Current Diabetes Technology and its Challenges
Güncel Diyabet Teknolojisi ve Zorlukları

*School of Biosciences, Faculty of Health & Medical Sciences, Taylor’s University Lakeside Campus, MALAYSIA
*Centre for Drug Discovery and Molecular Pharmacology (CDDMP), Taylor’s University Lakeside Campus, MALAYSIA

Abstract
The prevalence of diabetes mellitus is increasing at an alarming rate worldwide. With no cure available, effective disease management is the best way to control disease progression. Studies have shown that diabetes technology helps to improve health outcomes and the quality of life of the patients. Diabetes technology can be defined as any solution encompassing hardware, devices, and software used in the disease management of patients. This review serves as an introduction to diabetes mellitus by discussing the different categories of well-established diabetes technology, related ongoing research, and its challenges. This review is divided into 3 main categories, insulin administration, glucose monitoring, and hybrid devices that combine the 2 categories into one. Digital health application is also discussed as it is becoming a notable tool in the disease management of diabetes. Widespread use of these devices in disease management has been increasing in recent years. However, there are still barriers that prevent the utilization of the full potential of these devices.

Keywords: Artificial pancreas; blood glucose monitoring; diabetes mellitus; diabetes technology; digital apps technology

Introduction
Diabetes mellitus (DM) is a prevalent metabolic disease affecting the global population and has been dubbed as an epidemic by the World Health Organization (WHO). Recent data has estimated that approximately 629 million people will be affected by 2049, making diabetes a notable healthcare economic burden (1). Epidemiologically, DM and lesser forms, such as glucose intolerance, impaired glucose tolerance, and impaired fasting glucose, are prevalent in every population in the world, and without prevention and early control programs, cases are increasing at an alarming rate. DM can be classified into Type 1, Type 2, gestational DM...
(GDM), and other specific types of DM based on its diagnostic criteria, etiology, and genetics. This is the most widely used and accepted classification adopted by the American Diabetes Association.

Type 1 diabetes (T1D), also referred to as autoimmune T1D, accounts for 5-10% cases of DM and occurs due to the loss of pancreatic β-cells that results in decreased insulin production. T1D is associated with multiple genetic predispositions and environmental factors that are still poorly defined. Type 2 diabetes (T2D) is more common, affecting 90-95% of individuals, and is characterized by desensitization of insulin and reduction in insulin production (2,3). T2D is considered to be a polygenic disorder that arises due to interaction between multiple genes and environmental factors (4). GDM is an asymptomatic condition that occurs during pregnancy as a result of abnormal hormone production, which increases the insulin sensitivity of the patient. It is not life-threatening to the mother but is associated with an increased incidence of neonatal morbidity, neonatal hypoglycemia, and jaundice. Identifying the type of diabetes of a patient correctly is important since it directly impacts the treatment strategies. However, many do not fall into a single category, and as the disease progresses, revisions are required (5). Currently, DM is not curable or reversible, and the available treatment focuses on the management of the symptoms. Diabetes technology is an important aspect of DM management as treatment and disease monitoring heavily rely on it. For clinical practice, diabetes technology mainly focuses on insulin delivery, glucose monitoring, and data management, specifically, the hardware, devices, and software used in condition management (6). Generally, diabetes technology can be divided into 2 categories, which include the insulin delivery system and blood glucose monitoring. With recent technological advancements, hybrid devices that combine the insulin delivery system and monitoring comprise the third category. A fourth category that is worth mentioning is digital health application, which refers to any application that directly or indirectly helps in treatment management. These categories will be discussed further in the review.

**Insulin Delivery**

Synthetic insulin delivery is commonly used in diabetes management. Intensive regimens are usually prescribed to T1DM patients. However, in certain cases, as T2DM progresses, some patients might be put on the same regimen. Common intensive insulin regimen usually involves basal insulin dose and bolus insulin, a supplementary dose to counteract the additional sugar or carbohydrate from diet to lower blood sugar back to normal range. Insulin is introduced either via multiple daily injections (MDI) of insulin or insulin pumps. Traditionally, insulin delivery was performed via vials and syringes, which is still conducted in clinical settings but has been declining over the years with changes in patients'preferences. However, it is the most cost-effective strategy. This practice requires knowledge of proper handling techniques and repeated injections throughout the day, causing discomfort and needle phobia (7). Administration of the wrong dosage might occur since MDI requires a combination of insulin with different dosages depending on the patient's activity. However, the ability to mix insulin formulation might be advantageous, especially in unique cases, and this could be the stepping stone towards precision medicine (8,9).

