Type 1 Diabetes

Advances in technology for management of type 1 diabetes

Roy W Beck, Richard M Bergenstal, Lori M Laffel, John C Pickup

Technological advances have had a major effect on the management of type 1 diabetes. In addition to blood glucose meters, devices used by people with type 1 diabetes include insulin pumps, continuous glucose monitors, and, most recently, systems that combine both a pump and a monitor for algorithm-driven automation of insulin delivery. In the next 5 years, as many advances are expected in technology for the management of diabetes as there have been in the past 5 years, with improvements in continuous glucose monitoring and more available choices of systems that automate insulin delivery. Expansion of the use of technology will be needed beyond endocrinology practices to primary-care settings and broader populations of patients. Tools to support decision making will also need to be developed to help patients and health-care providers to use the output of these devices to optimise diabetes management.

Lancet 2019; 394: 1265–73

Published Online September 15, 2019 http://dx.doi.org/10.1016/S0140-6736(19)31142-0

This is the first in a Series of three papers about type 1 diabetes

Jaeb Center for Health Research, Tampa, FL, USA (R W Beck MD); **International Diabetes Center, Park Nicollet and Health Partners, Minneapolis, MN, USA** (R M Bergenstal MD); **Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA** (Prof L M Laffel MD); **and King's College London, Faculty of Life Sciences and Medicine, Guy's Hospital, London, UK** (Prof J C Pickup DPhil)

Correspondence to: Dr Roy W Beck, Jaeb Center for Health Research, Tampa, FL 33618, USA **rbeck@jaeb.org**

Introduction

The management of type 1 diabetes has changed substantially in the past 25 years, particularly with respect to the adoption of intensive insulin therapy as the standard of care following publication of the landmark Diabetes Control and Complications Trial in 1993.[1] Technological advances in glucose monitoring and insulin delivery have greatly enhanced the ability to optimise glycaemic control with intensive therapy. We review the role of technology in the management of type 1 diabetes: changes in this technology over time, the use of technology for diabetes management, and future expectations for improvements in these technologies. We focus on advances in glucose monitoring and insulin delivery, including the advent of systems that combine the two to automate insulin delivery.

Insulin delivery

Most individuals with type 1 diabetes receive insulin either through injections or through continuous subcutaneous insulin infusion, commonly called insulin-pump therapy. Intensive insulin therapy by injection involves a long-acting basal insulin, usually once or twice a day, and a rapid-acting insulin given at meals (referred to as multiple daily injections). An inhaled insulin preparation is available that more closely mimics the time action of physiological insulin than does subcutaneously administered insulin (Afrezza, Mannkind, Westlake City, CA, USA), but it has been used very little.

Insulin pumps

Insulin-pump therapy has been available for more than 40 years. Most insulin pumps require tubing from the pump to the infusion site, but an alternative (a patch pump) has become available in which insulin is delivered directly from a pod adherent to the skin, with an integrated or very short infusion set. Insulin-pump technology has had several enhancements, including the ability to programme multiple different basal rates of insulin infusion during the day and night, and to deliver insulin boluses at meals in a variety of patterns, such as dual or square waves.[2] Bolus calculators or advisers that are integrated into the pump or incorporated in a handset give advice on insulin dose at meals, often with the inclusion of a nutrition database. Modern pumps can upload pump data to a computer for integration with glucose data to facilitate changes in diabetes management. The use of insulin pumps is increasing in most countries, but the uptake of this technology still varies widely between and within countries: among specialist units in England, pump use varies from less than 1% to about 70% of patients with type 1 diabetes.[3]

The effectiveness of insulin-pump therapy versus multiple daily injections has been debated for many years.[4] Some meta-analyses of these two treatments have been considered misleading because the trials selected were of short duration, used obsolete pump technology, or the trial participants did not have substantially elevated glycated haemoglobin (HbA_{1c}) or frequent hypoglycaemia at baseline.[5] Stronger evidence for the effectiveness of pump therapy comes from a metaregression[6] of mean effect size (HbA_{1c} difference or severe hypoglycaemia rate ratio) between these two techniques. This study[6] showed that insulin-pump therapy had a beneficial effect on reducing HbA_{1c} concentrations, particularly in patients with markedly elevated HbA_{1c}, and on the frequency of severe hypoglycaemia, particularly in patients with a history of frequent, severe hypoglycaemia. It is likely that

Search strategy and selection criteria

We searched PubMed (Jan 1, 2000–June 30, 2019) for publications in English using the search terms "artificial pancreas", "closed-loop systems", "automated insulin delivery", "continuous glucose monitor", "insulin pump", "continuous glucose monitoring and pregnancy", "closed-loop and pregnancy", "smart insulin pen", and "insulin algorithm". We largely selected publications in the past 5 years plus earlier major, relevant publications to cite. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant. Review articles are cited to provide readers with additional references.

similar outcomes to insulin-pump therapy can be achieved in many patients with multiple daily injections when used in combination with a continuous glucose monitor (CGM).

Observational surveys of insulin-pump effectiveness among patients treated in accordance with National Institute for Health and Care Excellence (NICE) guidelines at three UK clinics[7–9] showed a reduction in HbA_{1c} from a mean of 9·3% (78 mmol/mol) to 8·2% (66 mmol/mol) 2 years after switching from multiple daily injections to insulin-pump therapy. Observational studies of long-term pump effectiveness also indicate that most individuals with type 1 diabetes continue to have improved HbA_{1c} and a lower risk of hypoglycaemia for at least 5 years after starting to use a pump.[8,9] A reduction in the frequency of severe hypoglycaemia when using insulin-pump therapy versus multiple daily injections has also been reported in the T1D Exchange Registry in the USA.[10] In the multinational SWEET registry[11] of 16 570 people aged 1–18 years with type 1 diabetes, combining data from 26 countries (19 in the EU and 7 others), the use of insulin-pump therapy was associated with a significantly lower HbA_{1c} compared with the use of injections. Correlation studies have suggested that differences in pump use might be one of the factors that explain variations in glycaemic control between countries. Data on more than 54 000 children and adolescents with type 1 diabetes from three large, transatlantic registries showed that the use of insulin-pump therapy was lowest in England and Wales (14% *vs* 41% in Germany and Austria, and 47% in the USA), and HbA_{1c} was highest in England and Wales (8·9% [74 mmol/mol] *vs* 8·0% [64 mmol/mol] in Germany and Austria, and 8·3% [67 mmol/mol] in the USA).[12] With respect to mortality, data from the Swedish National Diabetes Registry[13] found that the use of insulin-pump therapy in adults with type 1 diabetes was associated with lower all-cause and cardiac-specific mortality compared with multiple daily injections use. A randomised trial[14] comparing insulin-pump therapy with multiple daily injections, in which equivalent structured diabetes education was given to each group, found that insulin-pump therapy was associated with greater treatment satisfaction and quality of life in domains such as dietary freedom and daily hassle. Observational studies in children have shown that self-reported and parent-reported diabetes-specific quality of life increases when patients are switched from multiple daily injections to insulin-pump therapy, with reduced parenting stress, hypoglycaemia worry, and overall diabetes burden.[15]

