Home Blood Glucose Monitoring and Digital-Health in Diabetes

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Abstract

Diabetes is a disorder of glucose metabolism and a major cause of death and disability. It currently affects 387 million people worldwide and is expected to affect 592 million by 2035. Monitoring of glucose levels is an essential component of treatment - providing feedback to clinician and patient on management through lifestyle and pharmacotherapy. This chapter provides an overview of the evidence that monitoring levels of glycaemia leads to improved outcomes for diabetes; a brief history of the technologies used for monitoring; and an update on recent research into ways in which people can be supported with use of their medication. Clinical support systems are now available and have been refined to improve their effectiveness, and combined with systems that enable personal support for self-monitoring can help make better use of the data available. The chapter includes a brief overview of recent developments with continuous glucose monitoring, flash monitoring and closed loop systems.

Keywords

Diabetes · Glucose monitoring · Digital technologies · Insulin treatment · Self-management support · Adherence

Introduction

Diabetes is a disorder of glucose metabolism and a major cause of death and disability. It currently affects 387 million people worldwide and is expected to affect 592 million by 2035 (Guariguata et al. 2014). It is responsible for five million deaths a year, and $673 billion is spent on healthcare for diabetes (12% of global health expenditure) (International Diabetes Federation n.d.). A detailed analysis of costs highlighted the importance of both direct and indirect costs, with a marked impact on employment potential (Seuring et al. 2015). Detailed within country analysis in the UK has identified the contribution to costs arising from hospital admission, which can arise either from either the consequences of poor glycemic control or arising from complications of the disease, including cardiovascular disease, cerebrovascular disease, renal disease, and amputations (Hex et al. 2012). These amount to ten per cent of the healthcare budget. Although the complexity of the homeostatic mechanisms underpinning glucose metabolism is increasingly understood, this knowledge still remains to be effectively applied to deliver glucose levels constrained toward physiological levels in the range 4–6 mmol/L (80–110 mg/dL).

Technological progress, alongside pharmacological advances, has revolutionized the management of, and outcomes for, people with diabetes. Urine testing has now been largely replaced by self-monitoring of blood glucose. Accurate measurement of blood glucose levels using finger-prick devices allows targeting of therapy and can provide feedback on the impact of physical activity and food intake on glycemia. The impact of continuous monitoring, or monitoring using devices that avoid repeated fingertip sampling, is yet to be fully assessed in clinical practice.

This chapter describes the way in which blood glucose self-monitoring is currently being used to support the care of people with diabetes, the potential impact of linking glucose monitoring to digital health devices, and the potential for such devices to also provide better self-management of other aspects of care, including management of therapeutic regimens, diet, and physical activity. In providing an overview of these issues, this chapter highlights the way that digital technologies can be used to ensure that the benefits of monitoring are fully delivered for patients and for health services.

Background

Blood glucose levels vary throughout the day, and for many individuals with type 1 diabetes, awareness of these variations and adjustment of insulin dose is a means to avoid both the immediate consequences of symptoms arising from hyper- or hypoglycemia and a means to deliver an overall average glucose level that is associated with a lower risk of long-term complications. The average overall level of glucose control, however, can be judged by the level of HbA_{1c}, a glycated protein that reflects levels of control over the previous 120 days and has been shown to be closely linked to long-term morbidity and mortality.

Achieving Optimal Glycemic Control with Monitoring

For individuals with both type 1 and type 2 diabetes, maintenance of long-term levels of glycemia contributes to a lower risk of long-term complications. In the diabetes control and complications trial (type 1 diabetes) (the Diabetes Control and Complications Trial Epidemiology of Diabetes Interventions and Complications DCCT/EDIC Study Research Group 2005), the risk of cardiovascular events was reduced by 42% alongside substantial reductions in renal disease and eye complications for those with better glycemic control. For individuals with type 2 diabetes, long-term follow-up of the UKPDS study where glucose levels were lower in the intervention compared to a control group observed reductions of 24% for microvascular complications and 15% for myocardial infarction (Holman et al. 2008).

Tight control of other risk factors, including blood pressure, cholesterol, and smoking are also major contributors to reduction in complications, but the management of glycemia presents unique challenges, as well as providing an exemplar for management of other risk factors including blood pressure and cholesterol levels.

Poor glycemic control among people with diabetes remains a major public health problem. A recent prospective cohort study of European patients with type 2 diabetes identifies over 37% with an $HbA_{1c} \geq 7\%$ (53 mmol/mol), while the UK National Diabetes Audit identified 66% meeting a HbA1c target of ≤ 58 mmol/mol in 2014/2015. In the same UK audit, control of both blood pressure ($\leq 140/80$) and cholesterol (<5 mmol/L) were better at 74.2% and 77.5%, respectively (Health and Social Care Information Centre 2016).

