The evolution of technologies to manage diabetes has led to improvements in patient adherence, technique, and monitoring. Insulin pens, for example, have distinct advantages over vials and syringes; they allow for more accurate dosing, improved adherence, less injection site pain, and greater patient satisfaction (1,2). As the population with diabetes grows internationally, second-generation insulin pens have been engineered with USB or Bluetooth features to enable closer monitoring of pharmacotherapy. Similarly, many devices for self-monitoring of blood glucose have also become integrated with Bluetooth to enable wireless transmission of data to a smartphone.

As of 2016, the smart insulin pen market was valued at $59 million and is expected to increase to $123 million by 2023 in Latin America, the Middle East, and Africa (3). One report predicts that Europe will have the greatest smart insulin pen market growth, bringing in more than $2 million by 2027, based in part on high current utilization of such pen devices. The trend toward increased use of smart insulin pens can also be seen in North America; in fact, the same report estimates that, by 2027, the North American smart insulin pen market will have a continuous annual growth rate of 26.7% (4).

The emergence of new technologies such as smart insulin pens, caps, attachments, and virtual platforms can help both patients and health care providers (HCPs) overcome problems such as poor insulin adherence, incorrect insulin initiation and titration, and medication errors. Adoption of such new devices may increase even further if clinical trials can show long-term cost-effectiveness (5).

This review highlights the technologies now available on the market in the United States and internationally that are designed to improve insulin administration. A comprehensive literature review was conducted using manufacturer websites, press releases, commercial data resources, educational and training tools, news outlets, periodicals, and medical device databases. Clinical trial information was included where possible, but limited studies have been conducted in this field to date. This review only includes devices that can be used as stand-alone products.

Digital Health Advancements for Insulin Pens
The widespread adoption of the Internet of Things (integration of wireless connectivity sensors into devices and objects) and the proliferation of digital health tools has led to a phase of mass development of new tools in medical care. Taking the commonly used insulin pen and adding sensors or technological features to update it for care in the 21st century has become a small niche, with multiple companies creating their own platforms or devices. The two most pervasive models at present are pens with refillable insulin cartridges that

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feature built-in wireless communication abilities and sensors to track insulin delivery. Other companies are creating sensors that attach to disposable insulin pens, such as a cap or a device that attaches to the side of the pen. These two approaches are targeted to currently produced insulin pens (i.e., pens with refillable cartridges or disposable pens) and reflect geographic regional preferences for insulin pen utilization. The following sections describe these devices in more detail.

**Integrated Smart Pen Systems**

The features of available integrated smart pen systems are summarized in Tables 1 and 2.

In December 2017, Companion Medical had a limited launch of its InPen system. The product includes a reusable pen that is compatible with U-100 (3 mL) lispro (Humalog, Eli Lilly) and aspart (Novolog, Novo Nordisk) rapid-acting insulin cartridges. The system is available by prescription only through a mail-order pharmacy.

After the insulin cartridge is appropriately installed, the device sends real-time data via Bluetooth to an InPen application (app) available for iPhones. The app displays information such as whether the pen is exposed to temperature extremes. Users can record their most recent blood glucose levels and anticipated meals, and a dose calculator will recommend the correct amount of insulin to inject. Of note, InPen can make the distinction between insulin used to prime the device and insulin for administration. Once the insulin is injected, the amount injected is also recorded on the app. Each pen has a non-rechargeable battery that lasts ~1 year (6,7) (Table 1).

In 2007, Eli Lilly made an early investment in the digital health market when it released the HumaPen Memoir in Europe. At the time, the pen featured a digital display and memory of the dates and times of the most recent 16 insulin doses. The product was lauded for its ability to minimize insulin waste and for accurate dosing but was ultimately discontinued for commercial reasons (8,9).

