

REVIEW

Advantages and disadvantages of connected insulin pens in diabetes management

Kathryn Lingen¹, Talia Pikounis¹, Natalie Bellini² and Diana Isaacs^{1,3} ¹Close Concerns, San Francisco, California, USA²University Hospitals, Cleveland, Ohio, USA³Cleveland Clinic, Cleveland, Ohio, USACorrespondence should be addressed to D Isaacs: ISAACSD@ccf.org

Abstract

Insulin administration remains vital to the treatment of diabetes and although there have been advances in insulin delivery, evidence suggests that many people with diabetes on insulin therapy have suboptimal glycemic management. Recent advancements in insulin administration techniques include connected insulin devices, such as connected insulin pens and pen caps. In this review, we provide an overview of the literature on the use of connected insulin pens and pen caps to further elucidate the clinical benefits and drawbacks of these devices. We discuss the development of these devices, outlining the characteristics of insulin pens and pen caps with regulatory approvals. These devices have different features that can ease the burden of diabetes management, including automatic recording of insulin dose information, tracking of insulin-on-board, bolus calculators, and missed dose alerts. Despite the advantages of connected pens and pen caps, a small percentage of insulin users are currently using these devices, due to many factors, including lack of health-care professional awareness, initial training for prescribers, and setup of the device. Overcoming these barriers and publishing more data demonstrating the glycemic outcomes associated with these systems could improve diabetes management for people living with diabetes. As health-care systems become increasingly digital, connected insulin pens have the potential to allow a data-driven approach to diabetes management for people who are not interested in, cannot afford, or do not have intensive insulin regimens that might warrant use of insulin pumps or automated insulin delivery systems.

Key Words

- ▶ pens
- ▶ connected
- ▶ pen caps
- ▶ insulin
- ▶ smartpen

Endocrine Connections
(2023) 12, e230108

Introduction

Brief history of insulin pens and evolution to connected pens

Every person with type 1 diabetes requires insulin to live. Many people with type 2 diabetes also require insulin to achieve glycemic targets due to the progressive nature of the condition. For most people living with diabetes, insulin administration largely occurs through subcutaneous injections via insulin pens. However, the original method of administering insulin, which was used to deliver the first doses of insulin in 1922, occurred via syringes, needles, and glass vials of insulin. This original

injection method confers poor accuracy and a lack of discretion for people with diabetes (1, 2). Despite the advent of insulin over a century ago, it was only in the last 40 years that delivery via insulin pens rose in popularity, with approximately 60% of global insulin users using pens today (1, 3, 4, 5). Although pen usage varies country by country (6), insulin pens have numerous advantages over traditional vial and syringe injections, as they confer ease of use, improved accuracy, and enhanced quality of life for people with diabetes (7, 8). Insulin pens combine the vial and syringe into a single device and allow convenient push-button injections. Insulin pen usage has

also been demonstrated to be correlated with decreased frequency of hypoglycemia events (9) and increased injection frequency compared to those using the vial and syringe method (10). The American Diabetes Association's 2023 Standards of Care state that insulin pens are 'preferred in most cases' compared to vials and syringes (11). However, the 2023 American Diabetes Association (ADA) Standards of Care also emphasize the importance of individual preference for people with diabetes, stating that cost, insulin type, dosing therapy, and self-management capabilities should all be considered when choosing an insulin delivery system (11).

All major insulin manufacturers produce insulin pens. The pens can be classified as either reusable or disposable pens. The reusable pens require the user to load the pen with prefilled insulin cartridges. The disposable pens have a prefilled insulin cartridge preinstalled in the pen and the entire product is discarded once the cartridge is used. These pens vary in size and dosage, with dosing increments ranging from half-units to 2 units and maximum doses per injection varying from 30 units to 160 units. There have been a large number of clinical trials on the efficacy, safety, and clinical outcomes related to these pens (6). Overall, both disposable and reusable pens have been found to be easier, more discreet, and preferred by a majority of people with both type 1 and type 2 diabetes, their caregivers, and health-care providers (12, 13, 14, 15).

Further insulin pen innovation has occurred over the last few years leading to the invention of connected insulin pens and pen caps. These devices combine additional technology features like dose tracking and dose calculations with the established accuracy of insulin pens (6). This review will discuss the types of available connected insulin pens and pen caps, including the scientific research studies and the clinical implications of these devices.

Background on connected insulin pens and pen caps

Connected insulin pens are insulin pens that can record and/or transmit data about insulin doses, whereas connected insulin pen caps are devices placed on existing insulin pens, providing dose calculations and/or transmitting data. These devices have various features, but all currently available connected insulin pens can transmit data via Bluetooth or near-field communication (NFC) to mobile apps. The first connected pens were simpler than many on the market today. Lilly launched the first insulin pen with a memory function, the HumaPen®

Memoir, in 2007. Novo Nordisk followed with the launch of NovoPen® Echo in 2009, which also had dose memory capabilities. Further innovation continued, with modern-day connected insulin pens and pen caps able to track and transmit insulin dose information automatically to mobile apps and data portals. These pens and pen caps can help people with diabetes calculate real-time insulin dosing information and many keep track of active insulin-on-board to avoid stacking of insulin when correcting a high glucose level. They can enable accurate sharing of dosing data with users' health-care teams, without the need for traditional dose logbooks. This secure data sharing allows health-care professionals to retrospectively review insulin data, including dose timing and, with some devices, dosage specifics and glucose data. The ADA's 2023 Standards of Care recommend connected insulin pens as an option for people with diabetes on injectable insulin therapy, and the guidelines state that their use can be helpful for diabetes management in those on injectable therapy (11).

