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Diabetes Technology: The Present and the Future

Introduction

Diabetes technology has evolved over the past decades, and the evolution of diabetes management tools has improved clinical outcomes. These tools have developed from insulin vials to pre-filled pen devices to insulin pumps; from urine strips to glucometers to continuous glucose monitoring (CGM) systems; and from old-school pen and paper to record blood glucose results to detailed CGM graphs and reports. The incorporation of technology into diabetes management has decreased the intensity and frequency of hypoglycemia episodes and improved glycemic management for millions of patients with diabetes. The various technological advances explored in this article include smart insulin pens and accessories, CGM systems, insulin pumps, diabetes mobile applications, and remote glycemic monitoring platforms.

About 200 years ago, diabetes — resulting from insulin deficiency — was primarily a fatal condition within weeks to months following diagnosis. Since insulin was discovered in 1921, many therapeutic options have been made available to manage hyperglycemia and reduce its related complications. Despite the scientific advances, the prevalence of type 2 diabetes has continued to increase, especially in the most recent five decades, leading to a worldwide epidemic and becoming one of the most common and costly medical conditions humans face today.

In 2020, the National Diabetes Statistics Report, a periodic publication by the Centers for Disease Control and Prevention (CDC), showed that 34.2 million people — or 10.5% of the U.S. population — had diabetes, according to crude estimates for 2018.[1] In 2017, the total direct and indirect costs associated with diabetes were $327 billion.[1] Studies have shown that people with diabetes incur medical expenditures 2.3 times higher compared to people without diabetes.[2]

The American Diabetes Association (ADA) defines diabetes technology as devices, hardware, and software that people with diabetes can use for managing this chronic condition, from modifying lifestyle to monitoring blood glucose levels.[3] Diabetes technology is evolving rapidly, aiming to support the ever-changing individualized, patient-centered approach (considering a patient's wishes, needs, skill levels, and accessibility to devices) to keep up with the daunting tasks in effective diabetes management and its preventing complications.

Diabetes-specific support and guidance from healthcare professionals can be amplified and strengthened through incorporating diabetes technology into delivering care to those for whom an educational and motivational boost is

EXECUTIVE SUMMARY

Advances in technology for diabetes management have resulted in decreased intensity and frequency of hypoglycemic episodes and improved glycemic control for millions of patients.

- A recent report showed that 34.2 million people (or 10.5% of the population) in the United States have diabetes, with total and indirect costs of $327 billion.
- Insulin pens offer the advantages of ease of use, convenience, adherence, accuracy, and improved patient preference. The addition of sensors or technological features has created a new generation of pens, called smart insulin pens. These smart pens record the number of units of insulin administered and can make dosing recommendations and can format information that can be shared with healthcare professionals or caregivers.
- Self-monitoring of blood glucose was introduced in the 1970s and was considered the standard of care in type 1 diabetes until the introduction of continuous glucose monitoring in 1999. Several randomized studies have demonstrated a number of clinical benefits. The goal is to provide glucose monitoring data for preventing blood glucose variations of hypoglycemic and hyperglycemic episodes.
- Insulin pumps are used primarily in type 1 diabetes mellitus. However, the treatment option has become available for selected patients with type 2 diabetes mellitus, including a hybrid closed-loop system to optimize glycemic management.
- Although there has been an explosion of digital health apps, with 318,000 apps available worldwide (16% for diabetes, second only to mental health apps), there are no regulations or guidelines yet to standardize these apps for patient safety and clinical validity.

warranted.[4] For some time, technology has helped patients with their self-management activities, such as blood glucose monitoring, medication reminders, healthy eating, and staying physically active.[4] The continuous technological advances have brought a more comprehensive array of options to patients with diabetes, offloading fear, distress, anxiety, and the burden of disease management, and enhancing the prevention of complications.[5] Some patients have achieved optimal glycemic management and reduced hypoglycemia episodes because of these recent advances in diabetes technology.[6,7] New technologies enable the personalization of care, thus encouraging the user to consult with their healthcare professionals when selecting a system that would best fit their lifestyle and expectations. This article summarizes and explores the various forms of technology available to patients with diabetes: continuous glucose monitoring devices, insulin pumps, smart insulin pens and accessories, diabetes mobile applications, and remote glycemic monitoring platforms.

Continuous Glucose Monitoring Systems

The first self-monitoring of blood glucose (SMBG) measurement was introduced in the 1970s and was considered the standard of care in type 1 diabetes mellitus (T1DM) until the introduction of the first Food and Drug Administration (FDA)-approved continuous glucose monitoring (CGM) system in 1999.[8] Several randomized clinical trials have shown the benefits of CGM use in patients with T1DM and type 2 diabetes mellitus (T2DM).[9,10]

In comparison with SMBG, CGM allows the consistent indirect monitoring of blood glucose levels through detecting and analyzing glucose levels in the interstitial fluid at a predetermined time interval (e.g., every five minutes), thus leading to a considerable number of data points collected throughout the day and night. Moreover, its interoperability with insulin pumps and smart devices allows clinicians to obtain a complete capture of the user's glucose variability and frequencies of extreme glucose levels for optimizing the safety and effectiveness of antidiabetic regimens. Despite the well-documented benefits of CGM systems, these devices have barriers, such as the need for recalibrations and sensor replacement, limiting the acceptance and usability in both T1DM and T2DM populations.[11] With the hope of addressing the limitations of CGMs, manufacturers consistently have been redesigning and incorporating changes in the upcoming products that will further improve the accuracy in glycemic monitoring and provide greater consumer satisfaction.