More recently, Eli Lilly announced in December 2017 that it would start feasibility studies to create a connected ecosystem of diabetes management using its automated insulin delivery (AID) system (10). With this system, the company is aiming to bring a hybrid closed-loop platform (using an insulin pump, a continuous glucose monitoring [CGM] device, and a dosing algorithm) to the market that can help patients dose their insulin based on real-time CGM. In addition, another platform includes the use of a “connected insulin pen with glucose-sensing technologies and software applications” to give patients insulin dose recommendations (10). Currently, Eli Lilly has received U.S. Food and Drug Administration (FDA) 510K clearance for a dosing app called the Go Dose System that can supply insulin dosing information for patients using Eli Lilly insulin products (11). Two versions of the app will be available, “Go Dose” for patients and “Go Dose Pro” for HCPs, enabling providers to titrate patients’ insulin doses remotely. Further details regarding these new pen-related devices are not yet available.

Novo Nordisk has also started investing in and conducting clinical trials of decision-support systems to help minimize hypoglycemia in patients with type 1 diabetes (12). One of its newest pen models is called the NovoPen 5. These pens are compatible with U-100 (3 mL) aspart rapid-acting insulin cartridges and can administer 1- to 60-unit single doses. The pen clicks once a full dose has been administered. Its electronic display shows the last dose of insulin administered. It also has the capacity to display the hours elapsed since the last injection, the pen battery life, and information on malfunctioning pen memory (Table 2).

The NovoPen Echo is a similar pen device created for children. It offers the same features as the NovoPen 5, but allows for half-unit dosing and only administers up to 30 units of insulin per injection (13) (Table 2).

Novo Nordisk recently announced plans to release its NovoPen 6 and NovoPen Echo Plus in 2019. These products will eventually replace and improve on the designs of the NovoPen 5 and NovoPen Echo (14). The German company Pendiq Intelligent Diabetes Care has created Pendiq 2.0 digital insulin pens. To date, these devices are only available in Germany. Pendiq 2.0 pens are compatible with U-100 (3 mL) lispro and aspart rapid-acting insulin cartridges. They are able to store the last 1,000 entries of injection dates, times, and quantities, and users can view these entries on an OLED display. The pen’s Bluetooth compatibility allows it to transmit the data to a proprietary smartphone app called dialife, which is available for both Android and Apple smartphones. The pen comes with a USB cable used to both transmit data to a computer and recharge the pen battery. The device features a motor-driven apparatus that allows more precise dosing in increments of 0.1 units. Pendiq 2.0 also has a safety alarm that notifies users of any low insulin levels, low battery power, or malfunctions (15) (Table 1).

The ESYSTA system is another device in the smart connected insulin pen arena and is a product of Emperra Digital Diabetes Care. ESYSTA pens are compatible with U-100 (3-mL) lispro, aspart, and glulisine (Apidra, Sanofi) rapid-acting insulin cartridges. The device stores 1,000 entries, and its batteries must be replaced yearly. The display shows the last dose of insulin administered and a countdown during the actual insulin injection. The ESYSTA pen can wirelessly transfer insulin doses, times, and dates to the ESYSTA app, which is available for both Android and iPhone smartphones. The app provides users with blood glucose
### TABLE 1. Overview of InPen, ESYSTA, Pendiq, and YpsoMate SmartPilot Smart Insulin Pens

|                | InPen       | ESYSTA      | Pendiq    | YpsoMate SmartPilot |
|----------------|-------------|-------------|-----------|---------------------|
| Company        | Companion Medical | Emperra | Pendiq    | YpsoMed             |
| Country of origin | United States | Germany | Germany | Switzerland         |
| FDA approval   | 2016        | No          | No        | No                  |
| U.S. availability | Yes        | No          | No        | No                  |
| Cost           | $665        | $220 (€192)* | $193 (€169)* | Unable to verify |
| Insulin compatibilities | Lispro/aspart 3-mL cartridges | Lispro/aspart/glulisine 3-mL cartridges | Lispro/aspart 3-mL cartridges | Prefilled insulin |
| App service    | Apple, Android | Apple, Android | Apple, Android | Unable to verify |
| Bluetooth      | Yes         | Yes         | Yes       | Yes                |
| USB            | No          | No          | Yes       | No                 |
| Features       | • Lasts 1 year | • Cloud database accessible to providers | • Memory for recording last 1,000 injections (date, time, quantity) | • Tracks injection time and sequence of handling (pressing against skin, triggering the injection, positioning the injector, end of injection) |
|                | • Temperature sensor | • Replaceable batteries (last for up to 1 year) | • Alarms if low battery, needle blockage, or low insulin | |
|                | • Dose calculator | • Memory capacity for 1,000 data records | • Rechargeable battery | |
|                | • Reminders for patient | | | |
|                | • Prescription needed | | | |