Connected insulin devices can help overcome some of the challenges associated with insulin injections. People with diabetes treated with multiple daily insulin injections (MDI) must utilize numeracy skills to calculate their insulin doses, which has been found to frequently be done incorrectly, leading to dosing errors that can negatively impact glycemic outcomes. Without access to data on the timing and dosage of previous injections, it can also be difficult for people with diabetes to avoid 'stacked' doses and hypoglycemia (16). Connected insulin pens also can help people with diabetes treated with MDI remember to take an insulin dose at a certain time, reducing the number of missing or late doses that pose a significant challenge in diabetes management. Studies investigating people with diabetes on MDI found that missing only two meal-bolus doses of insulin a week is associated with a 0.4% increase in A1c (17, 18), demonstrating the importance of correct and timely mealtime insulin boluses. Connected insulin pens and caps have the possibility to overcome these barriers that people with diabetes on MDI therapy deal with every day. Studies conducted in Sweden and the USA have also found that connected insulin pens are associated with lower health-care costs (19, 20).

Connected insulin pens

Connected insulin pens are sometimes also referred to as 'smart' pens. Some devices provide reminders to bolus and can help calculate correct doses, allowing

people with diabetes to make informed insulin dose adjustments (see [Table 1](#) for a complete list of connected insulin pens with regulatory approvals). In 2017, Companion Medical's InPen was the first connected insulin pen to receive FDA clearance and was bought by Medtronic in 2020. InPen includes an FDA-cleared bolus calculator (21). Following InPen, other companies have entered the market with connected insulin pens, including Novo Nordisk's NovoPen® and Emperra's ESYSTA® pens. However, neither is available in the USA at this time. The pens outlined in [Table 1](#) have varying features, including the ability to recommend doses, remind users of missed doses, track an estimated 'insulin on board', which allows users to avoid stacking of insulin, and/or provide alerts for extreme temperature exposures that are dangerous for insulin stability (22). Some connected insulin pen systems, like InPen, can also integrate data from blood glucose monitors (BGM) and continuous glucose monitors (CGM), allowing users and health-care teams to view more information on the correlation between dosing behavior and glycemic management. In addition, the integration of glucose data allows the connected pen systems with dose calculators to make more informed insulin dosage recommendations by utilizing glucose data. These connected pen features are useful for both people with diabetes and their health-care teams in improving glycemic management via informed therapeutic decisions and more personalized recommendations. The reports containing this integrated dosing data are valuable to review to make therapy changes.

Connected pen caps

Connected insulin pen caps include a separate attachment to nonconnected insulin pens. These pen caps typically attach to the top or side of the insulin pen and display information about the insulin in the pen and integrate some insulin-related information within a Bluetooth-connected mobile app. The first connected pen cap, Bigfoot Biomedical's Bigfoot Unity, was FDA cleared in May 2021. The pen cap screen provides *recommended* insulin doses based on glucose data from Abbott's FreeStyle Libre 2 CGM, but does not record the *actual* dose of insulin a user takes (23). Other connected pen caps include Biocorp's Mallaya (24) and Lilly's Tempo Button (25). The Lilly Tempo Button also can integrate with Apple Health to incorporate physical activity into the data reports, and has education embedded in the mobile app. It also has a feature

that provides an estimated carbohydrate count of a picture of food to help a user calculate their meal-time insulin dose. See [Table 1](#) for more information on device features, compatibility, and availability for connected pen systems.

Scientific literature

Although more connected pen systems are entering the market, there remain few clinical studies investigating the outcomes of these devices. A Pubmed search was performed to determine any relevant articles including connected pens, connected pen caps, smart pens, or smart pen caps. To our knowledge, the first connected pen system clinical study was published in 2020 (26). Since then, eight clinical studies have been published ([Table 2](#)). Of the eight studies included in [Table 2](#), three are based on Novo Nordisk's NovoPen 6 (6), two investigate Medtronic's InPen (20, 28), two use the Insulclock pen (29, 30), and one investigates Bigfoot's Bigfoot Unity Diabetes Management System (31).

The published connected pen clinical studies utilize a range of methods, including observational proof-of-concept studies, randomized crossover pilot studies, and retrospective real-world analyses. Notably, there are no large, multicenter randomized control trials comparing connected pens or pen caps to vial and syringes or disposable insulin pens. Across all study types, these early studies show that connected pen systems are linked to higher time in range (26, 28, 30, 31), reductions in A1c (29, 31), reductions in severe hypoglycemia (20, 26), reductions in missed insulin doses (26, 28, 29, 30), and are a source of cost savings compared to standard insulin injections (nonconnected insulin pens or syringes) (19, 20). Eckberg *et al.* demonstrated that each missed basal insulin dose was associated with poorer glycemic management (27), illustrating that the dosage reminders from connected pen systems alone have the potential to improve glycemic outcomes. For more information on study design, type of insulin used, and results, see [Table 2](#). A more detailed clinical trials table is included in the Appendix (see section on [supplementary materials](#) given at the end of this article).