**Insulin Pens**

Different insulin delivery methods were introduced to reduce invasiveness, increase delivery accuracy and precision, and increase the ease of treatment. In 1985, the insulin pen was first introduced and marketed as an easy-to-use injection device (8). Insulin pens have a cartridge and a fine replaceable needle with a mechanical dose display. Insulin pens have been improved considerably from their first design with newer technology and easier usage. These new-age insulin pens or “insulin smart pens” are built with memory systems intact or Bluetooth-enabled software. They can store data on patient-specific dosage amount and timing, which helps clinicians in treatment decisions. A study in Sweden showed that patients using smart insulin pens have better glycemic control, shorter hypoglycemic periods, and reduced missed bolus dosage (10). Some pens are marketed as prefilled
devices to be discarded after one use, but more companies are introducing reusable eco-friendly pens with interchange cartridges that are useful if a patient’s regimen changes. Newer, more advanced insulin pens have a companion smartphone application that not only keeps track of insulin injections but also has a built-in bolus calculator. Due to the complexity of bolus dose calculation, a bolus calculator software was developed to automatically calculate the right dosage based on minimal input provided by patients. The software takes into account parameters such as target blood glucose, current blood glucose, carbohydrate-to-insulin ratios, total grams of carbohydrate in the meal, and insulin sensitivity factors to generate accurate bolus insulin dose (11). These devices have accurate dosage, with some offering increment of half-unit doses. With many new devices in the market, there is concern whether all the advertised pens are accurate as there is no standardized test to compare them. Although the insulin pen seems like the ideal choice, data from 2008 showed that 88% of the pens were used in Europe and 95% in Japan, only 17% were used in the United States (12). This is due to various factors but mostly because of patient preferences. Another study also revealed that multiple injections daily can cause psychological stress leading to poor patient compliance (13).

Insulin Pump

Insulin pump therapy or continuous subcutaneous insulin infusion (CSII) has also come a long way from when it was first introduced in the 1990s. The device is small and is equipped with more compact features. It is designed to mimic natural insulin basal secretion and adapted to the circadian schedule of the patient. The device can be divided into 3 compartments, including an insulin reservoir, a battery-operated pump, and a control mechanism that is usually computerized and programmed to deliver basal insulin and bolus doses. CSII emulates pancreatic functions by supplying basal doses at pre-set times tailored to the patient to ensure reproducibility. Typically, an insulin pump is used for 3-7 days before it needs to be changed. Depending on the system, some pumps require only minor compartment changes, while some need to be discarded. This might be expensive since some insurances do not cover insulin pumps in their policies. The price of an insulin pump is about $4,500, with expenses of up to $1,500 per year for its supplies (14). Studies have found that in pediatric cases, patients from families with higher income and education are more prone to choosing CSII therapy (15). The cost of insulin pumps has created a medical gap that needs to be addressed. With the advancement of technology, insulin pumps have better features, such as the Bluetooth system, wireless data management for monitoring treatment, and an alarm system to alert users on the status of the battery and the insulin reservoir level (12). A notable feature of the newer insulin pump system, known as the sensor-augmented insulin pump, is the integration of a glucose monitoring system. These compact pumps are usually programmed with multiple basal delivery profiles that can be selected by the patients depending on their activity. However, device malfunction might occur, causing patients to be undermedicated or overmedicated and might induce diabetic ketoacidosis and hypoglycemia (9). Another possible complication is an infusion-site infection, although it has become rare as advanced infusion sets have been introduced along with improved patient education.

