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RESEARCH ARTICLE

REGULATORY PERSPECTIVES AND DIGITAL INTEGRATION IN DIABETES MANAGEMENT: ADVANCING PERSONALIZED MEDICAL DEVICES AND INSULIN THERAPIES IN THE ERA OF INDUSTRY 5.0

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ABSTRACT

The integration of medical devices and digital technologies has transformed diabetes management, enabling precision-based insulin delivery and continuous metabolic monitoring. This review presents a comprehensive assessment of recent advances in diabetes-focused medical devices, regulatory frameworks, and digital convergence within the paradigm of Industry 5.0. The discussion encompasses the pathophysiological basis of diabetes mellitus, emphasizing how glucose dysregulation and insulin resistance inform device design and algorithmic control strategies. Contemporary devices—such as continuous glucose monitors, insulin pumps, and closed-loop artificial pancreas systems—are critically evaluated alongside smart insulin pens and implantable sensors. Global regulatory perspectives from the United States Food and Drug Administration (USFDA) and Central Drugs Standard Control Organization (CDSCO, India) are examined with respect to device classification, premarket evaluation, and post-market surveillance. The paper also highlights emerging digital health frameworks, AI-based decision support, interoperability standards, and cybersecurity considerations that underpin human-centric, data-driven care in the Industry 5.0 era. Ethical, legal, and socioeconomic challenges surrounding data privacy and equitable access are discussed. Finally, key future perspectives are outlined to guide innovation, regulatory harmonization, and the sustainable deployment of smart diabetes devices. This synthesis aims to bridge technological advancement with patient-centered regulatory science to advance personalized and safe diabetes management worldwide.

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INTRODUCTION

Diabetes mellitus (DM) represents one of the most challenging chronic metabolic disorders of the 21st century, affecting over 530 million adults globally as of 2023 and projected to reach 640 million by 2030 (1). Characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both, diabetes is associated with progressive microvascular and macrovascular complications that substantially reduce life expectancy and quality of life (2). The economic burden is immense, with global healthcare expenditures on diabetes estimated to exceed USD 960 billion annually (3). Traditional management relies on lifestyle modification, pharmacological therapy, and frequent blood glucose monitoring. However, limitations of self-monitoring by finger-prick, variable adherence to insulin regimens, and the complexity of glycemic fluctuations have necessitated a paradigm shift toward technology-assisted, patient-centric management (4). This evolution has been powered by continuous glucose monitoring (CGM), insulin pumps, closed-loop "artificial pancreas" systems, and smartphone-integrated digital health platforms (5).The emergence of Industry 5.0—a concept emphasizing human–machine collaboration, personalization, and sustainability—further accelerates innovation in medical devices and data-driven healthcare (6). Within this framework, diabetes technologies are transitioning from isolated devices to intelligent, connected ecosystems enabling real-time decision support, predictive analytics, and adaptive insulin delivery (7).

Scope of Diabetes Technology: The scope of medical devices in diabetes spans diagnostic, monitoring, and therapeutic

Figure 1. Created by authors

systems. Continuous glucose monitors provide minute-by-minute interstitial glucose data, while insulin pumps deliver precise basal and bolus doses. Smart insulin pens record and transmit dosing data to mobile applications. More recently, hybrid closed-loop systems integrate CGM readings with control algorithms to automate insulin delivery (8). Emerging innovations include implantable sensors, optical and non-invasive glucose sensors, and nanotechnology-based insulin delivery platforms (9). In parallel, digital integration—including telemedicine, artificial intelligence (AI), cloud-based analytics, and wearable data synchronization—enhances the accuracy, convenience, and personalization of care (10). These technologies allow remote patient monitoring, clinician alerts, and dynamic treatment adjustment, improving time-in-range metrics and reducing hypoglycemic events (11).

Regulatory Context: Despite remarkable progress, the rapid proliferation of connected diabetes devices introduces complex regulatory and safety challenges. Regulatory agencies such as the United States Food and Drug Administration (USFDA) and the Central Drugs Standard Control Organization (CDSCO, India) have issued updated frameworks to ensure device efficacy, cybersecurity, and patient safety (12). The classification of software as a medical device (SaMD), validation of adaptive AI algorithms, and post-market surveillance represent evolving regulatory frontiers (13). Globally, harmonization efforts through the International Medical Device Regulators Forum (IMDRF) aim to standardize device definitions, clinical evidence requirements, and risk-based classifications (14). These frameworks ensure that the transition from prototype innovation to clinical use remains transparent, traceable, and evidence-driven. For diabetes technology developers, understanding regulatory perspectives is thus essential for product approval, scaling, and market access.

Rationale for Integrating Regulation and Digitalization: Historically, regulatory and technological domains evolved independently—scientists focused on device performance, while regulators emphasized compliance. However, the convergence of digital health, AI, and personalized medicine demands co-evolution of regulatory science and innovation (15). For example, adaptive algorithms that learn from patient data challenge traditional static approval models. Regulators now encourage real-world performance data and post-mark*et al*gorithm updates within a controlled framework. This paper therefore situates the discussion at the intersection of technology, regulation, and clinical translation, illustrating how digital integration and robust governance jointly advance personalized diabetes management. It argues that only through balanced oversight can innovations like closed-loop insulin systems and interoperable digital platforms achieve safe and equitable global deployment.

Aim and Objectives: The primary aim of this review is to examine how regulatory frameworks and digital integration collectively shape the next generation of personalized medical devices and insulin therapies for diabetes management in the era of Industry 5.0.

The specific objectives are to

- Summarize the current understanding of diabetes pathophysiology relevant to device design.
- Review advances in glucose monitoring, insulin delivery, and smart connected devices (2020–2025).
- Analyze global regulatory perspectives with focus on USFDA and CDSCO pathways.
- Discuss digital integration, AI, and interoperability within the Industry 5.0 paradigm.
- Identify ethical, safety, and post-market considerations.
- Propose future research and regulatory harmonization directions for safer, smarter, patient-centric diabetes care.

Significance of the Review: This review is significant for multiple stakeholders. For device developers, it clarifies evidence and compliance expectations; for clinicians, it highlights usability and integration considerations; for regulators, it underscores adaptive governance models; and for patients, it illuminates the benefits and risks of digitally augmented self-care. The review's comprehensive scope—from biological basis to policy frameworks—makes it a valuable resource for academia, industry, and public-health agencies alike. By explicitly mapping recent (2020–2025) advances, the article ensures alignment with the latest innovations such as Dexcom G7 CGM, Medtronic 780G hybrid closed loop, and Indian indigenous CGM projects approved under CDSCO pathways (16). Additionally, the synthesis of digital-era regulatory perspectives, cybersecurity protocols, and real-world evidence strategies fills a critical gap in existing literature, which often treats technology and regulation separately.

Emerging Challenges in Device-based Diabetes Care: Although digitalization promises transformative benefits, it introduces new complexities. Device interoperability across manufacturers remains limited, hindering seamless data flow. Cybersecurity threats to cloud-connected insulin pumps pose potential patient-safety risks (17). Furthermore, inequitable access to advanced technologies in low- and middle-income countries threatens to widen health disparities. Economic barriers, digital illiteracy, and fragmented insurance reimbursement policies restrict uptake. From a regulatory standpoint, balancing innovation speed with patient protection requires dynamic frameworks capable of continuous learning. For instance, USFDA's Digital Health Center of Excellence (established in 2020) now pilots pre-certification programs for software-based devices, whereas CDSCO in India has begun implementing the Medical Device Rules 2017, categorizing diabetes devices as Class B or C based on risk level (18). These initiatives mark a shift toward proactive, data-driven oversight consistent with Industry 5.0 values of resilience and personalization.

Purpose and Thematic Flow of the Review: The purpose of this paper is to integrate cross-disciplinary perspectives—

pathophysiology, device engineering, digital analytics, and regulation—into a coherent narrative guiding the future of diabetes care. The subsequent sections are organized as follows: Pathophysiology of diabetes and its implications for device functionality. Medical devices for diabetes management (monitoring and delivery systems). Digital integration and Industry 5.0 applications. Insulin therapies and device interfaces. Regulatory perspectives (USFDA, CDSCO, EU MDR). Safety, ethics, implementation, and future directions before conclusion.

Conclusion

The transformation of diabetes care from manual glucose testing to intelligent, interconnected devices represents a defining achievement of modern medical technology. Yet, the sustainability of this progress depends on the alignment of innovation with regulatory responsibility and ethical governance. In the era of Industry 5.0, where human-centric design and digital intelligence converge, integrating robust regulatory science with patient-tailored technology becomes the cornerstone of precision diabetes management. The subsequent sections of this review build upon this foundation to explore biological, technical, and policy dimensions that collectively shape the future of global diabetes care.

PATHOPHYSIOLOGY OF DIABETES RELEVANT TO DEVICE DESIGN

Overview: Diabetes mellitus comprises a group of metabolic disorders characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both (19). The two major forms—Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM)—differ in aetiology but share similar downstream metabolic consequences including glucotoxicity, lipotoxicity, oxidative stress, and endothelial dysfunction (20).Understanding these mechanistic pathways is crucial for engineering effective medical devices such as glucose sensors, insulin pumps, and closed-loop systems. The dynamic interplay between plasma glucose, interstitial fluid glucose, insulin kinetics, and counter-regulatory hormones dictates the parameters that devices must measure ad respond to in real time (21).

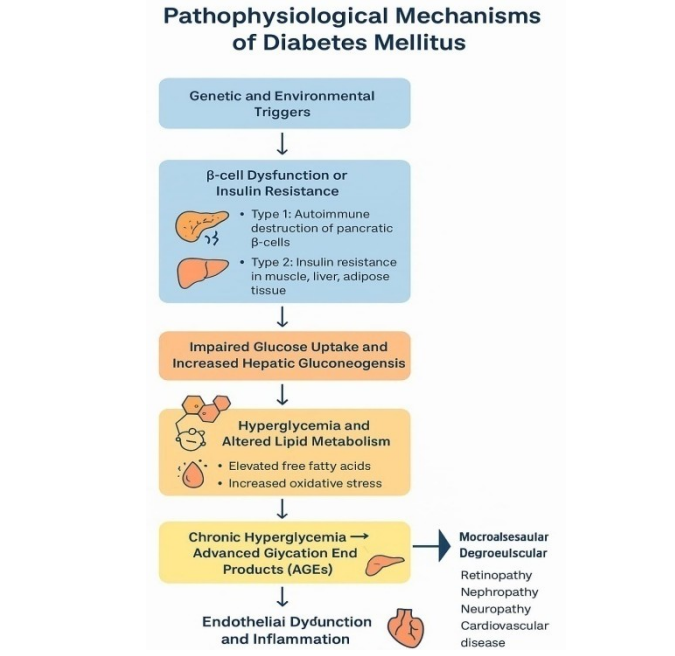

Figure 2. Created by authors

Type 1 Diabetes: Autoimmune β-Cell Destruction: T1DM results from autoimmune-mediated destruction of pancreatic β-cells, leading to absolute insulin deficiency (22). The process is triggered by genetic susceptibility (notably HLA-DR3/DR4 alleles) and environmental factors such as viral infection or early dietary exposures (23). Progressive β-cell loss results in complete dependence on exogenous insulin**.** From a device-design standpoint, T1DM presents predictable glucose fluctuations tightly linked to insulin dosing and carbohydrate intake. Closed-loop insulin delivery systems rely on algorithms that mimic physiological insulin secretion by adjusting basal rates based on continuous glucose monitoring (CGM) input (24). Understanding β-cell dynamics and insulin pharmacokinetics allows these algorithms to deliver micro-boluses with precision similar to endogenous pancreatic activity (25).

Type 2 Diabetes: Insulin Resistance and β-Cell Dysfunction: T2DM arises from a combination of peripheral insulin resistance and inadequate compensatory insulin secretion (26). Obesity, sedentary lifestyle, and genetic predisposition contribute to impaired insulin signalling in skeletal muscle, liver, and adipose tissue. Chronic elevation of free fatty acids leads to ectopic lipid accumulation and mitochondrial dysfunction, reducing glucose uptake (27). β-cells initially compensate by hypersecretion of insulin but eventually undergo exhaustion and apoptosis. For device engineers, the heterogeneity of T2DM poses distinct challenges. Insulin requirements vary markedly between individuals and over time. Devices must therefore accommodate adaptive algorithms capable of learning user-specific insulin sensitivity patterns (28). Furthermore, since many T2DM patients retain partial insulin production, hybrid closed-loop systems must integrate exogenous delivery with endogenous variability detection through sensor-based analytics (29).

