Devices for diabetes care: A practical guide

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Technology can be a help to many people with diabetes, from the large numbers undertaking self-monitoring of blood glucose to adjust their treatment and guide them in managing everyday life, to the few who are protected from the dangers of hypoglycaemia by sensor-augmented insulin pump therapy with an automated insulin suspension feature. This brief guide is designed to answer some of the questions that may arise about the place of such technologies in diabetes care.

Although much of the care of people using advanced technology to manage their diabetes is mainly conducted in secondary care, there are potentially significant advantages to making use of particular technologies in primary care. For example, continuous glucose monitoring (CGM) could be provided for people with diabetes for a short period of time as an educational tool.

In an age of readily available information, it is important to be able to answer questions people with diabetes may ask about current technologies and investigate all the possible options for each individual to optimise their care.

Self-monitoring of blood glucose

What is the technology?

Blood glucose levels can be measured using a drop of blood, usually from a fingertip. Most glucose meters use an electrochemical method, whereby the blood is sucked up by capillary action onto an enzyme electrode containing glucose oxidase, and a component of the resulting chemical reaction is measured by the meter to generate the blood glucose value.

What are the benefits?

There are a large variety of blood glucose meters on the market, which offer the user different advantages. Presentational features that may influence an individual's choice include size, shape, weight and even colour. More pragmatic reasons for choosing a particular meter may be the time it takes to calculate a glucose reading, which can be as little as 5 seconds, or the amount of blood the meter requires for analysis. Ease of use may include no need either for calibration or coding strips for the meter used.

The way the data from the meter are presented is often an important consideration. In most cases, it is possible to scroll through glucose readings on the screen, with the time displayed (provided the user has set it to the correct time initially), and to view mean blood glucose readings over a period of time, for example 7 or 14 days.

The most significant advance, however, has been the facility to upload data from the meter to a computer via a USB cable or other interface, such as infrared. This saves the user having to keep paper records (although many still find this helpful) and can allow identification of patterns of glucose change over days. Caution must be taken when capillary blood glucose readings are joined graphically, as this does not represent the true continuous blood glucose profile, but is simply joining the dots. Users can also download software, including smart phone applications that allow them to manage their blood glucose readings and log other information, such as meals and exercise.

Another feature that may appeal to the user is alternative site testing which is offered by most

Article points

1. Continuous glucose monitoring measures interstitial fluid glucose rather than blood glucose levels.
2. Insulin pump therapy delivers rapid-acting insulin continuously from a programmable pump, via a length of fine tubing attached to a teflon-coated plastic or metal infusion set inserted subcutaneously.
3. The concept of the artificial pancreas is an insulin-delivery system in which the rate of insulin administration is automatically adjusted according to the output of a glucose monitoring device to maintain normal blood glucose levels.

Key words

- Artificial pancreas
- Continuous glucose monitoring
- Insulin pump therapy
- Self-monitoring of blood glucose

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1. Continuous glucose monitoring (CGM) measures interstitial fluid glucose rather than blood glucose levels The commonly used continuous glucose monitors are based on an enzyme-tipped electrode that is inserted subcutaneously, usually into the abdominal wall.
2. The CGM user can see trends in glucose levels and can set high and low glucose alerts and predictive alarms to warn them when levels go significantly outside the target range. The user can then respond to this information to adjust therapy in real-time.
3. Before acting on an absolute interstitial glucose value it must be confirmed by checking a capillary blood glucose level.

meters currently on the market. This allows sites other than the fingertip to be used for blood sampling, such as the forearm or thigh. However, changes in glucose levels are usually picked up earlier at the fingertips, so alternative site sampling should not be used for non-routine tests, such as confirming hypoglycaemia.

What costs are involved?

The main focus on cost of self-monitoring of blood glucose (SMBG) has been in type 2 diabetes, where its cost-effectiveness has been questioned. The annual cost of SMBG in type 2 diabetes is estimated to be £30 million. In type 2 diabetes, NICE (National Collaborating Centre for Chronic Conditions, 2008) have advised that self-monitoring of plasma glucose should be available to:

- Those on insulin treatment.
- Those on oral glucose-lowering medications to provide information on hypoglycaemia.
- Assess changes in glucose control resulting from medications and lifestyle changes.
- Monitor changes during intercurrent illness.
- Ensure safety during activities, including driving.

