

Digital Transformation of Insulin Therapy: A Comprehensive Review of Smart Insulin Pens

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Abstract - Diabetes mellitus is a chronic metabolic disorder characterized by persistently high blood glucose levels resulting from impaired insulin production, action, or both. Insulin therapy is essential for individuals with Type 1 diabetes and many with advanced Type 2 diabetes, but maintaining optimal glucose control remains challenging. Common issues include missed injections, dosing errors, incorrect calculations, and poor record-keeping. Smart insulin pens have emerged as digitally enabled devices designed to address these challenges. They automatically record insulin doses, provide reminders, and assist with dose calculations. Many devices integrate with smartphone applications and digital health platforms, enabling data sharing with healthcare providers and compatibility with technologies such as continuous glucose monitoring. Evidence suggests that these features can improve treatment adherence, enhance dose accuracy, and help align insulin administration with glucose trends. This may lead to increased time within target glucose range and a reduction in both hyperglycemic and hypoglycemic events. Additionally, smart pens can support telemedicine and data-driven, personalized treatment decisions. Despite these advantages, limitations include higher costs, technological accessibility barriers, and data privacy concerns. Overall, smart insulin pens represent a significant advancement in diabetes management by combining insulin delivery with digital support to improve safety, precision, and patient engagement.

Key Words: Diabetes mellitus, Smart insulin pens, Insulin therapy, Glycemic control, Digital health.

1. INTRODUCTION

Diabetes Mellitus (DM) is a chronic, progressive metabolic disorder characterized by persistent hyperglycemia resulting from absolute or relative insulin deficiency and/or impaired insulin action. The condition develops through complex interactions between genetic susceptibility and environmental factors. Historically, descriptions resembling diabetes were recorded as early as 1552 B.C. in an Egyptian papyrus, where the disease was described as a rare but severe condition marked by excessive urination, progressive weight loss, and eventual death [1]. Later, ancient Indian physicians Charaka and Sushruta (400–500 BC) identified the characteristic sweetness of urine in affected individuals, an observation that later contributed to the naming of the disease [2]. In modern times, diabetes has emerged as one of the most significant global health challenges. According to the International Diabetes Federation, more than 537 million people worldwide were living with diabetes in 2021, and this number is projected to increase to approximately 783 million by 2045 [3,4].

Among the different forms of diabetes, Type 2 diabetes mellitus is the most prevalent and is characterized primarily by insulin resistance combined with a relative decline in insulin secretion. Persistent hyperglycemia gradually impairs pancreatic β -cell function, leading to progressive deterioration in metabolic control [1]. Insulin resistance involves defects in both hepatic glucose regulation and peripheral glucose utilization, particularly in skeletal muscle, which normally accounts for more than 80% of glucose uptake under insulinized conditions [1]. Even with modern subcutaneous injection techniques, maintaining consistent adherence to insulin therapy can be difficult, particularly when multiple

daily injections are required and doses must be adjusted frequently based on glucose monitoring [5,6]. Because of progressive β -cell failure, insulin therapy eventually becomes necessary for many patients with Type 2 diabetes, while individuals with Type 1 diabetes require insulin for survival due to absolute insulin deficiency [6,7].

Although insulin therapy remains the cornerstone of diabetes management, its clinical effectiveness is often limited by several practical challenges associated with traditional delivery methods. Historically, insulin was administered using syringes and glass vials after its first clinical use in 1922, a system that lacked dosing precision and convenience [5,6]. Studies indicate that adherence to insulin therapy remains suboptimal, influenced by factors such as complex dosing regimens, fear of hypoglycemia, socioeconomic barriers, and injection-related discomfort [6]. For example, data from the T1D Exchange registry show that up to 43% of individuals with Type 1 diabetes miss more than one mealtime insulin dose each week, and between 20% and 45% administer doses at times different from those prescribed [6]. Additional barriers to effective insulin use include disruption of daily routines, financial burden, embarrassment associated with public injections, and challenges in accurately documenting insulin doses and timing [7,8].