Clinical implications of connected insulin devices

Despite the advantages of connected pens and pen caps, a small percentage of insulin users are currently using

Table 1 Available Connected Pen and Pen Caps.

Device – company	Device features	Dose tracking	Dose calculating	GLP-1	Connectivity and integration	Mobile app features	Insulin compatibility	Availability
Available in the USA and internationally (FDA approved and CE marked)								
InPen – Medtronic (21)	<ul style="list-style-type: none"> Reusable pen that lasts 1 year Monitors insulin temperature Bluetooth pairs to smartphone app Tracks actual insulin dose and timing Reusable, with replaceable battery Smart pen cap 	x	x		Integrated with Dexcom, Medtronic CGMs View data via Insights Report or Medtronic's Carelink portal	<ul style="list-style-type: none"> iOS and Android Integrated bolus calculator Manually long-acting insulin doses and can set up basal and bolus dose reminders 	NovoLog, Humalog, Fiasp Cartridge only	FDA-cleared for type 1 or type 2 diabetes CE marked
InsulCheck Connect –Innovation Zed (34)	<ul style="list-style-type: none"> Reusable, rechargeable with seven to ten day battery life Smart pen cap Captures temperature and mounting data 	x			N/A	<ul style="list-style-type: none"> Compatible with diabetes mobile apps 	Compatible with Lilly's HumaPen Luxura and KwikPens; Novo Nordisk's FlexPen, NovoPen 3, and NovoPen 4; and Sanofi Aventis	CE marked FDA-cleared class 1 medical device
InsulCheck DOSE –Innovation Zed (34)	<ul style="list-style-type: none"> Reusable, rechargeable with seven to ten day battery life Smart pen cap Captures temperature and mounting data 	x			N/A	<ul style="list-style-type: none"> Compatible with diabetes mobile apps 	Compatible with Lilly's HumaPen Luxura and KwikPens; Novo Nordisk's FlexPen, NovoPen 3, and NovoPen 4; and Sanofi Aventis	CE marked FDA-cleared class 1 medical device
Mallya – Biocorp (24)	<ul style="list-style-type: none"> Reusable smart cap for disposable pens, lasts 2 years Two-piece cap with one piece clipped to top of pen and second piece over the control dial/button Pen cap USB rechargeable; needs recharge approximately once a month Sends dose, time, and date to app via Bluetooth Cap-specific versions for SoloStar, FlexPen, and KwikPen 	x		x	Data sharing partnership with DreaMed to send insulin dosing data to MDI/basal-only Advisor Pro clinical decision support system	<ul style="list-style-type: none"> iOS Sends dose reminders and alerts Records dose, time, and date 	SoloStar (LantusToujeo, Admelog, Apidra, Soliqua), KwikPen, FlexPen	FDA cleared for type 1 or type 2 diabetes CE marked

(Continued)



Table 1 Continued.

Device - company	Device features	Dose tracking	Dose calculating	GLP-1	Connectivity and integration	Mobile app features	Insulin compatibility	Availability
Tempo Smart Button and Pen - Eli Lilly (25)	<ul style="list-style-type: none"> Works with Lilly Tempo pens (Basaglar, Humalog, Lyumjev) Reusable Tempo Smart Button attaches to top of disposable Tempo Pen for data transfer via Bluetooth Tempo button battery lasts 8 months Button for both basal and bolus insulin doses Tracks insulin dose, timing, and type of insulin delivered 	x	x ^a		<p>Compatible with Dexcom CGMs or BGM</p> <p>Data integration with Roche (mySugr), Glooko, myDiabby, Dexcom apps</p> <p>Sync data with wearable devices (Fitbit, Garmin, Google Fit, Apple Health)</p> <p>View data in Tempo Insights Portal</p>	<ul style="list-style-type: none"> iOS and Android Tracks insulin dose Sends dosing reminders Monitors carb intake (can take picture of food and estimates carbs) and fitness activities App titrates basal, bolus, and basal + bolus In the USA, private label iteration of WellDoc's BlueStar app (titrates basal, bolus, and basal + bolus) Shares data with HCPs through clinician hub Tempo Insights 	Tempo Pens Basaglar 100 units/mL, Humalog 100 units/mL, and Lyumjev 100 units/mL	FDA cleared for type 1 or for type 2 diabetes CE marked
Available in the USA only (FDA approved)								
Bigfoot Unity - Biomedical (23)	<ul style="list-style-type: none"> Reusable smart cap for disposable and durable insulin pens White-colored insulin pen caps fits over rapid-acting insulin pens; black-colored insulin pen caps fit over long-acting insulin pens Rapid-acting pen cap uses data from Abbott's FreeStyle Libre 2 CGM to generate dose recommendations shown on cap's display; option to use blood glucose meter linked to an app to inform dose recommendations Sends insulin dose data to Bluetooth-paired smartphone app Track insulin dose time, temperature, and recommended dose 	x ^b	x		<p>Integrated with Abbott FreeStyle Libre 2 (FSL 2)</p> <p>View data in Bigfoot Clinic Hub Portal</p>	<ul style="list-style-type: none"> iOS and Android Real-time hypo alerts and can see glucose range/trends overtime from FSL 2 Notifies the user of potential missed doses 	Rapid-acting KwikPen Humalog (U-100 and U-200), Lispro, Lyumjev (U-100 and U-200); SoloSTAR: Apidra, Admelog; FlexTouch: Fiasp (U-100); FlexPen: NovoLog (U-100), ReliOn NovoLog (U-100), Aspart (U-100), Aspart Long-acting KwikPen: Basaglar; SoloSTAR: Lantus, Toujeo (U-300), Toujeo Max (U-300); FlexTouch: Tresiba (U-100 and U-200)	FDA cleared for type 1 or type 2 diabetes