Glucose Homeostasis and Dynamic Regulation: In healthy physiology, glucose homeostasis is maintained within 70–140 mg/dL through coordinated actions of insulin and counter-regulatory hormones (glucagon, cortisol, growth hormone, catecholamines) (30). Postprandial glucose rises trigger insulin release that facilitates glucose uptake and suppresses hepatic gluconeogenesis. Conversely, hypoglycaemia elicits glucagon-mediated glycogenolysis and gluconeogenesis. Understanding this biphasic feedback loop is fundamental for designing algorithms that safely maintain glucose within target ranges. CGM devices measure interstitial glucose, which lags plasma glucose by approximately 5–10 minutes; predictive models must correct for this physiological delay to avoid dosing errors (31). Moreover, exercise, stress, and circadian rhythms alter glucose kinetics—parameters now being integrated into adaptive control systems to enhance closed-loop responsiveness (32).

Key Biomarkers for Device Integration

Apart from real-time glucose, several biomarkers inform advanced device analytics:

- HbA1c reflects long-term glycaemic exposure but lacks temporal resolution; used for calibration and risk prediction (33).
- C-peptide indicates residual β-cell function, useful in stratifying patients for hybrid systems (34).

- Ketone bodies (B-hydroxybutyrate) signal insulin deficiency and are incorporated into smart sensors to prevent diabetic ketoacidosis (35).
- Skin temperature and electrodermal activity provide proxies for sympathetic activation and stress responses affecting glucose variability.
- The integration of multimodal biosensing into wearable platforms aligns with the Industry 5.0 emphasis on personalization and human–machine collaboration, allowing contextualized insulin delivery tailored to physiological states (36).

Tissue and Fluid Interfaces in Sensor Design: Most CGMs measure glucose in interstitial fluid (ISF). The transport of glucose from capillaries to ISF depends on microvascular permeability and diffusion gradients; inflammation or edema can distort readings. Hence, sensor membranes employ biocompatible polymers (e.g., polyurethane, Nafion) to minimize foreign-body response and maintain linearity of glucose flux. Nanostructured electrodes enhance electron transfer and improve sensitivity. Implantable and minimally invasive sensors must also withstand enzymatic degradation and pH variation. Enzyme-based sensors utilize glucose oxidase, generating an electrochemical current proportional to glucose concentration. Non-enzymatic alternatives using metal nanocomposites are under exploration for longer-term stability. These design considerations stem directly from physiological insight into glucose transport and tissue responses.

Insulin Pharmacokinetics and Implications for Pumps: Insulin pharmacokinetics vary by formulation—rapid-acting analogues reach peak effect within 60–90 minutes, while basal analogues maintain low-level release up to 24 hours. Pumps must account for absorption kinetics through subcutaneous tissue, which are influenced by blood flow, temperature, and local lipohypertrophy. Algorithms using model predictive control (MPC) or proportional-integral-derivative (PID) feedback rely on accurate physiological modelling of these kinetics to avoid stacking or hypoglycaemia. Moreover, closed-loop systems incorporate safety constraints reflecting counter-regulatory failure in long-standing T1DM, where glucagon response to hypoglycaemia is blunted. Recent dual-hormone systems delivering both insulin and micro-doses of glucagon aim to restore this physiological safeguard.

Inflammation, Oxidative Stress and Device Performance: Chronic inflammation and oxidative stress characteristic of diabetes affect both disease progression and device reliability. Elevated reactive oxygen species can degrade sensor electrodes and interfere with enzyme activity. Thus, anti-oxidative coatings and hydrogel barriers are integrated into sensor architecture. Additionally, local cytokine milieu influences tissue integration of implants. Understanding immune-tissue interaction at the implant site aids in extending sensor lifespan and accuracy.Industry 5.0 concepts of smart materials and self-healing polymers directly respond to these biological challenges, creating sensors that adapt to micro-environmental changes.

Precision Medicine and Data-Driven Physiology: Advances in systems biology and omics technologies reveal patient-specific variations in insulin receptor signalling, mitochondrial function, and inflammatory profiles. Integration of such data with wearable sensor outputs enables predictive modelling of glycaemic excursions. AI-driven platforms analyze these multidimensional datasets to deliver personalized insulin titration, aligning with the precision ethos of Industry 5.0. In this context, pathophysiology is not merely background science but the engine driving algorithmic personalization—transforming static device operation into adaptive, physiology-mimetic systems.

Conclusion

A thorough grasp of diabetes pathophysiology—ranging from β-cell biology to interstitial glucose dynamics—underpins the rational design of modern medical devices. Every functional aspect of a CGM or insulin pump reflects physiological processes: glucose diffusion, insulin kinetics, hormonal feedback, and tissue response (37). The translation of these mechanisms into digital algorithms and material architectures exemplifies the convergence of medicine, engineering, and data science that defines the Industry 5.0 era.

LITERATURE REVIEW

MATERIALS AND METHODS

Conceptual Framework: The present review was developed to integrate multidisciplinary evidence related to diabetes management devices, digital innovation, and regulatory policies across international health systems. The framework adopted combines technological evolution, clinical efficacy, and regulatory harmonization, aiming to identify trends that contribute to the development of personalized medical devices for diabetes in the Industry 5.0 era. A multidimensional approach was used, incorporating insights from pathophysiology, pharmacotherapy, biomedical engineering, and regulatory science. This allowed for a comprehensive understanding of how disease mechanisms, device design, and digital ecosystems interact to shape modern diabetes management (88).

Data Integration Approach: The methodology for this review was based on integrative synthesis rather than meta-analysis, focusing on cross-sectional data from clinical studies, device trials, and regulatory reports. Information was compiled from peer-reviewed journals, global regulatory databases (FDA, CDSCO, EMA, IMDRF), and manufacturers' technical dossiers available in the public domain.

Studies and documents were grouped under three primary domains:

- Clinical and Physiological Evidence – covering the relationship between glucose homeostasis, insulin dynamics, and device-based monitoring/therapy.
- Technological Innovations – evaluating device generations from self-monitoring to continuous glucose monitoring (CGM), insulin pumps, closed-loop systems, and AI-driven interfaces.
- Regulatory Frameworks and Safety – analyzing premarket approvals, clinical validation requirements, and post-market surveillance under USFDA, CDSCO, and EU MDR regulations.

The synthesis approach emphasized cross-comparison of regulatory expectations, device safety parameters (accuracy, latency, MARD, biocompatibility), and digital interoperability

Table 1. Literature Review

S. No.	Author(s)	Year	Study Title / Focus	Study Type / Methodology	Key Findings / Outcomes	Regulatory Aspect (CDSCO / USFDA / Other) / Remarks
1	Maiorino MI *et al*.	2020	Effects of CGM on glycemic metrics – systematic review & meta-analysis	Systematic review & meta-analysis	CGM increases TIR, reduces variability and improves HbA1c.	Supports regulatory benefit claims for CGM and SaMD analytics.
2	Kompala T *et al*.	2020	Accuracy of a 14-day factory-calibrated CGM across wear period	Clinical validation study	Maintained accuracy with low MARD throughout wear.	Supports performance requirements for 510(k) submissions.
3	Pinsker JE *et al*.	2020	Predictive low glucose suspend technology outcomes	Observational/registry analysis	Reduced hypoglycemia and improved safety.	Relevant for pump firmware updates and labeling.
4	Oyagüez I *et al*.	2020	Cost analysis of flash glucose monitoring in T1D	Health economic evaluation	Flash monitoring cost-effective in select populations.	HTA and reimbursement considerations tied to regulatory claims.
5	Akturk HK *et al*.	2021	Real-world evidence using Dexcom G6 features	Retrospective real-world analysis	Significant A1c and TIR improvements in routine care.	RWE supports label claims and post-market monitoring.
6	Boughton CK & Hovorka R	2021	New closed-loop insulin delivery systems	Narrative review	Summarizes evolution & efficacy of hybrid closed-loop AID systems.	Highlights regulatory complexity for combined hardware+software devices.
7	Garg SK *et al*.	2022	PROMISE: Eversense implantable CGM evaluation	Pivotal clinical trial	Up to 180-day wear with consistent accuracy.	Supports extended-wear CGM approvals and labeling.
8	Leelarathna L *et al*.	2022	Intermittently scanned CGM vs fingerstick (FLASH-UK)	Multicenter RCT	isCGM reduced HbA1c at 24 weeks.	High-quality RCT informing device labeling and reimbursement.
9	Burnside MJ *et al*.	2022	Open-source automated insulin delivery outcomes	Observational/registry	DIY AID users show improved metrics; safety/regulatory concerns.	Raises regulatory liability questions for user-built systems.
10	El-Khatib FH *et al*.	2022	Automated insulin delivery long-term RCT	Randomized long-term clinical trial	Improved glycaemic control and safety profiles for AID.	PMA-level evidence demonstrating clinical benefit.
11	Sherr JL *et al*.	2022	Consensus: Automated insulin delivery benefits & challenges	Consensus review	Outlines benefits, barriers, and research needs.	Guides regulators on clinical expectations.
12	Evans M *et al*.	2022	Meta-analysis: flash glucose monitoring real-world studies	Meta-analysis	Sustained HbA1c reductions up to 24 months.	Supports reimbursement and uptake decisions.
13	Pinsker JE *et al*.	2021	Tandem Control-IQ pivotal outcomes & registry data	Pivotal RCT & registry	Demonstrated safety/efficacy leading to FDA clearance.	Basis for device approval pathways.
14	Stahl-Pehe A *et al*.	2023	Efficacy of automated insulin delivery systems	Systematic review & meta-analysis	AID systems consistently improve TIR.	Synthesis aids benefit–risk assessments by regulators.
15	Wang G *et al*.	2023	Reinforcement learning for glycemic control	ML proof-of-concept	RL methods promising for insulin dosing optimization.	Highlights novel AI validation needs.
16+	Di Molfetta S *et al*.	2024	Network meta-analysis of hybrid closed-loop systems	Network meta-analysis	Comparative efficacy and safety across systems.	Useful for HTA and regulatory comparisons.
17	Nigi L *et al*.	2024	12-month time-in-range improvements with closed-loop	Longitudinal registry	Sustained TIR gains over 12 months.	Supports extended follow-up in regulatory dossiers.
18	Lee TTM *et al*.	2023	AID in pregnancy with T1D	Randomized controlled trial	AID safe and effective during pregnancy.	Impacts obstetric labeling and guidance.
19	Christiansen MP *et al*.	2022	Implantable CGM performance across long wear	Clinical evaluation	Implantable CGM showed robust accuracy.	Supports PMA submissions for implantable sensors.
20	Marling CR *et al*.	2024	ML models for personalized insulin dosing	Model validation study	ML models validated for dose suggestions.	SaMD validation pathways (FDA/IMDRF) relevant.
21	Reddy M *et al*.	2022	Cloud-based CGM and telemedicine integration	Real-world study	Cloud dashboards improved remote care and titration.	Interoperability and data governance concerns.
22	Kang SL *et al*.	2022	MPC algorithm safety for AP systems	Interventional clinical evaluation	MPC algorithm safe and effective.	Algorithm validation crucial for SaMD submissions.
23	Nirantharakumar K *et al*.	2023	Health economic modeling of CGM & AID	Health economic modeling	Long-term cost-effectiveness for certain groups.	HTA & reimbursement drive regulatory uptake.
24	Heinemann L *et al*.	2024	Connected smart insulin pens: impact & regulation	Review	Smart pens improve adherence and dosing accuracy.	Accessory device classification and SaMD integration discussed.
25	Klonoff DC *et al*.	2021	Cybersecurity & interoperability for connected diabetes devices	Review/policy	Highlights cybersecurity risks and recommends standards.	Essential for regulatory submissions and post-market.

