CHAPTER

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Recent Trends in Diabetes Technologies

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ABSTRACT

An array of new and advanced diabetes technologies is now available and many are in developmental stages which can make diabetes management more effective and less burdensome. Compared to the earlier technologies which allowed more often only a physician-centered one-way communication, the recently introduced ones also allow the patients to get involved. They allow the patients to better understand their disease and to play active roles in managing it. Be it minimally invasive and user-friendly glucose monitoring systems with better accuracy, insulin pumps that helps deliver near physiological insulin delivery, point-of-care testing devices that provide immediate and actionable information, various artificial intelligence (AI)-enabled mobile applications for diabetes management, each one of them can empower the patients, diabetes care providers as well as the caregivers, thereby facilitating an individualized, hassle-free and more productive disease management. Considering the long-term benefits associated with the use of these technologies in reducing the possible future complications, the costs associated with them should never be considered as a hindrance factor for employing them in the most deserving candidates. The current chapter throws light on some of the recently introduced technologies for diabetes care.

INTRODUCTION

With several technological advancements happening in the field of diabetes management since the past few decades, shortcomings of conventional diabetes care practices have started to resolve in an appreciable manner. Normalizing the glycemic component happens to be the most challenging part of diabetes management and these newer and smarter technologies can guide both the physician and the patient to take the most appropriate and timely treatment decisions in an individualized manner and thereby manage blood sugars with minimal or no glucose variability and also ward off complications. Blood glucose monitors integrated with mobile applications and web applications available today makes diabetes management much simpler and easier. Likewise, continuous glucose monitoring systems (CGMSs) can provide continuous insight into changing glucose levels and display information regarding glucose direction and rate of change enabling better diabetes management.[1-8] CGMSs with improved accuracy and user-friendliness are continuously being researched at.

Continuous subcutaneous insulin infusion therapy (insulin pump therapy) involves the use of a small device connected to the body via an infusion tube delivering a rapid-acting analog

insulin via the subcutaneous route continuously. Though originally meant for type 1 diabetes mellitus (T1DM), currently, it is approved for use in any type of diabetes as an advanced gadget for delivering insulin, replacing the conventional syringes and pens. The Indian insulin pump guidelines advocate the use of pumps in eligible and affordable patients as an alternative drug delivery device with proven benefits in reducing the glycemic burden, alleviating the pain of neuropathy and improving the quality of life.[9] First generation insulin pumps lacked many of the features that are now standard in modern pumps such as alarms for malfunction, low battery state, bolus dose adjustment and cannula occlusion. Integrated bolus calculators were included in the insulin pumps in 2002 and options for flexible basal rates were introduced later. Insulin pumps subsequently underwent tremendous technological innovation and bioengineering to closely approximate physiological insulin delivery. Open loop insulin delivery technologies are gradually being replaced with partially closed loop and hybrid closed-loop systems. Open-loop insulin delivery system combines an external insulin pump with a CGMS. Patients, however, need to manually use the information from their CGMS to determine how much insulin to infuse. Meanwhile, the partially closed loop and hybrid closed-loop systems enable direct communication between the CGMS and the insulin pump by means of a computer-controlled algorithm to automatically stabilize the blood glucose at an unprecedented level, with little or no input from the patient. Artificial pancreas (AP) systems with multiple glucoregulatory hormones in addition to insulin have also successfully completed clinical trials.

These new generation continuous glucose monitoring (CGM) devices, upcoming technologies in closing the loop, the recently approved AP algorithm, etc.,[10-13] are all supposed to be pathbreaking technologies that can help address and overcome the many major challenges in diabetes management. Though expensive, technologies are indispensable and worth investing, given the high cost of treating the complications of the disease. Some of the recently introduced technologies for diabetes care are discussed here.

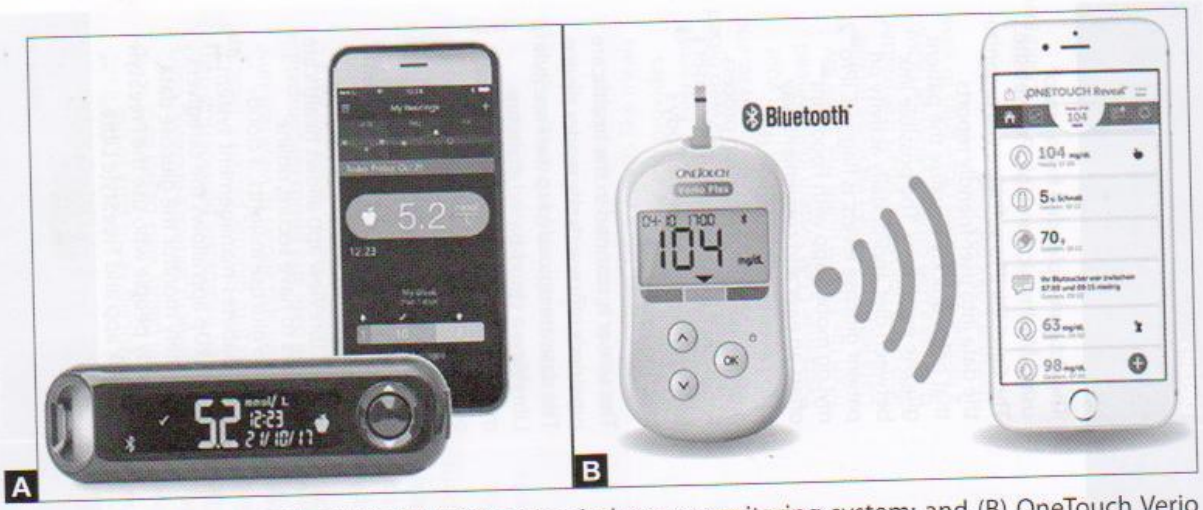
CONTOUR® NEXT ONE BLOOD GLUCOSE MONITORING SYSTEM