There is therefore an unmet need for improved glucose control for people with diabetes in the context of maintaining quality of life and reducing the burden of self-care. Utilizing data about levels of glucose control to bring glycemic control for people with diabetes back to physiological levels requires pharmacological and lifestyle measures. Measurement of blood glucose or HbA_{1c} is often considered in the context of a diagnostic test, with a reason for an abnormal measurement considered and an action prescribed. However, it is not just used as a single test, but as a test repeated over time with the aim of identifying excursions beyond a defined range of normal values or to modify an intervention intended to reestablish the parameter within a defined range.

Theoretical Approaches to Monitoring

The concept of a cycle of events in which the response of a system is measured and adjustment made to maintain a constant state is taken from engineering control theory (Del Toro and Parker 1960). For people with type 1 diabetes, short term and within day, measurement of glucose levels and adjustment of short-acting insulin dose is used to maintain glycemic control. The same control-cycle principles apply to adjustment of long-acting or basal insulin in response to glucose levels, although a more gradual adjustment of dose over a period of days reflects the longer period required to achieve a steady state of insulin levels for a change in insulin dose. Similar principles can be considered for people with type 2 diabetes and gestational diabetes where insulin treatment is used. The concept of a cycle of events can be applied to the use of HbA_{1c} to monitor long-term control for people with type 2 diabetes, where adjustment of oral medication can be carried out on the basis of knowledge of the average glucose control over a preceding period of weeks, with subsequent retesting to judge the need for further adjustment of medication.

The concept of a control cycle is more specifically referenced in behavior change theories such as control theory (Carver and Scheier 2002). This theory postulates that there is a synergistic association between receiving information about one's behavior (via "self-monitoring" or "feedback") and having a strategy for acting on this information ("action planning" or "information on where and when to perform the behavior"). The former provides a cue and motivation for the latter. Education that supports patients understanding associations between patterns of behavior (e.g., eating, physical activity, and medication adherence) and outcomes (blood glucose levels) has the potential to be more effective than education or blood glucose testing on their own.

For some people, the experience of self-monitoring extends to a greater understanding of the physiological processes and thus enables adjustment of lifestyle and pharmacological treatment to avoid the development of hyperglycemia, particularly during periods of illness. It can also allow recognition of low levels of blood glucose that could lead to hypoglycemia. The impact of self-monitoring on illness understanding can be difficult to interpret, particularly as the changes in beliefs and perceptions can be very personal, varies widely between individuals, and is not consistently linked with changes in behavior (French et al. 2008).

Increasing the Impact of Monitoring with Education and Technology

Diabetes self-management education and support (DSMES) is an important element of diabetes healthcare provision that has been shown to reduce the risks of developing diabetes-related complications and improve glycemic control, at least in the short term (Norris et al. 2002; Powers et al. 2015). However there are significant challenges in providing DSMES and uptake rates are often low (Coonrod et al. 1994; Centre 2016). Barriers to attendance at self-management education sessions (whether individual or in a group) include inconvenience, fear of stigma, and a lack of knowledge about the potential benefits (Winkley et al. 2015). Digital DSMES programs have the potential for delivery at multiple locations at convenient times, can be used anonymously, and present content in an attractive and tailored format (Pal et al. 2013). Delivering DSMES online can improve glycemic control and diabetes-related knowledge (Pereira et al. 2015; Arambepola et al. 2016).

Adherence with a recommended regimen for taking diabetes medication is needed to obtain maximal benefit from treatment (Farmer et al. 2015). A systematic review of medication adherence studies found that retrospective analyses showed adherence with oral hypoglycemic agents ranged from 36% to 93% and prospective analysis showed adherence between 67% and 85% (Cramer 2004). Around one-third of patients with type 2 diabetes stop their medication within 1 year of starting treatment, and this leads to poorer clinical outcomes and higher healthcare costs (Egede et al. 2012; Hertz et al. 2005; Pladevall et al. 2004). Recent studies of adherence to medication in type 2 diabetes report up to 30% primary nonadherence (Karter et al. 2009) with up to 13% of those continuing to use medication taking less than 80% of their prescribed medication (Farmer et al. 2015).