Currently, there are three categories of CGM devices: real-time CGM (rtCGM), intermittently scanned CGM (isCGM), and professional CGM.[3] rtCGM devices measure and display users' glucose levels in a continuous manner. On the other hand, isCGM devices monitor users' glucose levels continuously and display results only if a reader or smartphone scans the sensor. Professional CGM devices are placed on patients in healthcare providers' offices. These devices are worn for seven to 14 days and are clinic-owned to gather glycemic data remotely for obtaining glucose patterns. Data gathered might be blinded to the users wearing the sensors until downloaded by the providers.

All CGM systems have one goal: providing glucose monitoring data for optimizing pharmacotherapies for preventing blood glucose variations (e.g., hypoglycemic and hyperglycemic episodes). Since introducing the first CGM system, manufacturers have continued to improve their CGM systems to include daily glucose patterns, real-time data sharing, and integration with insulin pumps. The current FDA-approved CGMs are compared and contrasted in Table 1.

Dexcom

Dexcom, Inc. launched their newest CGM, Dexcom G6, in 2018. It was the first CGM to obtain an interoperable

Table 1. Comparison of Continuous Glucose Monitoring Systems[12]

	Dexcom G5	Dexcom G6	Enlite	Guardian Sensor 3	FreeStyle Libre 14-Day System	FreeStyle Libre 2	Eversense
Available in the United States	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Manufacturer	Dexcom	Dexcom	Medtronic	Medtronic	Abbott	Abbott	Sensesonics
Age for Use	≥ 2 years	≥ 2 years	≥ 16 years	≥ 7 years	≥ 18 years	≥ 4 years	≥ 18 years
Type of CGM	rtCGM	rtCGM	rtCGM	rtCGM	isCGM	isCGM	rtCGM
Sensor Wear Time	7 days	10 days	6 days	7 days	14 days	14 days	90 days
Warm-Up Period	2 hours	2 hours	2 hours	2 hours	1 hour	1 hour	24 hours
Required Calibration with SMBG	Two times per day	No	Two times per day	Two times per day	No	No	Two times per day
Confirmatory Fingerstick Testing Required	No	No	Yes	Yes	No	No	Yes
Provides Active Hyperglycemic and Hypoglycemic Alarms/Alerts	Yes	Yes	Yes	Yes	No	Yes	Yes
Real-Time Remote Monitoring (Data Sharing)	Yes	Yes	Yes	No	No	No	Yes
Connects with Insulin Pump	Yes	Yes	Yes	Yes	No	No	No
Interoperability with Other Devices	Yes	Yes	Yes	No	No	No	Yes
Smart Device	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Compatibility						App under FDA review	
Software for Data Reports	Dexcom Clarity	Dexcom Clarity	CareLink Personal	CareLink Personal	LibreView; LibreLink	LibreView; LibreLink	Eversense DMS
Cost		~$3,800 per year pre-insurance[a]		First transmitter: $699; sensors: $50-$75 (at least $3,000 per year)[c]		~$2,300 per year pre-insurance[a]	Bridge Program: $99 per sensor (up to two), plus sensor insertion/removal cost ($300-$400)[b]

a: Hoskins M. Around the online diabetes community: April 2021. Healthline Media. https://www.healthline.com/diabetesmine/around-the-diabetes-online-community-april-2021#7; b: Ryan E, Serino M. Senseonics' Eversense Bridge Program: Cost assistance for 90-day implantable CGM. diaTribe Learn. May 20, 2019. https://diatribe.org/senseonics-eversense-bridge-program-cost-assistance-90-day-implantable-cgm; c: Medtronic For Healthcare Professionals. Continuous glucose monitoring: The costs. https://hcp.medtronic-diabetes.com.au/cgm-subscriptions

CGM: continuous glucose monitoring; SMBG: self-monitoring blood glucose; rtCGM: real-time continuous glucose monitoring; isCGM: intermittently scanned continuous glucose monitoring; FDA: Food and Drug Administration; DMS: data management system

status from the FDA.[13] Its interoperability allows Dexcom G6 to be part of an integrated system, combining with a compatible medical device, such as an automated insulin dosing (AID) system, an insulin pump, or an electronic medical device.[13] A Dexcom G6 sensor can be worn for up to 10 days, and fingerstick blood glucose measurements

are not required for calibration or therapeutic modifications. The COVID-19 pandemic has delayed the pivotal trial of Dexcom G7, per Dexcom CEO Kevin Sayer.[14]

Awaiting FDA approval, Dexcom will launch Dexcom G7 in 2021. It will feature several updates: extended life wear for 14 to 15 days, a smaller and thinner design, a fully disposable construction; and a transmitter that is integrated for economic and environmental purposes.[15]

FreeStyle Libre

FreeStyle Libre and FreeStyle Libre Pro, manufactured by Abbott Diabetes Care, Inc., were approved by the FDA in 2016 and 2017, respectively, for adults ages 18 years or older with either T1DM or T2DM. The sensor has been upgraded from 10-day life wear to 14-day life wear.[16] Unlike other CGM systems, this sensor must be scanned with the Libre reader at least every eight hours to maintain 24-hour, continuous glucose data capturing. Additionally, the FreeStyle Libre sensor lacks the alarm function that alerts the user when hypoglycemia episodes occur.[17]