The CONTOUR® NEXT ONE smart meter and CONTOUR® DIABETES app seamlessly connect to capture the blood glucose readings via Bluetooth, which can be conveniently accessed on a smartphone, tablet or computer. The captured readings will be automatically synced and logged, and over time, help create meaningful insights regarding how one's lifestyle can affect the blood glucose levels. The CONTOUR® NEXT ONE smart meter system (**Fig. 1A**) has many salient features such as the (1) SmartLIGHT® feature (an instant indicator of the blood glucose levels, i.e., green for within target, amber for above target and red for below target); (2) Second-Chance® sampling (allows users to re-apply blood to the same test strip if the first sample was insufficient to take a reading, avoiding lancing a second time and wasting of test strips); (3) Options to add events like diet, activity, medication, photos, voice memos, etc., to put the results in context; (4) My patterns feature to detect the patterns in glucose readings that help the user gain more insights; (5) Smart alerts when your glucose readings are critically out of range; (6) Share reports with healthcare professionals, etc. As per the manufacturer, the smallest error range demonstrated by the glucose meter system was that, for subject fingertip tests, 95% of results met ±8.4 mg/dL or ±8.4% (vs. YSI reference) for glucose values <100 mg/dL or ≥100 mg/dL, respectively.[14]

ONETOUCH VERIO FLEX® METER AND THE ONETOUCH REVEAL® APPLICATION

The OneTouch Verio Flex® meter with ColorSure® technology (**Fig. 1B**) instantly shows the users if their blood glucose levels are in or out of range. The range indicator arrow points to the corresponding blue, green, or red color bar below the meter display.

The OneTouch Verio Flex® meter also connects wirelessly with the OneTouch Reveal® mobile app and synchronizes data directly to the patient's smartphone or tablet. The electronic visual logbook available in the mobile app automatically logs and organizes blood glucose



FIGS. 1A AND B: (A) CONTOUR® NEXT ONE blood glucose monitoring system; and (B) OneTouch Verio Flex® blood glucose monitoring system and OneTouch Reveal® application. ***(For color version, see Plate 6)***

results and transforms data into quick visual snapshots. ColorSure® technology highlights patterns and can motivate patients to perform structured self-monitoring of blood glucose (SMBG). The data can be shared with the healthcare provider as PDF, CSV, text or email without the glitches of contacting the physician's office. The app also facilitates the entry of data on insulin dosages, carbohydrate intake and physical activity. Details of the medications (oral drugs/type of insulin being used, i.e., whether a long-acting, mixed or rapid-acting insulin or insulin pump, etc.) can be entered which enhances the scope for setting and following customized targets. For the healthcare team, the OneTouch Reveal® web app facilitates setting of individualized short-term and long-term treatment goals, quick subgroup analysis of the patients, and generate ready-to-publish data.[15]

IPRO®2 CONTINUOUS GLUCOSE MONITORING SYSTEM

The iPro®2 (Medtronic, Inc. Diabetes) is a professional continuous glucose monitoring (PCGM) system that procures interstitial fluid (ISF) glucose profile for 6–7 days (listed in **Table 1**). The system consists of Enlite sensor, iPro®2 recorder and the Enlite serter. The Enlite sensor is small and comfortable and has a thin, flexible needle that can be inserted into the body. The iPro®2 recorder collects (up to 7 days of data, after which it shuts off automatically) and stores data from a glucose sensor and is intended for multiple patient use (each iPro®2 can be used up to 60 times). The data can be uploaded into CareLink® iPro® Therapy Management Software for Diabetes, to generate reports and store the data. An iPro®2 Docking Station enables to charge the iPro®2 and upload the data from the iPro®2 to CareLink® iPro®. The user-friendly reports provide a quick visualization of the patient's glucose excursions as well as possible explanations or suggestions based on glucose trends, thus allowing the healthcare provider to take optimal treatment decisions.[1,16,17]

FREESTYLE LIBRE PRO CONTINUOUS GLUCOSE MONITORING SYSTEM

Abbott's FreeStyle Libre flash glucose monitoring (FGM) system is available in two versions FreeStyle Libre (real time) and FreeStyle Libre Pro (professional version). Only the FreeStyle Libre Pro model is currently marketed in India. Both the versions of the system (listed in **Table 1**) consist of a small, round sensor that can be worn on the back of the upper arm, which measures ISF glucose every minute through a small (5 mm long, 0.4 mm wide) filament that is inserted just under the skin. The sensor comes in a factory-calibrated mode, thus eliminating the need for fingerstick calibrations. The recommended sensor wear-time is 14 days and the system captures as many as 1,340 glucose values.

In the professional version, the recorded glucose values can be procured by the healthcare provider's FreeStyle Libre Pro reader in as little

TABLE 1: Some of the currently available professional and personal continuous glucose monitoring systems.