*Currency conversions conducted on 29 January 2019.

### TABLE 2. Overview of NovoPen 5 Plus, NovoPen Echo, Vigipen, and KiCoPen Smart Insulin Pens

|                | NovoPen 5 Plus | NovoPen Echo | Vigipen | KiCoPen |
|----------------|---------------|--------------|---------|---------|
| Company        | Novo Nordisk  | Novo Nordisk | Diabnext | Cambridge Consultants |
| Country of origin | United States | United States | United States | United Kingdom |
| FDA approval   | No            | Yes          | No       | No      |
| U.S. availability | No          | Yes          | No       | No      |
| Cost           | $68 (~£52)*  | ~$54–$67 with discount | Unable to verify | Unable to verify |
| Insulin compatibilities | Aspart 3-mL cartridges | Aspart 3-mL cartridges | Unable to verify | Unable to verify |
| App service    | No            | No           | Apple    | Unable to verify |
| Bluetooth      | No            | No           | Yes      | Unable to verify |
| USB            | No            | No           | No       | Unable to verify |
| Features       | • Records time since and dose of last injection | • Designed for children | • Automatically records the time of injection as well as the amount of insulin injected | • Records time and amount injected |
|                | • Displays battery life and memory status | • Records time since and dose of last injection | • Displays battery life and memory status | |
|                | • Half-unit dosing | • Displays battery life and memory status | • Transfers the data via Bluetooth to app | |

*Currency conversions conducted on 29 January 2019.*
trends and targets and the ability to synchronize their data to the ESYSTA Portal, a real-time interface that users and their HCPs can use to track insulin administration and blood glucose levels. The data are encrypted and protected in compliance with the International Organization for Standardization and the International Electrotechnical Commission (16) (Table 1).

Cambridge Consultants, based in the United Kingdom, has pioneered the KiCoPen, which recently received the prestigious, international Red Dot Award for product design. The pen connects wirelessly to a smartphone app, which tracks the times and amounts of insulin injected and allows users to input glucose levels, exercise regimens, and carbohydrate consumption. The device derives its power not from battery storage, but rather from the kinetic energy of the cap being pulled off of the pen (17) (Table 2).

**Smart Sensors and Attachments for Insulin Pens**

YpsoMed’s YpsoMate SmartPilot is a reusable attachment to the proprietary YpsoMate pen, designed for an easy two-step injection process. The device has a sensor and memory that connects with an app to display injection timing and doses. The sleeve is intended for a single use and is disposable. The emphasis with this product is on injection process; the pen can provide audio and visual feedback to users. The app can also remind users when it is time to inject. When data are shared with an HCP, adherence and injection technique can be assessed—specifically any errors in the handling or administering of the insulin (18) (Table 1).

The features of available smart caps and insulin pen attachments are summarized in Tables 3 and 4.

The GoCap, by Common Sensing, is a device that replaces the caps of SoloStar (Sanofi), KwikPen (Eli Lilly), and FlexPen (Novo Nordisk) insulin pens. The Joslin Diabetes Center is conducting a clinical trial in which the app platform and GoCap devices are provided to a sample of patients using these pens. The primary outcome measure is missed insulin doses (19).