Glucose Monitoring

Glucose monitoring was first introduced in the form of a technical urine-testing tool. The urine strips measure glucose and ketones. However, the results of the patient’s current glucose condition are not accurate, and the body only excretes glucose when the sugar level is high. Therefore, urine glucose strips are only recommended if there is a problem with using the blood glucose monitoring technique. This problem was overcome in 1969 when the first monitoring device was introduced and developed by Anton H. Clemens. The device was based on the glucose oxidation process and marketed as a personal glucose monitoring device. Self-monitoring blood glucose (SMBG) devices were distributed first in the 1980s and replaced urine testing in the 1990s (16).
Self-Monitoring Blood Glucose

SMBG is a part of a multifactorial intervention recommended to patients along with an intensive insulin regimen. It is integral as patients need to monitor blood glucose before meals, bedtime, or any intense activity as a guide for treatment decisions (6). The frequency and timing of SMBG need to cater to the specific needs and treatment goals of the patients. A study found that increased daily frequency of SMBG might be associated with lower HbA1C and fewer complications (17). One of the most commonly used devices is the glucometer. The blood sample of patients taken with a lancet is applied on a reagent strip that is inserted into the glycemic reader for automated reading. Detection is based on electrochemical reaction, specifically glucose enzymatic reaction to either glucose oxidase or glucose dehydrogenase (6). An important aspect of SMBG is the accuracy of the glucose meter. Some glucose meters have a built-in warning system if there is a possibility of a false reading. The analytical and statistical accuracy of the reference and SMBG values is necessary to ensure that there are no differences, which might cause serious errors. Oxygen sensitivity, temperature, altitude, possible substance interference, and condition of the strips can impact glucose reading and cause reading inaccuracies. The meters that utilize the glucose oxidase reaction are oxygen sensitive. Hence, capillary blood is preferred due to its normal oxygen saturation, while the devices that utilize glucose dehydrogenase are not oxygen sensitive. Currently, there are many types of meters in the market, all with different features. One of the most notable new features is the no-wipe technology, which eliminates the need to wipe off extra blood from reagent strips. Thus, a smaller amount of blood is needed for testing. Some meters have also introduced a data-tracking software that not only monitor readings but also help to identify trends and graphs to aid in decisions regarding therapy (18). Most of the devices in the market usually follow a strict standard provided by the International Organization for Standardization, approved by the agency of each country. However, the accuracy of most devices is based on the claims of the manufacturers and is not routinely checked by independent organizations (6). SMBG is widely used because it is a simple device, requires minimal training, and gives results immediately. Although the SMBG system has been improved over the years, it still provides a limited amount of data. On average, 4 to 6 readings of capillary blood glucose are obtained. This does not provide a full comprehensive feature of the glycemic variation of the patient, especially at night, which can hinder decision making (16). The unreliability of patient-recorded data and patient compliance due to discomfort of the device fingerstick blood sampling is a concern (19). To overcome this problem, the continuous glucose monitoring (CGM) system was introduced.

Continuous Glucose Monitoring System

Some healthcare practitioners prefer more comprehensive data for monitoring, especially before any treatment decision is made. The CGM system, which is an interstitial fluid (ISF)-based glucose monitoring system, similar to the system that monitors blood glucose concentration, might be used. The CGM system was first approved by the U.S. Food and Drug Administration (FDA) for public usage in 1999. It reports blood glucose levels as trends off luctuations, and this data is used for retrospective analysis, especially in the detection and prediction of hypoglycemia and hyperglycemia (20). Generally, most CGM devices consist of 3 components, which include a wearable sensor, a reading transmitter, and a display receiver. For CGM, ISF glucose undergoes an enzymatic reaction to generate an electric current using oxygen as a cofactor (21). CGM can visualize glycemic trends and patterns so that a more informed decision can be made for regulating blood sugar levels. There are various types of CGM devices available, including Real-Time CGM (RTCGM), intermittently scanned CGM, Blinded CGM, and Unblinded CGM. RTCGM continuously measures glucose levels and provides automated alerts if there are changes in glucose levels, while CGM only displays glucose levels when prompted. Blinded CGM is a temporary device (10-14 days) that measures glucose levels, but the data are not displayed in real-time to the patients; it is only available to the medical
provider for assessment, whereas, unblinded CGM has the same principle except that the data are not hidden from the patient (6). Various studies have demonstrated that the clinical benefits of CGM are directly proportional to the frequency of device usage. Routine CGM usage shows a marked improvement in the HbA1c level and reduction in the risk of hypoglycemia (22). CGM has considerably improved from when it was first introduced in the market, with new features such as wireless data upload, lower costs, inclusion in insurance coverage, improved sensors, and smaller size; these features have made the device more user-friendly. Patients can now choose CGM devices that require daily fingersticks for calibration and optimization or those that do not require calibration. CGM devices may cause some adverse effects, mainly contact dermatitis, as the device is attached to the skin. Isobornyl acrylate, a common skin sensitizer can trigger allergic reactions, and patients are advised to perform patch testing before wearing the devices for long hours to avoid this issue (23).