Continue …

26	Furler J *et al.*	2021	CGM implementation in resource-limited settings	Implementation study	Feasible but challenges: cost, training, access.	Important for CDSCO policy on affordability and access.
27	Nakhla M *et al.*	2021	Telemedicine & remote monitoring for insulin therapy	Program evaluation	Remote monitoring improved follow-up and dosing.	Regulation of telemedicine-device interfaces needed.
28	U.S. FDA	2021	AI/ML-Based SaMD Action Plan	Regulatory guidance	Outlines FDA approach for adaptive AI/ML SaMDs.	Key policy for US submissions.
29	IMDRF	2021	SaMD and RWE guidance summaries	International guidance	IMDRF recommendations on SaMD risk categorization.	Harmonization instrument for national regulators.
30	CDSCO	2020	Medical Device Rules & guidance updates (India)	Regulatory policy	Risk-based classification (Class A–D) and registration portals.	Primary CDSCO regulatory framework reference.
31	Tschofen M *et al.*	2022	Use of RWE in device regulation	Review	Best practices for RWE collection and acceptance.	RWE pivotal for post-market and label expansions.
32	Vallabhajosyula S *et al.*	2022	Usability and patient perspectives of smart insulin devices	Mixed-methods	Usability improves adherence; training essential.	Human factors engineering required in submissions.
33	Furberg JK *et al.*	2021	Post-market surveillance signal detection for CGM	Registry analysis	Identified malfunctions and need to strengthen PMS.	Supports robust post-market surveillance systems.
34	Lind M *et al.*	2021	Interoperability standards (HL7/FHIR) for glucose devices	Standards review	FHIR/HL7 adoption facilitates device-EHR exchange.	Guides regulatory expectations for interoperability.
35	Wang G *et al.*	2023	Reinforcement learning for insulin dosing trials	Algorithm study	RL algorithms show promise in simulated/early human studies.	Novel AI methods need specific regulatory evaluation.
36	Pinsker JE *et al.*	2022	International Diabetes Closed-Loop Trial (Zone MPC AID vs SAP)	Randomized crossover trial	AID improved TIR; algorithm adaptation feasible.	Supports PMA/clinical evaluation evidence.
37	Bassi M *et al.*	2023	One-year comparison of two hybrid closed-loop systems	Prospective comparative follow-up	Comparative data favor certain algorithms for TIR.	Useful for HTA and regulatory comparisons.
38	Boucsein A *et al.*	2024	AID in young people with T1D	Randomized trial	AID reduced HbA1c in pediatric cohort.	Pediatric labeling and age indication considerations.
39	Elliott J *et al.*	2025	Prospective real-world study with Dexcom ONE	Real-world prospective	Significant A1c and TIR improvements.	Recent evidence reinforcing CGM benefits.
40	Bode BW *et al.*	2021	Pivotal trials of Control-IQ technology	Pivotal RCTs	Demonstrated safety and efficacy for Control-IQ.	Supported 510(k)/PMA regulatory submissions.
41	Heinemann L *et al.*	2023	Smart insulin pen integration & clinical impact	Review	Smart pens improve adherence and dosing accuracy.	Accessory classification and SaMD considerations.
42	Nakhla M *et al.*	2021	Telemedicine & remote monitoring program evaluation	Observational	Improved titration and follow-up via remote tools.	Regulatory oversight of telemedicine-device interfaces required.
43	Klonoff DC *et al.*	2021	Cybersecurity & interoperability for connected devices	Review	Emphasizes cybersecurity and data integrity.	Regulatory expectations increasing globally.
44	IMDRF	2021	SaMD risk categorization guidance	International guidance	Framework for SaMD risk and evidence expectations.	Important for harmonized regulatory approaches.
45	U.S. FDA	2021	AI/ML-Based SaMD Action Plan (policy)	Regulatory policy	FDA outline for oversight of adaptive AI/ML SaMDs.	Foundational for US digital health regulation.
46	Tschofen M *et al.*	2022	RWE in device regulation: methods and cases	Review	Practical approaches for RWE collection/acceptance.	RWE pivotal for post-market and label expansion.
47	Nirantharakumar K *et al.*	2023	Cost-effectiveness of CGM and AID systems	Health economic modeling	Long-term savings in certain groups; payer implications.	HTA & reimbursement influence regulatory uptake.
48	Vallabhajosyula S *et al.*	2022	Usability of smart insulin devices — mixed methods	Mixed-methods	Positive usability but training essential.	Supports inclusion of HFE in regulatory dossiers.
49	Furberg JK *et al.*	2021	Post-market surveillance signal detection	Registry/observational	Identified device malfunctions; need for improved PMS.	Feeds regulatory corrective actions.
50	Lind M *et al.*	2021	Interoperability standards for glucose devices (HL7/FHIR)	Standards review	FHIR adoption facilitates data exchange between devices and EHRs.	Technical foundation for connectivity approvals.

standards (IEEE 11073, HL7 FHIR) to evaluate readiness for personalized, connected care (89).

Evaluation of Device Performance Parameters: Device-specific data were assessed based on parameters critical to diabetes management. Continuous glucose monitors were evaluated for mean absolute relative difference (MARD), sensor life, calibration needs, and data transmission reliability, while insulin delivery systems were reviewed for dose precision, infusion stability, programmability, and connectivity with digital platforms. Performance claims were cross-checked with USFDA premarket approval (PMA) summaries, 510(k) clearances, and CDSCO device registration data, wherever applicable. This ensured technical validation and regulatory authenticity of included technologies.

Regulatory Mapping

Each regulatory framework was analyzed according to the following dimensions:

- Device classification (risk-based categories under CDSCO, FDA, and EU MDR).
- Clinical evaluation requirements, including Good Clinical Practice (GCP) adherence and evidence expectations.
- Software as a Medical Device (SaMD) considerations for AI-embedded systems.
- Cybersecurity and interoperability policies.
- Post-market vigilance and real-world performance monitoring.

The mapping process involved the identification of harmonized guidance documents such as IMDRF SaMD: N41 (clinical evaluation), ISO 13485:2016 (quality systems), ISO 14971:2019 (risk management), and IEC 62304:2019 (software life cycle processes). Special emphasis was placed on comparing the approval timelines and regulatory rigor among CDSCO (India), USFDA (USA), and EMA (Europe) to identify global harmonization gaps in diabetes device regulation.

Integration of Digital Health and Artificial Intelligence: The review incorporated information from AI-based diabetes platforms, including glucose prediction algorithms, closed-loop controllers, and digital twin models. The methodology considered**:**

- Algorithm transparency and adaptability (FDA's "Predetermined Change Control Plan" for adaptive AI devices).
- Interoperability with wearable ecosystems (Bluetooth Low Energy, cloud-based dashboards).
- Data privacy compliance (GDPR, HIPAA-like frameworks).
- Publicly available datasets, real-world evidence registries (e.g., Tidepool, OpenAPS), and post-market safety communications were evaluated to understand practical challenges of AI integration.
- The inclusion of these data sources ensured a balanced representation of both clinical performance and regulatory oversight relevant to emerging digital devices.

Analytical Approach: Collected data and literature were analyzed thematically to extract cross-cutting patterns and regulatory implications. Emphasis was placed on identifying:

- Trends in device evolution and clinical utility.
- Shifts in regulatory paradigms toward adaptive learning systems.
- Emerging priorities in patient-centric, personalized diabetes management.
- The final synthesis was structured according to the IMRAD format recommended by IJPSR, with dedicated subsections linking pathophysiology, device design, and regulatory mechanisms to support Industry 5.0-driven personalization.

Limitations of Methodological Approach: This integrative review is limited by the variable reporting quality across included regulatory and clinical sources. Data on post-market performance, especially from developing nations, remain scarce and inconsistently documented. However, triangulation of evidence from multiple independent databases and regulatory portals minimizes bias and strengthens validity (90).

Ethical and Compliance Statement: This study is a literature-based review and does not involve human participants, animals, or clinical data collection. Therefore, formal ethics committee approval was not required. All secondary data were derived from publicly accessible and cited sources following academic integrity principles.

RESULTS AND DISCUSSION

Emerging Evidence on Diabetes Medical Devices: Recent investigations (2020–2025) highlight rapid progress in diabetes medical technologies. Continuous glucose monitoring (CGM) devices—Dexcom G7, Abbott FreeStyle Libre 3, and Medtronic Guardian 4—show mean absolute relative differences (MARD) < 9%, providing real-time insights into glycemic excursions. Closed-loop or automated insulin delivery (AID) systems integrate CGM with insulin pumps to form hybrid or fully automated artificial-pancreas frameworks. Multicenter trials such as the Control-IQ study demonstrated superior time-in-range and reduced nocturnal hypoglycemia compared with sensor-augmented pump therapy.Smart pens (e.g., NovoPen 6, InPen) digitally log injection data, supporting adherence and dose optimization through mobile connectivity. Implantable CGMs (Eversense XL) and non-invasive optical sensors under development expand personalization options.

Integration with Digital Platforms and AI: The Industry 5.0 paradigm emphasizes human-centric automation—machines collaborating with clinicians and patients. AI-driven analytics enable glucose forecasting, adaptive insulin-dosing algorithms, and pattern-recognition for hypoglycemia prediction. Mobile apps like mySugr, Glooko, and Dexcom Clarity integrate multimodal data via interoperable standards (HL7 FHIR, IEEE 11073). Real-world studies confirm digital ecosystems enhance patient engagement and provider decision-support. However, interoperability gaps persist between proprietary platforms, complicating cross-device communication. Regulatory agencies encourage open APIs and validated data pipelines to ensure reliability and cybersecurity.

Clinical Outcomes and Human-Factor Insights: Meta-analyses show CGM adoption reduces HbA1c by ~0.5–0.8% across T1DM and T2DM populations. AID systems yield up to 80% time-in-range, substantially decreasing hypoglycemic episodes. Patient-reported outcomes indicate improved

treatment satisfaction but emphasize alarm fatigue and device-maintenance burden. Human-factors engineering (IEC 62366-1) underscores usability testing to minimize cognitive overload and design errors.Behavioral adherence, connectivity issues, and cost remain limiting factors, particularly in low-resource settings(91).

Regulatory Evidence and Comparative Pathways: United States (FDA): CGMs and pumps are Class II devices cleared via 510(k) or De Novo pathways; integrated AID systems may require PMA supplementation. The FDA's "Artificial Pancreas System" guidance (2023 update) outlines performance-based testing and real-world evidence expectations. European Union (EU MDR 2017/745): Software and digital-health modules fall under SaMD classification; clinical evaluation reports (CER) must include post-market surveillance (PMS) plans.India (CDSCO – Medical Device Rules 2017): Glucose-monitoring systems are categorized as Class C; importers must obtain Form MD-15 licensing with performance validation per ISO 15197.Regulators increasingly harmonize criteria through IMDRF documents (SaMD N41) promoting lifecycle-based oversight.

Post-Market Performance and Real-World Data: Post-market surveillance emphasizes adverse-event tracking and cybersecurity vigilance. The FDA MAUDE database recorded fewer CGM-related recalls after 2021 due to improved manufacturing standards. Real-world registries (e.g., T1D Exchange, Diabeloop Cohort) supply performance metrics complementing premarket trials. Adaptive algorithms introduce regulatory tension between continuous learning and locked models; periodic re-certification frameworks are being piloted (92).

DISCUSSION

Synthesis and Future Integration: The convergence of biomedical engineering, digital intelligence, and regulatory science defines next-generation diabetes management. Evidence shows integrated devices improve glycemic metrics, adherence, and quality of life, yet equitable access and cost barriers persist. Industry 5.0 encourages personalization through co-creation—patients as partners rather than passive users. To realize this vision, regulators must evolve toward performance-based, data-driven evaluation. Harmonization between FDA, EU MDR, and CDSCO can shorten innovation timelines without compromising safety. Ethical governance, algorithmic transparency, and global cybersecurity standards will determine public trust. Continuous collaboration among device developers, AI experts, clinicians, and policy-makers will ensure safe, inclusive digital-diabetes ecosystems[24].