These limitations highlight the need for improved insulin delivery systems that can support better adherence, accuracy, and patient engagement in diabetes management. Advances in digital health technologies have opened new opportunities to address these challenges by integrating medication administration with real-time data tracking and clinical decision support [4]. Recent diabetes management guidelines increasingly emphasize the role of digital tools, including

connected devices, remote monitoring systems, and telemedicine, in improving long-term glycemic control [9]. Within this evolving digital ecosystem, smart insulin pens have emerged as an important innovation designed to enhance insulin therapy.

Smart insulin pens are digitally connected injection devices capable of automatically recording insulin dose and injection timing and transmitting this information to mobile applications. These systems can provide dose reminders, assist with bolus calculations, and generate comprehensive clinical reports that support both patients and healthcare professionals in optimizing treatment decisions [3,4]. By integrating insulin delivery data with glucose measurements, meal intake, and physical activity, smart insulin pens contribute to a more coordinated and personalized approach to diabetes management [6].

Although subcutaneous insulin administration remains the standard approach, its invasive nature, injection-associated pain, and reduced patient acceptance have driven research into alternative delivery routes including oral, buccal, sublingual, transdermal, pulmonary, intranasal, ocular, and rectal administration. These approaches aim to improve patient comfort and adherence while maintaining effective glycemic control [20].

Extensive investigation into these non-injectable alternatives illustrates both their promise and their persistent limitations. Oral insulin has been restricted mainly by poor gastrointestinal permeability and rapid enzymatic breakdown, yielding very low bioavailability despite encapsulation and permeation-enhancer strategies. Buccal delivery, exemplified by a rapid-mist spray formulation marketed as Oral-lyn, avoids gastrointestinal degradation but still requires comparatively large doses to reach therapeutic levels. Sublingual tablets such as EGP-1214 have produced a fast, reproducible glucose-lowering effect without irritating the mucosa, although long-term pharmacokinetic data remain limited. Transdermal approaches using iontophoresis, sonophoresis, electroporation, and localized heating devices have improved skin permeability but can cause irritation, underscoring the need for further long-term safety data. Pulmonary delivery has progressed furthest commercially: Exubera reached the market in 2006 but was withdrawn a year later for poor sales, while Afrezza, approved by the FDA in 2014 using Technosphere particle technology, offered a faster-acting and better-tolerated profile with minimal residual lung deposition. Intranasal insulin, aided by absorption enhancers such as chitosan nanoparticles and enzyme inhibitors, avoids first-pass hepatic metabolism but has been associated with nasal irritation and transient blood pressure elevation. Rectal and ocular routes showed encouraging absorption in early studies but have not progressed to marketed products because of practical inconvenience. Collectively, these findings help explain why injectable delivery, refined through smart insulin pen technology, remains the most clinically dependable route for achieving precise, predictable glycemic control [20].

Therefore, the present article aims to review the role, technological features, and clinical significance of smart insulin pens in improving insulin therapy and enhancing diabetes management outcomes.

2. SMART INSULIN PENS

Insulin pens combine the insulin cartridge and injection mechanism into a single device, allowing insulin to be administered using a simple push-button method. Studies have shown that insulin pen users often experience fewer hypoglycemic events and tend to inject more consistently compared with those using the vial-and-syringe technique [5].

All major insulin manufacturers produce pen devices. These are generally categorized as reusable or disposable. Reusable pens require insertion of prefilled insulin cartridges by the user, whereas disposable pens come with a preinstalled cartridge and are discarded once empty. These devices vary in size and dosing capability, with increments ranging from half-unit steps to 2-unit steps, and maximum single doses typically ranging from about 30 to 160 units [5].

Connected insulin delivery devices help overcome several challenges associated with injection therapy. People using multiple daily injections (MDI) must frequently perform dose calculations, and research shows these calculations are often done incorrectly, leading to dosing errors that negatively affect glycemic outcomes [5].

Smart insulin pens are designed to extend beyond standard pen functionality and incorporate features similar to advanced insulin pumps. Unlike conventional pens, smart pens can automatically log doses, record carbohydrate and correction entries, help prevent insulin stacking, and connect via Bluetooth to enable detailed data tracking and sharing. These features support more accurate, personalized, and manageable insulin therapy [10].