(Continued)



Table 1 Continued.

Device – company	Device features	Dose tracking	Dose calculating	GLP-1	Connectivity and integration	Mobile app features	Insulin compatibility	Availability
Available internationally only (CE marked) ESYSTA – Emperra (35)	<ul style="list-style-type: none"> Reusable for 1 year Smart pen displays last dose, automatic transfer of insulin doses 	x			Beurer GL50 evo and GlucoCheck Gold BGMs	<ul style="list-style-type: none"> iOS and Android 	Lilly's Kwikpen, Novo Nordisk's Flextouch, and Sanofi's Solostar	CE marked
InsulClock – InsulClock (30)	<ul style="list-style-type: none"> Reusable for 5 years. Battery charge lasts 3 days with 1.5 h of charge via USB Smart cap tracking dose, time, and type of insulin Monitors insulin storage temperature 	x			Integrates with Dexcom CGMs	<ul style="list-style-type: none"> iOS and Android Allows for meal and exercise tracking Monitors insulin storage temperature 	Lilly's Kwikpen, Novo Nordisk's Flextouch, and Sanofi's Solostar	CE marked
NovoPen 6 – Novo Nordisk (36)	<ul style="list-style-type: none"> Reusable pen; 800-dose memory, 5-year battery life Last insulin dose and time of injection on end of pen Compatible with both basal and bolus insulin Adjustments of 1 U increments with 60 U max dose NFC connectivity 	x			Data integration with Abbott, Roche, Glooko, Dexcom apps	<ul style="list-style-type: none"> Connects to compatible iOS and android diabetes apps (Glooko, Abbott's FreeStyle LibreLink, mySugr, Dexcom Clarity) Sends insulin dose info to preferred diabetes app and shares with HCP Local app integrators in select markets (Japan: Health2Sync, Arkray; France: myDiabby, Glooko XT; Denmark, UK, Switzerland, Ireland, France, Luxembourg, Malta: Hedia) 	<ul style="list-style-type: none"> Levemir, Xultophy, Tresiba, NovoLog, Fiasp Cartridge only 	CE marked

(Continued)



Table 1 Continued.

Device - company	Device features	Dose tracking	Dose calculating	GLP-1	Connectivity and integration	Mobile app features	Insulin compatibility	Availability
NovoPen Echo Plus - Novo Nordisk (37)	<ul style="list-style-type: none"> Reusable pen; 800-dose memory, 5-year battery life Last insulin dose and time of injection on end of pen Compatible with both basal and bolus insulin Adjustments of 0.5 U increments with 30 U max dose NFC connectivity 	x			Data integration with Abbott, Roche, Glooko, Dexcom apps	<ul style="list-style-type: none"> Connects to compatible iOS and android diabetes apps (Glooko, FreeStyle Abbott's LibreLink, mySugr, Dexcom Clarity) Sends insulin dose info to preferred diabetes app and shares with HCP Local app integrators in select markets (Japan: Health2Sync, Arkray; France: myDiabby, Glooko XT; Denmark, UK, Switzerland, Ireland, France, Luxembourg, Malta: Hedia) 	Levemir, Tresiba, NovoLog, Fiasp Cartridge only	CE marked
YpsoMate On - Ypsomed (38)	<ul style="list-style-type: none"> Single use Connected smart insulin pen with prefilled autoinjector 	x			N/A	<ul style="list-style-type: none"> Bluetooth connectivity to Ypsomed mobile app 	Ypsomed Ypsomate insulin pens Cartridge only	CE marked
SmartPilot - Ypsomed (39)	<ul style="list-style-type: none"> Reusable, no charge required Smart cap tracking dose, time, and authenticates insulin Provides audio and visual feedback of dosing technique 	x			N/A	<ul style="list-style-type: none"> Bluetooth connectivity to Ypsomed mobile app 	Ypsomed YpsoMate insulin pens Cartridge only	Not yet CE marked

^aTitration feature only available in the USA; ^bOnly tracks that a dose was given, not the details of the actual dose. X, insulin device has insulin dose tracking and/or calculates insulin dose



Table 2 Connected Pens – Clinical Studies.