Continuous glucose monitoring

What is the technology?

CGM measures interstitial fluid glucose rather than blood glucose levels (*Figure 1*). The commonly used devices are based on an enzyme-tipped electrode that is inserted subcutaneously, usually into the abdominal wall. The information from this sensor is relayed to a monitor that displays the glucose data in graphical form. Values taken from the sensor every few seconds are averaged over a few minutes to produce this output. The CGM user can see trends in glucose levels and can set high and low glucose alerts and predictive alarms to warn them when levels go significantly outside the target range. The user can then respond to this information to adjust therapy in real-time.

Caution is needed in interpreting the information obtained on two counts. First, there is a lag time between blood and interstitial glucose levels, and when glucose levels are rapidly changing, this delay can be as great as 20 minutes. Therefore, before acting on an absolute interstitial glucose value it must be confirmed by checking a capillary blood glucose level. This is not as crucial if action is being taken on a trend in the glucose level, as this will usually be reliably demonstrated by the sensor. In this respect, CGM is like a CCTV camera giving a slightly fuzzy but continuous display of glucose levels, in contrast to the accurate digital snapshot provided by a single capillary glucose reading from a glucose meter.

Second, the user has to be careful to allow enough time for an intervention to take effect. For example, if a correction dose of insulin is given to bring down an elevated glucose level, the user must wait at least half an hour before giving a further correction dose. In some case reports the user has given five correction bolus doses in 20 minutes because the glucose levels on the monitor had not started to fall (Wolpert, 2008).

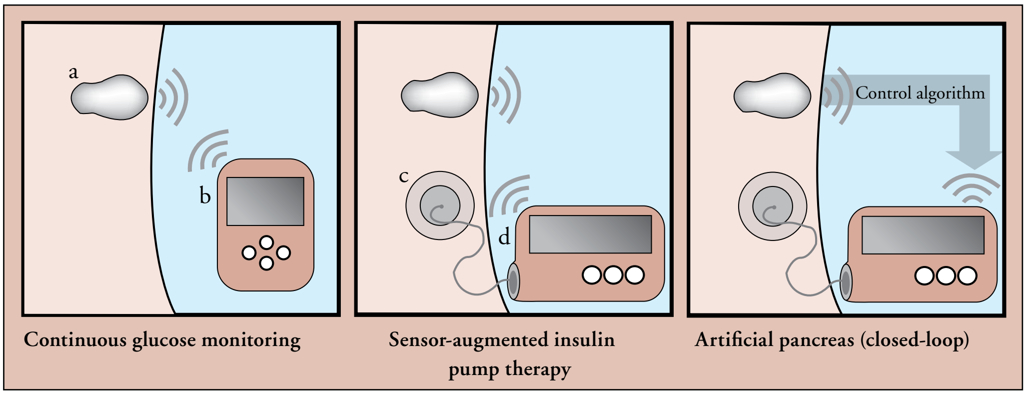

Figure 1. Illustration of devices for the management of diabetes progressing towards the closed-loop. a) Wireless continuous glucose monitoring (CGM) sensor. b) CGM receiver. c) Insulin infusion set. d) Sensor-augmented insulin pump.

The data from the sensor can also be uploaded to a computer so that changes can be made to treatment regimens on the basis of retrospective evaluation. This is most effectively done when the user has kept a record of meals, exercise and other daily activities that may influence blood glucose levels.

What are the benefits?

As well as real-time CGM, there is also the option of retrospective – or blinded – CGM, whereby the user wears a sensor for up to 6 days, but cannot see any readings displayed. The data from the sensor is uploaded to a computer at the end of this period and changes can be made to therapy according to the findings (*Figure 2*). There is limited evidence that this may produce glycaemic control benefits in populations, but in experienced hands there can be benefits when used in selected individuals.