The manufacturer acted on this deficiency and allocated resources for research and development to enhance their technology. In June 2020, the FDA cleared the FreeStyle CGM system's second-generation, the FreeStyle Libre 2, for adults and children ages 4 years and older. This same device was made available in Europe in 2018.[18,19] The integrated real-time alarm alerts the user at hyperglycemia (250 mg/dL and above) and hypoglycemia (< 70 mg/dL) episodes via Bluetooth connectivity without scanning the sensor with the reader. However, users are given the option to disable this alert function with the consultation from a healthcare professional.[19, 20] In terms of cost, the FreeStyle Libre 2 system is the same price as the FreeStyle Libre 14-day system.[19]

Eversense

The Eversense CGM system, manufactured by Senseonics, Inc., is the first implantable subcutaneous CGM, lasting for three months. It was approved by the FDA in 2019 for use in T1DM and T2DM populations who are 18 years of age and older.[21] The Eversense CGM is designed to improve glycemic management and reduce the inconvenience and discomfort of biweekly sensor insertions. In comparison with the other CGM systems, the Eversense CGM provides the lowest overall mean absolute relative difference (MARD) at 8.8%, as shown in Table 1.[21,22]

Senseonics initiated the PROMISE Trial (NCT03808376) in 2019 to assess the safety and efficacy of Eversense XL for more extended life wear to 180 days, which already has been approved in Europe.[23] With more extended life wear, users replace sensors only twice each year with the help of a certified healthcare professional. Senseonics also plans to move toward a 365-day wear sensor, integrating a built-in battery that allows the device to save the data when the transmitter is not attached to the skin.[24] This potential product also can reduce calibration frequency to once per week instead of twice daily, as with the 90-day life wear version.[24]

Medtronic Guardian Sensor 3

Unlike the other CGMs mentioned earlier, the Medtronic Guardian Sensor 3, manufactured by Medtronic, Inc., is compatible only with Medtronic MiniMed 630G and 670G insulin pump systems. This device also can function as a standalone CGM.[25] Although the Guardian Sensor 3 is an improvement from the Enlite sensor, this sensor is not compatible with the upcoming closed-loop systems that Medtronic is developing currently.[25] The current pipeline of products expected to be released includes the Guardian Sensor 3 Non-Adjunctive (NA), which eliminates meal-time fingersticks and allows for Medicare expansion; the Zeus Sensor, which aims for a 95% reduction in fingersticks, meeting the integrated CGM (iCGM) criteria; and the Synergy Sensor, which will have a 50% reduction in size, and calibration is needed only on day 1 instead of twice per day as with the current Guardian Sensor 3.[25]

In summary, CGM systems have various features, such as real-time data sharing and capturing daily glucose patterns/variability, to improve glycemic management in both T1DM and T2DM populations. The interoperability with smartphones and devices allows users to gain complete insight into their glucose levels. The real-time data sharing, providing detailed and practical information with clinicians and family members, encourages shared decision-making on refining the existing treatment regimen.

The coronavirus disease 2019 (COVID-19) pandemic urges continuous evolution in healthcare practices, especially in the hospital setting where frequent point-of-care (POC) blood glucose checking is warranted for hyperglycemia management. Maintaining this much-needed practice puts hospital staff at a higher risk of contracting the virus with frequent patient contact and the need for much personal protective equipment (PPE). Thus, the use of CGM in the hospital setting (although it has not received a formal FDA indication) has been explored continuously to meet the urgent needs. Some studies using real-time (rt) in non-intensive care unit (ICU) patients have shown initial favorable outcomes in both non-ICU patients and ICU patients.[26-29] In October 2020, the FDA released a revision on a guidance document relating to noninvasive remote monitoring devices during the COVID-19 public health emergency, allowing the integration of CGM devices at the hospital to facilitate patient monitoring.[30]

Insulin Pumps

Insulin pumps, or continuous subcutaneous insulin infusion (CSII) systems, are used mainly in the T1DM population to deliver exogenous insulin to manage hyperglycemia.[31] However, this treatment option has become available to the T2DM population with suboptimally managed diabetes on multiple daily injections (MDI) of insulin.[32] Diabetes technology is changing constantly and is expected to evolve in the future with what now is called a hybrid closed-loop system to optimize glycemic management, such as reduction of A1c and prevention of hypoglycemic episodes, without

compromising the user's preferences and needs. A hybrid closed-loop system automatically delivers micro-boluses of rapid-acting insulin as basal insulin in response to blood glucose readings collected from an integrated CGM. A comparison of available insulin pumps is displayed in Table 2 (*available at https://bit.ly/2RshsC4*).

Insulet

In 2005, Insulet Corp. developed the first commercially available "tubeless" insulin pump. The Omnipod insulin pump can store maximally 200 units of U-100 insulin, and it can be worn for up to 72 hours.[33] The pump is connected to a Personal Diabetes Manager (PDM) that features several functions, including alerts/alarms and data transmission. However, data transmission is achievable only when the PDM is close to the reservoir.