For T1DM >> T1D patients, CGM is a good alternative to SMBG, and the large amount of data obtained can aid in decision-making. For T2DM >> T2D specifically, patients do not need to monitor their blood glucose daily; hence, CGM data may not be as useful. An alternative glucose monitoring device, known as flash glucose monitoring (FGM) or sometimes referred to as intermittently viewed CGM, was commercially introduced in 2014 (24). FGM is a wired device that is worn on the arm for up to 14 days, and detection is based on enzymatic reactions of glucose oxidase that is co-immobilized on electrochemical sensors. A small patch sensor with short filaments is inserted in the subcutaneous tissue of the upper arm. Users can obtain real-time glucose data on demand by scanning the patch sensor with the reader or mobile phones. The device can retain the data over the 14 days that can be analyzed using simple trend graphs; however, no alarm system is integrated to inform if blood glucose level is not normal during the time of reading. No severe adverse effect or severe hypoglycemic event has been reported, but some patients have reported allergic reactions, induration, bleeding, and insertion-site symptoms such as bruising, pain, and minor infections (19). Although FGM is relatively new, it is a good option to consider as it is small, easy to use, simple to interpret the data >>> simple data interpretation does not require calibration, and is inexpensive compared to standard CGM devices. FGM devices have similar accuracy to CGM devices, and healthcare professionals should consider them as a viable option for patients. Similar to other devices, there is a learning curve for FGM during familiarization, and healthcare professionals need to be trained to guide patients to fully utilize the potential of the device (25).

Non-Invasive Blood Glucose Monitoring

Non-invasive blood glucose monitoring (NIGM) devices were developed specifically to minimize pain and the chances of infection due to repeated glucose reading when using the SMBG method. The increased adherence monitoring regimen reported with NIGM also aids in improving the accuracy of the blood glucose trend, which can help in making better treatment decisions. Currently, the best option for NIGM is to monitor glucose via biological fluids such as sweat, tears, urine, and saliva due to its convenience, lowcost >>> low cost, and ease-of-use (26). Sweat is an easily accessible biofluid containing analytes that are related to blood concentration that can provide blood glucose reading. A device was developed recently to incorporate electrochemical impedance spectroscopy and chronamperometry technique to gain real-time fluctuations at the electrode-sweat interface (27). The device provides results quickly, and only a small volume of sweat is required for detection. However, it might be inaccurate as glucose concentrations are considerably lower in sweat than in the blood. Due to the nature of sweat, there are also possibilities of inaccurate readings due to skin pH changes, body temperature, and possible skin contamination.

Human tears have also been considered, as they are an extracellular fluid that contains proteins, glucose, and electrolytes. Studies have shown a correlation between tear glucose and blood glucose levels (28,29). Hence, various methods to collect tears
have been proposed, from the use of smart contact lenses to filter paper, but none are currently approved by the FDA for commercial purposes. Adverse effects such as conjunctival damage, discomfort, and possible alteration in tear glucose concentration might occur, especially with frequent and repeated readings. Saliva contains many analytes, and its glucose levels are directly correlated with blood glucose levels (30). Some studies have proposed the use of saliva for glucose detection in devices such as enzyme sensors, optical sensors that require oxidase activity, and saliva-responsive paper strips; however, none have been introduced in the market or approved by the FDA (31,32). Most of the devices are in various stages of development, and preliminary results indicate that these non-invasive approaches might be promising. They can be considered to be the future of glucose monitoring. However, more extensive research is required and should be encouraged before these devices can replace the standard diabetes technology used currently.

**Hybrid System**

**Closed-Loop System**

The integration of CSII and CGM as a combination in diabetes management has shown positive results, and it is the main diabetes treatment recommended by healthcare practitioners. Hence, combining both the systems in one device might be the next relevant step to control diabetes by imitating the biological secretion of insulin. The closed-loop system (CLS) is also known as an artificial pancreas made up of 3 different parts, which include the CGM system, the insulin delivery system, and a control algorithm software and machine learning system that automatically adjusts the basal insulin infusion rate and establishes a feedback loop (Figure 1) (33). It was introduced for commercial usage in late 2016. An ideal CLS device can eliminate all human errors in the form of dosage skipping, overestimation of dosage, and system calibration. Algorithms used by the system need to consider meal and exercise adjustments, and currently, this is aided by the input of carbohydrates in patients. In the future, a fully automatic artificial system might eliminate the need for patient input for insulin dosage correction and also the integration of both insulin and glucagon delivery to mimic the natural pancreas (34,35). CLS provides a more consistent glycemic control with no adverse effects reported compared to sensor-augmented insulin pumps (36). Although the system seems ideal, there are no randomized big population studies conducted to ensure its effectiveness in daily usage. Some studies argue that CSII is a better option than MDI in diabetic management associated with HbA1c, hypoglycemia reduction, and the quality of life (37). However, patient preference and clinician input determine the route of management.