Study, year	Device	Sample size	Type 1 or type 2 diabetes	Type of trial	Primary outcome	Secondary outcome
Adolfsson (2020) (26)	NovoPen 6	94	T1D	Prospective, proof-of-concept study	Time in range ($P < 0.001$)	Missed bolus doses ($P = 0.1352$), time above range ($P = 0.003$), time below range ($P = 0.005$)
Gomez-Peralta (2020) (30)	Insulclock	16	T1D	Randomized pilot study	Time in range ($P = 0.038$)	Missed bolus doses, time above range ($P = 0.0026$), time below range
Jendle (2021) (19)	NovoPen 6	94	T1D	Prospective, proof-of-concept study (continuation of Adolfsson <i>et al.</i> 2020)	Cost-effectiveness, time in range	Mortality, quality of life, time above range, time below range
Vigersky (2021) (28)	InPen	529	T1D or T1D	Observational study	Time in range ($P < 0.05$)	Time above range, time below range, total insulin doses (all $P < 0.05$)
Ekberg (2022) (27)	NovoPen 6	32	T1D	Prospective, proof-of-concept study	Missed bolus doses ($P < 0.001$)	Time in range ($P = 0.005$), time above range ($P = 0.002$), time below range (ns)
Galindo (2023) (29)	Insulclock	80	T2D	Randomized, crossover pilot	Missed bolus doses (ns)	A1c ($P = 0.006$), mean glucose ($P < 0.01$), treatment satisfaction (ns)
Chien (2023) (20)	InPen	1681	T1D or T2D	Retrospective, real-world analysis	Number of severe hypoglycemia episodes ($P = 0.008$)	Cost savings
Baliga (2023) (31)	Bigfoot Unity	58	T1D or T2D	Retrospective, real-world analysis	Alc ($P < 0.001$)	Time in range ($P < 0.05$), time above range ($P < 0.05$), time below range, average glucose ($P < 0.05$)

these devices. There are multiple reasons for this. Because they are newer treatment options, many health-care professionals simply are not aware of this technology or how to go about obtaining it for their patients. For example, there may be uncertainty about what pieces and parts need to be sent to the pharmacy. In many cases, this includes the device, the insulin (cartridge or disposable pen), and pen needles. Some connected pens and pen caps do not go through the traditional pharmacy route. For example, Bigfoot Unity was initially only available through direct contracts with the company and a reimbursement model that relied on remote physiologic monitoring. As with any new product or device, insurance coverage can initially be limited. For this reason, many companies have cost-savings programs, however, prescribers and patients may not always be aware of these programs. Another important consideration is that each device has different insulins it is compatible with. For example, the manufacturer-specific devices usually only work with their company's specific insulins. Some only work with bolus insulin, such as

Medtronic's InPen, while others can work with basal and bolus insulins.

A second barrier is the initial education, training, and setup of the device. While connected pen systems are generally intuitive and easy for people with diabetes to use, any devices with dose calculators require users and/or HCPs to enter initial settings like a carbohydrate ratio, insulin sensitivity factor, insulin action time, and glucose target. Often, the doses a person was previously using with traditional pens can be used. For HCPs calculating doses for a connected pen system, Table 3 outlines some formulas that can be helpful when creating the settings. These formulas are just estimates and often doses need to be titrated more frequently in the initial weeks after starting insulin therapy. Additional barriers include prescriber's lack of knowledge of the connected pen systems and inability to interpret reports to adjust insulin doses. Some reports like the InPen report include a long-acting insulin assessment to provide guidance on how to adjust the long-acting insulin dose (21). However, studies show despite this feature, HCPs often

Table 3 Methods to Calculate Connected Pen Settings.

Setting	Explanation/calculation	Considerations
Total daily dose (TDD)	Use one of the following: Total daily dose of mealtime + long-acting insulin Or weight based: Weight (kg) × 0.5 Weight (lb) × 0.23	If consistent hypoglycemia, use lower amount If consistent hyperglycemia, use higher amount Can also average the results of the two calculations
Insulin carbohydrate ratio	450 or 500 ÷ TDD	These are starting points and should be adjusted based on CGM or BGM readings
Insulin sensitivity factor (correction factor)	1700 or 1800 ÷ TDD	These are starting points and should be adjusted based on CGM or BGM readings
Active insulin time or insulin on board	Usually set between 3 and 5 h Children, pregnancy: 3 h Older adults, impaired renal function: 5 h Most adults: 4 h	Based on the duration of action of rapid-acting insulin
Maximum bolus	Maximum amount delivered at one time	Safety precaution

Source: Warsaw (2020) (40); Grunberger (2014) (41).
BGM, blood glucose meter; CGM, continuous glucose monitor; TDD, total daily dose.

do not change a person’s dose (32). This could be related to not understanding this feature of the report or not being sure how to make an appropriate therapy change based on the data.