CGM Device	Maximum sensor wear duration	Finger-stick confirmation	Recommended calibration frequency	Frequency of glucose readings	Compatible with insulin pumps	MARD	Alarms, alers etc.	Details
Professional CGM system  Medtronic iPro™2 with Enlite sensor	7 days	Required	Every 12 h	Every 5 min	No	13.60%	None	The data are uploaded from sensor using Medtronic CareLink iPro website. The CareLink iPro software will organize the data into user-friendly reports that helps quickly visualize the patient glucose excursions. The possible link between diet and/or daily activity on patient glucose levels, is flagged. iPro™2 myLog mobile app with FoodPrint™ offers an easy and convenient way to log events and improves the professional CGM evaluation process. FoodPrint™ identifies and grades user's food choices based on the body's reaction to glucose
 FreeStyle Libre™ Pro	14 days	Not required	–	Every 15 min	No	12.30%	None	The sensor is scanned in the healthcare provider's office with the reader device. The data are uploaded to the FreeStyle LibreView a cloud-based diabetes-management system, to have secure, online access to glucose insights
Personal CGM system  FreeStyle Libre™	14 days	Not required	–	Available every minute; automatically records every 15 min	No	9.40%	None (newer version Freestyle Libre 2 will provide real-time alerts)	FreeStyle LibreLink app allows patients to monitor their glucose using their phone. LibreView app allows healthcare providers to have secure, online access to glucose insights, a cloud-based diabetes-management system. LibreLinkUp app allows the caregivers to remotely monitor the glucose data shared by people who use the FreeStyle LibreLink app and FreeStyle Libre sensors

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CGM Device	Maximum sensor wear duration	Finger-stick confirmation	Recommended calibration frequency	Frequency of glucose readings	Compatible with insulin pumps	MARD	Alarms, alers etc.	Details
 Dexcom G6™ CGM	10 days	Not required	–	The Dexcom G6 sends glucose readings to a smart device or the Dexcom receiver every 5 min	Yes (T:slim X2 Pump)	9.00%	Customisable alerts notify the users when glucose levels go below or rise above preset limits. The "Urgent Low Soon" alert warns uers in advance (within 20 min) of a severe hypoglycemic event (55 mg/dL) and thus gives them sufficient time to take appropriate action before an event happens	Automatically sends data to the Dexcom Clarity web-based data management software allowing users and their healthcare providers to gain insights into glucose patterns. Dexcom G6* CGM app allows to view real-time glucose data and trends on compatible smart devices and to share the data with their close ones. 'Dexcom Follow App' allows people to remotely follow the glucose readings and trends from their compatible smart device
 Eversense® CGM	3 months	Required	Every 12 h	The smart transmitter automatically collects the glucose readings every 5 min and sends it to the user's Eversense Mobile App.	NO	8.50%	Provide visual, audible, and on-body vibe alerts	The Eversense mobile app allows to receive and display the sensor glucose data from the Eversense Smart Transmitter, on a compatible mobile device. It allows to set customised glucose alerts, track events like meals and physical activities and provides reports on glucose patterns. Eversense Data Management System, a web based application allows to view, analyze, and store glucose information from your Eversense CGM System (data synced from the system using the Share My Data feature on the Eversense mobile app or by uploading smart transmitter data via a USB cable). Eversense NOW, a mobile app allows close ones to view the user's glucose data

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CGM Device	Maximum sensor wear duration	Finger-stick confirma-tion	Recom-mended calibration frequency	Frequency of glucose readings	Compatible with insulin pumps	MARD	Alarms, alers etc.	Details
 Guardian™ Connect CGM	7 days	Required	Every 12 h	The Guardian™ connect transmitter sends glucose data to the user's compatible device every 5 min	No	9.10%	Smart technology can predict where the user's glucose levels are headed and can give alerts from 10 to 60 min before a high or low. Unlike othe CGM systems, users do not require a separate receiver	Guardian™ connect app displays sensor glucose data, trends and alerts in a simple and easy to use design. The mobile app has the option to send the most recent sensor glucose readings from the sensor and any un-cleared alarm every 5 min to the CareLink™ Personal Software integrated Therapy Management Software. The mobile device can also send full details every 24 h, including sensor glucose readings and graphs, alerts, and event markers. The Sugar.IQ™ Diabetes Assistant allows to detect important patterns and trends, and offers real-time, personalized insights. It continually analyzes how the glucose levels respond to the user's food intake, insulin dosages, daily routines etc.

(CGM: continuous glucose monitoring; MARD: mean absolute relative difference)

as 5 seconds (a single reader can be used to scan FreeStyle Libre Pro sensors of multiple patients). FreeStyle Libre Pro system offers easy-to-interpret reports which can be procured either through the LibreView system, a secure free cloud-based diabetes management system, or the FreeStyle Libre Pro reporting software designed for desktop. The comprehensive glucose report "Ambulatory Glucose Profile (AGP)" generated provides a visual snapshot of glucose levels, trends and patterns over time and was found to be an effective basis for education, helping achieve a better understanding of glycemic variability and increasing involvement in diabetes self-management.[8,18,19]

DEXCOM G6® FACTORY-CALIBRATED REAL-TIME CONTINUOUS GLUCOSE MONITORING SYSTEM

The Dexcom G6® CGM is a factory-calibrated CGM system specified for 10-day wear (listed in **Table 1**). It is FDA (US Food and Drug Administration) permitted to make diabetes treatment decisions without confirmatory fingersticks or calibration and is indicated for patients aged 2 years and older. The system comprises of a sensor, transmitter and a display device (receiver and/or compatible smart device). The glucose readings procured by the sensor are sent to the smart device or the Dexcom receiver every 5 minutes. The web-based diabetes management software platform Dexcom CLARITY®, simplifies diabetes data reporting and management and uses the standardized glucose reporting format, AGP. It provides the users and their healthcare providers with relevant insights into glucose patterns and also allows them to access and track data, anywhere, anytime and features many time saving tools.