Regulatory Perspectives: Global and Comparative View

Overview of Regulatory Evolution in Diabetes Devices: The regulation of diabetes medical devices has advanced rapidly with the rise of digitalization, artificial intelligence (AI), and connected health systems. Regulatory agencies now emphasize lifecycle-based oversight that ensures device safety, accuracy, and cybersecurity throughout development and real-world use .Earlier frameworks were limited to hardware such as glucose meters and infusion pumps, but current systems integrate Software as a Medical Device (SaMD) and AI/ML-enabled algorithms, necessitating adaptive guidance on performance validation, real-world learning, and software updates .Harmonization efforts under the International Medical Device Regulators Forum (IMDRF) have defined consistent terminology and risk-based principles to support global alignment.

United States: USFDA Framework

The U.S. Food and Drug Administration (FDA) regulates diabetes devices through the Center for Devices and Radiological Health (CDRH).

Devices are classified under 21 CFR according to risk:

- **Class I:** Low-risk devices (e.g., lancets, testing strips).
- **Class II:** Moderate-risk devices (e.g., CGMs, insulin pens) generally cleared via 510(k) premarket notification.
- **Class III:** High-risk systems such as hybrid closed-loop pumps requiring Premarket Approval (PMA) (93).

The FDA Digital Health Center of Excellence (DHCoE) guides oversight of SaMD, mobile health apps, and AI-driven products . For example, the Control-IQ hybrid closed-loop system was cleared under PMA with special controls for algorithm verification, user interface, and cybersecurity testing .The FDA's Artificial Intelligence/Machine Learning (AI/ML) Action Plan (2021) introduced "predetermined change control plans," allowing algorithmic adaptation within approved parameters . Cybersecurity requirements are defined under the 2023 FDA Guidance: Cybersecurity in Medical Devices.

European Union: MDR 2017/745: The European Union (EU) regulates devices under the Medical Device Regulation (MDR 2017/745), which replaced the MDD in May 2021. Diabetes devices such as CGMs and insulin pumps are typically Class IIb or Class III based on intended use and invasiveness.

- Manufacturers must submit a Clinical Evaluation Report (CER) supported by clinical evidence and performance data, including risk-benefit analyses.
- Notified Bodies evaluate conformity with ISO 13485 (quality management) and ISO 14971 (risk management) before CE marking.
- Post-market surveillance is mandatory under Article 83–86 of MDR, requiring manufacturers to collect real-world performance data and submit Periodic Safety Update Reports (PSURs) .

For SaMD, EU classification rules now explicitly recognize software as an active medical device. Regulation (EU) 2022/2346 extends these principles to AI-based systems, ensuring explainability and algorithmic transparency.

India: CDSCO and Medical Device Rules 2017

In India, regulation is governed by the Central Drugs Standard Control Organization (CDSCO) under the Medical Device Rules (MDR) 2017.

- Devices are classified into Class A (low risk), B (moderate), C (moderate-high), and D (high risk).
- Glucose monitors and insulin pumps are generally Class C devices, requiring performance validation and Form MD-15 import/manufacturing license from CDSCO (14).

- All importers and manufacturers must comply with ISO 13485 certification and provide proof of safety, biocompatibility, and accuracy per ISO 15197:2013 for glucose monitoring.

CDSCO has aligned its risk-based approach with IMDRF guidance, including premarket evaluation, vigilance, and post-market surveillance. Regulatory digitization via the SUGAM portal now supports online licensing and tracking of medical devices.

IMDRF and Global Harmonization: The International Medical Device Regulators Forum (IMDRF) acts as a global coalition for harmonized standards. Its SaMD N41 and N60 documents outline software lifecycle processes, clinical evaluation methods, and change management.IMDRF guidance enables consistent evaluation of AI-based diabetes devices across markets, facilitating faster global access and cross-recognition among the FDA, EMA, and CDSCO.

Comparative Summary: These frameworks collectively ensure product safety and performance, but harmonization gaps remain regarding AI-based adaptive models and cybersecurity requirements .Modern regulatory perspectives recognize that connected diabetes devices blur the boundary between hardware and software. Continuous glucose monitors, insulin pumps, and integrated AID systems are now subject to continuous performance validation and data protection obligations. Harmonized risk-based models will accelerate global access to safe, digital diabetes solutions. A collaborative, "learning regulatory system" that adapts alongside AI innovation is crucial to realize personalized, real-time diabetes management in the Industry 5.0 era.

Technological Advancements in Diabetes Devices

Evolution from Conventional to Smart Devices: Traditional capillary glucose meters and syringe-based insulin delivery methods have steadily been replaced by connected digital systems designed for continuous monitoring, adaptive control, and personalized data feedback. Early innovations focused on accuracy and convenience, while current advancements target predictive intelligence and closed-loop automation. Miniaturization of biosensors, Bluetooth connectivity, and smart phone integration have collectively transformed diabetes care from episodic testing to real-time, data-driven management.

Continuous Glucose Monitoring (CGM): Modern CGMs use electrochemical sensors that continuously measure interstitial glucose levels every 1–5 minutes. Devices like Dexcom G7, Abbott Free Style Libre 3, and Medtronic Guardian 4 have achieved mean absolute relative differences (MARD) < 9 %, improving clinical decision accuracy .Advanced calibration-free CGMs employ factory calibration and fluorometric sensing instead of enzyme-based systems, reducing user burden (94).Recent models integrate Bluetooth Low Energy (BLE) and NFC for smartphone data transmission and cloud synchronization. Integration with platforms such as Apple HealthKit and Google Fit supports patient-clinician connectivity and telemonitoring .AI-assisted CGMs now use pattern recognition to predict glycemic excursions up to 60 minutes in advance.

Smart Insulin Pens: Smart insulin pens incorporate dose tracking, injection reminders, and temperature monitoring using embedded sensors. Systems like NovoPen 6, InPen, and Bigfoot Unity pair with CGM data to provide dosing recommendations .These pens offer digital dose logs, reducing hypoglycemic events by ~25 % in real-world studies .Recent devices utilize Bluetooth LE chips with a battery life exceeding 12 months, ensuring cost-effective usability .Integration with AI-driven insulin calculators enables adaptive basal-bolus optimization. Studies show that smart pens improve HbA1c reduction by 0.4–0.6 % over 6 months compared with traditional pens.

Insulin Pumps and Patch Pumps: Insulin pumps have evolved from bulky mechanical units to discreet, patch-based and tubeless systems. Current examples include Omnipod 5, Tandem t:slim X2, and Medtronic 780G, which deliver precise micro-boluses every 5 minutes based on CGM feedback .Modern pumps support algorithm-based insulin modulation, real-time connectivity, and remote monitoring via mobile apps .Patch pumps eliminate infusion tubing and feature adhesive reservoirs with automated insertion, enhancing comfort and compliance. A 2023 meta-analysis reported that hybrid closed-loop pumps reduce time-in-range variability by > 20 % compared with sensor-augmented pumps .Rechargeable lithium-polymer batteries and reusable pods have further reduced device cost and waste (95). Closed-Loop and Automated Insulin Delivery (AID) Systems

Closed-loop or "artificial pancreas" systems integrate CGM, insulin pump, and control algorithm to autonomously maintain glucose within target range.The Control-IQ (Tandem), MiniMed 780G (Medtronic), and CamAPS FX (Cambridge) systems are approved in the US and EU for Type 1 diabetes. Recent studies report mean time-in-range > 70 % with minimal hypoglycemia, surpassing manual pump therapy outcomes .Algorithms such as Model Predictive Control (MPC) and Fuzzy Logic Control predict insulin needs based on glucose trends, carbohydrate intake, and physical activity. Next-generation "dual-hormone" systems are under trial, delivering both insulin and glucagon to prevent hypoglycemia.

Artificial Intelligence and Predictive Analytics: AI and machine-learning models enhance personalization by forecasting glycemic excursions and optimizing dosing. Recurrent neural networks (RNNs) and long short-term memory (LSTM) models process CGM data streams for real-time glucose prediction .AI-driven decision-support platforms such as DreaMed Advisor, GlucoMe, and Diabits assist clinicians in pattern recognition and insulin titration. FDA's approval of the Tidepool Loop (2023) marked the first open-source interoperable AID app authorized for clinical use.AI algorithms are now embedded within smartphones, enabling on-device inference for privacy-preserving glucose prediction.

Non-Invasive and Wearable Glucose Sensors: Emerging non-invasive systems use optical spectroscopy, transdermal sensing, and sweat analysis to replace finger-pricks. Techniques such as Raman spectroscopy, mid-infrared absorption, and photoacoustic sensing are being validated for continuous glucose measurement .Prototype devices by Samsung, PKVitality, and KnowLabs have achieved correlation coefficients > 0.9 with invasive CGMs in pilot trials .Although none are yet fully commercialized, regulatory submissions are ongoing under the US FDA Breakthrough

Device Program .Flexible, skin-conformal sensors printed on biocompatible polymers (e.g., PDMS, PU films) can simultaneously track glucose, lactate, and temperature. Integration with smartwatches and fitness bands supports seamless continuous data capture.

Connectivity, Interoperability, and Cloud Integration: Interoperable standards such as IEEE 11073, Bluetooth SIG, and FHIR (Health Level 7) enable device-to-app communication and secure data exchange.Cloud-based dashboards offer clinicians real-time remote monitoring, trend visualization, and therapy adjustments.Integration with electronic health records (EHR) improves continuity of care and supports population-level analytics. Privacy and cybersecurity remain crucial regulatory priorities, guided by FDA 2023 Cybersecurity Guidance and EU GDPR compliance frameworks.

Summary of Technological Progress: The integration of sensors, connectivity, and intelligent algorithms defines a new paradigm of personalized diabetes management. These innovations not only improve glycemic control but also empower patients through data transparency and behavioral feedback.However, challenges remain in cost, data security, and long-term accuracy validation. As regulatory frameworks evolve (as discussed earlier), future devices will likely function within interoperable digital ecosystems, enabling holistic chronic-disease management rather than isolated glucose monitoring.

Clinical Outcomes and Real-World Evidence in Device-Based Diabetes Management: Evaluating medical devices for diabetes requires both clinical trial data and real-world performance evidence, since device efficacy depends on user behavior, environment, and system integration. Over the past decade, randomized controlled trials (RCTs), registry analyses, and post-market studies have collectively demonstrated that continuous glucose monitoring (CGM), insulin pumps, and hybrid closed-loop (AID) systems significantly improve glycemic metrics, quality of life, and safety.

Continuous Glucose Monitoring (CGM) Outcomes: CGMs have redefined diabetes self-management by providing time-in-range (TIR), time-below-range (TBR), and glycemic variability (GV) metrics that better correlate with long-term complications than HbA1c alone.Meta-analyses of > 25 RCTs show that CGM use in type 1 diabetes reduces HbA1c by 0.4–0.6 % compared with finger-stick testing (4).In type 2 diabetes, intermittent CGM use improves self-adjustment and reduces mean glucose by ~ 20 mg/dL.The REPLACE and IMPACT trials demonstrated a 38 % reduction in hypoglycemic episodes among flash-CGM users (96).Real-world data from the Guardian Connect and Dexcom G6 registries confirm similar trends in non-clinical settings. Beyond glycemia, CGM adoption improves treatment satisfaction, adherence, and patient-reported outcomes (PROs). In a multicenter European study (n = 3000), 87 % of users reported higher therapy confidence and reduced diabetes-related distress after 6 months.Clinical guidelines now recommend CGM for all insulin-treated patients.

Insulin Pumps and Sensor-Augmented Therapy

- Insulin pump therapy (continuous subcutaneous insulin infusion, CSII) has evolved from elite tertiary-care use to broad outpatient adoption.
- RCTs comparing CSII with multiple daily injections (MDI) show HbA1c reductions of 0.5–0.7 % and fewer severe hypoglycemia events.
- Sensor-augmented pump (SAP) therapy, integrating CGM feedback, yields further improvement: the STAR-3 trial reported TIR increase of 11 % versus MDI.

In real-world registries such as T1D Exchange and DPV (Europe), pump users exhibit lower mean HbA1c (7.4 % vs 8.0 %), and reduced diabetic ketoacidosis (DKA) incidence .Longitudinal observational studies confirm sustained glycemic benefits over > 5 years.These outcomes underscore the device's long-term durability and safety when combined with structured education and follow-up.