Some people with diabetes choose not to use these devices because they like the enhanced technology offered by insulin pumps, which often can pair directly with CGM to automate background insulin delivery, therefore achieving a higher time in range compared to insulin pens. However, there are numerous reasons why people may not want to be or may not be able to be on an insulin pump. These reasons include cost, lack of access, and lack of coverage for people with type 2 diabetes, along with the fact that there is a subset of people that do not like being attached to an insulin pump all the time and prefer pens. There are also people using insulin pumps that occasionally want a pump break, in which connected pens and pen caps can be a great alternative. Some also use connected insulin pen systems as a back up to their insulin pump in case of failure.

Future directions

As data becomes more available, there are many exciting future directions for connected pens and pen caps. The integration with CGM could allow for incorporation of trend arrows into dose calculators to increase or decrease recommended insulin doses for more precise insulin delivery. Meal detection technology, that detects when glucose starts to rise or can identify the act of eating through a smart watch to alert someone to bolus would be helpful. Other features could include an automatic

dose advisor if glucose is elevated. Current CGM systems have customized high and low alerts, but often people do not know how to act on the high alert. An automatic recommended dose based on previous insulin and glucose trends, may further improve time in range and place less burden on the patient to remember to use their bolus calculator to manually enter in the glucose numbers. Other potential features like weight based set up, as is available with the iLet insulin pump (33), could make start-up easier for people with diabetes and their HCPs. Integration with other types of data like sleep length and quality, nutrition, physical activity and screen time could also be helpful, along with using artificial intelligence to make personalized recommendations.

Within mobile apps, offering new features like more targeted education, gamification of the learning, and peer support in the form of moderated discussion boards or chats are all potential directions this technology could go.

Conclusion

Since the first insulin injection in 1922, the primary method of insulin administration remains injections. While this started with vials and syringes, insulin pens are more commonly used today. In the past 10 years, connected insulin pens and caps have allowed insulin users to track their dosing and time of injections. Connected devices hold all the benefits of traditional insulin pens – improved safety, convenience, and precision – while also offering users connectivity and the ability to track timing and dosing of insulin.

These pens can improve outcomes, by reducing dosing errors and optimizing insulin delivery. While there are few clinical studies evaluating the long-term outcomes of these devices, connected insulin pens and pen caps have the potential to allow people with diabetes on MDI to leverage the advantages of technology to deliver the right dose at the right time. These connected insulin devices can provide continuous insulin data transmission and have the potential to positively impact diabetes outcomes by allowing diabetes care teams to make more informed, data-driven treatment decisions for people on MDI.

Supplementary materials

This is linked to the online version of the paper at <https://doi.org/10.1530/EC-23-0108>.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector. Diana Isaacs is a speaker for Medtronic, Dexcom, and Abbott Diabetes. Natalie Bellini is a speaker for Abbott Diabetes. Kathryn Lingen and Talia Pikounis are employed by Close Concerns, a for-profit company that is funded by a number of diabetes therapeutic and technology companies.