These systems also allow secure sharing of dosing information with healthcare providers without relying on handwritten logbooks. Clinicians can review dose timing and — in some devices — dose amounts and glucose data to guide therapy adjustments [5].

A smart insulin pen can:

- Calculate recommended doses using current glucose values, carbohydrate intake, meal size, active insulin levels, and physician-defined parameters.
- Deliver doses with half-unit precision.
- Reduce the likelihood of skipped injections.
- Perform dosing calculations for meals and correction of high glucose levels.
- Record the time and amount of each injection and provide reminders for upcoming doses.
- Alert users if insulin has expired or has been exposed to temperatures outside the safe range.
- Transmit diabetes management data to healthcare professionals when required.
- Integrate with smartphones, smartwatches, and commonly used diabetes data platforms [11].

On December 14, 2017, the first FDA-cleared smart insulin pen was introduced. This device records both the timing and amount of each insulin dose and transmits the information wirelessly through Bluetooth to a dedicated mobile application. The companion app tracks insulin-on-board, provides dosing

guidance, and generates structured reports for healthcare providers [8].

Table 1. Evolution of insulin delivery systems [7,20]

Delivery System	Key Advantages	Main Disadvantages	Invasiveness
Vial and syringe	Lower cost compared with pens and pumps	More injection-site pain, less convenient, lower accuracy	Minimally invasive
Insulin pen	Convenient, efficient, portable, better low-dose accuracy	More expensive, no mixing, limited flexibility	Minimally invasive
Insulin pumps	Continuous infusion, improved control, flexible basal rates	High cost, infection risk, technical problems, skin irritation	Minimally invasive
Intra-peritoneal	Direct portal delivery, more physiologic	Invasive, expensive, infection and thrombosis risk	Invasive
Inhaled insulin	Noninvasive, better acceptance, rapid onset	Reduced bioavailability, device malfunction, lung concerns	Noninvasive
Oral insulin	Higher portal concentration	Reduced bioavailability	Noninvasive
Nasal insulin	No pulmonary interference	Reduced bioavailability, local irritation, discomfort	Noninvasive
Transdermal insulin	Needle-free approach	Possible skin irritation, redness, blistering, pain	Noninvasive
Buccal insulin	Bypasses GI degradation, rich buccal vasculature	Low bioavailability, requires larger doses	Noninvasive
Sublingual insulin	Fast, reproducible glucose-lowering action	Limited long-term pharmacokinetic data	Noninvasive
Rectal insulin	More efficacious absorption than other non-injectable routes	Practically inconvenient, no marketed product	Noninvasive
Ocular insulin	Potential for systemic absorption via conjunctival route	Inconvenient device placement, inconsistent efficacy	Noninvasive

3. STAGES OF DEVELOPMENT OF SMART INSULIN PENS

- **Stage 0 (Baseline pens):** Standard reusable or prefilled pens with no digital or connectivity features.
- **Stage 1 (Add-on trackers):** Clip-on or cap-based sensors attached to existing pens that log dose time and size and transmit data via Bluetooth to a companion app.
- **Stage 2 (Integrated smart pens):** Purpose-built reusable pens with built-in sensors, displays, and Bluetooth connectivity that eliminate the need for a separate add-on device.

- **Stage 3 (Connected ecosystem pens):** Smart pens integrated with continuous glucose monitors (CGM) and mobile applications to provide combined dose and glucose data.
- **Stage 4 (Decision-support pens):** Devices offering automated bolus-calculation guidance, insulin-on-board tracking, and alerts based on glucose trends and dosing history.
- **Stage 5 (AI-enabled predictive pens):** Emerging devices that apply machine-learning algorithms to historical dosing and glucose data to generate personalized, predictive dosing recommendations.

Table 2. Comparison of traditional vs. smart insulin pens [5,6]

Feature	Description
Dose recording	Traditional pens rely on manual logging; smart pens automatically record dose time and amount.
Dose calculation	Traditional pens require manual calculation; smart pens offer built-in bolus calculators.
Data sharing	Traditional pens have no data-sharing capability; smart pens transmit data to apps and clinicians via Bluetooth.
Reminders and alerts	Traditional pens provide none; smart pens issue missed-dose reminders and insulin-exposure alerts.
Integration	Traditional pens function as standalone devices; smart pens can integrate with CGMs and diabetes apps.
Cost	Traditional pens are generally lower in cost; smart pens carry a higher upfront cost with added functionality.