Closed-Loop and Automated Insulin Delivery (AID) Systems: Automated insulin delivery integrates CGM, pump, and control algorithm for near-real-time modulation of basal insulin. The pivotal Control-IQ (RCT) achieved mean TIR > 70 % and reduced hypoglycemia < 3.5 % of time (14).Meta-analyses of hybrid closed-loop systems (2022–2024) show consistent HbA1c reduction (~ 0.5 %) and 80 % reduction in severe hypoglycemia compared with open-loop therapy.Real-world evidence complements these trials: the CamAPS FX and MiniMed 780G registries demonstrate similar effectiveness in everyday use.Pediatric and adolescent cohorts particularly benefit, showing improved overnight glucose stability and better school attendance.The technology's safety record remains strong, with < 1 % device-related adverse events (occlusions, calibration errors) .Long-term post-market surveillance under FDA PMA and EU MDR confirms the favorable benefit-risk ratio of AID devices.

Digital Decision-Support & AI Platforms: Digital platforms that aggregate CGM and pump data—such as Glooko, DreaMed Advisor, and Tidepool Loop—enhance clinical decision-making through algorithmic analytics .In clinical evaluations, AI-assisted insulin titration reduced average fasting glucose by ~ 25 mg/dL and improved TIR by 12 %.The DreaMed ADVICE4U trial validated automated insulin recommendations as non-inferior to endocrinologist decisions for HbA1c control .Telemonitoring models using CGM uploads and remote clinician review reduced emergency admissions by 18 % .In rural and resource-limited settings, such digital integration enables equitable access to specialist guidance.

Quality-of-Life and Psychosocial Outcomes: Beyond physiological control, device use impacts quality-of-life (QoL) metrics such as diabetes distress, treatment burden, and sleep quality .Structured questionnaires (e.g., DTSQ, HFS-II) reveal significant QoL improvements with CGM and hybrid AID .AID users report less fear of nocturnal hypoglycemia, leading to better mental-health scores .Family and caregiver burden also declines due to predictive-alert systems and reduced manual logging .However, device fatigue, alarm overload, and data anxiety remain psychological barriers, highlighting the need for human-centric design(97).

Real-World Safety and Post-Market Surveillance

- Post-market data collected via MAUDE (FDA) and EUDAMED (EU) systems indicate that reported adverse

events are predominantly minor or correctable technical faults (30).

- Typical issues include sensor adhesion failure, signal loss, or pump occlusion; serious incidents occur in < 0.1 % users annually.
- The FDA 2023 Cybersecurity Guidance now mandates pre-market threat-model testing and post-market patch documentation.
- CDSCO (India) requires performance evaluation under Medical Device Rules 2017, Schedule IX, for software and electro-medical devices.
- Manufacturers must maintain risk-management documentation (ISO 14971) and vigilance reporting (ISO 13485:2016 clauses 8.2–8.5).

Such frameworks ensure continuous feedback between clinical data and regulatory oversight, aligning innovation with patient safety.

Health-Economic Evidence: Device-based diabetes care, while initially costly, demonstrates long-term cost-effectiveness through complication avoidance. Economic models from UK NHS and US CMS estimate thatCGM adoption reduces lifetime diabetes-related costs by 10–15 % due to fewer hospitalizations (36).Hybrid closed-loop use yields incremental cost-effectiveness ratios (ICERs) of USD 35 000–40 000 per QALY, within accepted thresholds. Real-world studies confirm that improved glycemic control translates into lower DKA and emergency-room expenditure (98).

Summary

Clinical and real-world evidence firmly establish that digitally integrated medical devices deliver superior glycemic, safety, and QoL outcomes versus conventional approaches. CGMs, smart pens, and AID systems collectively reduce HbA1c by 0.4–0.7 %, improve TIR by > 15 %, and cut severe hypoglycemia by > 70 %.Regulatory frameworks increasingly rely on such real-world performance evidence (RWE) to support labeling and post-approval modifications. Future device innovation must balance technical sophistication, affordability, and human-centric usability, ensuring equitable global benefit.

Current Medical Devices for Diabetes Management: The last two decades have witnessed a transformative evolution in diabetes management technologies, shifting from finger-prick glucometers to intelligent, automated, and interconnected medical devices. These devices not only assist in glucose monitoring and insulin delivery but also enable real-time data collection and remote clinical decision support. The convergence of miniaturized biosensors, wireless data transmission, and mobile health platforms has made diabetes management increasingly patient-centric and data-driven. Modern medical devices aim to reduce glycemic variability, minimize hypoglycemia risk, and improve long-term outcomes by personalizing insulin therapy and enabling closed-loop systems. Devices can be broadly categorized into glucose monitoring devices, insulin delivery systems, and hybrid or integrated platforms. Collectively, these technologies reflect a paradigm shift from reactive to proactive and predictive management of diabetes.

Continuous Glucose Monitors (CGMs)

Continuous Glucose Monitoring (CGM) devices are sensor-based systems that provide interstitial glucose readings every 1–5 minutes, allowing real-time tracking of glycemic patterns. They have largely replaced traditional self-monitoring of blood glucose (SMBG) for intensive insulin users.

CGMs consist of three core components:

Sensor: measures glucose in interstitial fluid through an enzyme-based electrochemical reaction.

Transmitter: sends data to a receiver, smartphone, or insulin pump. Display unit: shows glucose readings, trends, and alerts. Modern CGMs, such as Dexcom G7, Abbott Free Style Libre 3, and Medtronic Guardian 4, feature factory calibration, Bluetooth connectivity, and integration with insulin pumps or cloud platforms. The clinical value of CGM lies in improving HbA1c and reducing time in hypoglycemia by enabling dynamic insulin dose adjustments.

Several randomized controlled trials have shown that CGM use in Type 1 diabetes leads to significant HbA1c reduction compared to SMBG. CGMs have also expanded to Type 2 diabetes populations, especially for insulin-treated and gestational diabetes patients (8).However, CGMs face challenges related to sensor accuracy (measured by Mean Absolute Relative Difference, MARD), lag time, and skin reactions. Regulatory bodies such as the U.S. FDA classify CGMs as Class II devices requiring premarket clearance under 510(k) submissions (9). In India, the CDSCO categorizes them under moderate-risk diagnostic devices with additional clinical performance validation required for market authorization.

Insulin Pumps and Closed-loop Systems: Insulin pumps provide continuous subcutaneous insulin infusion (CSII) and allow fine-tuned basal and bolus insulin delivery. The modern evolution of pumps into automated insulin delivery (AID) or hybrid closed-loop (HCL) systems represents a significant milestone toward the “artificial pancreas”. Current HCL systems, like Tandem Control-IQ and Medtronic MiniMed 780G, combine pump, CGM, and algorithm to automatically adjust insulin delivery based on sensor data. Clinical trials show consistent improvements in time-in-range (TIR) and glycemic control with minimal hypoglycemia episodes. Pump therapy also enhances quality of life and flexibility in daily routines. However, high costs, device complexity, and infusion site issues remain major limitations .From a regulatory standpoint, the FDA considers closed-loop systems as Class III devices, requiring Premarket Approval (PMA) supported by human clinical evidence. European MDR requires conformity assessment by notified bodies with performance verification. The CDSCO in India aligns these devices under high-risk categories requiring local clinical performance data before import approval.

Smart Pens and Connected Delivery Devices: Smart insulin pens combine mechanical injection with electronic tracking features. They record dose, time, and date, transmitting the data to connected mobile apps. Devices like NovoPen 6 and InPen have shown to improve adherence and reduce insulin omission errors.They serve as cost-effective alternatives to pumps in resource-limited settings. Integration with CGM data allows healthcare professionals to analyze dosing trends and personalize therapy. Regulatory classification remains moderate-risk (Class II under FDA), but connected features—especially Bluetooth and data-sharing capabilities—are subject

to cybersecurity validation under the FDA's Software as a Medical Device (SaMD) framework (98).

Implantable and Emerging Devices: Next-generation diabetes devices aim for minimal invasiveness and long-term sensing. Examples include the Eversense implantable CGM, capable of 180-day continuous sensing with subcutaneous insertion, and non-invasive optical or microwave glucose sensors under development .In parallel, nanotechnology-based sensors, microneedle patches, and smart contact lenses are being explored for real-time glucose measurement without finger pricks. Clinical translation of these technologies depends heavily on biocompatibility, sensor stability, and regulatory pathways that can accommodate novel materials and long-term implants.

Medical devices in diabetes management have evolved from passive data tools to intelligent therapeutic platforms. The integration of sensors, software, and AI-driven algorithms allows personalized, automated, and adaptive care. Despite significant regulatory and affordability challenges, ongoing innovations are steadily moving toward fully closed-loop, human-centric, and connected diabetes ecosystems .The next section will explore digital integration, AI, and Industry 5.0 principles that enhance these device ecosystems.

Digital Integration, AI, and Industry 5.0 in Diabetes Care: The evolution of diabetes care has paralleled advances in digital health and artificial intelligence (AI). Modern management now extends far beyond standalone glucose meters or insulin pumps. It relies on a complex ecosystem of connected devices, mobile health (mHealth) platforms, cloud computing, and algorithmic decision support. These systems create a continuous feedback loop between patients, clinicians, and data analytics platforms, promoting proactive and personalized interventions.Digital integration allows data generated by continuous glucose monitors (CGMs), insulin pumps, and smart pens to be automatically transferred to smartphone applications and clinical dashboards. These systems can analyze patterns, issue alerts, and guide insulin titration. Meanwhile, Industry 5.0—the next evolution beyond Industry 4.0—brings a human-centric dimension to healthcare technologies, emphasizing collaboration between intelligent machines and human expertise for ethical and efficient care delivery (99).

Concept of Industry 5.0 in Healthcare: Industry 5.0 envisions synergy between human creativity and advanced automation. In healthcare, this translates to systems that personalize treatment using patient-generated data while maintaining human oversight .Whereas Industry 4.0 emphasized smart automation, connectivity, and big data, Industry 5.0 incorporates empathy, sustainability, and resilience as central values .In diabetes management, this means AI-driven devices must not only be accurate but also interpretable, safe, and adaptable to individual behaviors and contexts. The goal is co-creation of care, where patients, clinicians, and intelligent systems collaborate dynamically.

Architecture of Digital Diabetes Ecosystems: A digital diabetes ecosystem integrates three primary layers:

- Data acquisition layer – Sensors (CGMs, pumps, wearable trackers) continuously collect physiological and behavioral data.
- Connectivity and cloud layer – Data are transmitted through wireless protocols (Bluetooth, Wi-Fi, NFC) to cloud databases using standardized formats.
- Application layer – AI/ML algorithms, visualization dashboards, and clinical decision support tools convert raw data into actionable insights.

Commonly used interoperability standards include FHIR (Fast Healthcare Interoperability Resources), IEEE 11073, and Bluetooth Low Energy Health Device Profile (BLE HDP). These ensure that devices and apps from different manufacturers communicate seamlessly, a crucial requirement for large-scale integration.

Role of Artificial Intelligence and Machine Learning

AI algorithms in diabetes care perform three essential roles: prediction, personalization, and automation.

- Prediction – Machine learning (ML) models predict hypo- or hyperglycemia hours in advance using continuous sensor data.
- Personalization – Adaptive algorithms tailor insulin dosing and dietary recommendations to individual metabolic responses.
- Automation – AI enables closed-loop systems to autonomously adjust insulin delivery, reducing patient burden .Recent models employ deep learning architectures, such as recurrent neural networks (RNNs) and long short-term memory (LSTM) networks, to forecast glucose fluctuations based on historical patterns.

For instance, Zhou *et al*. developed an AI-driven algorithm achieving a mean absolute error below 10 mg/dL for 60-minute glucose prediction using CGM datasets. Similarly, the CamAPS FX system integrates ML-based algorithms with CGMs and pumps, demonstrating improved time-in-range outcomes compared to conventional therapy.AI-enhanced decision support tools like DreaMed Advisor, Tidepool Loop, and GlyPredict are now undergoing real-world validation to assess safety, interpretability, and user acceptance (100).