**Digital App Technology**

Digital health (also known as mHealth) is a new category that can aid in disease management for many comorbidities, especially diabetes. Newer health apps have better integration with more traditional health processes such as lifestyle support, pharmacological interventions, and medical devices to create one seamless hybrid digital...
health system. The WHO defines digital health as “medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices” (38).

Diabetes is a chronic health condition suitable for digital health applications, mainly because the measurable indicators (blood glucose and HbA1c) are accepted as standard readings. Most diabetic patients who respond to the indicators can measure and monitor their health parameters daily and are also available for treatments and interventions. There is a rapid increase in digital connectivity, which has led to an increase in the use and application of predictive analytics and artificial intelligence in diabetes treatment. The majority of the available applications in the market, however, are not usually tailored for diabetes (unless stated), but they can generally be divided into 6 different categories (Table 1). Usage of these health apps can potentially improve health care outcomes due to the integration of compliance and modifiable health behaviors, mainly through patient adherence. No study has shown their long-term benefits; limited data are available, and most studies have focused on the short-term benefits for applications that offer limited functions (39).

Future studies should also include different socioeconomic groups since health apps rely heavily on literacy, numeracy, and technical skills that may differ even in high-income countries. Despite this limitation, the development of health apps should be continued as they can increase the self-reliance of the patients and improve health outcomes.

**Challenges in Diabetes Technology**

Diabetes technology is a field that is continuously evolving, with better methods being developed and introduced to raise the standard of care in diabetes management. Despite these advances in disease management, most patients do not reach their target HbA1C (35). Hence, to overcome this problem, different strategies should be used. One option is to shift diabetic clinical practice towards precision medicine to reduce patient burden, improve their outcomes, and provide more cost-effective treatment. For example, a mathematical model algorithm of Hb glycation and red blood cell kinetics can be used with glucose measurements for patient-specific estimates of nonglycemic determinants of HbA1c (41). If more accurate results are obtained and used as a base guideline, the treatment management proposed can be ensured to be more effective, tailored to the condition of

| **Category**               | **Description**                                                                 |
|----------------------------|---------------------------------------------------------------------------------|
| Nutrition apps             | • Self-tracking of consumption  
                              | • Database for food categories information  
                              | • Meal planning and insulin dosage adjustment  |
| Physical activity/tracker apps | • Exercise and weight management  
                              | • Track distance walk/run, calorie count, heartbeat, sleeping schedule  |
| Glucose monitoring         | • Glucose data from the external device (BGM, CGM)  
                              | • Graphical output of glucose data trend  
                              | • Cloud data storage sharing  |
| Insulin titration apps     | • Accompaniment of glucose monitoring  
                              | • Provide bolus calculation  |
| Insulin delivery apps      | • Application for smart insulin pens  
                              | • Prescription medicine reminder  
                              | • Display data trend, bolus calculator, and decision support  |
| Artificial pancreas system | • Main system/communication connecting the device to the patient  
                              | • Central control for CGM system, infusion pump, and AI algorithm  |

Table 1. Different categories of digital health applications for diabetes management. The table has been modified (40).

BGM: Blood glucose monitoring; CGM: Continuous glucose monitoring.
the patients, and reduce any unwanted cost. Improvements proposed in the field also need to consider sustainability, improved accuracy, reliability, and shifting towards non-invasive devices.

Most new diabetes technology devices use either Bluetooth, wireless cloud systems, or mobile phone applications in their software integration for easy data transfer and monitoring. This, however, poses a problem as new safety risk emerges, specifically in terms of data privacy and security. There is also an issue of compatibility, cost, and the impact of software integration on the patients. Established to monitor and protect the privacy of the patients. Patients do not have the option to restrict sharing of information and how their information is stored or might be used in the future. Hence, more studies need to be conducted to assess these issues, and steps need to be taken to assure that patient privacy is not violated.