Possible reasons to refer for consideration of CGM would include recurrent unexplained hypoglycaemia or suboptimal glycaemic control for which an immediate cause cannot be identified using conventional SMBG.

What is the cost of the technology?

The main limitation to personal use of CGM is the cost. In contrast to SMBG, where meters are often given away free of charge to people with diabetes or sold at fairly low cost in pharmacies, and meter strips are reimbursable on prescription, CGM is not specifically funded on the NHS. Users must therefore either pay for it themselves, or rely on NHS funding from a secondary care provider or on an exceptional basis from primary care trusts.

The cost of the system is around £1000, with sensors costing around £40 per week. For continuous usage – the only way of using CGM of proven benefit – the cost to the individual for the sensors alone would be around £2000 per year. This has meant that there are few people funding CGM on their own. CGM will, therefore, be almost exclusively provided on the recommendation of secondary care clinicians.

Insulin pump therapy

What is the technology?

Insulin pump therapy delivers rapid-acting insulin continuously from a programmable pump, the size of a pager, via a length of fine tubing attached to a Teflon-coated plastic or metal infusion set inserted subcutaneously, usually into the lower abdominal wall. Depending on the make and model, the pump can deliver insulin at rates as low as 0.025 units/hour, and the rate can be altered every 30–60 minutes. It is this ability to alter the basal rate that principally distinguishes insulin pump therapy from multiple daily injections (MDI). In addition, the basal rate can be temporarily altered downwards, for example, to allow the user to take exercise, or upwards to cover intercurrent illness.

What are the benefits?

Randomised controlled trials comparing insulin pump therapy with MDI have shown that absolute reductions in HbA_{1c} levels of around 0.5 percentage points are associated with a significant reduction in episodes of severe hypoglycaemia (Pickup and Sutton, 2008). These benefits are shown in observational studies where the reductions in HbA_{1c} tend to be greater, of the order of 1.0 percentage point (Pickup and Sutton, 2008).

In addition to a variable rate basal insulin infusion, the insulin pump can deliver insulin bolus doses as needed, both with meals and snacks, and to correct high glucose levels.

In recent years, the technology to deliver the bolus has advanced, so that a conventional bolus

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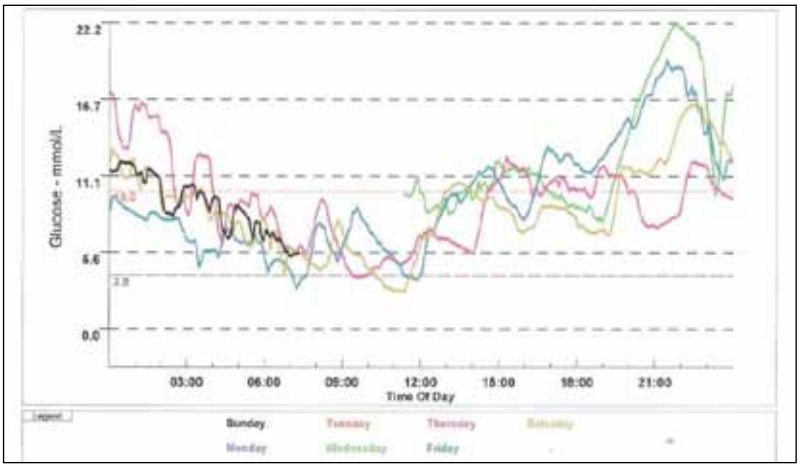

Figure 2. Retrospective continuous glucose monitoring data showing a daily profile overlay, which indicates a consistent trend with high levels in the late evening and early hours of the morning – further information is needed from the user to allow advice to be given as to therapy adjustment.