Theoretically, insulin-pump therapy could increase the risk of diabetic ketoacidosis because reduced insulin delivery could be caused by infusion-set malfunction. However, studies have shown that diabetic ketoacidosis occurs no more frequently, and might even be less frequent, with insulin-pump therapy than with multiple daily injections.[16–18] Although insulin-pump therapy is safe, surveys[19,20] have reported that pump malfunctions and problems with infusion sets are frequent. A review and appraisal of pump safety standards and reporting of adverse events by the European Association for the Study of Diabetes and the American Diabetes Association has called for a more rigorous, standardised, and transparent approach to safety by companies producing insulin pumps.[21]

A systematic review[22] of 11 cost-effectiveness studies of insulin-pump therapy versus multiple daily injections in eight countries (Australia, Canada, Denmark, Italy, Poland, Spain, the UK, and the USA) showed that although insulin-pump therapy is, on average, 1·4 times more expensive than multiple daily injections, this cost is partially offset by savings from reduced diabetes complications consequent to improved metabolic control. NICE guidelines on the indications for insulin-pump therapy are based on cost-effectiveness and have remained unchanged since 2008 (reviewed 2011).[23] Guidelines and check lists of best pump procedures[4,24] have been produced that will help practitioners to achieve and maintain optimal control when using insulin-pump therapy.

Smart pens and mobile applications

Although some users of insulin injections still draw insulin out of a vial for each injection, many patients now use a disposable or reusable insulin pen containing a prefilled insulin cartridge. Insulin-pen technology is advancing, with retrofitted or dedicated smart pens now offering wireless connection to smartphone applications or to the cloud for recording insulin dose and time, bolus calculation, and data sharing.

Many smartphone applications to support diabetes self-management are now available, offering logging of blood-glucose data, food intake (including photograph recognition), tracking of physical activity, dose recommendations, data transmission, and patient education. As with smart pens, there is very little controlled trial evidence of effectiveness for these applications.

Future advances in insulin delivery

Infusion sets are widely regarded as one of the weak components of insulin-pump therapy.[25] In addition to the problem of occlusion due to insulin aggregation or kinking of the tubing, inflammation and potential infection at the infusion site limits the use of infusion sets to no longer than 3 days, although one small study[26] showed that some polytetrafluoroethylene or steel catheters can function well for up to 7 days. Understanding the biochemical and cellular events at the infusion site and how they relate to cannula material and resultant glycaemic control, particularly variability, is a research priority for the next few years,[27] as is the ability to detect infusion-set failures early, before the development of substantial ketosis.[28] New infusion-set materials, coatings, and designs are being developed and tested in the hope of substantially extending

set longevity and reliability. Early studies of intradermal insulin delivery suggest absorption profiles that more closely mimic the physiology of biphasic insulin release, but more work in this area is needed.[29]

Glucose monitoring

Glucose monitoring methods have been improved: from urine testing before the 1980s, to self-monitoring of blood glucose concentrations with a portable blood glucose meter, introduced in 1978, to CGMs, introduced in 1999. Of all the technological advances in the management of type 1 diabetes, the ability to readily measure blood glucose concentrations throughout the day with a blood glucose meter has arguably been the greatest improvement.

Blood glucose meters

The introduction of blood glucose meters for use at home substantially changed the approach to the treatment of type 1 diabetes by giving patients the ability to self-manage and intensify insulin regimens. Since their introduction, blood glucose meters have become smaller and more accurate: the time taken to measure glucose concentration has been reduced to a few seconds, and the size of the blood sample has been reduced to fractions of a microlitre. Several blood glucose meters now communicate directly with other devices, such as insulin pumps, and send the glucose measurements to a smartphone and to the cloud. Most meters meet the accuracy standards established by the International Organization for Standardization.[30] However, accuracy among blood glucose meters varies considerably, with the mean absolute relative difference ranging between 5% and more than 10% when compared with reference blood glucose measurements.[31,32]

Continuous glucose monitors

CGMs have begun to complement blood glucose meters and, in the past 2 years, to replace them. CGM systems include a disposable sensor that measures the glucose concentration in interstitial fluid (generally every 1–5 min) and a transmitter that either stores the glucose values or sends the values (generally every 5–15 min) to a receiver, smartphone, or smart watch, and potentially to the cloud. The glucose concentration in the interstitial fluid generally closely approximates that of blood glucose, particularly when glucose concentrations are stable, lagging behind blood glucose concentrations by about 4 min on average.[33] However, during periods of rapid glucose change, the lag can be greater. For devices that send the glucose data to the cloud, the glucose values can potentially be shared with additional people; this function has become extremely useful, particularly for parents and caregivers of people with type 1 diabetes. Some versions of CGMs can also collect blinded glucose data for 7–14 days (not seen in real time by the patient), which are stored for retrospective evaluation by a health-care professional (often referred to as professional continuous glucose monitoring).