Recently, the Omnipod DASH system was launched to reflect the state-of-the-art technology with features such as the use of Bluetooth technology, touchscreen function, and compatibility with smartphones.[34] Also, mobile applications (e.g., Omni View and Omni DISPLAY) enable data sharing with caregivers and healthcare professionals for guiding adjustments in therapy.[35]

With an expected release in 2021, the Tidepool Loop Program collaborates with Omnipod DASH to build an algorithm in the iOS app, allowing any iOS smart device to monitor glycemic levels through integrating with Dexcom G6.[36] Insulet initiated the Pivotal Omnipod HORIZON Trial in 2019 and had expected to release results in late 2020; unfortunately, the company had to postpone to early 2021 because of a technical problem with the software.[37,38] Unlike the Omnipod DASH system, the HORIZON hybrid closed-loop system has the algorithm built into the pod itself, so proximity with a smart device or PDM is not required.

Tandem Diabetes Care

In 2019, Tandem Diabetes Care, Inc. launched the t:slim X2 insulin pump with Control-IQ technology, which is the first product approved with a new FDA category called the interoperable automated glycemic controller.[39] This new category is an entirely automated insulin dosing (AID) system that automatically adjusts and delivers insulin based on the glycemic measurements from a CGM.[40] The t:slim X2 with Control-IQ technology is composed of an alternate controller-enabled insulin pump (ACE pump) and an integrated CGM. Compared to the Basal-IQ technology, the t:slim X2 with Control-IQ technology has two additional features. These features include predicting high blood glucose levels 30 minutes ahead and delivering a corresponding insulin dose to keep glucose in range (70 mg/dL to 180 mg/dL) and providing optional settings to accommodate and match physiological needs during sleep and exercise activities.[41] Depending on which activities are enabled, the glucose range and the amount of insulin delivered can be adjusted.

Currently, Tandem is developing the next generation of the device, named the t:sport mini pump, with a design that is half the size of the t:slim X2 insulin pump.[42] Despite the smaller size, the reservoir can hold up to 200 units of insulin. The anticipated launch date is in the first half of 2021, but this will happen when the application to the FDA for approval is granted.[43] The intention of the t:sport mini pump is to provide users the flexibility to manage insulin delivery through a separate handheld device or via a mobile application.[43]

Medtronic

Medtronic has been in the insulin pump space for more than 30 years. They developed the first FDA-approved hybrid closed-loop system, called the MiniMed 670G, in 2017.[44] This system, often referred to as an "artificial pancreas," was approved for automatically adjusting basal insulin every five minutes based on glycemic levels in users with T1DM age 7 years or older.[44,45] As mentioned earlier, the Guardian Sensor 3 is not compatible with any of the MiniMed 600 series pumps; therefore, the Guardian Sensor 3 used in the MiniMed 670G contains a different transmitter than the one in the Guardian Connect system.[46] The CGM provides glucose readings every five minutes and alerts users to any potential hyperglycemic or hypoglycemic episodes 30 minutes in advance.

According to a presentation given at the ADA 2019 investor briefing, Medtronic Inc. had plans for the next-generation automated insulin delivery (AID) with improvements from the existing hybrid closed-loop system.[25] This new version, the MiniMed 780G, is an advanced hybrid closed-loop system (AHCL), including automatic basal rate adjustments and correction boluses.[47] The enabling of auto mode allows the algorithm to calculate the dose using the CGM data automatically. Moreover, the blood glucose target level can be adjusted from 120 mg/dL down to 100 mg/dL in response to the user's preference.[47] Currently, the MiniMed 780G is available in European countries, and Medtronic aims to launch this model in the United States in 2021.

Another system currently in development is called the personalized closed-loop (PCL) system.[25] With the PCL system, missed meals are taken into account automatically to replace the constant reminder of putting in carbohydrate count and missed meals manually.

A study compared the costs for 2,539 patients who transition to continuous subcutaneous insulin infusion (CSII) and 2,539 patients who stayed on multiple daily insulin injection (MDI) between July 1, 2009, and June 30, 2012. The difference in the average cost was about $20,565 per person within the three-year period.[48]

Smart Insulin Pens and Accessories

The use of technology in managing diabetes has improved patient medication adherence and achieved better glycemic levels. An insulin pen is an insulin delivery system that uses an insulin cartridge combined with disposable needles to deliver insulin into the subcutaneous layer. Compared with using vials and syringes, insulin pens offer the advantages of ease of use, convenience, adherence, accuracy, and patient preference, confirmed in numerous studies.[51-53] The addition

Table 3. Comparison of InPen, ESYSTA, and Pendiq 2.0[54-58]

	InPen	ESYSTA	Pendiq 2.0
Manufacturer	Companion Medical	Emperra	Pendiq Intelligent Diabetes Care
Origin	United States	Germany	Germany
Available in the United States	Yes	No	No
App Availability	iOS, Android	iOS, Android	iOS, Android
Insulin Compatibility	U-100, 3.0 mL pre-filled cartridges from Lilly Humalog, Novo Nordisk Novolog, Novo Nordisk Fiasp	Compatible with all U-100, 3.0 mL pre-filled cartridges	U-100, 3-mL, pre-filled cartridges from Berlin-Chemie, Lilly, Novo Nordisk, Sanofi-Aventis

of sensors or technological features to insulin pens has created a new generation of insulin pens, called smart insulin pens.[54] One type has a refillable insulin cartridge that enables built-in wireless communication and contains a sensor to track insulin delivery; the other has a sensor in the form of an attachment or a cap, linking to a disposable pen.

