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BEYOND THE ALGORITHM: A SYSTEMATIC REVIEW OF AI-DRIVEN DIGITAL TWINS IN GLYCEMIC CONTROL AND DECISION SUPPORT FOR TYPE 1 DIABETES

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ABSTRACT

Background: Managing type 1 diabetes requires continuous adaptation to metabolic fluctuations. Standard automated systems use static rules rather than dynamic, patient-specific models. AI-driven Digital Twins (DTs) overcome this by pairing continuous multimodal data with virtual patient representations for proactive therapy optimization.
Aim: This systematic review characterizes AI-driven DTs for T1D glycemic control, evaluating their underlying architectures (data-driven, mechanistic, hybrid), multimodal data integration, decision-support translation, and clinical validation levels.
Methods: Following PRISMA guidelines, a PubMed search yielded 443 unique records after duplicate removal. Five independent reviewers screened articles using PICOS criteria. Ultimately, 42 studies (including 11 randomized trials) evaluating AI-driven DTs or predictive models in T1D were included for qualitative synthesis.
Results: Most systems rely on continuous glucose monitoring (97.6%), while 40.5% incorporate the complete "metabolic triad" (CGM, insulin, carbohydrates). Architectures are shifting toward closed-loop paradigms combining patient-state estimation and adaptive feedback. Clinically, DT integration increased Time in Range by 7–26 percentage points (adding 3.0–6.2 hours daily), reduced Time Below Range (<4%), and lowered HbA1c by 0.32%–1.05% without severe adverse events. Capabilities range from short-term forecasting (30–120 minutes) to counterfactual simulation and autonomous closed-loop delivery. Hybrid models combining physiological mechanisms with machine learning represent the emerging standard.
Conclusions: AI-driven DTs advance T1D care by enabling dynamic, personalized decision-making and automated control. However, widespread clinical implementation requires addressing technical complexity, establishing standardized architectures, and conducting robust prospective validation under real-world conditions.

KEYWORDS

Type 1 Diabetes, Digital Twin, Artificial Intelligence, Continuous Glucose Monitoring, Machine Learning, Decision Support System

CITATION

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1. Introduction

Type 1 diabetes (T1D) is a chronic metabolic disorder characterized by absolute insulin deficiency and substantial variability in glucose regulation. Despite advances in continuous glucose monitoring (CGM), insulin pumps, and automated insulin delivery (AID), stable glycemic control remains challenging because glucose dynamics are influenced by meals, insulin absorption, physical activity, stress, illness, sleep, and other behavioral and physiological factors. Consequently, diabetes management increasingly requires not only continuous glucose monitoring but also prediction of future metabolic states and individualized therapeutic adaptation.

AID systems represent a major transition from reactive to algorithm-assisted diabetes management by integrating CGM, insulin delivery, and control algorithms that continuously adjust insulin administration. Clinical trials have demonstrated that closed-loop systems can substantially increase time in range while reducing hyperglycemia without increasing hypoglycemia [2,3]. For example, a six-month randomized trial of Control-IQ increased time in the 70–180 mg/dL range by approximately 11 percentage points compared with sensor-augmented pump therapy [3]. However, current systems generally optimize treatment within predefined algorithmic frameworks rather than maintaining a continuously evolving computational representation of the individual patient.

Artificial intelligence (AI) further extends this paradigm by enabling analysis of longitudinal diabetes data for prediction, classification, and individualized therapeutic recommendations [1]. AI-based approaches have been used to recommend insulin adjustments, predict impending hypoglycemia, and support behavioral decisions [1]. Nevertheless, accurate prediction or insulin-dose recommendation alone does not constitute a Digital Twin (DT), as AI models may remain detached from an explicit, patient-specific representation of the underlying physiological system.

Digital Twins provide a broader framework by representing an individual or physiological process computationally and continuously informing this representation with real-world data to simulate future states or interventions. In T1D, DTs have traditionally focused on individualized glucose–insulin models capable of reproducing responses to meals, insulin, and physical activity. A recent systematic review showed that existing T1D DT approaches predominantly model glucose–insulin metabolism and simulate therapeutic interventions rather than representing the patient at a comprehensive multiscale level [4]. The key value of a DT therefore lies not only in prediction but also in providing a patient-specific virtual environment for testing alternative therapeutic strategies before their real-world application.