Interventions using the Internet and digital devices have a growing evidence base. For example, using short messaging service (SMS) text messages to deliver behavioral support focused on medication adherence has been shown to be an effective way of improving medication adherence (Bobrow et al. 2016). The majority of the population in most countries could use such potentially low-cost scalable digital interventions. Reminders and online portals to track medication refills have also been shown to improve medication adherence in people living with type 2 diabetes (Misono et al. 2010; Sarkar et al. 2014). However, for such interventions to have a meaningful impact, they would need to become part of standard care, and, as with DSMES interventions above, providing patients with links between blood glucose levels and their use to diabetes medication would be a potent feedback mechanism to motivate and support adherence to treatment.

The Artificial Pancreas

The technological culmination of successful management of glucose homeostasis is the "artificial pancreas." The extent to which technology has been able to deliver a functioning system that replicates the physiological functions of the pancreas is discussed at the end of this chapter. However, the technology underpinning

monitoring, including glucose sensors, computer algorithms, patient education and advice, and insulin pumps, has all undergone transformations over recent years, offering potential for patient benefit.

Urine Testing to Home Blood Glucose Monitoring

The characteristic sweet urine of diabetes, described by Thomas Willis in 1674 in differentiating diabetes mellitus from diabetes insipidus, has been recognized for thousands of years. In 1776 Matthew Dobson established that the smell arose from sugar. In 1838 George Owen Rees showed how sugar could be isolated from the blood of people with diabetes. The development of the copper reduction test by Benedict in the early twentieth century gained widespread acceptance as a means of testing for glucose levels in urine. In the 1940s, Clinitest, a self-heating alkaline copper reduction test, gained widespread acceptance, to be superseded in 1957 by a urine test stick: the glucose oxidase-based Clinistix (Free et al. 1957).

In 1963, Ernie Adams developed Dextrostix, in which a glucose oxidase/peroxidase reaction was used with a semipermeable membrane through which glucose, but not red blood cells, could pass. The reaction led to a color change; the blue color produced was proportional to blood glucose levels. Although the method allowed an estimate of blood glucose levels, accurate results depended on having experience of the methods and being able to judge the intermediate color changes. In 1970, Anton Clemens was the first person to develop a blood glucose meter, the Ames Reflectance Meter. The meter used the light reflected from a Dextrostix to provide a more accurate estimate of blood glucose level. Despite its size and weight, and originally intended for physician office use, the meter was rapidly adopted by many clinicians and their patients for home use with the first case reports of use of a meter for home glucose monitoring dating from 1975, rapidly followed by detailed reports of its use (Tattersall 1979). Other meters were then developed using other chemicals to react with a dye and, depending on glucose levels, produce a color change.

In 1982 Hill and colleagues developed a ferrocene electrode in which the glucose oxidase reaction led to a change in electrical conductivity rather than a color change and thus opened the way to development of more accurate estimates of blood glucose levels using portable and convenient meters.

Current blood glucose meters are compliant with international standards for accuracy, but have lower levels of accuracy compared to laboratory methods, with a coefficient of variance/variation of around 4% to 6% compared to laboratory standards of less than 2%. Most meters are now factory calibrated, use very small quantities of blood, are quick, and record readings in an internal memory. Many also allow download of their readings to a computer for further review and interpretation. Current standards date from 2013 (ISO: 15197:2013) with the aim that 95% of blood glucose results should be within $\pm$ 0.83 mmol/L of laboratory results at concentrations of under 5.6 mmol/L (within $\pm$ 15 mg/dl of laboratory results at concentrations of under 100 mg/dL) and within $\pm$ 20% of laboratory results at concentrations of

5.6 mmol/L (100 mg/dL) or more. The guidance also requires 99% of readings to fall within zones A and B of the consensus error grid for type 1 diabetes.

Careful handling of test strips and attention to standardized procedures are important for accurate testing. Exposure of test strips to air reduces accuracy, and some reagents are affected by altitude and humidity. Contamination of strips from handling without hand-washing is also a potential problem.

There is a wide range of other equipment available for glucose and glycated hemoglobin. These also range from laboratory-based analyzers to small point of care analyzers and self-monitoring devices that can be used for finger-prick measurement. In addition, the measurement of finger-prick blood samples is now supplemented with technology for intermittent or continuous monitoring using implantable sensors, considered later in this chapter.

Using Blood Glucose Testing for Home Management

Regardless of the indication for using self-monitoring of blood glucose (SMBG), careful instructions in technique and knowledge and skills in using the data acquired to adjust therapy are needed. Regular review is needed to ensure that skills are maintained and that the type of monitoring carried out is relevant and contributing to maintaining health. Obtaining blood samples from finger tips is best done by using a lancet on the side of the finger rather than directly on the finger pad.