References

- Kesavadev J, Saboo B, Krishna MB & Krishnan G. Evolution of insulin delivery devices: from syringes, pens, and pumps to DIY artificial pancreas. *Diabetes Therapy* 2020 **11** 1251–1269. (<https://doi.org/10.1007/s13300-020-00831-z>)
- Selam JL. Evolution of diabetes insulin delivery devices. *Journal of Diabetes Science and Technology* 2010 **4** 505–513. (<https://doi.org/10.1177/193229681000400302>)
- Rex J, Jensen KH & Lawton SA. A review of 20 year' experience with the Novopen family of insulin injection devices. *Clinical Drug Investigation* 2006 **26** 367–401. (<https://doi.org/10.2165/00044011-200626070-00001>)
- Perfetti R. Reusable and disposable insulin pens for the treatment of diabetes: understanding the global differences in user preference and an evaluation of inpatient insulin pen use. *Diabetes Technology and Therapeutics* 2010 **12**(Supplement 1) S79–S85. (<https://doi.org/10.1089/dia.2009.0179>)
- Marcus A. Diabetes care – insulin delivery in a changing world. *Medscape Journal of Medicine* 2008 **10** 120.
- Masierek M, Nabrdalik K, Janota O, Kwiendacz H, Macherski M & Gumprecht J. The review of insulin pens—past, present, and look to the future. *Frontiers in Endocrinology* 2022 **13** 827484. (<https://doi.org/10.3389/fendo.2022.827484>)
- Coscelli C, Lostia S, Lunetta M, Nosari I & Coronel GA. Safety, efficacy, acceptability of a pre-filled insulin pen in diabetic patients over 60 years old. *Diabetes Research and Clinical Practice* 1995 **28** 173–177. ([https://doi.org/10.1016/0168-8227\(95\)01092-R](https://doi.org/10.1016/0168-8227(95)01092-R))
- Summers KH, Szeinbach SL & Lenox SM. Preference for insulin delivery systems among current insulin users and nonusers. *Clinical Therapeutics* 2004 **26** 1498–1505. (<https://doi.org/10.1016/j.clinthera.2004.09.009>)
- Asche CV, Luo W & Aagren M. Differences in rates of hypoglycemia and health care costs in patients treated with insulin aspart in pens versus vials. *Current Medical Research and Opinion* 2013 **29** 1287–1296. (<https://doi.org/10.1185/03007995.2013.825590>)
- Grabner M, Chu J, Raparla S, Quimbo R, Zhou S & Conoshenti J. Clinical and economic outcomes among patients with diabetes mellitus initiating insulin glargine Pen versus Vial. *Postgraduate Medicine* 2013 **125** 204–213. (<https://doi.org/10.3810/pgm.2013.05.2656>)
- ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, *et al.* Diabetes technology: standards of care in diabetes—2023. *Diabetes Care* 2023 **46**(Supplement_1) S111–S127. (<https://doi.org/10.2337/dc23-S007>)
- Korytkowski M, Bell D, Jacobsen C, Suwannasari R & FlexPen Study Team. A multicenter, randomized, open-label, comparative, two-period crossover trial of preference, efficacy, and safety profiles of a prefilled, disposable pen and conventional vial/syringe for insulin injection in patients with type 1 or 2 diabetes mellitus. *Clinical Therapeutics* 2003 **25** 2836–2848. ([https://doi.org/10.1016/S0149-2918\(03\)80337-5](https://doi.org/10.1016/S0149-2918(03)80337-5))
- Ignaut DA, Schwartz SL, Sarwat S & Murphy HL. Comparative device assessments: Humalog KwikPen compared with vial and syringe and FlexPen. *Diabetes Educator* 2009 **35** 789–798. (<https://doi.org/10.1177/0145721709340056>)
- Campos C, Lajara R & Deluzio T. Usability and preference assessment of a new prefilled insulin pen versus vial and syringe in people with diabetes, physicians and nurses. *Expert Opinion on Pharmacotherapy* 2012 **13** 1837–1846. (<https://doi.org/10.1517/14656566.2012.713350>)
- Pfützner A, Bailey T, Campos C, Kahn D, Ambers E, Niemyer M, Guerrero G, Klonoff D & Nayberg I. Accuracy and preference assessment of prefilled insulin pen versus vial and syringe with diabetes patients, caregivers, and healthcare professionals. *Current Medical Research and Opinion* 2013 **29** 475–481. (<https://doi.org/10.1185/03007995.2013.775112>)
- Schmidt S & Nørgaard K. Bolus calculators. *Journal of Diabetes Science and Technology* 2014 **8** 1035–1041. (<https://doi.org/10.1177/1932296814532906>)
- Zaugg SD, Dogbey G, Collins K, Reynolds S, Batista C, Brannan G & Shubrook JH. Diabetes numeracy and blood glucose control: association with type of diabetes and source of care. *Clinical Diabetes* 2014 **32** 152–157. (<https://doi.org/10.2337/diaclin.32.4.152>)
- Randløv J & Poulsen JU. How much do forgotten insulin injections matter to hemoglobin A1c in people with diabetes? a simulation study. *Journal of Diabetes Science and Technology* 2008 **2** 229–235. (<https://doi.org/10.1177/193229680800200209>)
- Jendle J, Ericsson Å, Gundgaard J, Møller JB, Valentine WJ & Hunt B. Smart insulin pens are associated with improved clinical outcomes at lower cost versus standard-of-care treatment of Type 1 diabetes in Sweden: a cost-effectiveness analysis. *Diabetes Therapy* 2021 **12** 373–388. (<https://doi.org/10.1007/s13300-020-00980-1>)
- Chien A, Thanasekaran S, Gaetano A, Im G, Wherry K, MacLeod J & Vigersky RA. Potential cost savings in the United States from a reduction in sensor-detected severe hypoglycemia among users of the InPen smart insulin pen system. *Journal of Managed Care and Specialty Pharmacy* 2023 **29** 285–292. (<https://doi.org/10.18553/jmcp.2023.22283>)
- Companion Medical. InPen system. *Instructions for use*. Minneapolis, MN, USA: Medtronic, 2023. (available at: <https://www>)