The GoCap app is available for both iPhone and Android users. The cap itself uses light sensors to detect how much insulin remains and has a screen that shows the quantity of insulin in the pen once a dose has been administered and the pen properly recapped. It also shows that the insulin has been administered successfully by displaying a check mark on the screen. The cap can be recharged with the provided micro-USB cable, and its battery lasts for 10 days.

The cap needs to be paired via Bluetooth to the mobile app. The app not only displays the type and time of insulin administration, but also allows users to enter blood glucose levels and meals. Alerts let users know when their next injection should be and whether there are any temperature fluctuations. The information provided can be shared by entering an e-mail address on the app (20) (Table 3).

Timesulin, by Bigfoot Biomedical, is a cap that records the time since the last injection. When the cap has been removed from the pen for 8 seconds, it resets. When the cap is put back on the pen, it begins timing again. The caps are compatible with KwikPen, FlexPen, FlexTouch (Novo Nordisk), and SoloStar insulin delivery devices. The product is meant to minimize extra or missed doses of insulin and can be used for -1 year (21) (Table 3).

Dukada Trio is a cap with novel features that place an emphasis on proper injection technique. The cap is compatible with FlexPen and SoloStar devices. Dukada, a company based in Denmark, has designed the cap to have a flexible grip feature that, when extended, allows for more stability for patients with dexterity problems. The cap also features a light above the needle to improve visibility when injecting. The cap has small lights that illuminate every hour after insulin administration to remind the user when the last dose was injected. According to Dukada, the cap has a replaceable battery that lasts for 6–8 months (22) (Table 3).

InsulCloud, based in Spain, created a product called InsulClock. This is an attachment currently used with the KwikPen, although the company plans to make it available for several major insulin pens, including the FlexTouch, Flexpen, and SoloStar. Unlike the caps, this attachment snaps on to the back of the insulin pen and logs how much insulin is administered on an app available for both iPhone and Android smartphones. Similar to the other apps and devices, the platform shows the type, time, and quantity of insulin administered and can provide users with reminders. The app also reports any temperature fluctuations and allows users to store their food or blood glucose data (23) (Table 4).

Diabnext has made a similar product called Clipsulin. The device is compatible with the majority of pen devices on the market, including the SoloStar, ClikSTAR (Sanofi), KwikPen, Luxura (Eli Lilly), FlexPen, and FlexTouch brands. Clipsulin records the amount of insulin injected. As the user turns the knob to adjust the insulin dose, the device detects the units of insulin being queued for injection, and its LED display shows that number. Once injected, the quantity is transmitted to the app via Bluetooth. Clipsulin uses the Diabnext app available for both iPhone and Android smartphones. Similar to the other platforms, the app allows for long-term blood glucose trending, diet logging, and medication reminders. According to Diabnext, the device’s battery lasts for ~1,800 injections and the device can hold 200 injections in memory (24) (Table 4).

InsulCheck, by the Irish company Innovation Zed Ltd., is a similar attachment that records time elapsed between injections. The green light on the attachment displays after the user
### TABLE 3. Overview of Smart Caps

|                | GoCap               | Timesulin          | Dukada Trio        |
|----------------|---------------------|--------------------|--------------------|
| **Company**    | Common Sensing      | Bigfoot Biomedical | Dukada             |
| **Country of origin** | United States   | United Kingdom     | Denmark            |
| **Year created** | 2013               | 2010               | 2012               |
| **FDA approval** | No                  | No                 | No                 |
| **U.S. availability** | Yes                 | No                 | No                 |
| **Cost**       | $25/month           | $15.72 (~£12)*     | $46 (~ €40)*       |
| **Insulin compatibilities** | SoloStar pens, FlexPen, and KwikPen (2019) pens | KwikPen, FlexPen, FlexTouch, SoloStar pens | FlexPen, SoloStar pens |
| **App service** | Apple, Android      | No                 | No                 |
| **Bluetooth**  | Yes                 | Yes                | No                 |
| **USB**        | Yes                 | No                 | No                 |
| **Features**   | • Displays remaining insulin<br>• App displays type/time of insulin administration<br>• App allows for blood glucose monitoring and meal entry<br>• Lasts 1 year | • Tracks the time since last injection<br>• Battery life of 1 year | • Flexible grip allows for more stability<br>• Has a light above needle for better visibility<br>• Shows time elapsed since last injection |

*Currency conversions conducted on 29 January 2019.