Most blood glucose meters in current use allow measurements to be stored and tagged to indicate whether the readings are made before or after food. Detailed records of blood glucose levels alongside changes in treatment, physical activity, and food intake are needed for self-management and adjustment of treatment. Increasingly blood glucose meters include the facility for charting or displaying data in graphical form and downloading data to computer or other digital devices. These technological developments are considered later in the chapter.

Use of Home Blood Glucose Monitoring Type 1 Diabetes

With the potential for enabling people with type 1 diabetes to adjust their insulin dose and check for hypoglycemia, self-blood glucose monitoring is widely accepted on the basis of early case studies showing a clear impact on diabetes control (Walford et al. 1978), although randomized studies of insulin treatment in type 1 diabetes have SMBG as part of the treatment and not separately evaluated. Self-monitoring, along with education and experience in adjustment of insulin levels to reflect lifestyle, provides the tool with which desired blood glucose levels can be accurately targeted.

Adults with type 1 diabetes are recommended to aim for a fasting plasma glucose level of 5–7 mmol/liter on waking and a level of 4–7 mmol/liter before meals at other times of the day. For those individuals testing after meals, a target of 5–9 mmol/liter 90 min after eating is recommended (National Institute for Health and Clinical Excellence 2015). People should be supported to aim for an HbA1c of 48 mmol/

mol (6.5%), but an individualized target should take into account a wide range of factors. To achieve these levels, testing is recommended four times a day including before each meal and before bed. Testing up to ten times a day can be needed if the agreed target for blood glucose control measured by HbA_{1c} is not met; hypoglycemia becomes a problem, during illness, when taking part in a sport, during pregnancy, and if there are legal reasons for doing so (e.g., when driving) (National Institute for Health and Clinical Excellence 2015).

Use of Home Blood Glucose Monitoring for Insulin Treated Type 2 Diabetes

Evidence from a small number of trials does not provide convincing evidence that intensive monitoring of individuals with type 2 diabetes using insulin leads to clinically significant benefits from HbA_{1c} reduction. Never the less, the use of regular blood glucose testing is needed to safely achieve control of glycemia in a timely manner without leading to hypoglycemia. Incremental increases in insulin required to reach an acceptable level of control without testing would be unsafe and risk hypoglycemia. Individuals with type 2 diabetes starting insulin using a basal (once daily long acting) regimen can titrate insulin requirements straightforwardly using once daily testing (Holman et al. 2007); as fasting glucose levels fall, additional tests may be needed where hypoglycemia is a possibility (e.g., with physical activity or changing meal patterns). If basal insulin treatment fails to reduce HbA_{1c} to an acceptable level, then additional testing may be needed to adjust insulin dose with introduction of prandial insulin or mixed insulin regimens.

Use of Home Blood Glucose Monitoring for Non-insulin-Treated Type 2 Diabetes

For many people with type 2 diabetes, measurements of HbA_{1c} are sufficient to guide any necessary changes in non-insulin glucose-lowering treatments. Many treatments for type 2 diabetes now available do not lead to hypoglycemia and do not, therefore, need routine monitoring. However there remain concerns that some drugs, for example, sulfonylurea drugs, may increase risk of hypoglycemia, and therefore SMBG should be available. The circumstances through which SMBG for non-insulin treated type 2 diabetes came into widespread use, and then following careful examination of the evidence moved to a more restricted role, highlights the need for careful evaluation of technology intended to improve outcomes.

Following the development and wider use of blood glucose meters for self-monitoring for people with type 1 diabetes, the potential for blood glucose meters to be used by people with type 2 diabetes to control their blood glucose levels was suggested. This was followed by much research intended to evaluate the extent of benefit of using self-monitoring of blood glucose to support self-management by people with non-insulin-treated type 2 diabetes. The first reported randomized trial

was in 1986 (Wing et al. 1986), and a series of subsequent trials were reported up to 2000.

Two important reports published at that time raised concerns about the use of current strategies for SMBG. A systematic review identified that the pooled data from randomized trials to date comparing the effectiveness of people using SMBG, to those not using SMBG, did not show any additional benefit in reducing blood glucose levels (Coster et al. 2000). A cohort study also showed that people treated with insulin using SMBG showed improvements in blood glucose control, but no benefit was observed for people treated with diet or with oral glucose-lowering drugs. In addition, the possibility of increased distress, worry, and depressive symptoms for those using SMBG was raised (Franciosi et al. 2001). A number of well-designed trials were established to establish whether structured education in the use of medication, closer attention to medication titration, use soon after diagnosis, or other factors might improve the impact of the technology when routinely for non-insulin treated people (Farmer et al. 2007; Davidson et al. 2005; O'Kane et al. 2008; Schwedes et al. 2002). In addition, the largest of these trials included an integral cost-effectiveness analysis (Simon et al. 2008).