This simulation capability enables DTs to support decisions involving insulin dosing, meals, physical activity, and control policies. For example, Young et al. developed an exercise decision-support system using individualized DT models to simulate glucose responses to aerobic and resistance exercise. In silico evaluation across exercise sessions from 247 individuals suggested that DT-supported recommendations could increase time in range and reduce time below range compared with no intervention [5]. Such approaches illustrate how patient-specific virtual representations can transform prediction into actionable decision support.

The maturation of AID technologies further supports this transition. Early studies demonstrated that closed-loop systems could safely automate insulin delivery in real-world settings, while subsequent randomized trials confirmed clinically meaningful improvements in glycemic control [2,3]. The next generation of diabetes technology may therefore depend not only on more sophisticated control algorithms but on integrating prediction, physiological modeling, contextual information, continuous learning, and decision support into a coherent patient-specific framework. Such systems could address clinically relevant questions such as how a patient is likely to respond to a given insulin dose or exercise intervention, rather than simply predicting future glucose levels.

Recent work has begun to connect DTs with AI, real-time data assimilation, automated control, and cyber-physical-human systems [6]. However, the field remains heterogeneous, with substantial differences in

mathematical foundations, data requirements, personalization, validation, and real-time interaction [4,6]. Moreover, many approaches remain limited to retrospective or in silico evaluation, while prospective clinical validation is comparatively scarce. Terminology is also inconsistent, with glucose forecasting models, physiological simulators, personalized computational models, AI-based decision-support systems, and Digital Twins often discussed within overlapping technological landscapes. Recent research evaluating glucose predictions within a DT framework illustrates the emerging shift from prediction alone toward assessing clinical impact on glycemic control [7].

Therefore, this systematic review aims to characterize AI-driven Digital Twins designed for glycemic control and decision support in T1D, focusing on how patient-specific virtual representations are constructed, which AI/ML methods and data streams are integrated, and how predictions are translated into therapeutic recommendations or automated interventions. Particular attention is given to data-driven, mechanistic, and hybrid DT architectures; personalization and real-time adaptation; clinical validation outcomes; and the progression from retrospective or in silico studies toward prospective evaluation. By examining these dimensions together, this review seeks to determine whether Digital Twins represent merely an evolution of glucose prediction algorithms or a broader paradigm for individualized, predictive, and simulation-assisted diabetes care.

2. Methodology

To investigate the impact of AI-driven digital twins and predictive models on glycemic control and decision support in patients with type 1 diabetes, a systematic literature search was conducted on August 18, 2026, using the PubMed electronic database.

The following search query was applied:

(("Diabetes Mellitus, Type 1"[Mesh] OR "Type 1 Diabetes" [TiAb] OR "T1D"[TiAb] OR "T1DM"[TiAb] OR "Insulin-Dependent Diabetes Mellitus" [TiAb]) AND ("Artificial Intelligence"[Mesh] OR "Machine Learning"[Mesh] OR "Deep Learning"[Mesh] OR "Computer Simulation"[Mesh] OR "Algorithms"[Mesh] OR "Digital Twin"[TiAb] OR "Digital Twins"[TiAb] OR "In Silico"[TiAb] OR "Predictive Model*"[TiAb] OR "Artificial Intelligence"[TiAb] OR "Machine Learning" [TiAb] OR "Neural Network*"[TiAb] OR "Reinforcement Learning"[TiAb]) AND ("Blood Glucose Self-Monitoring" [Mesh] OR "Decision Support Systems, Clinical" [Mesh] OR "Insulin Infusion Systems" [Mesh] OR "Blood Glucose"[Mesh] OR "Glycemic Control" [TiAb] OR "Decision Support"[TiAb] OR "Automated Insulin Delivery" [TiAb] OR "Closed-Loop" [TiAb] OR "Artificial Pancreas" [TiAb] OR "Continuous Glucose Monitoring" [TiAb] OR "CGM"[TiAb] OR "Dose Calculation*"[TiAb]))*

As a result of applying this strategy, 449 records were identified. The results were exported to the Rayyan platform, which is dedicated to literature review management and analysis. Using this platform, six duplicates were identified and removed after manual verification by our research team. This process allowed for the identification of 443 unique articles that qualified for the next selection stage.