Smart Insulin Pens

Smart insulin pens record the number of insulin units administered and the time/date of administration, then transmit the information via Bluetooth to a dedicated application (app). The app then can make dosing recommendations based on specific personal information, such as blood glucose levels, and track residual active insulin. The collected data are formatted to be shared with healthcare professionals or caregivers. (*See Table 3*.)

InPen

InPen is an FDA-approved device manufactured by Companion Medical and was made available in 2017.[54] This device is a reusable pen injector that can deliver up to 30 units of insulin by dialing in half-unit increments.[54] This pen injector is compatible with Humalog, Novolog, and Fiasp U-100, 3.0 mL pre-filled cartridges, as well as single-use detachable and disposable pen needles.[55,56]

InPen technology integrates a Bluetooth wireless insulin pen with smartphone apps for iOS 10 or later and Android 6 or later devices.[55,56] The InPen app can calculate insulin doses based on the current blood glucose level, amount of carbohydrates or meal-type and/or size, active insulin, insulin-to-carbohydrate ratio (ICR), insulin sensitivity factor (ISF), and target blood glucose.

The dose calculator on the app also tracks residual bolus insulin to limit insulin stacking, thus preventing hypoglycemia. The app can remind the user to take their long-acting/basal insulin. The InPen app for iOS integrates with Dexcom G5 and G6 through the Health app on an Apple device.

ESYSTA

ESYSTA from Emperra is an automatic documentation and monitoring system, which provides continuous automatic transmission of all relevant data to the ESYSTA portal. Users check their blood glucose levels through the ESYSTA blood glucose monitors, and the results are transmitted to the ESYSTA portal via the ESYSTA Basis. The ESYSTA Basis is equipped with a subscriber identity module (SIM) card, enabling data transmission from the pen and glucometer to the portal.

The ESYSTA portal provides users with a complete and continuous record of measured blood glucose values, carbohydrate amounts consumed, and insulin doses in an analyzed format personalized for every user. Users can log into their portal accounts through a web browser or the iOS/Android app. The insulin cartridge adaptor for the ESYSTA pen is compatible with all U-100, 3.0 mL insulin cartridges available. [57]

Pendiq 2.0

Pendiq 2.0 is produced by Pendiq Intelligent Diabetes Care. The Pendiq 2.0 pens are compatible with U-100, 3.0 mL insulin cartridges from Sanofi-Aventis, Lilly, Berlin-Chemie, and Novo Nordisk. This device can be adjusted in micro increments of 0.1 unit.

The pen can store information, such as date, time, and doses of insulin delivered for up to 1,000 injections, which can be uploaded via Bluetooth to a diabetes management app called dialife (available for Android and iOS devices). The device alerts the user when the pen needle is blocked or the amount of residual insulin is too low.

In summary, smart pens can track the dose history and the timing of injections, and this information can be retrieved easily on an app. Data captured by smart pens can be shared with healthcare professionals, family members, and caregivers.

Additionally, in conjunction with apps, smart pens import glucose readings, recommend insulin doses, and keep track of dosing history to ensure the insulin therapy's safety and effectiveness.[58]

Table 4. Comparison of Gocap, Timesulin, and Dukada Trio[59-61]

	Gocap	Timesulin	Dukada Trio
Manufacturer	Common Sensing	Bigfoot Biomedical	Dukada
Origin	United States	United Kingdom	Denmark
Available in the United States	Yes	Yes	No
App Availability	iOS, Android	N/A	N/A
Insulin Compatibility	Lantus SoloStar, Apidra SoloStar	Novo Nordisk FlexPens, Novo Nordisk FlexTouch pens, Sanofi SoloStar pens, Lilly KwikPens	Novo Nordisk FlexPens, Sanofi SoloStar pens

Accessories for Insulin Pens: Smart Caps

Insulin smart caps are battery-operated caps for insulin pens that replace their standard caps. Smart caps can record the time and date of insulin injections and doses. (*See Table 4.*)

Gocap

Gocap, manufactured by Common Sensing, is a Bluetooth-enabled smart cap. This cap uses light-sensing technology to detect how much insulin is remaining in the pen and communicates that to the Gocap app via Bluetooth. The app shows the dose, dosing time, temperature, and type of insulin, and it alerts the user when it is time to inject the next dose. This device also differentiates between long-acting and rapid-acting insulins, reminding the user to take the correct medication at the right time for the right purpose. If needed, the information can be shared with others by entering their email addresses on the app.[59]

Timesulin

Timesulin by Bigfoot Biomedical is a cap for insulin pens that shows users how long ago the last insulin injection was administered. When the cap is removed for longer than eight seconds, the timer is reset to zero. After the cap is placed back onto the pen, the timer resets itself. The timer on the cap helps the user remember whether the dose was administered and how long ago the previous dose was administered. Timesulin is compatible with most of the major insulin pens, such as Novo Nordisk FlexPens and FlexTouch pens, Sanofi SoloStar pens, and Lilly KwikPens.[60]

Dukada Trio

Dukada Trio smart cap is an insulin timer for Novo FlexPens and Sanofi Solostar pens. The Dukada Trio smart cap replaces the original cap of the compatible insulin pen and records the time elapsed since the last injection. The Dukada Trio also features an LED light above the needle to improve visibility.[61]

Attachments for Insulin Pens

Attachments are anchored onto insulin pen devices and include features for recording injection time and insulin dose.