These trials and a number of others have been examined for evidence of benefit from using SMBG. Pooling of composite data (Clar et al. 2010; Malanda and Welschen 2012) did not provide evidence for a clinically important effect, and pooling of individual data from six trials using a prespecified protocol and intention to treat analysis confirmed a benefit of 1–2 mmol/mol (0.2%) in $HbA_{1c}$and did not identify any subgroups in which there might be more benefit from using SMBG. Further studies have identified and carried out proof-of-principal studies to establish whether focusing on further structuring of the delivery of SMBG might improve effectiveness, but trials have not identified a clinically important benefit (Polonsky and Fisher 2013; Franciosi et al. 2011).

In 2015 the UK National Institute for Health and Clinical Excellence reviewed the evidence for use of blood glucose self-monitoring for people with type 2 diabetes. The guideline development group examined a range of trials that might have identified a potential benefit. Of the 17 trials comparing SMBG with no SMBG, there was only a small, clinically unimportant reduction in HbA_{1c} levels, although hypoglycemic events were increased. However, the extent to which this might have been due to increased awareness of low blood glucose levels is unclear. Different forms of SMBG were examined, including SMBG plus education versus conventional SMBG in three studies. Overall differences between the groups were not significant. SMBG plus telecare versus conventional SMBG was tested in five trials, but the only trials reporting benefit did not report the types of glucose-lowering treatment being used. Trials looking at frequency of monitoring did not find any differences in HbA_{1c} when comparing less frequent with more frequent monitoring. The health economic evidence suggested that use of SMBG resulted in a lower benefit in terms of quality of life year estimates, as well as being more costly.

Although measurement of blood glucose levels may provide some insight into the impact of lifestyle on glucose control, the extent to which this can be achieved when used routinely at a wide-scale is therefore unproven. Similarly, although the extent to

which SMBG might be used for people with type 2 diabetes to support self-management and improve communication with clinicians is often discussed, evidence of benefit remains limited.

Following the widespread introduction and standardization of HbA_{1c} measurement, along with the observation that for many individuals, HbA_{1c} levels remain relatively stable over time, regular measurement of blood glucose levels has been replaced with HbA_{1c} testing. Two to three monthly measurements allow titration of medication, and annual tests allow maintenance of control to be confirmed in those who have a stable treatment regimen. The potential for self-monitoring to provide information about the pattern of blood glucose levels throughout the day and the extent to which the measurements can provide additional motivation and support remain a matter of debate.

NICE has therefore recommended that SMBG should not be used routinely, although it may still have a place where there is an increased risk of hypoglycemia, for example in sulfonylurea drug treatment.

Digital Health and Glucose Control for Type 2 Diabetes

Progress in technology has greatly expanded the potential for supporting better blood glucose control through multiple channels, not only those directly relating to glucose measurement. Over the past 20 years, connectivity between devices and computing power has evolved rapidly. Systems used by health professionals to maintain electronic medical records have developed to allow patient access to their data through the Internet. Mobile phones now support wearable smart devices allowing for increasingly sophisticated information processing and sharing (van Rooij and Marsh 2016). Digital health interventions based on these technologies (often referred to as mHealth) offer a range of functions that support self-monitoring and self-management including distance-based care, education, support for medication adherence, clinical decision support, and personal applications and devices. This section will look at digital interventions to support better self-management of type 2 diabetes, focusing on blood glucose monitoring and control.

Distance-Based Care

Blood glucose self-monitoring solutions involve data recording and displays. The use of these facilities on blood glucose meters has been described earlier in this chapter. These facilities can be complemented by software that allows logging and visual displays of the information stored on the meters. Early telehealth interventions added the ability to share this data with healthcare professionals and support distance-based care. An early systematic review of telehealth interventions to support self-blood glucose monitoring in patients with diabetes did not find evidence of improvements in HbA_{1c} (Farmer et al. 2005). Simply keeping a record of blood glucose readings does not improve long-term outcomes, and transferring data

collection from paper to computer, using technology to record data, or sharing data remotely do not influence this. However, a systematic review of the use of information technology to manage diabetes found that more sophisticated interventions that included computerized insulin dose adjustment, remote case-management, or distance learning were more likely to show improvements in outcomes like glycemic control (Riazi et al. 2015).

