testing in people with diabetes receiving insulin treatment. It is painless, convenient and discreet, and thus may reduce the barriers to optimal frequency of SMBG, which is key to managing glycaemia in many people with diabetes. The current financial cost may restrict routine use of flash glucose monitoring in some people. There is still potential to improve accuracy in future technology, particularly during times of hypoglycaemia and rapidly changing glucose levels. **ET**

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COMPETING INTERESTS: Professor Twigg is on the National Advisory Board for the FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care). Professor Twigg and Dr Lee are planning clinical studies in which Abbott Diabetes Care will supply product.