- medtronicdiabetes.com/sites/default/files/library/download-library/user-guides/InPen-user-guide.pdf
- 22 Sangave NA, Aungst TD & Patel DK. Smart connected insulin pens, caps, and attachments: a review of the future of diabetes technology. *Diabetes Spectrum* 2019 **32** 378–384. (doi:[10.2337/ds18-0069](https://doi.org/10.2337/ds18-0069)).
 - 23 Bigfoot Biomedical. Bigfoot Unity™ diabetes management system. Milpitas, CA, USA: Bigfoot Biomedical, 2023. (available at: <https://www.bigfootbiomedical.com/bigfoot-unity>)
 - 24 Biocorp. Instructions for use Mallya. Issoire, Auvergne, France: Biocorp, 2021. (available at: https://my-mallya.com/wp-content/uploads/2021/01/IFU_MAL_EN_V9_210319.pdf)
 - 25 Eli Lilly. Instructions for use (Tempo Smart Button). Indianapolis, IN, USA: Eli Lilly, 2023. (available at: <https://pi.lilly.com/us/tempo-smart-button-ug.pdf>)
 - 26 Adolfsson P, Hartvig NV, Kaas A, Møller JB & Hellman J. Increased time in range and fewer missed bolus injections after introduction of a smart connected insulin pen. *Diabetes Technology and Therapeutics* 2020 **22** 709–718. (<https://doi.org/10.1089/dia.2019.0411>)
 - 27 Ekberg NR, Hartvig NV, Kaas A, Møller JB & Adolfsson P. Smart pen exposes missed basal insulin injections and reveals the impact on glycemic control in adults with Type 1 diabetes. *Journal of Diabetes Science and Technology* 2022 19322968221104142. (<https://doi.org/10.1177/19322968221104142>)
 - 28 Vigersky R, Smith M, Thanasekaran S, Gaetano A, Heungyong IM, Cordero TL & MacLeod J. 219-OR: impact of inpen smart insulin pen use on real-world glycemic and insulin dosing outcomes in individuals with poorly controlled diabetes. *Diabetes* 2021 **70**(Supplement 1) 219. (<https://doi.org/10.2337/db21-219-OR>)
 - 29 Galindo RJ, Ramos C, Cardona S, Vellanki P, Davis GM, Oladejo O, Albury B, Dhruv N, Peng L & Umpierrez GE. Efficacy of a smart insulin pen cap for the management of patients with uncontrolled Type 2 diabetes: a randomized cross-over trial. *Journal of Diabetes Science and Technology* 2023 **17** 201–207. (<https://doi.org/10.1177/19322968211033837>)
 - 30 Gomez-Peralta F, Abreu C, Gomez-Rodriguez S & Ruiz L. Insulclock: a novel insulin delivery optimization and tracking system. *Diabetes Technology and Therapeutics* 2019 **21** 209–214. (<https://doi.org/10.1089/dia.2018.0361>)
 - 31 Baliga BS, Tillman JB, Olson B, Vaughan S, Sheikh FN & Malone JK. First real-world experience with bigfoot unity: a 6-month retrospective analysis. *Clinical Diabetes* cd220126 1–10. (<https://doi.org/10.2337/cd22-0126>)
 - 32 Smith MB, Gaetano A, Vigersky R, Cordero T & MacLeod J. Abstract #1003586: Smart insulin pens uncover the need for long acting insulin dose optimization in multiple daily insulin therapy. *Endocrine Practice* 2021 **27** S49–S50. (<https://doi.org/10.1016/j.eprac.2021.04.576>)
 - 33 Beta Bionics. iLet® bionic pancreas system user guide. Boston, MA, USA: Beta Bionics, 2023. (available at: <https://www.betabionics.com/resources/user-guides/>)
 - 34 Innovation Zed. Injection pen technology. Dublin, Ireland: Innovation Zed, 2021. (available at: <https://innovationzed.com/research-and-development-projects-draft>)
 - 35 Emperra. Quick user guide ESYSTA. Potsdam, Germany: Emperra, 2016. (available at: https://www.emperra.com/wp-content/uploads/2017/02/ESYSTA_Kurzbedienungsanleitungen_EN.pdf)
 - 36 Novo Nordisk. NovoPen 6 user guide. Bagsværd, Denmark: Novo Nordisk, 2021. (available at: <https://www.novonordisk.com/content/dam/nncorp/global/en/our-products/pdf/instructions-for-use/novopen-6/Novopen6-IR.pdf>)
 - 37 Novo Nordisk. NovoPen Echo Plus user guide. Bagsværd, Denmark: Novo Nordisk, 2021. (available at: <https://www.novonordisk.com/content/dam/nncorp/global/en/our-products/pdf/instructions-for-use/novopen-echo-plus/Novopen-echo-plus-IR.pdf>)
 - 38 Ypsomed. Ypsomate – quick guide. Burgdorf, Switzerland: Ypsomed, 2022. (available at: <https://yds.ypsomed.com/en/products/autoinjectors/ypsomate/ypsomate-quick-guide.html>)
 - 39 Ypsomed. SmartPilot – transforming Ypsomate into a smart product system. Burgdorf, Switzerland: Ypsomed, 2021. (available at: <https://yds.ypsomed.com/en/injection-systems/smart-devices/smartpilot-for-ypsomate.html>)
 - 40 Warshaw H, Isaacs D & MacLeod J. The reference guide to integrate smart insulin pens into data-driven diabetes care and education services. *Diabetes Educator* 2020 **46**(4_suppl) 3S–20S. (<https://doi.org/10.1177/0145721720930183>)
 - 41 Grunberger G, Abelseth JM, Bailey TS, Bode BW, Handelsman Y, Hellman R, Jovanović L, Lane WS, Raskin P, Tamborlane WV, *et al.* Consensus statement by the American Association of Clinical Endocrinologists/American college of endocrinology insulin pump management task force. *Endocrine Practice* 2014 **20** 463–489. (<https://doi.org/10.4158/EP14145.PS>)

Received 26 March 2023

Accepted 22 August 2023

Available online 23 August 2023

Version of Record published 27 September 2023