Clinical Decision Support

Clinical decision support systems (CDSS) are computer programs that offer patient-specific, actionable recommendations or management options to improve clinical decisions (Hunt et al. 1998; Kawamoto et al. 2005; Roshanov et al. 2013). Older reviews suggested that the features that lead to improved outcomes were automatic decision support as part of clinician workflow, provision of recommendations rather than assessments, and provision of decision support at the time and location of decision-making. However recent reviews suggest that there is potential for clinicians to be at risk of "alert fatigue" and that integration of support with workflow risks generating too many alerts that are subsequently overridden or ignored (Roshanov et al. 2013; van der Sijs et al. 2006). However, ensuring that patients are also informed of outputs from the CDSS appears to be an effective strategy. Thus, there are opportunities for systems that have traditionally been clinician focused to be improved by taking a more patient-centered approach through collection of patient-reported data and using suitable user-interfaces (O'Connor et al. 2016). Self-reported blood glucose monitoring data feeding into such systems could be used to guide clinical decision-making and be analyzed to provide suggestions for changes to lifestyle and medication. This data would be uploaded automatically without manual input of values. This integrated and holistic approach to digital health could target individuals who might benefit from the regular use blood glucose monitoring or highlight circumstances when it could be valuable in people who would not otherwise need regular SMBG.

Personal Self-Monitoring and Self-Management Support

Mobile phone-based applications (apps) are becoming increasingly popular with over half of adults in the United States owning a smartphone (Eng and Lee 2013). However even though there are more than 1000 publically available smartphone apps for diabetes, a recent review found only 20 peer-reviewed evaluations of these apps (Garabedian et al. 2015). Most apps do not adhere to evidence-based guidance and lack an empirical or theoretical basis for development, and there are no universal standards to help users judge apps by such criteria (Breland et al. 2013; Boulos et al. 2014). In spite of the large volume of apps for diabetes, the majority offer similar functionalities and combine only one or two functions, usually manual blood glucose recording (Arnhold et al. 2014). Given the evidence discussed previously

in this chapter, these apps are unlikely to have any impact on outcomes, yet they are marketed and sold to users. However most apps score quite highly on assessments of usability and acceptability, even for adults aged over 50, and the fewer the functions, the higher the usability (Arnhold et al. 2014; Payne et al. 2015). The challenge that lies ahead is work to combine the usability of commercially created apps with a theoretical and empirical basis that can create usable and effective interventions, within a regulated framework, that can link glucose meters, personal records, electronic medical records, and CDSS (Klonoff 2013).

However, it is also worth noting that not all mHealth is high-tech or smartphone based. SMS text messaging is a cheap and widely available technology that can be used in most parts of the world and is another popular area of research (Bin Abbas et al. 2015; Capozza et al. 2015). It has also been shown to be an effective way of improving outcomes in a range of long-term conditions (Free et al. 2013; Leon et al. 2015; Lester et al. 2010). Algorithm-driven SMS-advice based on patient-entered blood glucose data has been shown to reduce HbA_{1c}, and although it is not widely used, it can be effective (Liang et al. 2011). A systematic review of computerized diabetes support trials suggests mobile phone-based interventions that provided tailored feedback and advice based on blood glucose reading have significantly larger improvements in HbA_{1c} than other digital self-management interventions (Pal et al. 2014).

A wide range of behavioral approaches has been combined with monitoring to provide smartphone-based health coaching: health-related education, behavior change, and support for patients (Sherifali et al. 2016). Health professionals or peers can lead these interventions, and they have been shown to help reduce HbA_{1c} and improve patient outcomes (Quinn et al. 2011; Thom et al. 2013; van der Wulp et al. 2012; Wayne and Ritvo 2006).

Potential Challenges with Digital Interventions

Although digital health interventions have potential to improve care through the wide range of functions described above, they also have a number of barriers to their effectiveness that need to be overcome. These include engaging people with their use, inequity in provision, facilitating their adoption by health systems, security, and rapid changes in systems as technology evolves.

Disengagement with digital interventions is a significant concern as the usage of digital interventions is associated with their effectiveness (Couper 2010; Donkin 2011). It is particularly important for digital interventions to have active strategies to facilitate uptake and engagement with users (van Vugt et al. 2016). Technology-based prompts can help with this (Alkhaldi et al. 2016), and human input and support in using digital interventions by facilitators and peers have also been shown to increase exposure (Brouwer 2011).