4. COMPONENTS OF SMART INSULIN PENS

- Reusable or disposable pen body housing the insulin cartridge.
- Embedded electronic sensor module that captures dose time and dose amount.
- Bluetooth Low Energy (BLE) module for wireless data transmission.

- Digital display (in most integrated devices) showing dose history and reminders.
- Companion mobile application for logging, visualization, and report generation.
- Rechargeable or replaceable battery to power the electronic components.

5. KEY FEATURES OF SMART INSULIN PENS

- **Automatic dose logging:** captures the exact time and units delivered with each injection, removing the need for manual logbooks.
- **Bolus calculation support:** helps determine appropriate mealtime and correction doses using current glucose values and carbohydrate intake.
- **Insulin-on-board tracking:** estimates residual active insulin to reduce the risk of insulin stacking and hypoglycemia.
- **Missed-dose reminders:** alerts users when a scheduled dose has not been taken.
- **Temperature and expiry alerts:** notify users when insulin may have been exposed to unsafe storage conditions or has expired.
- **Data sharing and reporting:** generates structured reports that can be shared with healthcare providers to support treatment decisions.

6. REQUIREMENTS FOR CLASSIFYING SMART INSULIN PENS

For a device to be classified as a smart insulin pen, it should generally meet the following requirements:

- Accurate recording of dose time and dose size.
- Wireless connectivity (typically Bluetooth) to a companion application.
- A user interface for reviewing dosing history and reminders.
- Compliance with relevant regulatory standards for medical devices.
- Data security and privacy safeguards for transmitted health information.

7. FACTORS AFFECTING THE PERFORMANCE OF SMART INSULIN PENS

7.1. Human Factors

- User familiarity with digital devices and comfort with mobile applications.

- Willingness to consistently pair the pen with a smartphone or CGM system.
- Manual dexterity and vision, particularly in elderly patients.
- Motivation and health literacy affecting engagement with dose-tracking features.

7.2. Technological Factors

- Reliability of Bluetooth connectivity and app synchronization.
- Battery life and charging requirements of the pen.
- Compatibility with different smartphone operating systems and CGM brands.
- Sensor accuracy in detecting dose time and dose amount.

7.3. Commercial Factors

- Upfront device cost and ongoing subscription or replacement expenses.
- Insurance coverage and reimbursement policies.
- Availability of the specific pen model and compatible insulin cartridges in local markets.
- Manufacturer support, including software updates and customer service.

8. SETUP, ONBOARDING AND CLINICAL INTEGRATION OF SMART INSULIN PENS (SIP)

1. Device selection: choosing a smart pen compatible with the patient's insulin type and, where relevant, existing CGM system.
2. Initial pairing: connecting the pen to the companion mobile application via Bluetooth.
3. Profile configuration: entering patient-specific parameters such as insulin sensitivity factor, carbohydrate ratio, and target glucose range.
4. Patient education: training on dose logging, reminder settings, and interpretation of app-generated reports.
5. Clinical review setup: establishing data-sharing permissions so that healthcare providers can access dosing history remotely.
6. Ongoing monitoring: periodic review of adherence and dosing patterns, with adjustments made as follows:
 - Reviewing missed-dose frequency and timing patterns.
 - Adjusting bolus-calculator parameters based on glycemic trends.
 - Reinforcing education where adherence gaps are identified.

Table 3. Key milestones in insulin pen development [5,8]

Year	Milestone	Reference
1985	Introduction of the first reusable insulin pen	[5]
1990s	Widespread adoption of disposable prefilled insulin pens	[5]
2016	Early Bluetooth-enabled add-on dose-tracking caps introduced	[8]
2017	First FDA-cleared smart insulin pen launched (Dec 14, 2017)	[8]
2019–2021	Integration of smart pens with CGM platforms and diabetes apps	[5]

Year	Milestone	Reference
2022–present	Emergence of AI-assisted, predictive dosing features in smart pens	[5]

9. INTEGRATION OF SMART INSULIN PENS WITH DIGITAL HEALTH AND ARTIFICIAL INTELLIGENCE

- **Predictive analytics:** machine-learning models analyze historical dosing and glucose data to forecast glycemic trends and suggest proactive dose adjustments.
- **Personalized treatment:** AI-driven insights help tailor insulin sensitivity factors and correction doses to individual patient patterns over time.
- **Integration with multiple technologies:** smart pens increasingly interoperate with CGMs, automated insulin-delivery systems, and telehealth platforms to support coordinated, data-driven diabetes care.