2.1. Inclusion criteria

The research inclusion criteria were structured based on the PICOS framework (population, intervention, comparison, outcome, and study design) in accordance with the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The selected articles aimed to answer the following research question: "What is the clinical efficacy, predictive accuracy, and safety profile of AI-driven digital twins and predictive models compared with standard clinical care, conventional closed-loop systems, or baseline models in optimizing glycemic control and therapeutic decision support for individuals with type 1 diabetes?". The main inclusion criteria were as follows: (1) clinical trial, cohort, case-control, prospective pilot/observational studies, or experimental studies validating in-silico models on patient datasets; (2) a population of patients of any age with a confirmed diagnosis of type 1 diabetes (T1D); (3) documented application of digital twins or predictive models based on artificial intelligence (AI), machine learning (ML), or in-silico modeling supporting automated insulin delivery, glucose trajectory prediction, or therapeutic decision-making; (4) inclusion of a control/comparator group receiving standard clinical care (manual MDI), standard closed-loop/AID systems without digital twin modules, before-and-after baseline comparisons, or standard simulators/real clinical data for in-silico models; (5) measurement of primary outcomes including

Time in Range (TIR, 70–180 mg/dL), glycated hemoglobin (HbA1c), Time Below Range (TBR, <70 mg/dL), Time Above Range (TAR, >180 mg/dL), and/or glycemic variability parameters (CV%, SD); and (6) reporting of secondary outcomes such as predictive accuracy metrics (e.g., RMSE, MAE), adverse event rates (including severe hypoglycemia and diabetic ketoacidosis), quality of life (QoL), diabetes distress, or technology satisfaction. The exclusion criteria were as follows: (1) literature reviews, meta-analyses, expert opinions, letters to the editor, and case reports; (2) studies covering populations with type 2 diabetes (T2D), gestational diabetes (GDM), or other rare diabetes types (unless data for the T1D cohort were independently extracted and reported); and (3) interventions evaluating classic, rigid algorithms without adaptive/AI elements, basic static bolus calculators, or traditional paper/electronic logbooks lacking predictive models.

2.2. Data collection and analysis

The literature selection process was carried out in multiple stages, strictly following PRISMA guidelines. Initially, a team of five independent reviewers assessed the titles and abstracts of 443 articles, examining their compliance with the main objective of the study. To ensure maximum objectivity and minimize systematic error, this stage was conducted independently on the Rayyan platform. Studies that failed to meet the basic assumptions of the PICOS protocol were excluded. The next step involved an independent full-text assessment of the remaining publications by all review authors, based on detailed inclusion and exclusion criteria. Potential disagreements and conflicting assessments were subjected to joint analysis and discussed until a final consensus was reached. Forty-two studies were included in this systematic review. Of these, 11 were randomized controlled trials (RCTs) or randomized crossover trials.

2.3. Data Extraction

The following data were extracted from the qualified publications: DOI number, first author's name, year of publication, study type, follow-up period, number of participants in the study and control groups, mean/median age of participants, duration of diabetes, baseline HbA1c, prior treatment modality, digital twin classification (data-driven/ML, hybrid, or mechanistic), specific AI algorithm/model architecture utilized, input data sources (such as CGM streams, carbohydrate intake, insulin dosing history, wearable sensor data, and demographic variables), comparator group characteristics, model clinical application (including multi-horizon glucose forecasting [30–60 min], automated bolus calculation, basal dose adaptation, and early hypoglycemia warning systems), mean changes and levels of TIR (70–180 mg/dL), TBR (<70 mg/dL and <54 mg/dL), TAR (>180 mg/dL), HbA1c, and glycemic variability parameters (SD, CV%), model prediction error metrics (RMSE, MAE), and adverse events (including severe hypoglycemia, ketoacidosis, and rescue carbohydrate interventions).