One of the biggest concerns with new technologies is equity and access, often referred to as the digital divide. The digital divide can be defined as an economic and social inequality arising from lack of access or impact from information and

communications technology (ICT) (US Department of Commerce, National Telecommunications and Information Administration (NTIA) 1995) – and it has been noted that use of the Internet and access is highly associated with income, age, education, and occupation (van Dijk 2006). However access to ICT is improving rapidly – for example, in the UK in 2015, 86% of adults had used the Internet within the last 3 months and that number is increasing (Statistics 2015). Digital interventions increasingly have the potential to be a channel through which health outcomes can be improved across society and used to reach those with the greatest need and the most potential to benefit.

Effective digital interventions consist of multiple components, often referred to as complex interventions, and are not always widely adopted in healthcare settings, and when they are, the process is often much slower than other sectors of business and society (Chaudoir et al. 2013; Cresswell and Sheikh 2013). The process of implementing such complex interventions into routine clinical practice faces a number of challenges (Murray et al. 2010). There is a general difficulty perceived in making the transition "from clinical studies to everyday clinical practice and health decision making" (Woolf 2008). Therefore approaches to implanting digital technologies for diabetes need to adapt to address the likely barriers (Grol 1997) and address the interdisciplinary nature of the problem. A review of the implementation literature identified more than ten different academic disciplines that contribute to the uptake of innovations in health services (Greenhalgh et al. 2005). There are more than 60 theories and frameworks that have been developed to guide the process of implementation (Tabak 2012). Although there is no simple solution to the challenges of the implementing digital health technologies, taking a theoretically informed approach to anticipating barriers and generating possible solutions as part of the conception, development, and evaluation of the technologies is likely to be key to success.

Increasing dependence on technology for care for people with diabetes carries with it a number of risks. These include risks for patients from unauthorized access to their data and loss of data. These could arise unintentionally through human error, power failure, or malicious tampering. Security standards required for devices, for example, insulin pumps, are rapidly developing and are addressing such threats.

Technical obsolescence is a major risk facing all IT systems (Samy et al. 2010). Hardware and software systems are rapidly evolving: Moore's law predicts that processing power of computers doubles every 2 years, and this has remained true for nearly five decades (Roberts 2000; Schaller n.d.); Lehman's laws predict that the software size and complexity will increase with time and system quality will decline with time unless the system is rigorously monitored and adapted to these changes (Yu and Mishra 2013). The digital landscape has further evolved with the advent of multiple computing devices that now include tablets, smartphones, and wearable technology. IT systems now need to be compatible with multiple ecosystems (e.g., Windows, Android, IOS) with different interfaces and devices sizes – and also factor in planned obsolescence with annual iterations of many hardware and software platforms. Achieving sustainability by gaining sufficient adoption and use, while keeping up with an evolving environment, is an increasingly complex task. The time

taken to evaluate and implement healthcare services puts digital health interventions as risk of obsolescence before they have a chance to be widely adopted.

Developing Technology Around Home Glucose Monitoring

Continuous Blood Glucose Monitoring

The possibility of using more frequent glucose measurements than feasible with blood glucose meters to guide insulin therapy has stimulated the development of increasingly practical technologies for continuous glucose monitoring (CGM), capable of providing up to 300 measurements a day.

All the currently available systems require calibration using capillary blood glucose measurement and use a subcutaneously implanted sensor that can remain in place for up to 7 days. This sensor usually transmits data wirelessly to a monitor. CGM systems are intended for intermittent use to identify periods of hyperglycemia that can be corrected by changing therapy (e.g., increasing the dose of insulin or changing timing of injections) or detecting periods of biochemical hypoglycemia that may be too brief to cause symptoms but may nevertheless cause some impairment in cognitive function. These devices are not as accurate as conventional blood glucose meters, so blood glucose levels need to be confirmed before a change in treatment.

Evidence for effectiveness of CGM in selected people with T1DM aged over 25 years using intensive insulin therapy comes from a randomized trial with 322 people with T1DM (Juvenile Diabetes Research Foundation 2008). Those allocated to the CGM arm experienced a 0.5% (6 mmol/mol) reduction in HbA1c from 7.6% to 7.1% (60 to 54 mmol/mol) compared to conventional therapy. Evidence for HbA1c lowering is less strong in children, teenagers, and younger adults, although there may be specific clinical circumstances in which CGM might be helpful. Success correlates with adherence to the ongoing use of the device. Many people with type 1 diabetes indicate that CGM is a valued addition to diabetes care with a perceived improvement in HbA1c and reduction in hypoglycemia (Pickup et al. 2015).