The Dexcom G6® CGM application allows viewing real-time glucose data and trends on the user's phone and sharing data with their close ones. The "Dexcom Follow app" allows up to five people to remotely follow the glucose readings and trends from their compatible smart device. In a recent study among adults and children with either T1DM or type 2 diabetes mellitus (T2DM), the system's "Urgent Low Soon" (predictive of hypoglycemia within 20 min) hypoglycemia alert was correctly provided 84% of the time within 30 minutes before impending biochemical hypoglycemia (<70 mg/dL). The 10-day sensor survival rate was found to be 87%.[20]

EVERSENSE® 90-DAY IMPLANTABLE CONTINUOUS GLUCOSE MONITORING SYSTEM

Eversense® CGMS (listed in **Table 1**) recently received FDA approval for using the system in people 18 years of age and older with diabetes. This is the first and only CGMS to feature an implantable glucose sensor and provides long-term continuous monitoring for up to 90 days.

The system includes a pill-sized sensor implanted in the upper arm (by a physician in a short office procedure) for 90 days, an on-body transmitter, and a mobile application that displays glucose data and issues alert to high and low blood glucose values. Eversense's 90-day wear thus eliminates the need for frequent sensor insertions required by other CGMs, which currently last only for 7–14 days. This is also the first CGM to issue on-body vibration alerts and thus notifies the user in the event of highs and lows—a particularly useful feature for individuals who are visually impaired or have trouble hearing.[21]

GUARDIAN™ CONNECT CONTINUOUS GLUCOSE MONITORING SYSTEM

The FDA recently approved the Guardian™ Connect CGMS (listed in **Table 1**) for use among people with diabetes using multiple daily insulin injections and aged 14–75 years. It works with three elements: (1) A thin sensor, (2) A small transmitter attached to the sensor, and (3) The Guardian Connect app on a compatible iOS device. It is, thus, the first smart standalone CGM system that does not require a receiver and directly sends continuous sensor glucose data from the sensor transmitter to a smartphone.

The Sugar.IQ™ smart diabetes assistant app with AI technology from IBM Watson Health continually analyzes how an individual's glucose

levels respond to their food intake, insulin dosages, daily routines, and other factors. Like other CGMs, the Guardian™ Connect CGM reports glucose readings every 5 minutes. The system has customizable alerts that allow the users to get notified about future high and low glucose events up to 60 minutes in advance, and also allows the caregivers to track the user's glycemic status remotely in real-time or via text alerts. It uses Guardian Sensor 3, the latest and most advanced sensor which is FDA approved to be used to control the AP system, MiniMed™ 670G hybrid closed-loop insulin delivery system.[22] However, Guardian Connect, which has been launched in the last quarter of 2018 in India, uses the sensor used with 640G insulin pump and does not connect with Sugar.IQ™ app.

ALERE AFINION™ HBA1C

Point-of-care (POC) testing devices provide immediate, actionable information, contributing to better clinical, operational, and economic outcomes. Alere Afinion™ glycosylated hemoglobin (HbA1c) (**Fig. 2**) is one such POC HbA1c testing device designed for use in a physician's office, a treatment room, or at a bedside. It is a desktop-size analyzer, weighs 5 kg and is able to store 500 patients' results. It uses a finger-prick capillary blood sample which when applied to a test cartridge, is analyzed within several minutes. The system has several potential advantages over laboratory A1C testing such as: Simple to perform without a lab technician and accurate and rapid test results expedite medical decision-making, more convenient for patients, can be useful for convincing the patients on changes in therapy or even a behavior, can improve health system efficiency, can improve access to testing for underserved populations.

The Afinion™ HbA1c Dx system includes a compact multi-assay analyzer (the Alere Afinion™ AS100 Analyzer) which is also capable of testing for lipid levels, albumin/creatinine ratios, and C-reactive protein, and can accept samples of whole blood, plasma, or urine. A small connectivity device facilitates automatic transfer of data from the analyzer to a laboratory, information system, or other electronic record systems (the Alere Afinion™ Data Connectivity Converter). The single-use Afinion™ test cartridges are used to collect patients' capillary blood samples.[23] Alere has now been acquired by Abbott.

MINIMED 640G INSULIN PUMP

The MiniMed 640G Insulin Pump (listed in **Table 2**), the first-generation AP made available in India since 2015, is a sensor-augmented pump (SAP)—the latest type of insulin pump that includes CGM capabilities and is indicated for both T1DM and T2DM. The 640G system has built-in intelligent features for increased protection including the SmartGuard™ technology, active insulin tracking, bolus progress bar and predictive battery life. The SmartGuard technology, which

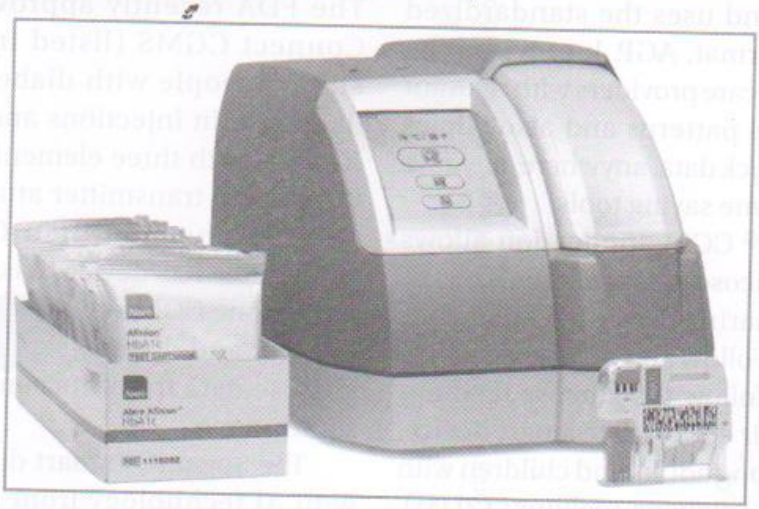

FIG. 2: Point-of-care glycosylated hemoglobin (HbA1c) testing device—Alere Afinion™ HbA1c Dx.