3. Results

3.1. Digital Twin-architecture and modeling

The architecture of AI-driven Digital Twins for glycemic control in type 1 diabetes (T1D) is heterogeneous, ranging from purely data-driven predictive models to mechanistic and hybrid patient-specific representations. At the input layer, most systems integrate continuous glucose monitoring (CGM) data, while more advanced architectures additionally incorporate insulin delivery, carbohydrate intake, meal characteristics, demographic and anthropometric variables, physical activity, and wearable-derived physiological signals [8, 12, 13, 18, 26, 34, 36]. The central component is the virtual representation of the patient, which may be constructed using mechanistic physiological models describing glucose–insulin dynamics, data-driven machine-learning models, or hybrid approaches combining both paradigms. Mechanistic representations were frequently implemented through validated T1D simulators, particularly the UVA/Padova framework, enabling simulation of individual glucose–insulin dynamics and testing of control strategies in silico [11, 16, 19, 20, 39, 44, 48]. In contrast, data-driven architectures primarily learned patient-specific temporal patterns directly from CGM and associated clinical or behavioral data, using recurrent neural networks, LSTM/BiLSTM architectures, convolutional networks, temporal fusion transformers, gradient-

boosting methods, and ensemble learning [8, 9, 10, 14, 15, 22, 34, 38, 40, 42, 45, 47]. Hybrid architectures represent a particularly relevant development for Digital Twin applications because they combine physiological knowledge with adaptive machine learning, allowing the model to retain clinically meaningful physiological constraints while continuously adapting to inter-individual and intra-individual variability [12, 18, 26, 36, 39, 44, 49].

From an architectural perspective, the reviewed systems can be conceptualized as a closed information loop comprising four interconnected components: (1) multimodal data acquisition, (2) patient-state estimation and virtual patient modeling, (3) AI-based prediction or decision-making, and (4) feedback to insulin delivery or clinical decision support. The first component provides continuously updated information about the patient's current metabolic state, predominantly through CGM and, in some systems, insulin, meal, activity, and wearable data [13, 18, 26, 34]. The modeling layer then estimates latent physiological states or patient-specific parameters, such as insulin sensitivity, glucose dynamics, or postprandial response, which can subsequently be updated as new observations become available [12, 22, 26, 36]. The decision layer employs predictive and adaptive algorithms, including reinforcement learning, model predictive control, Bayesian optimization, deep neural networks, and ensemble methods, to forecast future glucose trajectories or determine insulin interventions [17, 18, 24, 25, 29, 37, 39, 43, 44].

Finally, the resulting predictions or recommendations can be translated into automated basal-rate adaptation, correction or meal boluses, hypoglycemia prevention, or decision-support recommendations [10, 11, 19, 24, 25, 26, 28, 32, 43, 44]. Importantly, several studies included in the present review describe sophisticated patient-specific AI or physiological models but do not formally define them as Digital Twins [10, 14-18, 20, 41]. Therefore, the current evidence suggests that the field is moving toward Digital Twin-like architectures rather than a uniformly established Digital Twin paradigm. The defining feature of the more mature approaches is not the use of AI alone, but the combination of a continuously updated representation of the individual patient with bidirectional prediction, adaptation, and decision support, enabling the virtual model to reflect changing metabolic conditions and inform subsequent therapeutic actions [26, 36, 39, 44].

3.2. Data and sources inputs

The efficacy, accuracy, and adaptive capabilities of digital twins and artificial intelligence or machine learning algorithms in diabetes management depend directly on the quality, sampling frequency, and diversity of input data sources. In the analyzed dataset of 42 studies [8–49], a broad spectrum of features was identified, ranging from single-dimensional time series of continuous glucose levels to complex, multimodal feature vectors incorporating insulin dynamics, carbohydrate intake, wearable telemetry, and clinical-demographic patient profiles. Among the 42 analyzed studies, continuous glucose monitoring (CGM) represented the core modality and was utilized in 97.6% of the studies [8–15, 17–49]. Insulin delivery data, including both meal or correction boluses and basal rate infusions, were incorporated in 52.4% of the studies [8, 11–14, 17–22, 24–27, 29–31, 34–37], while carbohydrate intake and meal data were included in 50.0% of the studies [8, 11–14, 16–19, 21–24, 26–29, 31, 32, 34, 36]. Demographic, anthropometric, and clinical parameters were integrated in 21.4% of the studies [10, 15, 22, 32, 34–37, 41], and physical activity or wearable telemetry was incorporated in 7.1% of the studies [18, 30, 34].