Insulclock

Insulclock is an electronic device that can be anchored onto insulin pen devices. This device connects to an app on smartphones. Insulclock tracks the date, time, dose, type of insulin, temperature, and intervals between insulin injections. The data are readily available on the app, and both patients and healthcare professionals can retrieve the information.[62]

Clipsulin

Clipsulin, made by Diabnext, is an attachment that clips to the side of almost all available insulin pens, e.g., SoloStar, KwikPen, FlexPen, and FlexTouch. Clipsulin automatically records the time and amount of insulin after the dose is dialed. An LED screen on Clipsulin displays the dose. After the dose is confirmed, the information regarding the dose, date, and time is sent via Bluetooth to the Diabnext app on any iOS or Android device.[63]

InsulCheck

InsulCheck is an accessory that clips onto an insulin pen and automatically records the time elapsed since the last injection. This device is compatible with most insulin pens, including FlexPen, NovoPen, KwikPen, and SoloStar. A green light is displayed on the attachment after a dose is delivered and the timer is reset. InsulCheck alerts the user when insulin is exposed to extreme temperature fluctuations.[64,65]

In the Pipeline: Mallya

Mallya, a smart cap for pen injectors from Biocorp, has been made available in Europe. Mallya can track injection data, such as dose and date/time of injections, and sync via Bluetooth technology. This device is compatible with all disposable pen injectors. Mallya can be connected to Gluci-Chek, a smartphone application. After this device is paired with the app, information such

Table 5. Comparison of Insulclock, Clipsulin, and InsulCheck[62-65]

	Insulclock	Clipsulin C3 xs	InsulCheck
Manufacturer	Insulcloud	Diabnext	Innovation Zed
Origin	Spain	United States	Ireland
Available in the United States	No	Yes	Available to order online
App Availability	iOS, Android	iOS, Android	N/A
Insulin Compatibility	Compatible with Novo Nordisk FlexPen and FlexTouch, Lilly KwikPen, Sanofi SoloStar pen	Connects to almost all available insulin pens using the Diabnext app	Compatible with Novo Nordisk FlexPen, NovoPen (3,4,5 and Echo); Sanofi SoloStar, ClickStar; Lilly KwikPen, Luxura HD, Savvio

as dose, date, and time of injections will be visible.

In summary, smart caps and attachments record the time, date, and doses of insulin injections. Most of these devices can be connected to a smartphone via an app, allowing the captured information — showing a user's behavioral patterns — to be accessed by the user and shared with those who are members of the care team.

Currently, this category of devices is not popular in the United States. One of the reasons is that these devices generally are not covered by health insurance; thus, obtaining prior authorization is rather difficult.[66,67]

Apps Most Commonly Used by People with Diabetes

There has been a rapid development of digital health apps that assist people with diabetes in managing this chronic condition.[68] However, there are no regulations or guidelines yet to standardize these apps for patient safety and clinical validity.[68]

Evidence suggests that diabetes apps improve patients' knowledge of the condition, achieve better glycemic management, and assist with tracking physical activities, nutrition, and blood glucose monitoring.[69-71] More than 318,000 mobile health applications are available worldwide, and diabetes apps account for 16%, second only to mental health apps.[71,72] For this article, we have chosen to limit the discussion to some of the most popular apps used by people with diabetes, based on findings from Kebede and Pscheke.[73]

mySugr

The mySugr app allows entries for blood glucose, mood, carbohydrate, and medications, providing a 24-hour overview on its home screen and showing the estimated hemoglobin A1c (HbA1c) based on the collected blood glucose readings. All data then are summarized as PDF reports, which can be emailed from the app. mySugr's bolus insulin calculator currently is available only in selected countries.[74]

MyFitnessPal

MyFitnessPal is a tracking tool for exercise and food consumption. This app can connect with fitness trackers and other apps, such as Fitbit, Strava, Garmin, and many more. One of this app's critical features is its extensive food database, with more than 300 million items, supporting customization based on sex, age, and weight loss goal.[75]

One Drop

One Drop is designed for people with T1DM and insulin-dependent T2DM. The One Drop app is available on iOS and Android devices. Blood glucose measurements can be entered manually or synced automatically via Bluetooth from a One Drop glucose meter. This app can be linked with Apple Health, Apple Watch, Fitbit, Dexcom G5/G6, and many other platforms, allowing data from these platforms to be retrievable easily on the One Drop app.

This app also reminds the user to take medications and tracks insulin pump basal rates. Containing a sizable built-in food and nutrition database, One Drop thus can assist with carbohydrate counting. One Drop automatically tracks the physical activities of the user via a smartphone's pedometer.[76]

Diabetes:M

Diabetes:M is a mobile application for diabetes management available on both iOS and Android devices. Users can use the logbook feature on the app to enter glucose readings, medications, dose and type of insulin used, food intake, injection sites, weight, and types of physical activities.

This app also has a bolus insulin calculator function. The nutrition database on this app provides nutritional information, conveniently assisting the tracking of food intake. Diabetes:M can be connected to other diabetes management software, such as Glucose Buddy, mySugr, Diasend, and many others.