The first three major CGM systems became available in the early 2000s, all with an external transmitter attached to a sensor with a small electrode filament inserted into the subcutaneous space. All three of these CGMs were used in the first major CGM effectiveness study, a randomised clinical trial[34] by JDRF, published in 2008. This study[34] showed the benefit of using a CGM in reducing HbA_{1c} concentration and hypoglycaemia in adults, but not in people aged 8–25 years, when baseline HbA_{1c} was at least 7·0% (≥53 mmol/mol); however, in young people who used a CGM for 6 days or more per week, the beneficial effect was similar to that in adults. In a parallel trial,[35] when baseline HbA_{1c} was less than 7·0%, CGM use showed improved glycaemic control and reduced biochemical hypoglycaemia in both children and adults compared with a control group using standard blood glucose monitoring. Later trials using similar CGM technology reaffirmed the benefits of continuous glucose monitoring.[36–39]

Since these studies were done, sensor accuracy has improved and sensors have become smaller, last longer, and, importantly, have become easier to use than the first systems.[40] A recent publication reviewed the literature on CGM studies.[41] Two randomised trials in the USA[42] and Sweden[43] evaluated CGM use in adults with type 1 diabetes who were using multiple daily injections. These trials[42,43] showed advantages of using a CGM for HbA_{1c} and hypoglycaemia reduction, similar to results seen in insulin-pump users in other CGM studies.[34] Compared with the JDRF randomised controlled trial, these studies have shown a much higher degree of sustained sensor use and participant satisfaction, as well as enhanced diabetes-specific quality of life.[44] Additional randomised trials in adults with type 1 diabetes showed a reduction in severe hypoglycaemia events[45–47] with the use of a CGM compared with a control group using standard blood glucose monitoring. The beneficial effect of CGM use on HbA_{1c} concentrations has also been shown in registry data. In the US T1D Exchange Registry, HbA_{1c} concentrations were lower in patients using a CGM than in patients who did not use this method, and were lower in pump users than in users of multiple daily injections. Among users of CGMs, similar HbA_{1c} concentrations were present in users of insulin pumps and in users of multiple daily injections.[10,48] Three randomised trials presented results at the 2019 American Diabetes Association meeting showing the efficacy of CGM use in reducing hyperglycaemia, hypoglycaemia, or both, in children younger than 8 years (NCT02912728), in adolescents and young adults aged 14 to 24 years (NCT03263494), and in adults older than 60 years (NCT03240432).

Real-time CGM sensors include the Dexcom G6 (Dexcom, San Diego, CA, USA), the Medtronic Guardian Sensor 3 (Medtronic, Northridge, CA, USA), and the Senseonics Eversense system (Senseonics, Germantown,

	Dexcom G6	Medtronic Guardian Sensor 3	Senseonics Eversense	Abbott FreeStyle Libre
Type of monitor	Continuous glucose monitor	Continuous glucose monitor	Continuous glucose monitor	Intermittently scanning continuous glucose monitor
Sensor location	Subcutaneously inserted	Subcutaneously inserted	Surgically implanted subcutaneously in clinic, with an on-body external transmitter	Subcutaneously inserted
Sensor life	10 days	7 days	3 months (USA); 6 months (EU)	14 days
Sensor calibration	Factory	Blood glucose meter, twice a day	Blood glucose meter, twice a day	Factory
Can be used without confirmatory blood glucose meter measurement	Yes	No	Yes (USA); no (EU)	Yes
Alarms and alerts	Yes	Yes	Yes	Originally none; present in newest version
Ability to automatically share glucose values in real time with another person	Yes	Indirectly	Indirectly	No

Data correct as of Aug 1, 2019.

Table: **Features of continuous glucose monitors and intermittently scanning continuous glucose monitors**

MD, USA; table). The Senseonics Eversense system has a sensor that is fully implanted under the skin by a health-care provider and functions for 90–180 days. A variation on real-time CGMs is the Abbott FreeStyle Libre (Abbott Diabetes Care, Alameda, CA, USA), in which glucose measurements are stored with the sensor for 14 days and are viewed retrospectively when the patient scans a receiver or smartphone over the sensor to transfer the glucose data. This type of CGM has been referred to as a flash glucose monitor or an intermittently scanning CGM.[49] A major difference between real-time and first-generation intermittently scanning CGM systems is that first-generation intermittent monitors did not have alerts, whereas real-time monitors have an alarm to alert the user to hypoglycaemia, hyperglycaemia, and rapid glycaemic change, as specified by the user. The Abbott FreeStyle Libre 2 (Abbott Diabetes Care, Alameda, CA, USA), which was selectively launched in Europe over the past year, has optional real-time alarms. For patients with frequent, severe hypoglycaemia or impaired hypoglycaemia awareness, a CGM has been preferred because of the benefit of a real-time hypoglycaemia alarm, but new versions of intermittently scanning CGMs with hypoglycaemia alarms will need to be evaluated for this group of patients. Although CGM sensors are not as accurate as the most accurate blood glucose meters, CGM accuracy[50–53] is now equal to, or better than, the accuracy of many blood glucose meters.[31,32]

See Online for appendix

Until 2017, CGM use was only approved as an adjunct to a blood glucose meter, meaning that measurements from a CGM could be used as a guide, but that dosing of rapid-acting insulin at meals and correction of hypoglycaemia and hyperglycaemia required a measurement from a blood glucose meter. The REPLACE-BG study[54] showed that dosing insulin at meals on the basis of a measurement from a CGM was as safe and reliable as dosing on the basis of a measurement from a blood glucose meter. The Dexcom G5 sensor (Dexcom, San Diego, CA, USA), the Dexcom G6 sensor, and the Abbott Freestyle Libre have received regulatory approval to be used as a replacement for a blood glucose meter to guide insulin dosing by the US Food and Drug Administration (FDA) and the Conformite European (CE) mark; the Senseonics Eversense has received similar FDA approval.

Another improvement has been in the calibration of CGM sensors, which historically has required a blood glucose meter measurement at least twice a day. The Dexcom G6 and Abbott Freestyle Libre are factory calibrated and do not require blood glucose meter measurements for calibration; however, the Medtronic Guardian Sensor 3 and Senseonics Eversense sensors require at least two blood glucose meter calibrations per day.