The most comprehensive input data configuration employed for building a digital twin of glucose metabolism is the metabolic data triad, which combines continuous glucose monitoring, logged insulin dosages, and carbohydrate consumption logs. Complete triad inputs were employed in 40.5% of the studies [8, 11, 12, 13, 14, 17, 18, 19, 21, 22, 24, 26, 27, 29, 31, 34, 36], demonstrating the highest degree of physiological fidelity. In studies such as [11, 19], derived parameters were also incorporated, including active insulin in the body, active carbohydrates, individual insulin-to-carbohydrate ratios, and insulin sensitivity factors. In contrast, the glucose-insulin dyad without carbohydrate logs was present in 11.9% of the studies [20, 25, 30, 35, 37]. The omission of manual meal logging in this group is primarily intended to reduce the patient burden or to leverage reinforcement learning algorithms capable of autonomously estimating the unannounced metabolic impact of meals [17, 37]. The glucose-meal dyad without explicit insulin logs was present in 7.1% of the studies [23, 28, 32], focusing predominantly on evaluating postprandial glycemic response curves and forecasting meal-induced glucose excursions. Finally, single-modality or CGM-only configurations were employed in 38.1% of the studies [9, 10, 15, 33, 38-49], relying on advanced time-series predictive architectures forecasting future glucose concentrations solely based on auto-correlation and historical temporal trends extracted from CGM sensor feeds, such as Medtronic Enlite [9, 15] or FreeStyle Libre [35].

A detailed examination of the input components shows that the CGM signal serves as the core foundation across the sample, although studies differ regarding sampling frequency and pre-processing. The most common sampling standards are 5-minute [9, 33] or 10-minute intervals [19]. Several studies derive summary glycemic metrics rather than relying solely on raw sequences, such as preprandial glucose levels, area under the curve, and glycemic extrema in [21], or up to 49 distinct glycemic features covering exercise and recovery periods in [33]. Alongside real-patient datasets and clinical repositories such as OhioT1DM [10, 14, 15, 42, 45], ShanghaiDM [10, 15], and Tidepool Big Data [49], physiological in silico simulators are widely represented, most notably the UVA/Padova T1DM Simulator [11, 12, 20, 39, 43, 44, 48].

Insulin administration is modeled either as discrete meal and correction bolus events defined by dose magnitude and timestamps [8, 12, 21, 22, 25, 26] or as continuous basal delivery profiles, including 48-hour historical basal infusion profiles [19] and dynamically adjusted basal delivery in automated insulin delivery systems [11, 17, 29, 36]. Meal information enters models through estimated carbohydrate mass in grams [8, 11, 19, 23, 24, 27, 34], total meal weight [22], or unquantified meal announcement flags [31]. Study [16] employs gold-standard triple-tracer meal data to model the specific rate and shape of gut carbohydrate absorption, whereas frameworks in [17, 18] feature embedded automated meal detection and estimation modules triggered by glucose rate changes. Furthermore, a growing trend involves enriching digital twins with individual clinical profiles, such as age, biological sex, BMI, diabetes type, baseline HbA1c, and micro-or macrovascular complications [10, 15, 22, 32, 34, 35, 41]. Finally, the integration of wearable telemetry and smartwatches [18, 30, 34] provides continuous measurements of heart rate, energy expenditure, step counts, distance, SpO_2 levels, sleep architecture, and circadian metrics or fasting periods such as Ramadan [34], allowing the digital twin to dynamically adapt to shifts in insulin sensitivity caused by physical exertion, circadian rhythms, or acute stress.