TABLE 2: Some of the insulin pump or artificial pancreas systems that are currently available or are expected to hit the market in the near future.

Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details
 MiniMed™ 640G	Yes	Enlite™ Sensor, 6 days	n/a	The system providers the user with alarms, alerts or messages, depending on the seriousness of the problem. Alarms warn the user when something needs to be addressed right away, e.g., insulin delivery is being prevented due to the blockage in insulin flow or because battery needs to be replace. Alerts make the user aware of a situation that may need attention, for example, a low insulin reservoir, a low battery or if sensor glucose levels are predicted to reach preset high or low levels in the next 30 min, or are rapidly changing. Messages give information about the pump status. Users are notified of alarms and alerts using sound or vibration. If an alarms is not cleared within 10 min, a siren is sounded	180-unit/ 300-unit	Works with CareLink Personal and Professional data management software. Compatible with Windows and Mmac operating systems	SmartGuard™ technology can warn the user when he is approaching low glucose levels 30 min in advance and automatically stops insulin delivery. As the glucose levels recover, SmartGuard™ will automatically resume insulin delivery. It allows the users to set multiple low limits and thus extends enhanced protection. The CONTOUR® Next Link 2.4 m wirelessly communicates with the system, eliminating manual entries for calibration, insulin dosing, or remote bolus delivery

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Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details
 MiniMed™ 670G	Yes	Guardian™ Sensor 3, 7 days	n/a	The system provides the user with alarms, alerts or messages, depending on the seriousness of the problem. Alarms warn the user when something needs to be addressed right away, e.g., insulin delivery is being prevented due to the blockage in insulin flow or because battery needs to be replaced. Alerts make the user aware of a situation that may need attention, for example, a low insulin reservoir, a low battery or if sensor glucose levels are predicted to reach preset high or low levels, or are rapidly changing. Messages give information about the pump status. Users are notified of alarms and alerts using sound or vibration. If an alarm is not cleared within 10 min, a siren is sounded.	300-unit	Works with CareLink Personal and Professional data management software. Compatible with Windows and Mac operating systems	The MiniMed™ 670G system offers SmartGuard™ technology which provides two levels of automated insulin delivery. The Suspend before low feature automatically stops insulin delivery for upto 30 min before hitting the preset low limits, and automatically restarts insulin when the levels recover thus avoiding lows and rebound highs. The Auto Mode feature automatically adjusts basal insulin delivery every 5 min by continuously increasing, decreasing, or suspending insulin delivery based on the user's sensor glucose values and recent insulin delivery. However, the user must still manually deliver insulin therapy during meals. The system uses the new Guardian Sensor 3 for enhanced accuracy. The Contour® Next Link 2.4 m wirelessly communicates with the system, eliminating manual entries for calibration, insulin dosing, or remote bolus delivery

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Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details

Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details
 Tandem t:slim X2™	Yes	Dexcom G6 CGM System, 10 days	n/a	Built-in hypoglycemia safety alarm gives warning when the glucose reached 55 mg/dL. Customizable alerts can notify the user when glucose falls below or rises above preset limits and when glucose is rapidly fluctuating.	300-unit	Works with web-based t:connect® Diabetes Management Application. The application is compatible with Mac® and other personal computers, and can be accessed by both patients and providers. It allows for a fast and easy way to access and save data from pumps, supported glucose meters, and Continuous Glucose Monitors, and provides meaningful insights and trends. Compatible with many other data management systems	Color touch screen. Flat reservoir design and micro-delivery technology allow for a thinner pump. The Tandem Device Updater is a Mac® and PC-compatible tool for the remote update of Tandem insulin pump software, and provides in-warranty customers access to new and enhanced features faster than the industry has been able to in the past, and separate from the typical multi-year warranty cycle
 Omnipod DASH™	No	n/a	No. The system has connectivity to the Contour NEXT ONE glucose meter. Users who utilize the Omnipod DISPLAY™ app on their iOS smartphone, a Today View Widget will be available and can be configured alongside the Dexcom System Widget. This will provide an integrated view of both PDM and insulin data next to their Dexcom CGM data. HCPs and patients can also see their CGM and insulin data together via Insulet Provided Glooko	The PDM provides audible and vibratory alarms, alerts, and reminders related to insulin delivery, reservoir level, pod functioning, and battery life. The settings also allow for PDM alarms to first be seen or heard on an iPhone	200-unit	Full market release is expected in early 2019 in the United States. The Omnipod DASH™ System will feature a suite of mobile applications such as Omnipod DISPLAY and Omnipod VIEW, that will allow users quick and easy access to their Personal Diabetes Manager (PDM) data on their smartphone and the ability to share their status with up to 12 persons. The Today View Widget would allow the users to see their CGM and insulin delivery information together on a single screen on their iOS mobile devices. Users can upload the data from Omnipod DASH™ System to Glooko Universal diabetes management platform and at full market release, users would be able to set DASH™ PDM to automatically upload the data to Insulet Provided Glooko	No tubing. The system includes a waterproof pod that can be worn up to 72 h and the PDM, which is a handheld device used to wirelessly control the Pod. Various features include: customizable basal insulin profile and bolus calculator, intuitive graphical displays, CalorieKing® food library with carbohydrate content for up to 80,000 foods etc.