Page points

1. An insulin pump costs around £2000–3000, with a 4-year warranty, and the annual cost of consumables (infusion sets, tubing, insulin reservoirs) is around £1000.
2. A patch pump adheres directly to the skin and has an integrated mini-catheter sited subcutaneously. It is controlled by a remote unit linked by a wireless connection.
3. Sensor-augmented pump therapy can help to protect the user from hypoglycaemia, particularly if they have lost hypoglycaemia awareness, because the sensor alarms warn of glucose levels outside the user's target range, or predict when these may soon occur.

can be administered, or a bolus extended over as long as 8 hours, or a combination of the two in different proportions. The latter can be very useful following meals with high fat or carbohydrate content, which tend to be absorbed over longer periods of time. The user can also consult in-built algorithms that take into account insulin previously administered, blood glucose level and carbohydrate intake to calculate how many units of insulin should be given with a particular meal.

What is the cost of the technology?

An insulin pump costs around £2000–3000, with a 4-year warranty, and the annual cost of consumables (infusion sets, tubing, insulin reservoirs) is around £1000. In view of the cost, NICE have twice appraised insulin pump therapy, publishing their latest review in July 2008 (NICE, 2008).

The guidance concluded that insulin pump therapy was indicated for adolescents and adults (≥12 years of age) with type 1 diabetes using MDI and after structured education (in the case of adults) who either fail to achieve their target HbA_{1c} level because of disabling hypoglycaemia, or cannot achieve an HbA_{1c} of <8.5% (<69 mmol/mol) despite fully optimised MDI. In children younger than 12 years of age an insulin pump can be considered for delivery of intensified insulin therapy from diagnosis, without the need for an initial trial of MDI (NICE, 2008).

NICE specified that pump therapy was not indicated for people with type 2 diabetes. However, there may be exceptional circumstances where those with type 2 diabetes using MDI therapy might be considered for an insulin pump. Other rare indications include insulin allergy, hypoglycaemia unawareness, needle phobia, intractable painful neuropathy, and gastroparesis or other severe symptomatic autonomic dysfunction.

What recent advances in insulin pump therapy have there been?

Patch pumps

A patch pump is a semi-disposable pump that does not need tubing to deliver the insulin. It does not necessarily need to be sited on the abdomen, and can be placed on the upper arm, for example. The pump adheres directly to the skin and has an integrated mini-catheter sited subcutaneously. It is controlled by a remote unit linked by a wireless connection.

Sensor-augmented pump therapy

The combination of an insulin pump and CGM can improve optimisation of insulin pump therapy. Sensor-augmented pump therapy (*Figure 1*) can help to protect the user from hypoglycaemia, particularly if they have lost hypoglycaemia awareness, because the sensor alarms warn of glucose levels outside the user's target range, or predict when these may soon occur. Protection against hyperglycaemic excursions is less immediately beneficial but, in the longer term, can lower HbA_{1c} levels (Raccah et al, 2009).

The expense of sensor-augmented pump therapy means that it will not be routinely considered for insulin pump users. The most likely indication would be if insulin pump therapy alone does not solve the concerns for those with hypoglycaemia unawareness, but another important need might be to avoid both hypoglycaemic and hyperglycaemic excursions in pregnant women.

A further sophistication of sensor-augmented insulin pump therapy is the automated suspend feature, whereby if the user fails to respond to two consecutive hypoglycaemia alarms, basal insulin delivery from the pump is automatically stopped for 2 hours, unless the user intervenes in the interim. The suspend mode can be activated again after a further half hour. This feature may be helpful for those with recurrent severe hypoglycaemia, usually in the context of unawareness.

What is the artificial pancreas?

The concept of the artificial pancreas (or closed-loop system) is an insulin-delivery system in which the rate of insulin administration is automatically adjusted according to the output of a glucose monitoring device to maintain normal blood glucose levels (*Figure 1*). While this has been achieved in one individual using an intraperitoneal insulin pump controlled by a sensor implanted in the jugular vein (Renard et al, 2003), this solution is too invasive to be routinely used in clinical practice. A number of research centres – mostly in the USA, with one in the UK based in Cambridge – are working on a system that combines currently available insulin pumps and CGM devices, developing algorithms that adjust insulin delivery from the insulin pump according to the interstitial glucose values from the sensor. These algorithms have to predict what will happen to the interstitial glucose levels allowing for the lag time between interstitial and blood glucose levels mentioned previously.