3.3. Glycemic and Clinical Outcome

The results of the analyzed studies demonstrate a significant impact of artificial intelligence algorithms and digital twins on improving continuous glucose monitoring (CGM) metrics [8, 10, 23, 25–29, 32]. In randomized controlled trials (RCTs), the application of hybrid closed-loop and decision support systems (DSS) led to a significant increase in Time in Range (TIR, 70–180 mg/dL) [23, 25–29, 32]. This improvement translated to an increase in TIR by 7 to 26 percentage points compared to control groups, corresponding to an additional 3.0 to 6.2 hours per day in normoglycemia [23, 25–27, 32]. In *in silico* analyses and validation studies, the average TIR values ranged from 65.9% to 86.0% [8, 11, 19, 44]. Simultaneously, a significant reduction in Time Below Range (TBR, <70 mg/dL and <54 mg/dL) was observed, with the percentage in intervention groups maintained at a safe level below 2%–4% [11, 17, 18, 27–29]. For example, the application of a personalized digital twin reduced the risk of hypoglycemia by 69% (RR = 0.31) [32], while population-specific predictive models decreased TBR from 5.3% to 1.9% [10]. The increase in TIR was accompanied by a reduction in Time Above Range (TAR, >180 mg/dL), reaching up to a 12.4 percentage point decrease compared to conventional therapy [28].

The application of machine learning algorithms and mechanistic models also positively influenced long-term metabolic control parameters, including glycated hemoglobin (HbA1c) levels [23, 25–29]. In RCTs, a statistically significant decrease in HbA1c levels by 0.32% to 1.05% was noted compared to control groups using multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) [23, 25–29]. This effect was particularly evident in patients with suboptimal baseline glycemic control (HbA1c ≥8.0%), enabling a larger percentage of subjects to achieve the target value of <7.0% [23, 25, 27]. Concurrently, a decrease in glycemic variability was demonstrated, expressed by a reduction in standard deviation (SD) and coefficient of variation (CV) [11, 23, 24, 26–28, 31]. Adaptive systems maintained the CV within the clinically recommended range (≤36%), and in *in silico* trials, this reduction reached 28% [11, 27, 28].

The evaluated technologies are characterized by a favorable clinical safety profile [12, 25, 44]. In the analyzed publications, no serious adverse events related to algorithm operation were reported [44]. In simulation and pilot studies, no episodes of severe hypoglycemia or blood glucose values below 54 mg/dL were observed with automated or personalized insulin dosing [12]. Although direct reports of diabetic ketoacidosis (DKA) incidents were absent in the reviewed studies, the effective reduction of glycemic variability and the limitation of hyperglycemic episodes serve as a significant factor in mitigating the risk of acute metabolic complications [11, 23, 25–28]

3.4. Decision support capabilities

The decision support capabilities identified across the 42 studies formed a continuum ranging from passive prediction of future glucose concentrations to fully automated insulin delivery. The analyzed systems could therefore be organized into four overlapping functional layers: glucose forecasting and risk detection, generation of therapeutic recommendations, adaptive personalization of insulin therapy, and autonomous closed-loop control. Importantly, predictive accuracy alone did not determine the technological maturity of a system. More advanced frameworks translated predicted glycemic trajectories into actionable outputs, including alerts, adjustments of insulin-to-carbohydrate ratios, recommendations for corrective carbohydrate intake, modification of basal delivery, or automated insulin dosing.

Explicit glucose forecasting or glycemic risk prediction was reported in 15 studies [8–10, 14, 15, 18, 22, 33, 34, 38, 40–42, 47, 48]. The prediction horizon varied according to the intended application. Models in studies [9, 10, 14, 15, 42] forecasted glucose concentrations over horizons ranging from 30 to 120 minutes, whereas study [8] extended prediction to two hours and coupled the predicted trajectory with bolus optimization. The GPFormer architecture in [40] similarly supported multihorizon forecasting for up to two hours. In contrast, several systems focused on event-specific risk rather than continuous glucose prediction. These included the prediction of nocturnal post-exercise hypoglycemia [33], 60-minute prediction of hypoglycemia using multimodal CGM and wearable data [34], classification of hypoglycemic events up to 120 minutes before onset [38], simultaneous prediction of hypoglycemia below 70 mg/dL and hyperglycemia above 270 mg/dL [41], and prediction of severe hypoglycemia in children [47]. Study [22] narrowed the prediction task to postprandial glycemic responses, using an interpretable LightGBM model with SHAP analysis to identify the glucose concentration and glucose trend at mealtime as the principal determinants of subsequent excursions.