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Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details
 Dana Diabecare RS	No	n/a	Possible. The Bluetooth Low Energy 4.0 wireless connectivity will allow DANA RS pump's firmware to be updated remotely like smartphones. This enables future CGM integration allowing data to go directly to the phone instead of a separate receiver or paired device	Alarms for low battery, low reservoir, occlusion, missed bouls, shutdown	300-unit	The mobile apps iOS – AnyDANA-I, and Android AnyDANA-A work together with the DANA RS pump, the former being the iOS version (pending regulatory approval) and the later for Android devices (received CE mark)	A smart insulin pump enabled with Bluetooth low energy 4.0 connectivity which allows discrete remote control from smartphone application to operate the pump, deliver boluses, change basals and change settings. Merely weight 62 g including battery. Basal features like basal increments, temporary basal, 4 profiles. Bolus features like bolus increments, extended bolus, dual pattern bolus. Many safety features including button lock. 21 languages supported. Enables integration with CGM
 iLet™ Bionic pancreas	No	n/a	Yes, Dexcom G5 CGM System and EVERSENSE® CGM	Alerts and alarms enabled	Insulin cartridge = 1.6 mL, Glucagon cartridge = 1mL	The main insulin-dosing algorithm uses a custom model-predictive control (MPC) strategy to determine dosing requirements (beyond the basal insulin requirement) every 5 min. The MPC insulin controller eliminates the need to determine or use insulin correction factors. Another insulin-dosing controller, running in parallel with the MPC controller, determines the basal insulin requirements, every 5 min. The basal insulin controller eliminates the need to determine or use basal rates. Both the MPC and basal insulin controllers adapt continually to	Not yet approved by the FDA or any other regulatory body. The iLet bionic pancreas platform consists of a dual-chamber infusion pump for subcutaneous delivery of insulin alone, glucagon alone, or both insulin and glucagon, and has an integrated continuous glucose monitor. The insulin and glucagon dosing algorithms integrated into the iLet require only the user's body weight for initialization and then autonomously adapt in real-time to changes

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Insulin pump model	Integrated CGM	Sensor used and its duration	Compatible with CGM	Alarms, alerts etc.	Reservoir	Software	Details
						the user's ever-changing insulin needs. The adaptive meal-announcement insulin controller eliminates the need to set or know the carbohydrate-to-insulin ratios, as it makes automatic adjustments based on dosing history for similar past meal announcements, and customizes its doses to the individual and time of day. The bihormonal configuration of the dosing algorithms integrated into the iLet also consists of a proportional-derivative glucagon dosing algorithm, which determines micro-doses of glucagon based on CGM readings	in an individual's insulin need, whether acute (e.g., due to circadian hormonal fluctuations, intercurrent illness, physical activity, or emotional state), or gradual (e.g., due to hormonal changes that occur during puberty or menopause). The iLet can be initialized by entering only the body weight and does not require the patient to count carbohydrates, set insulin delivery rates or deliver bolus insulin for meals or corrections. The glucagon-only configuration might find application in rare, chronic, low blood-sugar conditions like congenital hyperinsulinism and insulinoma syndrome

(CGM: continuous glucose monitoring)

is one step closer to AP, predicts when a patient is approaching low glucose levels 30 minutes in advance and automatically stop insulin delivery (Suspend before low option). When the glucose levels recover, SmartGuard will automatically resume insulin delivery. It is also possible to set multiple low limits throughout the day to give increased protection in times of need.[24]

MINIMED 670G INSULIN PUMP

The Medtronic's MiniMed 670G, the world's first hybrid closed-loop insulin pump (listed in **Table 2**) is a major milestone for diabetes technology a little over a decade after the "AP" project in 2005 was launched. Considered the first generation AP in USA, 670G is not yet available in India. The MiniMed 670G System consists of the following devices: MiniMed 670G insulin pump, the Guardian Link 3 transmitter, the Guardian sensor 3, One-Press serter, and the Contour® NEXT Link 2.4 glucose meter. The MiniMed 670G system features an advanced algorithm to date, the SmartGuard™ HCL, which enables greater glucose control with reduced user input. The "suspend before low" option can stop insulin up to 30 minutes before reaching the preset low limits, and the system automatically restarts insulin when the glucose levels recover without bothersome alerts. The system will thus reduce time at dangerous high and low blood sugar levels, improve time-in-range, reduce glucose variability, bring much greater nighttime safety and target morning blood sugars.

The system has two modes; manual mode and auto mode. The manual mode allows the user to program the system so as to deliver basal insulin at a preprogrammed constant rate (Bolusing can be done using either the Bolus Wizard™ feature or with manual boluses. May be used with or without CGM). Whereas, in auto mode, the system can automatically adjust basal insulin by continuously increasing, decreasing, or suspending the insulin delivery, every 5 minutes based on the CGM readings (Bolusing for carbohydrates before meals is necessary). The new Guardian Sensor 3 is the first and only sensor approved by the FDA to control a hybrid closed-loop system.[25]