This app provides users with detailed graphs to summarize trends and highlight extreme glucose levels. The timeline graph generated considers blood glucose readings, medications, physical

Table 6. Comparison of Tidepool and Glooko/Diasend

Tidepool	Glooko/Diasend
Similarities	
• Integrates activities, such as meals, exercise, and daily events • Provides educational aspects to patients • Works with Mac and Windows, as well as Android and iOS • Allows users to copy and paste blood glucose data to the electronic medical records systems • Allows users to and form teams and collaborate with endocrinologists, dieticians, certified diabetes care and education specialists (CDCES), and families and friends • Allows clinicians to monitor and adjust doses of medications remotely between visits	
Differences	
• Indicated for patients 13 years of age and older • Eversense continuous glucose monitoring is not supported • Data can be uploaded through both Tidepool Mobile and Health app on iOS 11 and newer	• Age is not indicated • Eversense continuous glucose monitoring is supported • Data can be uploaded through a transmitter via Bluetooth onto Android and iOS phones

activity, insulin administered, and carbohydrate intake.[77]

Dario

The Dario app from Dario Health is used in conjunction with the Dario smart meter and test strips. The Dario smart meter can be connected directly to a smartphone or tablet. When the users are ready to check blood glucose levels, they open the Dario app on the smartphone or tablet, connect the Dario meter to the device, insert a test strip into the meter port, and obtain a drop of blood. The blood glucose reading then appears on the app.

The Dario app provides the users with an average blood glucose level. This app features a logbook in which the users can record physical activity, insulin doses, and carbohydrate intake. The information from Dario can be shared with providers and caregivers.

In summary, mobile apps enhance the abilities of people with diabetes to effectively manage the condition. These apps record the users' physical activities, nutrition, and blood glucose levels, and improve their knowledge about diabetes management.[78]

Remote Glycemic Monitoring Platforms

Companies such as Tidepool, Diasend, and Glooko each have separately developed free online platforms for data sharing among patients, caregivers, and clinicians to implement safe and effective diabetes management strategies.[79,80] These free online platforms are comprehensive in the sense that data can be collected from various types and brands of insulin pumps, CGM systems, blood glucose meters, and insulin pens, and can be integrated into these online data management platforms.[81,82]

Diasend and Glooko have merged into one company and will release upcoming products under the name Glooko.[83] Tidepool and Glooko/Diasend share various similarities, as shown in Table 6, but they have different features that set them apart from each other. For example, Glooko and Diasend clients can upload their data using the corresponding uploader software or through the Glooko or Diasend transmitter at the clinician's office.[84]

In terms of device compatibility, both Glooko and Diasend can collect data from major brands, except for Medtronic insulin pumps (which are integrated only with the Tidepool platform).

In 2018, Glooko obtained FDA approval for its Mobile Insulin Dosing System (MIDS), which recommends long-acting insulin dosing based on fasting blood glucose readings from a patient's blood glucometer; this system is intended for patients with T2DM.[85] MIDS is a prescription-only device, and healthcare providers must program patient-specific parameters to activate MIDS.

Discussion

Diabetes technology has been incorporated into the treatment plans of most patients with diabetes, from the use of a glucometer and a pen device to the use of a hybrid system combining blood glucose monitoring and insulin delivery. The rapid advances and the complexities in the field of diabetes technology have led to an individualized approach based on users' preferences, needs, and skills. Incorporating all the encompassing data to support decision-making and treatment plan adjustments can be a daunting task for healthcare professionals. A real clinical case illustrating a patient with full insulin replacement therapy is described in "A Real Clinical Case: Before and After Starting a Continuous Glucose Monitoring and Insulin Pump System."

Specific resources, such as not-for-profit websites (e.g., DiabetesWise.org, the ADA's Standards of Medical Care in Diabetes and other publications, and numerous continuing education sessions, conferences, and device manufacturer training programs) are available to keep all people involved up-to-date with this ever-changing field, targeting to create positive health benefits for the end-users of the technology.

To initiate the integration of diabetes technology into patients' treatment

Continued on page 71

A Real Clinical Case: Before and After Starting a Continuous Glucose Monitoring and Insulin Pump System

A 52-year-old Caucasian male, who was diagnosed with latent autoimmune diabetes in adults (LADA) at age 35 years, was referred to our diabetes center for further diabetes management. At the time he was diagnosed, his hemoglobin A1c was at 17.9%; the A1c obtained during his initial visit at the diabetes center was at 12.1% (May 2020). His past medical history includes depression, erectile dysfunction, hyperlipidemia, hypertension, and lumbar radiculitis.

Before using diabetes technology, his medications included:

- Lantus, 45 units daily
- Humalog, 6-8 units for breakfast; 20 units for lunch and dinner (carbohydrate ratio: 5 units of insulin per 15 grams of carbohydrate)

Glucometer data (June to July 2020):

- Before breakfast: 122 mg/dL to 259 mg/dL
- Before lunch: 100 mg/dL to 158 mg/dL
- Before dinner: 98 mg/dL to 196 mg/dL
- Bedtime: 93 mg/dL to 249 mg/dL

He reported experiencing two episodes of hypoglycemia in the early morning, thus he self-reduced his basal insulin dose. He also expressed feeling comfortable titrating his insulin regimen, including both insulin and mealtime insulin, based on his fingerstick blood glucose readings. In addition, he would like to start on an insulin pump without a tube attached.