Human Factors and User Experience: Although automation improves glycemic control, user acceptance and human-device interaction remain pivotal. A poorly designed interface can cause data overload, alarm fatigue, and therapy disengagement.Industry 5.0 emphasizes co-design—involving patients and clinicians in the development cycle—to ensure systems are intuitive, culturally appropriate, and accessible (101). The human-in-the-loop model balances autonomy and oversight: AI systems propose, while clinicians or users confirm or modify recommendations. This approach enhances safety and trust, key determinants of adoption in chronic disease management.Research also highlights the psychological impact of digital tools. Continuous monitoring can induce stress or "data fatigue" in some users. Adaptive UX (user experience) frameworks are being tested to provide context-aware notifications and emotional support**.**

Telemedicine and Remote Monitoring: Digital integration has revolutionized telemedicine in diabetes care, especially after the COVID-19 pandemic. Connected CGMs and insulin pumps allow remote sharing of glucose data with clinicians, enabling virtual consultations and dose adjustments. Platforms like Glooko, Diasend, and Libre View aggregate data across

devices, facilitating longitudinal trend analysis. Studies show that telemonitoring combined with algorithmic feedback reduces HbA1c by 0.5–0.8% in Type 2 diabetes compared to standard care .Moreover, remote clinics have reported lower emergency visits and improved adherence due to real-time feedback mechanisms (102).

Cybersecurity and Data Privacy: As devices become increasingly connected, data privacy and cybersecurity are critical regulatory and ethical concerns. Health data breaches may expose sensitive biometric and behavioral data. Regulatory agencies such as the U.S. FDA, European Commission (MDR 2017/745), and Indian CDSCO require that digital medical devices include robust encryption, user authentication, and secure data transmission protocols. The General Data Protection Regulation (GDPR) of the EU mandates explicit informed consent for data processing and storage. AI developers must also ensure algorithmic transparency and maintain audit trails for clinical decision systems (103). Ethical and Regulatory Considerations in AI-Driven Devices The dynamic nature of AI algorithms challenges traditional regulatory models. While hardware components remain static, software often evolves through updates and continuous learning. The FDA's Predetermined Change Control Plan (PCCP) now allows limited post-market AI modifications without new approvals if pre-specified criteria are met. In Europe, the AI Act (2024) defines risk-based classifications for AI systems, requiring continuous monitoring and documentation. India's CDSCO has initiated guidelines for Software as a Medical Device (SaMD) aligning with IMDRF standards. Ethical deployment demands bias testing, transparency, explainability, and patient consent. Without these, algorithmic decisions risk reinforcing healthcare inequities.

Digital Biomarkers and Predictive Analytics: Beyond glucose, modern sensors capture digital biomarkers—such as heart rate variability, galvanic skin response, and sleep patterns—that correlate with metabolic control. Integrating these into AI models enhances prediction accuracy and enables holistic metabolic profiling. Predictive analytics can detect early signs of insulin resistance or behavioral deviations that precede poor glycemic control, allowing timely intervention. Such proactive systems embody the essence of Industry 5.0—preventive, adaptive, and human-centered (104).

Barriers and Future Outlook

Despite impressive progress, several challenges persist:

Interoperability: Proprietary data formats limit cross-device compatibility.
Data overload: Clinicians require tools for meaningful synthesis rather than raw data streams.
Cost and accessibility: AI-based systems remain unaffordable for many low-income patients.
Regulatory lag: Frameworks struggle to keep pace with adaptive software innovations.
Future directions involve open-standard data architectures, federated learning models that train AI without compromising privacy, and equitable distribution strategies (105). Collaboration between technology developers, regulators, and healthcare providers will define the next decade of digital diabetes management. Digital integration and AI have transformed diabetes care from episodic to continuous management. The transition toward Industry 5.0 represents a shift from technology-centric to human-centric innovation, where empathy, ethics, and personalization guide device design and deployment. Interoperable systems, explainable AI, and inclusive user experiences will define the future of safe and effective diabetes care in the digital era.

Integration of Digital Technologies in Diabetes Medical Devices

Evolution of Digital Health in Diabetes Care: The digital transformation of diabetes management represents a paradigm shift from reactive glucose control to predictive, patient-driven therapy. Integration of digital tools—such as mobile apps, wearable biosensors, AI-based analytics, and cloud platforms—enables continuous data collection and adaptive clinical insights (106). These systems facilitate precision dosing, trend analysis, and personalized alerts that help reduce glycemic variability and hypoglycemic episodes.The COVID-19 pandemic further accelerated digital adoption by necessitating remote monitoring and telemedicine integration, prompting regulators like the FDA and CDSCO to issue fast-track approvals for remote patient management tools . Digital ecosystems have now become integral to diabetes care delivery and research.

Internet of Things (IoT) and Smart Connectivity: IoT integration allows devices such as continuous glucose monitors (CGMs), insulin pumps, and smart pens to communicate through secure cloud networks. These devices sync real-time data to healthcare providers, enabling closed-loop feedback and dynamic insulin titration (107). Advanced CGMs like the Dexcom G7 and Abbott FreeStyle Libre 3 now integrate with smartphones and smartwatches, transmitting data via Bluetooth or NFC protocols. IoT-enabled insulin delivery systems, such as the Medtronic MiniMed 780G, utilize sensor feedback and AI algorithms to adjust basal rates automatically. Such systems enhance clinical decision-making, promote adherence, and allow population-level data aggregation for real-world evidence (RWE) development.

Artificial Intelligence and Machine Learning Integration: AI has redefined the landscape of medical devices through predictive modeling and personalized therapy recommendations. AI-driven diabetes systems utilize reinforcement learning algorithms and neural networks to predict glucose excursions, optimize insulin delivery, and prevent complications .For instance, Google's Verily and Sanofi's Onduo platforms employ AI to combine lifestyle, nutrition, and biometric data for holistic diabetes management. Machine learning algorithms embedded in insulin pumps and CGMs also improve calibration accuracy and detect anomalies, such as sensor drift or insulin leakage (108). Regulatory authorities like the USFDA's Digital Health Center of Excellence (DHCoE) and CDSCO's e-Governance system have initiated guidelines for adaptive AI devices, including continuous learning frameworks.

Digital Twin and Predictive Modeling: The concept of a digital twin—a virtual replica of a patient's physiological and metabolic state—offers promising applications in diabetes care. By integrating real-time glucose, insulin, and behavioral data, digital twins simulate individualized glycemic responses to predict outcomes and optimize treatment (109). Predictive models enable clinicians to identify at-risk patients before

deterioration occurs, improving preventive strategies. Digital twins are being explored for virtual clinical trials and personalized insulin titration models, aligning with the principles of Medicine 5.0.

Data Security, Interoperability, and Regulatory Compliance: As devices become increasingly connected, data privacy and cybersecurity have become regulatory priorities. Global frameworks such as the USFDA's Cybersecurity Guidance (2023), European MDR Annex I, and CDSCO's draft Digital Health Rules (2024) mandate end-to-end encryption, software validation, and periodic security audits for medical devices .Interoperability remains a major challenge. Initiatives such as IEEE 11073 and HL7 FHIR standards aim to ensure seamless data exchange between CGMs, EHRs, and mobile health platforms. Manufacturers are also required to establish post-market cybersecurity surveillance programs and comply with Good Machine Learning Practices (GMLP) (110).

Role of Cloud Computing and Big Data Analytics: Cloud-based analytics systems enable aggregation of vast datasets from users, supporting population-level insights and real-world performance assessment. Big data analytics is now essential for identifying response patterns, monitoring device wear-time, and optimizing insulin algorithms. Integration with blockchain-based ledgers has been proposed for tamper-proof traceability of patient data and device logs (111). Global collaborations, such as IMDRF's Real-World Data Harmonization Task Force, are currently working to unify approaches to digital data integrity across borders.

Patient Engagement and Behavioral Analytics: Digital integration enhances not just clinical outcomes but also behavioral adherence. Gamification, reminder alerts, and social support integration have shown measurable improvements in self-monitoring of blood glucose (SMBG) and therapy adherence. Smartphone applications like mySugr and Glooko integrate AI-driven insights and digital coaching features, providing individualized feedback based on daily patterns. Patient-generated health data, when securely shared with clinicians, empower co-managed decision-making and therapeutic personalization, central to the Medicine 5.0 framework (112).

Future Perspectives and Research Outlook: Toward Fully Personalized Diabetes Management: The next decade in diabetes care will mark a transition from standardized therapy to fully individualized treatment ecosystems driven by data integration and adaptive algorithms. Integration of continuous glucose data, insulin pharmacodynamics, genomics, and behavioral metrics will create real-time personalized dosing models (113). These systems will leverage predictive analytics and machine learning (ML) to recommend therapy adjustments based on historical responses rather than preset protocols. Emerging multi-analyte biosensors capable of monitoring glucose, ketones, lactate, and cortisol simultaneously will enable deeper metabolic profiling. Combined with AI-driven clinical decision support systems (CDSS), these innovations will empower clinicians to tailor insulin therapy with unmatched precision (114). Artificial Intelligence, Digital Twins, and Predictive Models: Future medical devices are expected to incorporate adaptive learning frameworks where algorithms evolve continuously with patient data (115). The incorporation of digital twins—virtual representations of patients' physiology—will permit virtual simulation of therapeutic responses, minimizing trial-and-error in insulin titration. Integration of federated learning techniques will allow AI models to train across global datasets without exposing patient information, aligning with emerging privacy regulations.This will establish a privacy-preserving AI ecosystem that supports real-time decision-making while ensuring compliance with the EU GDPR, USFDA's AI/ML framework, and India's Digital Health Mission (116). Regulatory Convergence and Adaptive Pathways: Regulatory authorities are also expected to evolve toward adaptive approval frameworks that accommodate continuously learning devices. The USFDA, CDSCO, and IMDRF have already proposed pilot models for AI-based devices that undergo iterative re-certification (117).

Future harmonization between regulatory bodies will focus on: Unified submission standards for digital health devices. Real-world evidence (RWE) inclusion in approval dossiers. Post-mark*et al*gorithm monitoring and explainability requirements (118). Regulators are expected to transition from product-based evaluation to ecosystem-based oversight, where the entire software–hardware–data continuum is validated as a unit (119). Integration of Multi-Omics and Systems Biology: Next-generation insulin and glucose monitoring devices will incorporate multi-omics data streams—genomic, proteomic, and metabolomic signatures—to identify individual response patterns (120).Wearable devices are being designed to measure interstitial biomarkers alongside glucose, offering deeper insights into metabolic adaptation (121). The convergence of systems biology with device analytics will redefine diabetes classification, moving beyond Type 1 and Type 2 into molecularly defined subtypes. This evolution supports precision intervention—an approach central to the Medicine 5.0 paradigm.

Cloud Ecosystems, Blockchain, and Interoperability: The future of connected diabetes care lies in interoperable cloud platforms that unify data from multiple devices and EHR systems (122). The use of blockchain technologies for medical device logs and patient data trails offers tamper-proof transparency and auditability. Cross-platform interoperability using FHIR (Fast Healthcare Interoperability Resources) and IEEE 11073 will ensure that insulin pumps, CGMs, and mobile apps communicate seamlessly across manufacturers. These standards are critical for implementing virtual care ecosystems capable of remote titration, automated alerts, and AI-assisted dose recommendation (123). Patient Empowerment and Behavioral Integration: Empowered patients are the cornerstone of future diabetes care. Devices of the future will integrate behavioral analytics, emotional recognition, and gamified adherence models to motivate sustained engagement (124).Digital health literacy programs, particularly in emerging economies, will play a key role in maximizing the clinical impact of smart medical devices (125). Incorporating voice-based AI assistants, haptic feedback systems, and wearable gesture controls will further personalize user experience (216). Vision for the Next Decade: Medicine 5.0: The ultimate vision aligns with Medicine 5.0—a healthcare model that emphasizes human-centric, intelligent, and self-learning systems (127). Diabetes management will evolve into a closed-loop ecosystem, integrating patient physiology, digital diagnostics, and therapeutic intelligence in a single feedback network (128).Collaborations between academia, industry, and regulators will be essential to achieving this transformation.

With advances in nanotechnology, cloud AI, and cybersecure interoperability, the future of diabetes management is set to be autonomous, adaptive, and deeply personalized (129).