TANDEM t:slim X2™ INSULIN PUMP WITH PREDICTIVE LOW GLUCOSE SUSPEND FEATURE

The t:slim X2™ insulin pump (listed in **Table 2**) is manufactured by Tandem Diabetes Care®, Inc., the manufacturer of the only touchscreen insulin pumps with CGM integration. The insulin pump comes with Basal-IQ™ technology, a predictive low glucose suspend (PLGS) feature and happens to be the first automated insulin delivery system that is approved for use by children as young as 6 years old. The t:slim X2™ insulin pump is integrated with the Dexcom G6® CGM System (which requires no fingersticks for calibration or diabetes treatment decisions). Basal-IQ™ algorithm of the pump helps reduce the frequency and duration of hypoglycemic events by predicting where glucose levels are heading 30 minutes in advance, suspending insulin delivery when low glucose (<80 mg/dL) is predicted and automatically resuming insulin delivery once glucose level increases. The Basal-IQ™ feature has no complicated settings to manage and operates without constant input or interaction. The t:slim X2 pump is up to 38% smaller than other pumps, yet can hold up to 300 units of insulin. Insulin delivery and glucose history can be seen directly on the insulin pump's bright color screen. t:connect® diabetes management application allows the users to upload the insulin delivery and CGM data from the pump to their computer and generate insightful reports and helps them review the data and adjust the settings, as well as allows the healthcare team to conduct an in-depth analysis.[26]

OMNIPOD DASH™ INSULIN MANAGEMENT SYSTEM

Insulet Corporation's Omnipod, first approved by FDA in 2005, was a tubeless insulin pump where the insulin is contained in a waterproof pod which can be worn on the body for 3 days for continuous insulin delivery, avoiding the hassles of tubings and daily injections. A separate device called the Personal Diabetes Manager (PDM) wirelessly communicates with the pod and allows to make discreet insulin delivery

including boluses, perform basal settings, and "insulin on board" calculations. The PDM has a built-in FreeStyle blood glucose meter.

United States Food and Drug Administration recently cleared Insulet Corporation's Omnipod DASH Insulin Management System (listed in **Table 2**) and the commercial release of the device is anticipated for early 2019. This tubeless, wearable insulin pump can hold up to 200 units of insulin and allows customizable basal rates and bolus amounts. Similar to the earlier version, the DASH system also consists of the Pod and the PDM, where the PDM has a modern, simple, colorful and intuitive touch-screen interface. However, PDM does not include a glucose meter but works with a separate CONTOUR® NEXT ONE blood glucose meter so that blood glucose readings can be viewed on the PDM and entered into the bolus calculator. Bluetooth® wireless technology enables connectivity between the DASH™ Pod and DASH™ PDM as well as to the CONTOUR® NEXT ONE blood glucose meter, and also provides the capability to see the Omnipod DASH™ system data on a user's smartphone via a suite of mobile apps (Omnipod DISPLAY™ app for the display of PDM data on the user's smartphone. Omnipod VIEW™ app for the care partners to remotely view the subjects' Omnipod DASH™ System data on their smartphone).

DANA DIABECARE RS

Dana Diabecare RS insulin pump (listed in **Table 2**) from SOOIL Developments Co., Ltd., Korea, is a smart insulin pump with discrete remote control. The icon-based interface in the pump makes it intuitive and easy to program and easy to learn. It has many key advantages like multiple language options (21 languages supported), small and light weight (62 g including battery) making it very comfortable and easy to wear, low basal rates (to go as low as 0.01 U/h), etc. The system also has many safety settings like alarms for low reservoir, line occlusion, low battery, missed bolus etc.; bolus frequency restriction; and active insulin monitoring. With two-way Bluetooth Low Energy 4.0 connectivity, the DANA RS can communicate with a smartphone app to operate the pump remotely, change settings, and change basals or deliver boluses. It will in future, allow the DANA RS pump's firmware to be updated remotely and also integration with CGM so that data can go directly to the phone instead of a separate receiver or paired device.[27,28]

BIONIC PANCREAS

"Bionic pancreas" refers to a dual-chambered investigational device that comprises a pump for delivering insulin and glucagon, a CGM, and a control algorithm. This device is the first and only of its kind to integrate glucagon delivery and makes therapeutic decisions every 5 minutes. Bionic pancreas platform was initially developed in an academic research setting and was then taken over by "Beta Bionics"—a "public benefit corporation" and integrated it into a single medical device, the "iLet" (listed in **Table 2**). It looks like a thick iPhone, with two ports on the end for the tiny drug delivery tubes (one for insulin and other for glucagon). iLet requires minimal patient input and can be initiated simply by providing data on the patient's body weight and the device essentially takes over, whereas other peers still require the user to count carbohydrates, take an insulin bolus before meals, and program their insulin doses.

Safety and efficacy of bionic pancreas have been demonstrated in a series of clinical trials involving T1DM adults, adolescents and preadolescents in different real life settings and has been found to reduce (i) on average, time spent with low blood sugars, (ii) on average, mean blood sugars and (iii) intersubject variability in blood sugar control. They expect potential FDA approval of the insulin-only configuration in the second half of 2020 and that of bihormonal configuration 12–24 months later. The automated glucose control (by employing insulin only, glucagon only or bihormonal configuration, as required) is also expected to find utility in managing other conditions such as T2DM, hypoglycemia in T1DM patients managing their own insulin therapy, post bariatric hypoglycemia and congenital hyperinsulinism.[29]