After Starting Diabetes Technology

The patient chose Omnipod, pairing with Dexcom G6. The pump settings are summarized below (after a telephone encounter on March 23, 2021):

- Basal rate: 2.2 units per hour (12 a.m.- 5 a.m.); 2.1 units per hour (5 a.m.-12 a.m.)
- Insulin to carbohydrate ratio: 1 unit per 6 grams
- Insulin sensitivity factor: 1 unit per 25 mg/dL

The following table shows his most recent sets of CGM summary data:

Time Frame	March 10-23, 2021	March 27-April 9, 2021
Average Glucose	203 mg/dL	188 mg/dL
Standard Deviation	67 mg/dL	61 mg/dL
Time in Range (Target Range: 70 mg/dL to 180 mg/dL)	> 180 mg/dL: 57% In range: 43% < 70 mg/dL: 0%	> 180 mg/dL: 47% In range: 53% < 70 mg/dL: 0%

His most recent A1c was at 8% (January 2021).

Thoughts on Progression: Telephone Encounter on April 9, 2021

Assessment: After the last phone encounter, the patient's average glucose improved from 203 mg/dL to 188 mg/dL; time-in-range for glucose levels improved from 43% to 53% without experiencing hypoglycemia. Since the patient still had a pattern of significant elevations between 12 a.m. and 6 a.m. (reflected in 47% of the time above 180 mg/dL), consider increasing basal rate between 12 a.m. and 5 a.m. by 10% to optimize glycemic management.

Plan:

- Basal rate: 12 a.m.-5 a.m.: 2.4 units per hour (increased from 2.2 units per hour)
- 5 a.m.-12 a.m.: 2.1 units per hour
- Bolus settings: Leaving all the settings below the same, the patient most likely will need to change his carbohydrate ratio in the future to help manage postprandial high
- Insulin to carbohydrate ratio: 6 grams/unit
- Sensitivity: 25 mg/dL/unit
- Active insulin time: 4.0 hours
- Glucose target: 120 mg/dL
- Glucose correction threshold: 150 mg/dL

Continued from page 69
plans, appropriate selection is a critical step, where the healthcare team will guide the patient and provide follow-up, ongoing education, and training to ensure a high level of engagement between the user and the devices/programs. A source for up-to-date diabetes technology-related, evidence-based information to be shared with patients is danatech, powered by the American Diabetes Care and Education Specialists (ADCES) and a benefit for its members.[86] The danatech platform is created to provide technological access and evaluation needs for healthcare professionals who take care of patients with diabetes and other chronic diseases.

The increasing digitalization in diabetes management enhances the quality of care provided to patients as well as supplements the human interactions between clinicians and patients. This has been true especially during the COVID-19 pandemic, when telehealth has become an important modality for continued healthcare delivery to minimize exposure to the virus. Although it remains a challenge for many, patients have the option to upload their personal glucose data onto a cloud portal where their clinicians can easily access the most up-to-date glycemic data to assist in refining patients' diabetes regimens as well as providing personalized education and guidance.

Conclusion

This article has discussed the various types of technology options available for people with diabetes to optimize diabetes management. Moreover, advanced technology, such as data sharing with multiple smart devices, not only allows caregivers and providers to better understand patients' glycemic profiles but also provides clinicians with a more complete picture of patients' blood glucose levels, thus supporting safe adjustments to diabetes regimens. Each product has specific and unique key features that allow enhancing flexibility, thus meeting the user's preferences and needs in terms of lifestyle and convenience, as well as therapeutic safety and effectiveness.

References

A complete list of references is available at https://bit.ly/3whaqic

CME Questions

1. InPen is compatible with which of the following insulin cartridges?
   a. Lyumjev
   b. Fiasp
   c. Basaglar
   d. Lantus
2. Which of the following statements regarding ESYSTA is *false*?
   a. It currently is available in the United States.
   b. The ESYSTA pen is compatible with all U-100, 3.0 mL pre-filled insulin cartridges.
   c. Users check their blood glucose using ESYSTA blood glucose monitors.
   d. The ESYSTA application is available on iOS and Android devices.
3. Which of the following categories of continuous glucose monitors (CGM) are available on the market?
   a. Real-time CGM (rtCGM)
   b. Intermittently scanned CGM (isCGM)
   c. Professional CGM
   d. All of the above
4. Which of the following is an intermittently scanned continuous glucose monitor (isCGM)?
   a. Dexcom G6
   b. Enlite
   c. Guardian 3
   d. FreeStyle Libre
5. The sensor for the FreeStyle Libre has to be scanned by the reader at least every eight hours to continuously capture 24-hour glucose data.
   a. True
   b. False
6. Which of the following insulin pumps has been approved by the Food and Drug Administration as an interoperable automated glycemic controller?
   a. OmniPod
   b. Medtronic 780G
   c. Tandem X2: Slim
   d. Medtronic 670G
7. The OmniPod is approved for use in which patients?
   a. Patients ≥ 2 years of age
   b. Patients ≥ 6 years of age
   c. Patients ≥ 7 years of age
   d. Patients of all ages
8. Which of the following is an example of a remote glycemic monitoring platform?
   a. Glooko
   b. MyFitnessPal
   c. One Drop
   d. Pendiq 2.0

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