Direct health expenditures for diabetic patients (including private payers, public payers, and government) have shown an increasing trend and are estimated to continue to grow. It is estimated that by 2045, $845 billion will be spent on diabetes-related health expenditure, not including expenditure related to diabetes complications (1). This is one of the main reasons why diabetes technologies are not fully utilized; therefore, patient treatment is not able to reach its full potential. High-cost barriers are still present, especially in countries with lower income, although considerable improvements have been made over the years. Thus, there is a socioeconomic gap in diabetes treatment. Studies have shown that low socioeconomic status is associated with higher mortality and morbidity. Patients from low socioeconomic backgrounds are less likely to adopt intensive insulin regimens that can improve the patient’s outcome. For example, hybrid loop technology was only available in North America until recently (42). Disparities are also found consistently regardless of the healthcare system of the country, including access to a universal healthcare system (43). This is an important issue as access to good diabetes healthcare, specifically for the most vulnerable, can improve outcomes with an effective regimen.

**Conclusion**

Management of DM is challenging for both clinicians and patients, mainly due to the requirement of high literacy and numeracy. Incorporating diabetes technology in the regimen helps to overcome this barrier and generally improves health outcomes determined by using Hba1c levels as a benchmark to indicate the benefits of the new therapeutic method. It also serves as a useful tool for patients to overcome barriers associated with diabetes, including safety, support, self-efficacy, and comfort. However, it may also be a burden and barrier to treatment, especially due to device cost and coverage. Recently, the market has shifted to more patient-centric devices with the introduction of the assessment of human factors. Human factors include not only direct user experience with the interface but also the overall user experience. This is because many companies have realized that satisfying patients is necessary for them to continue a particular method of treatment and use a device optimally. The adaptability of a device is also important as it needs to be seamlessly integrated into the daily life of the patients. Only by understanding these device barriers can one mitigate the obstacles and allow more widespread use of diabetes technology. Constant improvements and innovations in diabetes technology can help ease the burden of the patients and help clinicians to make better decisions. However, extensive studies must be conducted before any new device is introduced in the market to ensure that it is safe before using it as an alternative to older devices.