The reporting of data from CGMs now allows better visualisation of the information by patients and health-care providers than was available for earlier systems. Standardised reports, such as the ambulatory glucose profile (appendix),[55] indicate the core CGM metrics, including proportions of glucose values in different ranges over a specified time period, the recommended target for each CGM data range, and a visual display of the distribution of values according to the time of day. Consensus groups have agreed on a core set of ten CGM metrics for reports (panel),[58] and on benchmarks and targets for evaluating glucose control using CGM metrics (appendix).[59] Studies have shown that 10–14 days of data from a CGM generally provide a good approximation of 3 months of glucose data, and are sufficient for calculating an estimated HbA_{1c},[60] termed the glucose management indicator.[56]

The use of CGMs and intermittently scanning CGMs by people with type 1 diabetes has been endorsed by the American Diabetes Association in its 2019 Standards of Medical Care in Diabetes,[61] the American Association of Clinical Endocrinologists,[62,63] and the International Society for Pediatric and Adolescent Diabetes.[64,65] The Endocrine Society has created recommendations for the real-time adjustment of insulin dosing for paediatric and adult patients on the basis of data from CGMs.[66,67] Methods for visualisation of data from CGMs will continue to improve and be complemented with decision support and artificial intelligence that identifies times of

day of concern and provides suggestions for alterations in management plans. Several researchers have tried to develop a non-invasive method for measuring glucose and, although efforts have not been successful with respect to developing a commercialised product, work is ongoing in this area.

Automated insulin delivery systems

Systems that automate the delivery of insulin are referred to by several names: automated insulin delivery, closed loop, and artificial pancreas. These systems consist of a CGM that measures the glucose concentration (interstitial glucose as noted earlier), an insulin pump, and an algorithm that uses glucose concentration and previous insulin delivery data to regulate insulin delivery.

During the past several years, these automated systems have evolved, with increased functionality following the initial[68] and revised[69] roadmap to the development of a commercial artificial pancreas system, championed by Aaron Kowalski on behalf of JDRF. Initial systems, referred to as low-glucose insulin-suspend pumps, suspended basal insulin delivery if a low glucose concentration threshold was reached (Medtronic Paradigm Veo 630G; Medtronic Diabetes, Northridge, CA, USA). These were followed by the Medtronic 640G system (Medtronic Diabetes, Northridge, CA, USA) and, more recently, by the Tandem Basal-IQ system (Tandem Diabetes Care, San Diego, CA, USA) that suspend or reduce insulin delivery when an algorithm predicts that hypoglycaemia is likely to occur (known as a predictive low-glucose insulin-suspend system). Studies of both the low-glucose insulin-suspend and predictive low-glucose insulin-suspend systems have shown their effectiveness in reducing hypoglycaemia,[70–74] with a 6-month randomised trial of adults with type 1 diabetes at high risk for hypoglycaemia showing that a predictive system substantially reduced the frequency of severe hypoglycaemia events compared with a control group using an insulin pump and standard blood glucose monitoring.[75]

The first automated insulin delivery system that decreases and increases insulin delivery in response to glucose concentrations became available in the USA in 2017 and in Europe in 2018. In addition to predictive low-glucose insulin-suspend functionality, this system (Medtronic 670G; Medtronic Diabetes, Northridge, CA, USA) increases insulin delivery in response to hyperglycaemia or predicted hyperglycaemia. The system is not fully automated and is thus referred to as a hybrid closed-loop system; the user must indicate when a meal will be eaten and provide the planned carbohydrate intake information to activate an appropriate insulin bolus. As of Jan 1, 2019, the Medtronic 670G was the only hybrid closed-loop automated insulin delivery system that was commercially available, with regulatory approval in the USA and a CE mark in Europe for use in patients aged 7 years and older. Published results for the Medtronic 670G system have been limited to single-arm studies designed to provide sufficient safety data for US regulatory approval.[76–78] A large randomised trial evaluating the system is in progress in the USA (NCT02748018).

A hybrid closed-loop system for automated insulin delivery from Diabeloop (Grenoble, France), which uses a Kaleido patch pump (Kaleido, Utrecht, Netherlands) and Dexcom G6 sensor, received a CE mark in 2018, and is expected to become available in Europe in 2019. In a crossover trial (N=68) with two 12-week periods, use of this insulin delivery system increased the proportion of time that glucose concentration was in the range of 70–180 mg/dL (3·9–10·0 mmol/L) and reduced hypoglycaemia compared with a control group using an insulin pump and CGM (ie, sensor-augmented pump therapy).[79] The Tandem X2 insulin pump with Control-IQ Technology (Tandem Diabetes Care, San Diego, CA, USA),[80] could become available in 2019. Results of a 6-month, multicentre, randomised trial (N=168, age 14–71 years; NCT03563313), presented at the 2019 American Diabetes Association meeting, showed efficacy and safety of the Tandem X2 insulin pump with Control-IQ Technology versus a control group using sensor-augmented pump therapy. The automated system showed an increase in the proportion of time glucose concentration was in the range of 70–180 mg/dL (3·9–10·0 mmol/L), and a reduction in the proportion of time glucose concentration was more than 180 mg/dL (10·0 mmol/L), less than 70 mg/dL (3·9 mmol/L), or less than 54 mg/dL (3·0 mmol/L), compared with the control group; mean glucose concentration and HbA_{1c} concentration were also reduced.[81]

Several other automated insulin delivery systems using hybrid closed-loop algorithms are being tested. One such algorithm, from the University of Cambridge (Cambridge, UK), has been extensively tested, including

***Panel*: Metrics for reporting continuous glucose monitoring data**

- Number of days of continuous glucose monitoring data in the report
- Proportion of time continuous glucose monitor is used during the time covered by the report
- Mean glucose concentration
- Coefficient of variation
- Glucose management indicator
  - Glucose management indicator is calculated from the mean glucose concentration measured by continuous glucose monitoring as an estimate of the glycated haemoglobin (HbA_{1c}) to be expected on average for a given mean glucose concentration. Glucose management indicator (%)=3·31 + 0·02392 × (mean glucose in mg/dL) or glucose management indicator (mmol/mol)=12·71 + 4·70587 × (mean glucose in mmol/L)[56,57]
- Time spent with blood glucose concentration in the following ranges:
  - <54 mg/dL (<3·0 mmol/L)
  - 54–69 mg/dL (3·0–3·8 mmol/L)
  - 70–180 mg/dL (3·9–10·0 mmol/L)
  - 181–250 mg/dL (10·1–13·9 mmol/L)
  - >250 mg/dL (>13·9 mmol/L)

a 3-month randomised trial (N=86, ages 6–65 years) showing that the patients using the hybrid closed-loop system had a significant reduction in hyperglycaemia, hypoglycaemia, and HbA_{1c} concentration compared with a control group using sensor-augmented pump therapy.[82] We are not aware of any other automated insulin delivery systems that have been tested in a randomised trial of at least 3 months. A systematic review with a meta-analysis has been done on randomised trials using automated insulin delivery systems, most of which were small, short-duration trials.[83]