ARTIFICIAL INTELLIGENCE-ENABLED PLATFORMS FOR DIABETES MANAGEMENT/DETECTION OF DIABETES COMPLICATIONS

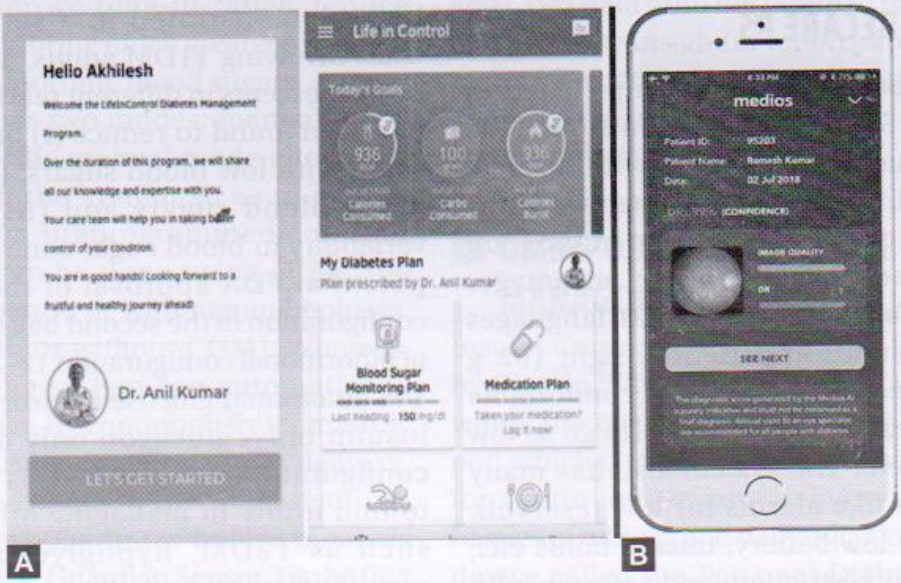
Numerous disease management or disease detection platforms are currently available as mobile apps and many of them are geared with the latest artificial intelligence (AI) technology. They have made the detection as well as management of the disease much simpler, accurate, affordable and accessible. The multi-model bot enabled diabetes care platform—Life in Control™ Diabetes Coach, and Medios Technologies AI Assistant to detect Diabetic Retinopathy (DR) are two such recently introduced disease management/detection platforms in the field of diabetes.

Life in Control™ Diabetes Care Platform

The Life in Control™ Diabetes Coach (**Fig. 3A**) is a multi-model bot enabled diabetes care program available both in Android and iOS platforms. It is designed to keep clinicians and the patients connected so as to achieve better diabetes management and allows integration with hospital electronic medical records (EMR) and monitoring devices. For clinicians, the platform allows for unprecedented access to the patient's diet, lifestyle and vital information for a greater insight into their condition, help increase patient engagement and treatment compliance, and thereby drive better patient outcomes. It can also analyze the user's medical history to predict secondary complications. The platform has been shown to improve their overall productivity and is proven to be a highly cost-effective and time-saving option.[30,31] For patients, it guides and supports them to set goals and daily tasks, improve their lifestyle, track calorie intake and physical activities, and get glycemic rating, nutritional information and personalized diet plans.[30,31]

Medios Technologies AI Assistant to Detect Diabetic Retinopathy

Medios Technologies uses deep learning to help doctors diagnose DR during a typical diabetes check-up in a convenient and efficient way without a specialist (**Fig. 3B**). It works by taking an image of the eye, running it through a software program which then provides an almost-immediate diagnosis. AI automatically grades fundus images, detects all cases of referable DR including moderate nonproliferative diabetic retinopathy (NPDR), severe NPDR



FIGS. 3A AND B: Artificial intelligence-enabled platforms for diabetes management or detection of diabetes complications. (A) Life in Control™ Diabetes Coach; (B) Medios Technologies artificial intelligence assistant to detect diabetic retinopathy. ***(For color version, see Plate 7)***

and proliferative DR. The first model is capable of detecting if a retinal image needs a referral with 98% sensitivity.[32]

CONCLUSION

We are witnessing rapid technological advancements in the healthcare sector whereby, conventional diabetes treatment and management practices are undergoing tremendous changes. Conventional diabetes care practices were usually centered around hospitals and primary care physicians which had their own limitations. In these practices, communication was mostly one way (physician-centered), and they were unable to provide any systematic assistance via social support to address the psychological needs of the patients and were unable to readily adopt advanced health information technologies that could otherwise facilitate effective healthcare. A constant gap always existed between the diabetes care practices and the recommended diabetes care standards.

Advancements achieved in various technologies like gadgets, mobile apps, and diabetes management platforms have empowered the healthcare providers, patients as well as the caregivers to be active players in improving diabetes care. The newer technologies are a lot simpler, user friendly, cost-effective and can also ensure successful short-term and long-term diabetes care outcomes. Physicians should adopt technologies in eligible and affordable candidates to successfully overcome the major barriers in treatment and help patients retain the quality of life while surviving longer with the disease. With the current faster pace of obtaining regulatory approvals, these technologies are for sure going to change the overall outlook and outcomes of diabetes management, provided they are rationally utilized.

EDITOR'S NOTE

Although there are a number of barriers to using technology related to physical, socioeconomic, and educational factors, the use of advanced technologies for diabetes management is on the rise among patients with diabetes. In contrast to the earlier physician-centered one-way communication, advanced technologies allow the patients to better understand their disease and more importantly allow the patients to get involved in the management of diabetes. It is now well conceived that advanced technologies pave way for meaningful improvements in A1c as well as hypoglycemia. In this chapter, Dr Jothydev summarizes different aspects of a technological approach to diabetes care, lists currently available devices and systems in the pipeline, and discusses the clinical evidence that supports for their use. The need of the day is to make these technologies much simpler, user-friendly, cost-effective, and to make sure that they ensure successful short- and long-term diabetes care benefits.

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