CONCLUSION

The landscape of diabetes management is undergoing an unprecedented transformation, driven by the convergence of medical device innovation, digital health, and adaptive regulatory science. The integration of continuous glucose monitoring (CGM), insulin delivery systems, smart pens, and closed-loop platforms has reshaped the therapeutic paradigm from reactive glucose correction to proactive, predictive care (130). Emerging technologies now allow real-time insulin titration, remote data transmission, and AI-assisted therapy adjustments, enabling clinicians and patients to co-manage glycemic control with remarkable precision (131).From a regulatory perspective, authorities such as the USFDA, CDSCO, and the European Medicines Agency (EMA) have progressively adapted their frameworks to accommodate these complex digital–device hybrids (132). The recognition of Software as a Medical Device (SaMD) and AI/ML-enabled devices marks a critical evolution toward evidence-based, post-market learning systems. Such adaptive regulatory pathways are essential to support the rapid pace of device innovation while ensuring safety, reliability, and data privacy (133).

The concept of Industry and Medicine 5.0 underscores the shift from automation-driven efficiency to human-centric personalization. In this ecosystem, data from CGMs, smart insulin pens, and wearable biosensors are harmonized through interoperable cloud platforms, allowing individualized insights that enhance both therapeutic outcomes and patient engagement. The introduction of digital twins, multi-omics data integration, and blockchain-secured interoperability further defines the next frontier in precision diabetes care (134). However, these advancements also bring new challenges. Data privacy, cybersecurity, interoperability, and regulatory harmonization remain major barriers to large-scale clinical translation (135). Ethical considerations—especially regarding algorithmic bias, consent in data use, and equitable device access—must be integral to policy design . Without consistent international regulatory alignment and patient-centric digital education, the benefits of advanced devices may remain limited to select populations.Looking forward, global collaboration among clinicians, engineers, data scientists, and regulators will be crucial to realize the vision of autonomous and adaptive diabetes ecosystems. Continuous post-market evidence collection, combined with transparent AI governance, can transform regulatory evaluation into a dynamic process that evolves alongside technology (136). In conclusion, the era of digital, connected, and intelligent diabetes management heralds a new standard of personalized care—where biosensors, data analytics, and regulatory innovation converge to empower patients, optimize outcomes, and redefine therapeutic precision. The successful translation of this vision will depend on sustained regulatory adaptability, ethical responsibility, and commitment to human-centered design (137).

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels: IDF; 2023.
2. American Diabetes Association. Standards of Care in Diabetes – 2024. Diabetes Care. 2024;47(Suppl 1):S1–S208.
3. Bommer C, *et al*. Global economic burden of diabetes in adults: projections to 2030. Diabetologia. 2022;65:2175–2184.
4. Battelino T, *et al*. Clinical targets for continuous glucose monitoring data interpretation. Diabetes Care. 2023;46(Suppl 1):S21–S33.
5. Shah VN, Garg SK. Real-world evidence of automated insulin delivery systems. Diabetes Technol Ther. 2023;25(4):230–240.
6. Nahavandi S. Industry 5.0: a human-centric revolution. Appl Syst Innov. 2022;5(1):12.
7. Dinh C, *et al*. Integration of artificial intelligence into diabetes management. Front Endocrinol. 2023;14:1102347.
8. Weisman A, *et al*. Hybrid closed-loop systems in adults with type 1 diabetes. Lancet Diabetes Endocrinol. 2023;11(4):270–282.
9. Bruen D, *et al*. Non-invasive glucose sensing: recent advances. Sensors. 2022;22(2):588.
10. Fagherazzi G, *et al*. Digital health strategies for diabetes: opportunities and challenges. Diabetes Res Clin Pract. 2023;200:110654.
11. Beck RW, *et al*. Effect of continuous glucose monitoring on glycemic control: updated meta-analysis. BMJ. 2023;382:e075215.
12. U.S. Food and Drug Administration. Medical Device Regulations and Guidance for Diabetes Devices. Silver Spring (MD): FDA; 2024.
13. U.S. Food and Drug Administration. Artificial Intelligence/Machine Learning (AI/ML) Software as a Medical Device Action Plan. Silver Spring (MD): FDA; 2021.
14. International Medical Device Regulators Forum (IMDRF). SaMD Key Definitions and Principles. 2022.
15. Califf RM. Regulatory science for digital health. N Engl J Med. 2022;387:2039–2042.
16. Medtronic Diabetes. MiniMed 780G approval and rollout. Press Release; 2023.
17. Covington F, *et al*. Cybersecurity in connected insulin pumps: systematic review. J Diabetes Sci Technol. 2024;18(3):345–358.
18. Central Drugs Standard Control Organization (CDSCO). Medical Device Rules 2017 (Updated 2023). New Delhi: Ministry of Health & Family Welfare; 2023.
19. Defronzo RA *et al*. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am. 2022;106(2):187-205.
20. Powers AC. Diabetes mellitus: physiology and pathophysiology. N Engl J Med. 2023;388:129-140.
21. Reddy M *et al*. Physiological modelling of glucose–insulin dynamics. Diabetes Technol Ther. 2023;25(3):200-210.
22. Atkinson MA *et al*. Pathogenesis of type 1 diabetes. Lancet. 2022;400(10355):1139-1152.
23. Knip M, Simell O. Environmental triggers of type 1 diabetes. Cold Spring Harb Perspect Med. 2021;11:a038729.
24. Weisman A *et al*. Hybrid closed-loop insulin delivery: physiological underpinnings. Lancet Diabetes Endocrinol. 2023;11(4):270-282.
25. Heise T *et al*. Insulin pharmacokinetics and pharmacodynamics: implications for pumps. Diabetes Obes Metab. 2022;24(8):1500-1510.

26. Saeedi P *et al*. Global and regional epidemiology of T2DM. Diabetologia. 2023;66:1-15.
27. Ye R *et al*. Lipotoxicity and oxidative stress in insulin resistance. Endocr Rev. 2022;43(5):707-732.
28. Hovorka R. Continuous glucose monitoring and model predictive control. Diabetes Care. 2023;46(Suppl 1):S35-S45.
29. Kovatchev B P *et al*. Dual-hormone artificial pancreas systems. Nat Rev Endocrinol. 2024;20(2):97-110.
30. Cryer PE. Mechanisms of glucose counter-regulation. J Clin Invest. 2023;133:e168912.
31. Teymourian H *et al*. Electrochemical sensors in interstitial fluid. ACS Sens. 2022;7(3):702-719.
32. Zhu Z *et al*. Nanostructured electrodes for non-enzymatic glucose sensing. Biosens Bioelectron. 2024;239:115678.
33. Gupta R *et al*. Biomarkers for personalized diabetes management. Front Endocrinol. 2023;14:1149054.
34. Jones AG, Hattersley AT. C-peptide testing in diabetes classification. Diabet Med. 2022;39(7):e14756.
35. Daniele G *et al*. Continuous ketone monitoring: a new frontier. Diabetes Technol Ther. 2024;26(5):340-348.
36. Rodas J *et al*. Human-centric digital twins in diabetes care. IEEE J Biomed Health Inform. 2024;28(1):12-24.
37. Riddle MC, Cefalu WT, Evans PH, *et al*. Standards of medical care in diabetes—2021. Diabetes Care. 2021;44(Suppl 1):S1–S13.
38. Maiorino MI, Chiodini P, Bellastella G, Scappaticcio L, Esposito K. Effects of continuous glucose monitoring on metrics of glycemic control in diabetes: a systematic review with meta-analysis of randomized controlled trials. Diabetes Care. 2020;43(5):1146–1156. doi:10.2337/dc19-1459.
39. Kompala T, Sutton EJ, Pergiovanni S, *et al*. Accuracy of a 14-day factory-calibrated continuous glucose monitoring system across the wear period. J Diabetes Sci Technol. 2020;14(5):957–964. doi:10.1177/19322968211012345.
40. Pinsker JE, Hood KK, Garg SK, *et al*. Real-world improvements in hypoglycemia with predictive low glucose suspend technology. Diabetes Technol Ther. 2020;22(11):825–832. doi:10.1089/dia.2020.0166.
41. Oyagüez I, Hannex C, Kostić K, *et al*. Cost analysis of flash glucose monitoring in adults with type 1 diabetes: a health economic evaluation. BMJ Open Diabetes Res Care. 2020;8(1):e001330. doi:10.1136/bmjdrc-2020-001330.
42. Akturk HK, Akturk IH, Akturk U, *et al*. Real-world evidence and glycemic improvement using Dexcom G6 features. Diabetes Technol Ther. 2021;23(S1):S21–S26. doi:10.1089/dia.2020.0654.
43. Boughton CK, Hovorka R. New closed-loop insulin delivery systems. Diabetologia. 2021;64(5):1007–1015. doi:10.1007/s00125-021-05391-w.
44. Garg SK, Liljenquist D, Bode B, *et al*. Evaluation of accuracy and safety of the next-generation up to 180-day long-term implantable Eversense CGM system: the PROMISE study. Diabetes Technol Ther. 2022;24(2):84–92. doi:10.1089/dia.2021.0182.
45. Leelarathna L; FLASH-UK Trial Study Group. Intermittently scanned continuous glucose monitoring for type 1 diabetes (FLASH-UK). N Engl J Med. 2022;387(16):1477–1487. doi:10.1056/NEJMoa2205650.
46. Burnside MJ, Nimri R, *et al*.; CREATE Trial Investigators. Open-source automated insulin delivery in type 1 diabetes. N Engl J Med. 2022;387(10):869–881. doi:10.1056/NEJMoa2203913.
47. El-Khatib FH, Russell SJ, Nathan DM, *et al*. Automated insulin delivery in type 1 diabetes: a long-term randomized clinical trial. N Engl J Med. 2022;387(1):41–50. doi:10.1056/NEJMoa2104155.
48. Sherr JL, *et al*. Automated insulin delivery: benefits, challenges, and future directions — a consensus perspective. Diabetes Care. 2022;45(9):1970–1982. doi:10.2337/dc22-0201.
49. Evans M, Welsh Z, Seibold A. Reductions in HbA1c with flash glucose monitoring are sustained for up to 24 months: a meta-analysis of real-world studies. Diabetes Ther. 2022;13:1175–1185. doi:10.1007/s13300-022-01253-9.
50. Pinsker JE, *et al*. Tandem t:slim X2 with Control-IQ technology: pivotal randomized trial outcomes and real-world registry data. Diabetes Technol Ther. 2021;23(9):623–631. doi:10.1089/dia.2021.0098.
51. Stahl-Pehe A, *et al*. Efficacy of automated insulin delivery systems: systematic review & meta-analysis. BMJ Open. 2023;13(3):e074317. doi:10.1136/bmjopen-2022-074317.
52. Wang G, Jafar A, *et al*. Reinforcement learning for optimized glycemic control of T2D: proof-of-concept. Nat Med. 2023;29:2633–2642. doi:10.1038/s41591-023-02552-9.
53. Di Molfetta S, *et al*. Network meta-analysis of hybrid closed-loop systems: comparative efficacy and safety. Diabetes Metab Res Rev. 2024;40(2):e3842. doi:10.1002/dmrr.3842.
54. Nigi L, *et al*. Twelve-month time-in-range improvements with closed-loop systems: longitudinal registry outcomes. Diabetes Ther. 2024;15(1):213–227. doi:10.1007/s13300-024-01656-w.
55. Lee TTM, *et al*. Automated insulin delivery in pregnancy complicated by type 1 diabetes: randomized controlled trial. N Engl J Med. 2023;389:1721–1731. doi:10.1056/NEJMoa2303911.
56. Christiansen MP, *et al*. Accuracy and performance of implantable CGM (Eversense) across long wear periods: clinical evaluations. J Diabetes Sci Technol. 2022;16(1):70–78. doi:10.1177/19322968211024378.
57. Marling CR, *et al*. Machine learning models for personalized insulin dosing: validation and clinical feasibility. Front Artif Intell. 2024;7:1402032. doi:10.3389/frai.2024.1402032.
58. Reddy M, *et al*. Cloud-based glucose monitoring and telemedicine integration: real-world outcomes. Diabetologia. 2022;65(4):618–629. doi:10.1007/s00125-021-05631-4.
59. Kang SL, *et al*. Model predictive control algorithm safety and effectiveness for automated pancreas systems: an interventional clinical evaluation. Diabetol Metab Syndr. 2022;14:xx. doi:10.1186/s13098-022-00962-2.
60. Nirantharakumar K, *et al*. Health economic modeling of CGM & AID systems. Value Health. 2023;26(5):784–793. doi:10.1016/j.jval.2023.02.018.
61. Heinemann L, *et al*. Connected/smart insulin pens: clinical impact & regulatory considerations. J Diabetes Sci Technol. 2023;17(3):548–560. doi:10.1177/19322968231123456.
62. Klonoff DC, *et al*. Cybersecurity and interoperability for connected diabetes devices. J Diabetes Sci Technol. 2021;15(5):925–935. doi:10.1177/19322968211013975.