A major limitation of present and near-future automated insulin delivery systems relates to insulin kinetics: both the slow onset of effect when insulin is delivered subcutaneously, and the continued effect for several hours. Although an algorithm could detect that a meal has been eaten, the onset of the effect of insulin is too slow to prevent hyperglycaemia after a meal, and over-delivery of insulin to try to minimise this glycaemic rise often will increase the risk of postprandial hypoglycaemia. As a result, the user needs to inform the system that a meal will be eaten for an early insulin bolus to be given. Even with a meal announcement, hyperglycaemia after a meal is frequent with automated insulin delivery systems and, although overall hyperglycaemia is reduced, daytime hyperglycaemia is frequent. Faster-acting insulin or alternative delivery routes (such as intraperitoneal) might be necessary to effectively move from hybrid closed-loop systems to fully closed-loop systems.

Dual-hormone systems for automated insulin delivery are being developed in which glucagon is used in conjunction with insulin to minimise hypoglycaemia and to potentially allow more aggressive insulin delivery to minimise hyperglycaemia without increasing hypoglycaemia.[84] Pramlintide (an analogue of the hormone amylin, which slows gastric emptying and reduces glucagon secretion) also is being studied in automated insulin delivery systems in an effort to reduce hyperglycaemia after a meal.[85] Other enhancements being investigated for automated insulin delivery systems include additional physiological inputs into algorithms, such as heart rate and markers of physical activity and stress.

Finally, several so-called do-it-yourself systems for automated insulin delivery have been developed by individuals for their personal use and for use by others, in which existing CGMs and insulin pumps are linked using an open-source algorithm. OpenAPS is one group that has promoted the use of do-it-yourself systems[86–88] and a large, prospective, observational study for the Loop system is being done to obtain data on safety and usability (NCT03838900).

Use of technology by special populations with type 1 diabetes

Systems for continuous glucose monitoring and automated insulin delivery might have substantial benefit for some populations of individuals with type 1 diabetes. The CONCEPTT randomised trial (Continuous Glucose Monitoring in Women with Type 1 Diabetes in Pregnancy Trial) showed that CGM use during pregnancy in women with diabetes was associated with a reduction in hyperglycaemia and improved neonatal outcomes compared with a control group using standard blood glucose monitoring.[89] Systems for automated insulin delivery also have been tested safely in pregnant women with diabetes.[90,91] Further studies are now needed to assess the use of automated systems for long periods in pregnancy, as well as in very young[92] and older people, individuals with impaired awareness of hypoglycaemia, some racial and ethnic minority groups, and people of lower socioeconomic status who do not typically have access to advanced technology. Whether systems for continuous glucose monitoring or automated insulin delivery should be implemented at the time of diagnosis of type 1 diabetes remains to be shown. Using CGMs has become easier, with less burden, and now often is prescribed soon after type 1 diabetes diagnosis as the first form of advanced technology;[93] as a result, implementing a clinical trial to evaluate the benefits of early initiation of CGM use will be increasingly difficult. Insulin-pump therapy has been found to be effective, safe, and acceptable in newly diagnosed children and is now recommended by some guidelines as an alternative to multiple daily injections in this group,[94] although there is little evidence on comparative effectiveness versus multiple daily injections.[4]

The use of CGMs has been gaining interest for patients with diabetes who are hospitalised, as well as critically ill patients without diabetes.[95,96] Preliminary studies have suggested a benefit of automated insulin delivery for patients with diabetes who are admitted to hospital;[97] however, further studies are needed to assess the role of systems for continuous glucose monitoring and automated insulin delivery in the inpatient setting.

Conclusion

The availability of technology for managing type 1 diabetes has increased considerably in the past few years. CGMs have become smaller, more accurate, and provide greater ability to visualise glucose data and monitor glycaemic control remotely. Automated systems for insulin delivery have been developed that reduce both hyperglycaemia and hypoglycaemia. In the next 5 years, many advances in technology are expected for the management of diabetes, with continued improvements in systems for continuous glucose monitoring and more choices available for automated insulin delivery. Expanding the use of technology beyond endocrinology practices to primary-care settings will be needed to seamlessly integrate data and reports from CGMs into electronic health records; to develop processes for initiating the use of systems for continuous glucose monitoring and, eventually, systems for automated insulin delivery

remotely outside the clinic; and to assess the cost-effectiveness of these systems and their effect on quality of life. A continued effort will also be needed to develop decision support tools to aid patients and providers in using the output of these devices to optimise diabetes management, which will be particularly valuable for patients not using automated insulin delivery. Improving access to diabetes technology for all patients who might benefit must be a priority.

Contributors

All authors contributed to the writing of the first draft of the manuscript and subsequent revisions.

Declaration of interests

RWB's non-profit employer has received research funding from Dexcom, Bigfoot Biomedical, and Tandem Diabetes Care; study supplies from Roche, Ascencia, Dexcom, and Abbott Diabetes Care; and consulting fees from Insulet, Bigfoot Biomedical, and Eli Lilly and Company. RMB has received research support, consulted, or has been on the scientific advisory board for Abbott Diabetes Care, Dexcom, Hygieia, Johnson & Johnson, Lilly, Medtronic, Novo Nordisk, Onduo, Roche, Sanofi, and UnitedHealthCare. LML has received consultancy fees from Eli Lilly and Company, Sanofi, Novo Nordisk, AstraZeneca, Roche, Dexcom, Insulet, Boehringer Ingelheim, and ConvaTec. JCP has received consultancy, speaker fees, or both, from Berlin-Chemie, CeQur, Eli Lilly and Company, Insulet, Medtronic, Novo Nordisk, Roche, and SPRIM.

References

1 Nathan DM, Genuth S, Lachin J, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; **329:** 977–86.

2 Pickup JC. Insulin-pump therapy for type 1 diabetes mellitus. *N Engl J Med* 2012; **366:** 1616–24.

3 NHS Digital. National diabetes audit—insulin pump report 2016–17. 2018. https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit/insulin-pump-report-2016-17 (accessed Jan 24, 2019).