10. CASE STUDIES

10.1. Case Study 1

- A cohort of adults with Type 1 diabetes using a Bluetooth-enabled smart pen showed improved adherence to mealtime dosing schedules over a 12-week period.
- Missed-dose frequency declined notably after users began receiving automated reminders through the companion application.
- Participants reported greater confidence in dose accuracy compared with their prior logbook-based routine.

10.2. Case Study 2

- A pediatric diabetes clinic integrated smart pen data with remote monitoring to support caregivers of children with Type 1 diabetes.
- Caregivers were able to review dosing history remotely, allowing earlier identification of missed or duplicate doses.
- Clinicians noted that structured dose reports simplified treatment-plan adjustments during routine follow-up visits.

11. ADVANTAGES OF SMART INSULIN PENS

- **Improved adherence:** automated reminders reduce missed and duplicated doses.
- **Greater dosing accuracy:** built-in calculators reduce manual calculation errors.
- **Reduced hypoglycemia risk:** insulin-on-board tracking helps prevent stacking of doses.
- **Better clinical decision-making:** structured reports give clinicians objective dosing data rather than relying on patient recall.
- **Enhanced patient engagement:** visual feedback and trends encourage active participation in self-management.
- **Remote monitoring capability:** supports telehealth follow-up and caregiver oversight for pediatric or elderly patients.

12. LIMITATIONS AND CHALLENGES OF SMART INSULIN PENS

- **Cost:** higher upfront and, in some cases, subscription costs limit accessibility.
- **Connectivity issues:** Bluetooth pairing failures or app synchronization errors can disrupt data logging.
- **Battery dependence:** device function relies on adequate battery charge, introducing a new point of failure.
- **Learning curve:** some patients, particularly older adults, may find the technology difficult to adopt.
- **Limited interoperability:** not all smart pens are compatible with every CGM system or diabetes app.
- **Data privacy concerns:** transmission of personal health data raises concerns that must be addressed through robust security measures.

13. REGULATORY CONCERN

Regulatory oversight of smart insulin pens generally addresses the following areas:

- a. Accuracy and reliability of dose-sensing hardware.
- b. Cybersecurity of Bluetooth data transmission.
- c. Data privacy and compliance with health information protection regulations.
- d. Clinical validation of bolus-calculation algorithms.
- e. Software update and version-control procedures for companion applications.
- f. Post-market surveillance for device malfunction reporting.
- g. Interoperability standards with CGMs and other connected devices.
- h. Labeling clarity regarding intended use and limitations.
- i. Manufacturer quality-management system compliance.

14. FUTURE PROSPECTS

- Wider integration of predictive, AI-driven dosing recommendations into routine clinical workflows.
- Expansion of interoperability standards to allow seamless data exchange across pen, CGM, and app manufacturers.
- Development of fully closed-loop systems combining smart pens with automated insulin delivery.
- Broader insurance coverage and cost reduction to improve accessibility in low-resource settings.
- Enhanced cybersecurity frameworks to protect patient data as connectivity features expand.

15. CONCLUSION

Smart insulin pens represent a meaningful advancement in insulin therapy, addressing many of the practical limitations associated with traditional injection devices. By combining automatic dose logging, bolus-calculation support, and connectivity with digital health platforms, these devices help

improve adherence, dosing accuracy, and clinical decision-making. While challenges related to cost, connectivity, and interoperability remain, continued technological development and broader integration with artificial intelligence and continuous glucose monitoring systems are expected to further enhance their clinical value. As the digital health ecosystem for diabetes management continues to evolve, smart insulin pens are likely to play an increasingly central role in supporting personalized, data-driven diabetes care.

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