In the UK, the National Institute for Health and Care Excellence (NICE) does not currently recommend routinely offering real-time CGM to adults with type 1 diabetes. However it can be considered for use where individuals are willing to use the systems and treatment is otherwise optimized, in those with severe hypoglycemia, loss of awareness of hypoglycemia, frequent asymptomatic hypoglycemia, or HbA_{1c} levels above 9% (77 mmol/mol) (National Institute for Health and Clinical Excellence 2015).

Continuous glucose monitoring during pregnancy is also an area where periods of intermittent continuous monitoring may offer benefit. To date, studies have not shown an improvement in glycemic control or clinical outcomes (Secher et al. 2013), but further work on the abnormalities detected by monitoring may be needed to better target glycemia. For example, using closed-loop systems in a proof-of-concept setting shows the potential for improved glycemic control (Law et al. 2015).

Flash Monitoring Systems

Innovative approaches to interstitial glucose measurement have now been developed, building on the experience of continuous glucose monitoring. These are referred to as flash monitoring – using an implantable sensor that is scanned to read the current glucose level, rather than providing a continuous stream of data. For example, the FreeStyle® Libre device uses a sensor worn for up to 2 weeks. It is designed for continuous use and does not require calibration, but is scanned, giving readings over the previous 8 hours, using a handheld device that avoids the need for a direct connection between a sensor and the recording device.

Insulin Bolus Advisor

For people with type 1 diabetes, adjustment of short-acting insulin is required to target recommended blood glucose levels. To achieve this, the insulin dose is adjusted based on carbohydrate intake and current glucose intake, taking into account insulin sensitivity. However, the required insulin dose is frequently miscalculated (Ahola et al. 2010). Some newer meters contain algorithms that can either be programmed with the required insulin sensitivity ratios. These meters appear to be safe and acceptable to patients in proof-of-concept studies (Schmidt et al. 2012).

Closed-Loop Systems

The language of engineering, noted at the beginning of this chapter, is reflected in the considerable advances that have been made in the management of diabetes where continuous glucose monitoring and continuous insulin infusion devices have been linked. Technologies evaluated include systems that suspend delivery of insulin when levels reach or are predicted to reach a preset lower limit and closed-loop systems that provide autonomous graduated modulation of insulin above and below preset insulin amounts in a glucose responsive manner (Hovorka et al. 2014).

Many people with type 2 diabetes have welcomed the development of such systems and the way they can provide "time off..." from the demands of diabetes (Hovorka et al. 2014; Barnard et al. 2015).

The control algorithms used in such closed-loop systems include a wide range of predictive approaches based on mathematical models that account for delays in absorption of food and delays in absorption of insulin. Strategies that have been used to overcome the inaccuracies of predictions include the use of hybrid systems that allow use of manual bolus of short-acting insulin.

The major limitations of these systems include the slow absorption of insulin and the difficulties of predicting insulin requirements around exercise and the postprandial state. In addition, there is a lag in blood glucose levels changing in the interstitial fluid compared to plasma. All of these factors limit the performance of closed-loop systems during the daytime, with clinical evaluations to date largely focusing on the overnight phase.

CGM systems are now being evaluated as a sensor within a closed-loop system in which insulin delivery through a pump device is regulated by the use of a control algorithm that automatically reduces and increases subcutaneous insulin delivery according to sensor glucose levels. Recent short-term studies in young adults with diabetes in a home setting indicate that glucose control is improved during the day and night with fewer episodes of hypoglycemia (Hovorka et al. 2014).

Summary

Monitoring of blood glucose levels is appropriate where the purpose of doing so is clear, the technology robust, and it can be done by individuals. Technology for blood glucose monitoring is increasingly simple to use and, although not as accurate as laboratory measurement, offers information on which to adjust insulin therapy. However, the extent to which routine monitoring offers advantages over HbA_{1c} monitoring for adjustment of medication in type 2 diabetes is unclear. Further advances in the technologies linked to SMBG are currently being tested. The rapidly evolving nature of technology and the increasingly ubiquitous presence of devices with significant computing ability represent significant opportunities to support patients with blood glucose control and improve outcomes for people with type 2 diabetes.

Although there is evidence of promise for many solutions across the technology spectrum, there are important barriers posed by the rapid pace of change and significant fragmentation in an environment with different devices, software ecosystems, and stakeholders with different needs (patients, healthcare professionals, and administrators). Together with the known difficulties in establishing uptake and engagement of health professionals and users at scale, there are significant challenges that need to be overcome to deliver sustainable, comprehensive, and accessible technology solutions. Health services need to address these issues to ensure that the potential of new technology is fulfilled to help deliver the increasing cost-efficiencies that are urgently needed to deal with the increasing demands facing health services in the twenty-first century.

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