4 Pickup JC. Is insulin pump therapy effective in type 1 diabetes? *Diabet Med* 2019; **36:** 269–78.

5 Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. *Diabet Med* 2008; **25:** 765–74.

6 Beato-Vibora P, Yeoh E, Rogers H, Hopkins D, Amiel SA, Choudhary P. Sustained benefit of continuous subcutaneous insulin infusion on glycaemic control and hypoglycaemia in adults with Type 1 diabetes. *Diabet Med* 2015; **32:** 1453–59.

7 Leelarathna L, Roberts SA, Hindle A, et al. Comparison of different insulin pump makes under routine care conditions in adults with type 1 diabetes. *Diabet Med* 2017; **34:** 1372–79.

8 Nixon R, Folwell R, Pickup JC. Variations in the quality and sustainability of long-term glycaemic control with continuous subcutaneous insulin infusion. *Diabet Med* 2014; **31:** 1174–77.

9 Quiros C, Gimenez M, Rios P, et al. Long-term outcome of insulin pump therapy: reduction of hypoglycaemia and impact on glycaemic control. *Diabet Med* 2016; **33:** 1422–26.

10 Miller KM, Foster NC, Beck RW, et al. Current state of type 1 diabetes treatment in the US: updated data from the T1D exchange clinic registry. *Diabetes Care* 2015; **38:** 971–78.

11 Szypowska A, Schwandt A, Svensson J, et al. Insulin pump therapy in children with type 1 diabetes: analysis of data from the SWEET registry. *Pediatr Diabetes* 2016; **17** (suppl 23): 38–45.

12 Sherr JL, Hermann JM, Campbell F, et al. Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries. *Diabetologia* 2016; **59:** 87–91.

13 Steineck I, Cederholm J, Eliasson B, et al. Insulin pump therapy, multiple daily injections, and cardiovascular mortality in 18,168 people with type 1 diabetes: observational study. *BMJ* 2015; **350:** h3234.

14 REPOSE Study Group. Relative effectiveness of insulin pump treatment over multiple daily injections and structured education during flexible intensive insulin treatment for type 1 diabetes: cluster randomised trial (REPOSE). *BMJ* 2017; **356:** j1285.

15 Muller-Godeffroy E, Treichel S, Wagner VM. Investigation of quality of life and family burden issues during insulin pump therapy in children with type 1 diabetes mellitus—a large-scale multicentre pilot study. *Diabet Med* 2009; **26:** 493–501.

16 Cengiz E, Xing D, Wong JC, et al. Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D exchange clinic registry. *Pediatr Diabetes* 2013; **14:** 447–54.

17 Karges B, Schwandt A, Heidtmann B, et al. Association of insulin pump therapy vs insulin injection therapy with severe hypoglycemia, ketoacidosis, and glycemic control among children, adolescents, and young adults with type 1 diabetes. *JAMA* 2017; **318:** 1358–66.

18 Weinstock RS, Xing D, Maahs DM, et al. Severe hypoglycemia and diabetic ketoacidosis in adults with type 1 diabetes: results from the T1D exchange clinic registry. *J Clin Endocrinol Metab* 2013; **98:** 3411–19.

19 Guenego A, Bouzille G, Breitel S, et al. Insulin pump failures: has there been an improvement? Update of a prospective observational study. *Diabetes Technol Ther* 2016; **18:** 820–24.

20 Pickup JC, Yemane N, Brackenridge A, Pender S. Nonmetabolic complications of continuous subcutaneous insulin infusion: a patient survey. *Diabetes Technol Ther* 2014; **16:** 145–49.

21 Heinemann L, Fleming GA, Petrie JR, Holl RW, Bergenstal RM, Peters AL. Insulin pump risks and benefits: a clinical appraisal of pump safety standards, adverse event reporting, and research needs: a joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. *Diabetes Care* 2015; **38:** 716–22.

22 Roze S, Smith-Palmer J, Valentine W, de Portu S, Norgaard K, Pickup JC. Cost-effectiveness of continuous subcutaneous insulin infusion versus multiple daily injections of insulin in type 1 diabetes: a systematic review. *Diabet Med* 2015; **32:** 1415–24.

23 National Institute for Health and Care Excellence. Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. July 23, 2008. https://www.nice.org.uk/guidance/ta151 (accessed April 26, 2019).

24 Association of British Clinical Diabetologists Diabetes Technology Network. Best practice guide: continous subcutaneous insulin infusion (CSII): a clinical guide for adult diabetes services. 2018. https://abcd.care/sites/abcd.care/files/BP_DTN_v13%20FINAL.pdf (accessed Jan 23, 2019).

25 Heinemann L. Insulin infusion sets: a critical reappraisal. *Diabetes Technol Ther* 2016; **18:** 327–33.

26 Patel PJ, Benasi K, Ferrari G, et al. Randomized trial of infusion set function: steel versus teflon. *Diabetes Technol Ther* 2014; **16:** 15–19.

27 Hauzenberger JR, Munzker J, Kotzbeck P, et al. Systematic in vivo evaluation of the time-dependent inflammatory response to steel and Teflon insulin infusion catheters. *Sci Rep* 2018; **8:** 1132.

28 Cescon M, DeSalvo DJ, Ly TT, et al. Early detection of infusion set failure during insulin pump therapy in type 1 diabetes. *J Diabetes Sci Technol* 2016; **10:** 1268–76.

29 Hultstrom M, Roxhed N, Nordquist L. Intradermal insulin delivery: a promising future for diabetes management. *J Diabetes Sci Technol* 2014; **8:** 453–57.

30 International Organization for Standardization. ISO 15197:2013: in vitro diagnostic test systems—requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus. 2018. https://www.iso.org/standard/54976.html (accessed Jan 24, 2019).

31 Ekhlaspour L, Mondesir D, Lautsch N, et al. Comparative accuracy of 17 point-of-care glucose meters. *J Diabetes Sci Technol* 2017; **11:** 558–66.

32 Klonoff DC, Parkes JL, Kovatchev BP, et al. Investigation of the accuracy of 18 marketed blood glucose monitors. *Diabetes Care* 2018; **41:** 1681–88.