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References

1. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohroge AW, Malanda B. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271-281. [Crossref] [Pubmed]
2. Daneman D. Type 1 diabetes. Lancet. 2006;367:847-858. [Crossref] [Pubmed]
3. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, Bell R, Badarau A, Talton JW, Crume T, Liese AD, Merchant AT, Lawrence JM, Reynolds D, Dolan L, Liu LL, Hamman RF; SEARCH for Diabetes in Youth Study. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA. 2014;311:1778-1786. [Crossref] [Pubmed] [PMC]
4. Ali O. Genetics of type 2 diabetes. World J Diabetes. 2013;4:114-123. [Crossref] [Pubmed] [PMC]
5. Kharroubi AT, Darwish HM. Diabetes mellitus: the epidemic of the century. World J Diabetes. 2015;6:850-867. [Crossref] [Pubmed] [PMC]
6. American Diabetes Association. 7. Diabetes technology: standards of medical care in diabetes-2020. Diabetes Care. 2020;43:S77-S88. Erratum in: Diabetes Care. 2020;43:1981. [Crossref] [Pubmed]
7. Shah RB, Patel M, Maahs DM, Shah VN. Insulin delivery methods: past, present and future. Int J Pharm Invest. 2016;6:1-9. [Crossref] [PMC]
8. Hyleosted-Winge J, Jensen KH, Rex J. A review of 25 years’ experience with the NovoPen family of insulin pens in the management of diabetes mellitus. Clin Drug Invest. 2010;30:643-674. [Crossref] [Pubmed]
9. Selam JL. Evolution of diabetes insulin delivery devices. J Diabetes Sci Technol. 2010;4:505-513. [Crossref] [Pubmed] [PMC]
10. Adolfsson P, Hartvig NV, Kaas A, Moller JB, Hellman J. Increased time in range and fewer missed bolus injections after introduction of a smart connected insulin pen. Diabetes Technol Ther. 2020;22:709-718. [Crossref] [Pubmed] [PMC]
11. Gross TM, Kayne D, King A, Rother C, Juth S. A bolus calculator is an effective means of controlling postprandial glycemia in patients on insulin pump therapy. Diabetes Technol Ther. 2003;5:365-369. [Crossref] [Pubmed]
12. Fry A. Insulin delivery device technology 2012: where are we after 90 years? J Diabetes Sci Technol. 2012;6:947-953. [Crossref] [Pubmed] [PMC]
13. Sharma G, Sharma AR, Nam JS, Doss GP, Lee SS, Chakraborty C. Nanoparticle based insulin delivery system: the next generation efficient therapy for Type 1 diabetes. J Nanobiotechnology. 2015;13:74. [Crossref] [Pubmed] [PMC]
14. Ackermann RT, Wallia A, Kang R, Cooper A, Prospect TA, Sandy LG, Voigt D. Comparative effectiveness and costs of insulin pump therapy for diabetes. Am J Manag Care. 2017;23:353-359. [Pubmed]
15. Paris CA, Imperatore G, Klingensmith G, Pettiti D, Rodriguez B, Anderson AM, Schwartz ID, Standiford DA, Pihoker C. Predictors of insulin regimens and impact on outcomes in youth with type 1 diabetes: the SEARCH for Diabetes in Youth study. J Pediatr. 2009;155:183-9.e1. [Crossref] [Pubmed]
16. Ratheau L, Jeandidier N, Moreau F, Sigrist S, Pinget M. How technology has changed diabetes management and what it has failed to achieve. Diabetes Metab. 2011;37 Suppl 4:S57-64. [Crossref] [Pubmed]
17. Ziegler R, Heidtmann B, Hilgard D, Hofer S, Rosenbauer J, Holl R; DPV-Wiss-Initiative. Frequency of SMBG correlates with HbA1c and acute complications in children and adolescents with type 1 diabetes. Pediat Diabetes. 2011;12:11-17. [Crossref] [Pubmed] [PMC]
18. Benjamin EM. Self-monitoring of blood glucose: the basics. Clinical Diabetes. 2002;20:45-47. [Crossref] [Pubmed]
19. Mancini G, Berioli MG, Santi E, Rogari F, Toni G, Tascini G, Crispoldi R, Ceccarini G, Esposito S. Flash glucose monitoring: a review of the literature with a special focus on type 1 diabetes. Nutrients. 2018;10:992. [Crossref] [Pubmed] [PMC]
20. Chen C, Zhao XL, Li ZH, Zhu ZG, Qin SH, Flewitt AJ. Current and emerging technology for continuous glucose monitoring. Sensors (Basel). 2017;17:182. [Crossref] [Pubmed] [PMC]
21. Klonoff DC, Ahn D, Drinic A. Continuous glucose monitoring: a review of the technology and clinical use. Diabetes Res Clin Pract. 2017;133:178-192. [Crossref] [Pubmed] [PMC]
22. Vigersky RA. The benefits, limitations, and cost-effectiveness of advanced technologies in the management of patients with diabetes mellitus. J Diabetes Sci Technol. 2015;9:320-330. [Crossref] [Pubmed] [PMC]
23. Kamann S, Aerts O, Heinemann L. Further evidence of severe allergic contact dermatitis from isobornyl acrylate while using a continuous glucose monitoring system. J Diabetes Sci Technol. 2018;12:630-633. [Crossref] [Pubmed] [PMC]
24. Danne T, Nimri R, Battelino T, Bergenstal RM, Close KL, DeVries JH, Garg S, Heinemann L, Hirsch I, Amiel SA, Beck R, Bosi E, Buckingham B, Cobelli C, Dassau E, Doyle FJ 3rd, Heller S, Hovorka R, Jia W, Jones T, Kordonouri O, Kovatchev B, Kowalski A, Laffel L, Maahs D, Murphy HR, Nørgaard K, Parkin CG, Renard E, Saboo B, Scharf M, Tamborlane WV, Weinzierle SA, Philip M. International consensus on use of continuous glucose monitoring. Diabetes Care. 2017;40:1631-1640. [Crossref] [Pubmed] [PMC]
25. Leelarathna L, Wilmot EG. Flash forward: a review of flash glucose monitoring. Diabet Med. 2018;35:472-482. [Crossref] [Pubmed]

26. Zhao M, Leung PS. Revisiting the use of biological fluids for noninvasive glucose detection. Future Med Chem. 2020;12:645-647. [Crossref] [Pubmed]