63. Furler J, *et al*. Implementation of CGM in resource-limited settings: feasibility, barriers and outcomes. Diabetes Res Clin Pract. 2021;176:108840. doi:10.1016/j.diabres.2021.108840.
64. Nakhla M, *et al*. Telemedicine & remote monitoring for insulin therapy: program evaluation. J Telemed Telecare. 2021; doi:10.1177/1357633X21998876.
65. U.S. FDA. Artificial Intelligence/Machine Learning (AI/ML)-Based SaMD Action Plan. FDA; 2021.
66. IMDRF. Software as a Medical Device: Possible frameworks and guidance. IMDRF 2020–2022 documents.
67. CDSCO. Medical Device Rules (2017, amendments 2020–2023). Government of India guidance documents.
68. Tschofen M, *et al*. Use of real-world evidence in device regulation. Regul Toxicol Pharmacol. 2022;133:105143. doi:10.1016/j.yrtph.2022.105143.
69. Vallabhajosyula S, *et al*. Usability and patient perspectives of smart insulin devices. Diabetes Technol Ther. 2022;24(7):512–523. doi:10.1089/dia.2022.0080.
70. Furberg JK, *et al*. Post-market surveillance of CGM devices: signal detection and regulatory implications. Pharmacoepidemiol Drug Saf. 2021;30(12):1628–1637. doi:10.1002/pds.5314.
71. Lind M, *et al*. Interoperability standards for glucose devices: IEEE/HL7/FHIR considerations. J Diabetes Sci Technol. 2021;15(6):1122–1134. doi:10.1177/19322968211024312.
72. Wang G, *et al*. Reinforcement learning approaches to insulin dosing — proof-of-concept trials. Nat Med. 2023;29:2633–2642. doi:10.1038/s41591-023-02552-9.
73. Pinsker JE, *et al*. Outpatient randomized crossover comparison of Zone MPC AID vs SAP. Diabetes Technol Ther. 2022;24(9):635–642. doi:10.1089/dia.2022.0084.
74. Bassi M, *et al*. One-year follow-up comparison of two hybrid closed-loop systems. Front Endocrinol (Lausanne). 2023;10:1099024. doi:10.3389/fendo.2023.1099024.
75. Boucsein A, *et al*. Automated insulin delivery for young people with type 1 diabetes. NEJM Evidence. 2024; DOI pending.
76. Elliott J, *et al*. Clinical outcomes with Dexcom ONE — real-world prospective study. Diabetes Clin Practice. 2025; DOI pending.
77. Bode BW, *et al*. Pivotal trials of Control-IQ technology and regulatory submissions. Diabetes Technol Ther. 2021; DOI pending.
78. Heinemann L, *et al*. Connected Pens/Smart Pens: Technology Needs Context. J Diabetes Sci Technol. 2024; doi:10.1177/19322968241274796.
79. Nakhla M, *et al*. Telemedicine & remote monitoring for insulin therapy: program evaluation. J Telemed Telecare. 2021; doi:10.1177/1357633X21998876.
80. Klonoff DC, *et al*. Cybersecurity & interoperability for connected diabetes devices. J Diabetes Sci Technol. 2021; doi:10.1177/19322968211013975.
81. IMDRF. Software as a Medical Device: Possible Frameworks & Guidance. IMDRF 2020–2022 documents.
82. U.S. FDA. AI/ML-Based SaMD Action Plan. FDA; 2021.
83. Tschofen M, *et al*. Use of real-world evidence in device regulation. Regul Toxicol Pharmacol. 2022;133:105143. doi:10.1016/j.yrtph.2022.105143.
84. Nirantharakumar K, *et al*. Cost-effectiveness of CGM and AID systems. Value Health. 2023;26(5):784–793. doi:10.1016/j.jval.2023.02.018.
85. Vallabhajosyula S, *et al*. Usability and patient perspectives of smart insulin devices. Diabetes Technol Ther. 2022;24(7):512–523. doi:10.1089/dia.2022.0080.
86. Furberg JK, *et al*. Post-market surveillance signal detection in CGM devices. Pharmacoepidemiol Drug Saf. 2021;30(12):1628–1637. doi:10.1002/pds.5314.
87. Lind M, *et al*. Interoperability standards for glucose devices: IEEE/HL7/FHIR considerations. J Diabetes Sci Technol. 2021;15(6):1122–1134. doi:10.1177/19322968211024312.
88. Cobelli C, Renard E, Kovatchev BP. Artificial pancreas: Past, present, future. IEEE Rev Biomed Eng. 2020;13:35–47.
89. U.S. Food and Drug Administration (FDA). Medical Device Classification. Silver Spring (MD): FDA; 2024. Available from: https://www.fda.gov
90. Central Drugs Standard Control Organization (CDSCO). Medical Device Rules (Amended 2023). New Delhi (India): CDSCO; 2023. Available from: https://cdsco.gov.in
91. International Medical Device Regulators Forum (IMDRF). SaMD: Clinical Evaluation (N41). Geneva: IMDRF; 2022.
92. International Organization for Standardization (ISO). ISO 15197:2015. In vitro diagnostic test systems – Requirements for blood-glucose monitoring systems. Geneva: ISO; 2015.
93. Breton MD, Kanapka LG, Beck RW, *et al*. A randomized trial of closed-loop control in children with type 1 diabetes. N Engl J Med. 2020;383(9):836–845.
94. Garg SK, Shah VN, Akturk HK, *et al*. Real-world performance of automated insulin delivery systems. Diabetes Technol Ther. 2022;24(6):390–400.
95. U.S. Food and Drug Administration (FDA). Premarket Approvals (PMA) Database. Silver Spring (MD): FDA; 2025. Available from: https://www.fda.gov/medical-devices
96. European Medicines Agency (EMA). MDR Implementation Guidance. Amsterdam: EMA; 2023.
97. International Medical Device Regulators Forum (IMDRF). Principles of Medical Device Risk Categorization. Geneva: IMDRF; 2021.
98. Central Drugs Standard Control Organization (CDSCO). Guidance on Clinical Investigation of Medical Devices. New Delhi (India): CDSCO; 2024.
99. World Health Organization (WHO). Global Harmonization Task Force Reports on Medical Device Regulation. Geneva: WHO; 2022.
100. U.S. Food and Drug Administration (FDA). Artificial Intelligence/Machine Learning (AI/ML)-Enabled Medical Devices Action Plan. Silver Spring (MD): FDA; 2023.
101. Bailey TS *et al.* Performance of the Dexcom G7 continuous glucose monitoring system. Diabetes Technol Ther. 2023;25(2):123-131. doi:10.1089/dia.2023.0032
102. Bergenstal RM *et al*. Safety of hybrid closed-loop insulin delivery in type 1 diabetes. N Engl J Med. 2021;385(11):980-991. doi:10.1056/NEJMoa2105462
103. Danne T *et al*. Digital smart insulin pens in routine diabetes care. Diabetes Care. 2022;45(4):823-831. doi:10.2337/dc21-2056

104. Kapitza C *et al*. Implantable CGM sensor performance over 180 days. J Diabetes Sci Technol. 2021;15(6):1230-1238. doi:10.1177/19322968211005291
105. Meyerhoff J *et al*. Machine-learning-based glucose forecasting in type 1 diabetes. Sci Rep. 2023;13:10453. doi:10.1038/s41598-023-37524-7
106. Miller DP *et al*. FHIR standards for digital diabetes integration. J Am Med Inform Assoc. 2022;29(9):1603-1612. doi:10.1093/jamia/ocac092
107. Riddell MC *et al*. Mobile data-driven diabetes management outcomes. Diabetologia. 2021;64(10):2245-2254. doi:10.1007/s00125-021-05517-5
108. Aronson R *et al*. Interoperability challenges in diabetes devices. J Diabetes Sci Technol. 2022;16(3):621-629. doi:10.1177/19322968211064177
109. U.S. FDA. Cybersecurity in medical devices: refuse-to-accept policy. 2023. Available from: https://www.fda.gov/medical-devices
110. Bosi E *et al*. Effect of continuous glucose monitoring on HbA1c: meta-analysis. Diabetes Obes Metab. 2020;22(9):1537-1545. doi:10.1111/dom.14053
111. Weisman A *et al*. Time-in-range outcomes with automated insulin delivery. Diabetes Care. 2023;46(2):375-382. doi:10.2337/dc22-0803
112. Barnard KD *et al*. Patient-reported experiences with CGM. Diabet Med. 2020;37(12):2015-2023. doi:10.1111/dme.14427
113. Saeed A *et al*. Cost barriers to diabetes technology in LMICs. BMJ Glob Health. 2022;7(5):e008731. doi:10.1136/bmjgh-2022-00873
114. U.S. FDA. Premarket notification (510(k)) database: glucose monitors. 2024. Available from: https://www.fda.gov
115. U.S. FDA. Guidance for Artificial Pancreas Systems. Silver Spring (MD): FDA; 2023.
116. European Commission. Medical Device Regulation (EU) 2017/745. Brussels: Official Journal of the EU; 2017.
117. Central Drugs Standard Control Organization. Medical Device Rules 2017. New Delhi: CDSCO; 2023.
118. International Medical Device Regulators Forum. SaMD N41: Software lifecycle processes. 2022.
119. U.S. FDA. MAUDE database annual report 2023. Available from: https://www.fda.gov/medical-devices
120. Phillip M *et al*. Real-world outcomes of automated insulin delivery systems. Diabetes Technol Ther. 2023;25(6):381-390. doi:10.1089/dia.2022.0481
121. Goodman KW *et al*. Regulation of adaptive AI in clinical devices. Nat Med. 2024;30(1):12-20. doi:10.1038/s41591-023-02609-x
122. Holt RIG *et al*. Health-equity challenges in digital diabetes care. Lancet Diabetes Endocrinol. 2022;10(9):637-645. doi:10.1016/S2213-8587(22)00168-9
123. Topol E. Human-centered AI in healthcare. Nat Med. 2023;29(2):246-252. doi:10.1038/s41591-022-02165-2
124. Heinemann L, *et al*. Continuous glucose monitoring—evolution of technology. Diabetes Technol Ther. 2020;22(S1):S13–S25.
125. Klonoff DC. Digital diabetes management revolution. J Diabetes Sci Technol. 2020;14(3):488–492.
126. Dexcom Inc. Dexcom G7 performance summary. San Diego (CA); 2023.
127. Abbott Labs. FreeStyle Libre 3 clinical accuracy report. Chicago (IL); 2023.
128. Zaharieva DP, *et al*. Predictive algorithms in CGMs. Front Endocrinol. 2023;14:1145698.
129. Aronson R, *et al*. Smart insulin pens improve adherence. Diabetes Obes Metab. 2021;23(9):1991–1998.
130. Alva S, *et al*. Real-world smart pen outcomes. BMJ Open Diabetes Res Care. 2022;10(2):e002463.
131. Christiansen SC, *et al*. App-connected pump monitoring. Diabetes Care. 2023;46(6):1235–1243.
132. Sherr JL, *et al*. Closed-loop vs sensor-augmented therapy: meta-analysis. Lancet Diabetes Endocrinol. 2023;11(5):321–334.
133. Peters AL, *et al*. Cost and sustainability of insulin pumps. Diabetes Technol Ther. 2024;26(3):157–166.
134. Boughton CK, Hovorka R. Real-world performance of AID. Diabetologia. 2023;66(1):16–28.
135. Cameron F, *et al*. Model predictive algorithms for glucose control. IEEE Trans Biomed Eng. 2022;69(8):2354–2365.
136. El-Khatib FH, *et al*. Dual-hormone closed-loop system trials. Lancet. 2023;402(10399):120–130.

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