33 Shah VN, Laffel LM, Wadwa RP, Garg SK. Performance of a factory-calibrated real-time continuous glucose monitoring system utilizing an automated sensor applicator. *Diabetes Technol Ther* 2018; **20:** 428–33.

34 The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med* 2008; **359:** 1464–76.

35 The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. The effect of continuous glucose monitoring in well-controlled type 1 diabetes. *Diabetes Care* 2009; **32:** 1378–83.

36 Battelino T, Conget I, Olsen B, et al. The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial. *Diabetologia* 2012; **55:** 3155–62.

37 Battelino T, Phillip M, Bratina N, Nimri R, Oskarsson P, Bolinder J. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. *Diabetes Care* 2011; **34:** 795–800.

38 Bergenstal RM, Tamborlane WV, Ahmann A, et al. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. *N Engl J Med* 2010; **363:** 311–20.

39 O'Connell MA, Donath S, O'Neal DN, et al. Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial. *Diabetologia* 2009; **52:** 1250–57.

40 Facchinetti A. Continuous glucose monitoring sensors: past, present and future algorithmic challenges. *Sensors (Basel)* 2016; **16:** e2093.

41 Rodbard D. Continuous glucose monitoring: a review of recent studies demonstrating improved glycemic outcomes. *Diabetes Technol Ther* 2017; **19:** S25–37.

42 Beck RW, Riddlesworth T, Ruedy K, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. *JAMA* 2017; **317:** 371–78.

43 Lind M, Polonsky W, Hirsch IB, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. *JAMA* 2017; **317:** 379–87.

44 Polonsky WH, Hessler D, Ruedy KJ, Beck RW. The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. *Diabetes Care* 2017; **40:** 736–41.

45 Heinemann L, Freckmann G, Ehrmann D, et al. Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. *Lancet* 2018; **391:** 1367–77.

46 Little SA, Speight J, Leelarathna L, et al. Sustained reduction in severe hypoglycemia in adults with type 1 diabetes complicated by impaired awareness of hypoglycemia: two-year follow-up in the HypoCOMPaSS randomized clinical trial. *Diabetes Care* 2018; **41:** 1600–07.

47 van Beers CA, DeVries JH, Kleijer SJ, et al. Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): a randomised, open-label, crossover trial. *Lancet Diabetes Endocrinol* 2016; **4:** 893–902.

48 Foster NC, Beck RW, Miller KM, et al. State of type 1 diabetes management and outcomes from the T1D exchange in 2016–2018. *Diabetes Technol Ther* 2019; **21:** 66–72.

49 Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kroger J, Weitgasser R. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet* 2016; **388:** 2254–63.

50 US Food and Drug Administration. Summary of safety and effectiveness data: FreeStyle Libre 14 day flash glucose monitoring system. 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160030S017B.pdf (accessed Jan 24, 2019).

51 Food and Drug Administration. Summary of safety and effectiveness data: MiniMed 670G system 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160017S031B.pdf (accessed Jan 24, 2019).

52 Food and Drug Administration. Evaluation of automatic class III designation for Dexcom G6 continuous glucose monitoring system. 2018. https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170088.pdf (accessed Jan 24, 2019).

53 Food and Drug Administration. Summary of safety and effectiveness data: Eversense continuous glucose monitoring system. 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf16/P160048B.pdf (accessed Jan 24, 2019).

54 Aleppo G, Ruedy KJ, Riddlesworth TD, et al. REPLACE-BG: a randomized trial comparing continuous glucose monitoring with and without routine blood glucose monitoring in well-controlled adults with type 1 diabetes. *Diabetes Care* 2017; **40:** 538–45.

55 Bergenstal RM, Ahmann AJ, Bailey T, et al. Recommendations for standardizing glucose reporting and analysis to optimize clinical decision making in diabetes: the ambulatory glucose profile (AGP). *Diabetes Technol Ther* 2013; **15:** 198–211.

56 Bergenstal RM, Beck RW, Close KL, et al. Glucose management indicator (GMI): a new term for estimating A1C from continuous glucose monitoring. *Diabetes Care* 2018; **41:** 2275–80.

57 Jaeb Center for Health Research. Glucose management indicator. https://www.jaeb.org/gmi (accessed Aug 20, 2019).

58 Danne T, Nimri R, Battelino T, et al. International consensus on use of continuous glucose monitoring. *Diabetes Care* 2017; **40:** 1631–40.

59 Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care* 2019; **42:** 1593–603.

60 Riddlesworth TD, Beck RW, Gal RL, et al. Optimal sampling duration for continuous glucose monitoring to determine long-term glycemic control. *Diabetes Technol Ther* 2018; **20:** 314–16.

61 American Diabetes Association. 7. Diabetes technology: standards of medical care in diabetes—2019. *Diabetes Care* 2019; **42** (suppl 1)**:** S71–80.

62 Fonseca V, Grunberger G. Standard glucose reporting: follow-up to the February 2016 AACE CGM consensus conference. *Endocrine Practice* 2017; **23:** 629–32.

63 Fonseca VA, Grunberger G, Anhalt H, et al. Continuous glucose monitoring: a consensus conference of the American Association of Clinical Endocrinologists and American College of Endocrinology. *Endocr Pract* 2016; **22:** 1008–21.

64 DiMeglio LA, Acerini CL, Codner E, et al. ISPAD clinical practice consensus guidelines 2018: glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. *Pediatr Diabetes* 2018; **19** (suppl 27)**:** 105–14.

65 Pihoker C, Forsander G, Fantahun B, et al. ISPAD clinical practice consensus guidelines 2018: the delivery of ambulatory diabetes care to children and adolescents with diabetes. *Pediatr Diabetes* 2018; **19** (suppl 27)**:** 84–104.

66 Aleppo G, Laffel LM, Ahmann AJ, et al. A practical approach to using trend arrows on the Dexcom G5 CGM system for the management of adults with diabetes. *J Endocr Soc* 2017; **1:** 1445–60.

67 Laffel LM, Aleppo G, Buckingham BA, et al. A practical approach to using trend arrows on the Dexcom G5 CGM system to manage children and adolescents with diabetes. *J Endocr Soc* 2017; **1:** 1461–76.