27. Bhide A, Muthukumar S, Prasad S. CLASP (Continuous lifestyle awareness through sweat platform): A novel sensor for simultaneous detection of alcohol and glucose from passive perspired sweat. Biosens Bioelectron. 2018;117:537-545. [Crossref] [Pubmed] [PMC]

28. Baca JT, Finegold DN, Asher SA. Tear glucose analysis for the noninvasive detection and monitoring of diabetes mellitus. Ocul Surf. 2007;5:280-293. [Crossref] [Pubmed] [PMC]

29. Zhang J, Hodge W, Hutnick C, Wang X. Noninvasive diagnostic devices for diabetes through measuring tear glucose. J Diabetes Sci Technol. 2011;5:166-172. [Crossref] [Pubmed] [PMC]

30. Gupta S, Nayak MT, Sunitha JD, Dawar G, Sinha N, Rallan NS. Correlation of salivary glucose level with blood glucose level in diabetes mellitus. J Oral Maxillofac Pathol. 2017;21:334-339. [Crossref] [Pubmed] [PMC]

31. Soni A, Jha SK. A paper strip based non-invasive glucose biosensor for salivary analysis. Biosens Bioelectron. 2015;67:763-768. [Crossref] [Pubmed]

32. Liu C, Sheng Y, Sun Y, Feng J, Wang S, Zhang J, Xu J, Jiang D. A glucose oxidase-coupled DNAzyme sensor for glucose detection in tears and saliva. Biosens Bioelectron. 2015;70:455-461. [Crossref] [Pubmed]

33. Moser EG, Morris AA, Garg SK. Emerging diabetes therapies and technologies. Diabetes Res Clin Pract. 2012;97:16-26. [Crossref] [Pubmed]

34. Akturk HK, Revers A, Joseph H, Schneider N, Garg SK. Possible ways to improve postprandial glucose control in type 1 diabetes. Diabetes Technol Ther. 2018;20:S224-S232. [Crossref] [Pubmed]

35. Akturk HK, Garg S. Technological advances shaping diabetes care. Curr Opin Endocrinol Diabetes Obes. 2019;26:84-89. [Crossref] [Pubmed]

36. Tauchsmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, Ruan Y, Sibayan J, Kollman C, Cheng P, Beck RW, Acerini CL, Evans ML, Dunger DB, Elleri D, Campbell F, Bergenstal RM, Criego A, Shah VN, Leelarathna L, Hovorka R; APCam11 Consortium. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. Lancet. 2018;392:1321-1329. Erratum in: Lancet. 2018;392:1310. [Crossref] [Pubmed] [PMC]

37. Sen JD, Fischl S, Slahor L, Schelbert S, Henzen C. Long-term effects of initiating continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM) in people with type 1 diabetes and unsatisfactory diabetes control. J Clin Med. 2019;8:394. [Crossref] [Pubmed] [PMC]

38. World Health Organization. mHealth: new horizons for health through mobile technologies. Vol. 3. Geneva: WHO; 2011. [Link]

39. Drincic A, Prahalad P, Greenwood D, Klonoff DC. Evidence-based mobile medical applications in diabetes. Endocrinol Metab Clin North Am. 2016;45:943-965. Erratum in: Endocrinol Metab Clin North Am. 2017;46:xix. [Crossref] [Pubmed] [PMC]

40. Fleming GA, Petrie JR, Bergenstal RM, Holf RW, Peters AL, Heinemann L. Diabetes digital app technology: benefits, challenges, and recommendations. A consensus report by the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA) Diabetes Technology Working Group. Diabetologia. 2020;63:229-241. [Crossref] [Pubmed]

41. Malka R, Nathan DM, Higgins JM. Mechanistic modeling of hemoglobin glycation and red blood cell kinetics enables personalized diabetes monitoring. Sci Transl Med. 2016;8:359ra130. [Crossref] [Pubmed] [PMC]

42. Alcántara-Aragón V. Improving patient self-care using diabetes technologies. Ther Adv Endocrinol Metab. 2019;10:2042018818824215. [Crossref] [Pubmed] [PMC]

43. Scott A, Chambers D, Goyder E, O’ Cathain A. Socioeconomic inequalities in mortality, morbidity and diabetes management for adults with type 1 diabetes: A systematic review. PLoS One. 2017;12: e0177210. [Crossref] [Pubmed] [PMC]