Preliminary studies have used these systems in controlled laboratory conditions (Hovorka et al, 2010). Overnight, when the basal insulin delivery is unaffected by external interference, blood glucose control is superior with the closed-loop system than with conventional pump therapy. At other times the closed-loop system is better at preventing the user from becoming hypoglycaemic.

It is likely that automated insulin delivery based on these closed-loop systems will gradually be integrated into existing pump technology. While a commercially available closed-loop system is probably over a decade away, extending automated insulin suspension to other situations, such as overnight, or automatic administration of correction bolus doses to correct significant hyperglycaemia under certain circumstances, may be introduced much sooner.

What about remote management using modern technology?

Web-based solutions can allow a healthcare professional to advise those using insulin pumps or sensors or both without the need for face-to-face consultation. The user can upload data from these devices to a password-protected website, and allow their healthcare professional remote access to the website. Useful information obtained may include the use of bolus doses, both in terms of type and dosage, temporary basal rate changes, and episodes of hypoglycaemia or hyperglycaemia. In addition, the user can log information such as meal carbohydrate content and physical activity. By considering the output from these devices together (*Figure 3*) the healthcare professional can give advice about adjustments to therapy or potential mistakes in self-management by the user.

Conclusion

Technology can be a useful adjunct in the management of many people with diabetes. It is important not to overstate what technology can do for the individual, nor to introduce technology for its own sake rather than addressing a specific need for the user. However, almost everyone with diabetes will at some point benefit from SMBG and, increasingly, people will reap the benefits from technological advance in insulin pump therapy and continuous glucose monitoring, and ultimately closed-loop insulin delivery systems.

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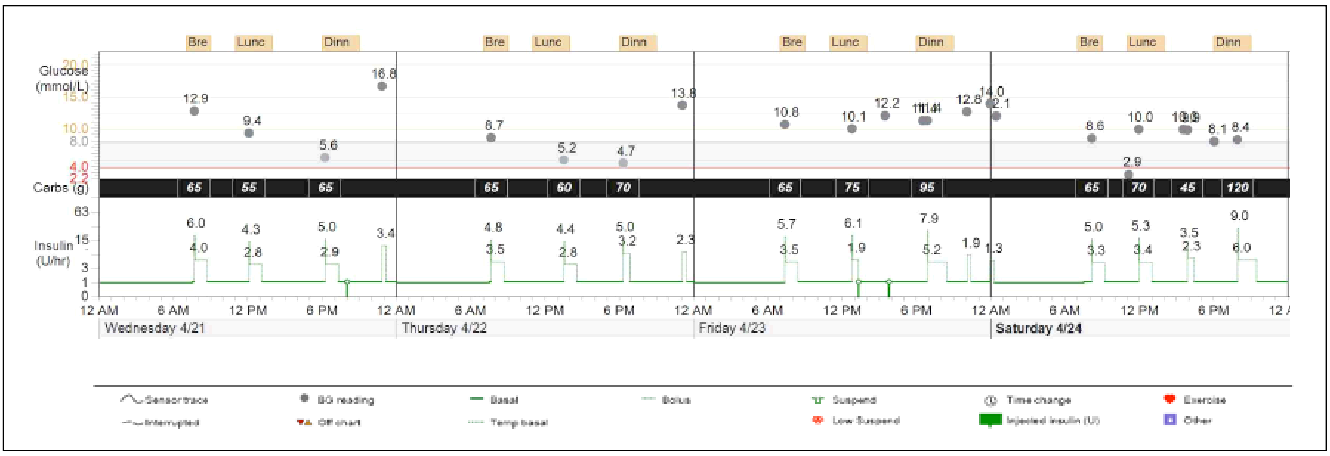

Figure 3. Carelink upload showing blood glucose meter data on the top panel; carbohydrate intake in the black middle panel; and pump insulin delivery data on the bottom panel, showing a flat basal rate, with bolus doses, most of which are dual wave.