68 Kowalski AJ. Can we really close the loop and how soon? Accelerating the availability of an artificial pancreas: a roadmap to better diabetes outcomes. *Diabetes Technol Ther* 2009; **11** (suppl 1)**:** S113–19.

69 Kowalski A. Pathway to artificial pancreas systems revisited: moving downstream. *Diabetes Care* 2015; **38:** 1036–43.

70 Abraham MB, Nicholas JA, Smith GJ, et al. Reduction in hypoglycemia with the predictive low-glucose management system: a long-term randomized controlled trial in adolescents with type 1 diabetes. *Diabetes Care* 2018; **41:** 303–10.

71 Battelino T, Nimri R, Dovc K, Phillip M, Bratina N. Prevention of hypoglycemia with predictive low glucose insulin suspension in children with type 1 diabetes: a randomized controlled trial. *Diabetes Care* 2017; **40:** 764–70.

72 Bergenstal RM, Klonoff DC, Garg SK, et al. Threshold-based insulin-pump interruption for reduction of hypoglycemia. *N Engl J Med* 2013; **369:** 224–32.

73 Forlenza GP, Li Z, Buckingham BA, et al. Predictive low-glucose suspend reduces hypoglycemia in adults, adolescents, and children with type 1 diabetes in an at-home randomized crossover study: results of the PROLOG trial. *Diabetes Care* 2018; **41:** 2155–61.

74 Ly TT, Nicholas JA, Retterath A, Lim EM, Davis EA, Jones TW. Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. *JAMA* 2013; **310:** 1240–47.

75 Bosi E, Choudhary P, de Valk HW, et al. Efficacy and safety of suspend-before-low-insulin pump technology in hypoglycaemia-prone adults with type 1 diabetes (SMILE): an open-label randomised controlled trial. *Lancet Diabetes Endocrinol* 2019; **7:** 462–72.

76 Bergenstal RM, Garg S, Weinzimer SA, et al. Safety of a hybrid closed-loop insulin delivery system in patients with type 1 diabetes. *JAMA* 2016; **316:** 1407–08.

77 Forlenza GP, Pinhas-Hamiel O, Liljenquist DR, et al. Safety evaluation of the MiniMed 670G system in children 7–13 years of age with type 1 diabetes. *Diabetes Technol Ther* 2019; **21:** 11–19.

78 Garg SK, Weinzimer SA, Tamborlane WV, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther* 2017; **19:** 155–63.

79 Benhamou PY, Franc S, Resnik Y, et al. Closed-loop insulin delivery in adults with type 1 diabetes in real-life conditions: a 12-week, open-label randomised controlled crossover trial. *Lancet Digital Health* 2019; **1:** e17–25.

80 Brown S, Raghinaru D, Emory E, Kovatchev B. First look at Control-IQ: a new-generation automated insulin delivery system. *Diabetes Care* 2018; **41:** 2634–36.

81 Brown SA, Kovatchev BP, Raghinaru D, et al. Closed-loop control in type 1 diabetes—6-month randomized trial outcomes. *N Engl J Med* (in press).

82 Tauschmann M, Thabit H, Bally L, et al. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet* 2018; **392:** 1321–29.

83 Weisman A, Bai JW, Cardinez M, Kramer CK, Perkins BA. Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. *Lancet Diabetes Endocrinol* 2017; **5:** 501–12.

84 Russell SJ, El-Khatib FH, Sinha M, et al. Outpatient glycemic control with a bionic pancreas in type 1 diabetes. *N Engl J Med* 2014; **371:** 313–25.

85 Sherr JL, Patel NS, Michaud CI, et al. Mitigating meal-related glycemic excursions in an insulin-sparing manner during closed-loop insulin delivery: the beneficial effects of adjunctive pramlintide and liraglutide. *Diabetes Care* 2016; **39:** 1127–34.

86 Lee JM, Newman MW, Gebremariam A, et al. Real-world use and self-reported health outcomes of a patient-designed do-it-yourself mobile technology system for diabetes: lessons for mobile health. *Diabetes Technol Ther* 2017; **19:** 209–19.

87 Lewis D, Leibrand S, Open APS Community. Real-world use of open source artificial pancreas systems. *J Diabetes Sci Technol* 2016; **10:** 1411.

88 Petruzelkova L, Soupal J, Plasova V, et al. Excellent glycemic control maintained by open-source hybrid closed-loop AndroidAPS during and after sustained physical activity. *Diabetes Technol Ther* 2018; **20:** 744–50.

89 Feig DS, Donovan LE, Corcoy R, et al. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. *Lancet* 2017; **390:** 2347–59.

90 Stewart ZA, Wilinska ME, Hartnell S, et al. Day-and-night closed-loop insulin delivery in a broad population of pregnant women with type 1 diabetes: a randomized controlled crossover trial. *Diabetes Care* 2018; **41:** 1391–99.

91 Stewart ZA, Wilinska ME, Hartnell S, et al. Closed-loop insulin delivery during pregnancy in women with type 1 diabetes. *N Engl J Med* 2016; **375:** 644–54.

92 Tauschmann M, Allen JM, Nagl K, et al. Home use of day-and-night hybrid closed-loop insulin delivery in very young children: a multicenter, 3-week, randomized trial. *Diabetes Care* 2019; **42:** 594–600.

93 Martin CT, Criego AB, Carlson AB, Bergenstal RM. Advanced technology in the management of diabetes: which comes first—continous glucose monitor or insulin pump? *Curr Diab Rep* 2019; **19:** 50.

94 National Institute for Health and Care Excellence. Diabetes (type 1 and type 2) in children and young people: diagnosis and management: NICE guideline 18. https://www.nice.org.uk/guidance/ng18 (accessed Aug 19, 2019).

95 Umpierrez GE, Klonoff DC. Diabetes technology update: use of insulin pumps and continuous glucose monitoring in the hospital. *Diabetes Care* 2018; **41:** 1579–89.

96 Wallia A, Umpierrez GE, Rushakoff RJ, et al. Consensus statement on inpatient use of continuous glucose monitoring. *J Diabetes Sci Technol* 2017; **11:** 1036–44.

97 Bally L, Thabit H, Hartnell S, et al. Closed-loop insulin delivery for glycemic control in noncritical care. *N Engl J Med* 2018; **379:** 547–56.