### TABLE 4. Overview of Insulin Pen Attachments

|                | InsulClock | Clipsulin | EasyLog | InsulCheck |
|----------------|------------|-----------|---------|------------|
| **Company**    | InsulCloud | Diabnext  | BioCorp | Innovation Zed, Ltd. |
| **Country of origin** | Spain       | United States | France | Ireland  |
| **FDA approval** | No          | No        | No      | No         |
| **U.S. availability** | No         | No        | No      | No         |
| **Cost**       | $285 (€249)* | ~$40     | <$50    | ~$32       |
| **Insulin compatibilities** | KwikPen, FlexTouch, SoloStar pens | SoloStar pens, ClikSTAR, KwikPen, Luxura, FlexPen, FlexTouch | Unable to verify FlexPen, KwikPen, SoloStar pens, NovoPen 3/4/5/Echo, Luxura HD, Savvio, ClikSTAR |
| **App service** | Apple, Android | Apple, Android | Unable to verify | No |
| **Bluetooth**  | Yes        | Yes       | Yes     | No         |
| **USB**        | No         | No        | No      | No         |
| **Features**   | • Shows the type, time, and quantity of insulin administered<br>• App provides dose reminders, food/glucose input, temperature fluctuations | • Shows the type, time, and quantity of insulin administered<br>• Battery life of 1,800 injections<br>• Memory of 200 injections | • Detects time, date, amount of insulin injected<br>• Alerts patients about missed, extra, and next doses | • Records elapsed time between injections<br>• Green light flashes when dose injected<br>• Temperature sensor<br>• Replaceable battery |

*Currency conversions conducted on 29 January 2019.*
companies have sought to create sensors to
market. Whereas many startup companies
are dynamic in the integration of digital
management.
Ultimately, costs and payor coverage
will likely determine which companies
will become direct competitors with fully
integrated smart insulin pen devices. These
devices have even been tailored to
other conditions such as asthma and
tension, showing that the landscape for chronic disease man-
agement is significantly adapting to new technologies. Smart
connected pens, devices, and attachments may aid in minimizing
the long-term costs and complications of diabetes and improve
diabetes care overall.

Duality of Interest
D.K.P. has been a consultant to and serves
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N.A.S., T.D.A., and D.K.P. all equally
researched, wrote, and edited the manu-
script. All three authors are the guarantors
of this work and, as such, had full access to
all of the research and take responsibility for
the integrity and accuracy of the informa-
tion presented.

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Discussion
This brief article illustrates a changing
dynamic in the integration of digital
health technologies in the insulin pen
market. Whereas many startup com-
panies have sought to create sensors
that attach to insulin pens or other
devices that work with insulin cartri-
ges for patient dosing and management,
the past few years have seen a shift
within the pharmaceutical sphere.
Currently, insulin manufacturers,
including but not limited to Eli Lilly,
Sanofi, and Novo Nordisk, appear
true to be expanding their interest in this
area and creating their own systems
and products that may either integrate with
current companies in this arena
(based on previous investments) or
become direct competitors with fully
integrated smart insulin pen devices.
Ultimately, costs and payor coverage
will likely determine which compa-
nies will emerge as the main players in
the digital health sphere for diabetes
management.

In summary, the development of
new pens, caps, and attachments for
insulin delivery holds great promise
for improving diabetes management.
These devices may offer the potential
for improved adherence, adminis-
tration, and quality of care. Smart
devices have even been tailored to
other conditions such as asthma and
tension, showing that the landscape for chronic disease man-
agement is significantly adapting to
new technologies. Smart connected
pens, devices, and attachments may
aid in minimizing the long-term costs
and complications of diabetes and improve
diabetes care overall.
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