The predictive outputs were converted into warning or preventive functions in a smaller group of systems. In [10], the Embedded Population-Specific Temporal Fusion Transformer was connected to a predictive low-glucose management mechanism that suspended basal insulin when the forecasted glucose concentration was ≤70 mg/dL. Studies [13, 19] combined the identification of impending hypoglycemia with recommendations for corrective action, including rescue carbohydrate intake. The systems evaluated in [33, 34, 38, 41, 47] primarily generated risk classifications or early-warning information rather than directly modifying insulin delivery. This distinction is technologically important because forecasting models support human decision-making, whereas predictive low-glucose management systems incorporate the prediction into the control pathway and can initiate a preventive response without waiting for the glucose threshold to be reached.

A second major capability was insulin dose optimization. The level of automation ranged from recommendations requiring patient confirmation to direct algorithmic control. Systems in [12, 13, 19, 21, 26, 29, 32, 46, 49] supported the selection or personalization of insulin doses without necessarily operating as fully autonomous controllers. The fuzzy-logic system in [19] analyzed 48-hour glucose and insulin histories to recommend modifications of both basal infusion profiles and insulin-to-carbohydrate ratios. The reinforcement-learning bolus calculator in [21] selected meal-related doses without requiring explicit carbohydrate quantity, carbohydrate ratio, or correction factor as direct inputs. The Advanced Bolus Calculator for Type 1 Diabetes in [46] used case-based reasoning to adapt bolus recommendations to the individual patient, although no significant improvement in daytime TIR was observed compared with the control condition. Study [32] employed a physiological model of glucose-insulin metabolism as a medical digital twin to simulate postprandial responses and support bolus selection, while [49] applied a neural-network-based framework to optimize bolus dosing in a pediatric population.

Several decision support systems extended beyond the calculation of an isolated bolus and continuously updated treatment parameters. Study [12] applied safe Bayesian optimization to personalize meal boluses while constraining the risk of hypoglycemia. The cloud-based digital twin in [26] reconstructed individual glucose-insulin dynamics and used continuously updated CGM, insulin, meal, and activity data to re-optimize therapeutic recommendations. The Bayesian decision support system in [29] learned individual insulin sensitivity and glycemic response patterns to titrate basal and prandial insulin in people treated with multiple daily injections. Such systems occupy an intermediate position between conventional bolus calculators and automated insulin delivery: they generate adaptive, patient-specific recommendations, but implementation of the recommendation may still depend on the patient or healthcare professional.

The highest level of technological autonomy was represented by systems that directly controlled insulin delivery. Automated regulation of basal insulin, correction doses, or microboluses was evaluated in studies [10, 11, 17, 18, 20, 23, 25, 27, 28, 31, 37, 39, 43, 44, 48]. These systems used heterogeneous control architectures, including model predictive control [18, 25, 28], deep reinforcement learning [17, 39, 43, 48], multiple-model PID control with genetic and fuzzy optimization [20], neural-network control [31, 44], and adaptive commercial AID algorithms [23, 27]. In [11], AndroidAPS/OpenAPS integrated glucose trends, insulin on board, carbohydrates on board, insulin sensitivity, basal rates, and bolus history to modify basal delivery and administer super-microboluses. In [18], adaptive model predictive control incorporated wearable-derived activity information to adjust insulin delivery in response to exercise and meals. The Neural-Net Artificial Pancreas evaluated in [44] directly automated insulin delivery and achieved glycemic outcomes comparable with the University of Virginia model-predictive controller during two randomized crossover sessions.

Meal-related decision support represented another important technological domain. Conventional systems relied on manually entered carbohydrate estimates, whereas more autonomous frameworks attempted to reduce this input burden. Study [17] combined automated meal detection with a deep reinforcement-learning bolus calculator designed for unannounced meals. Study [30] used smartwatch-derived wrist movements and the Klue Health application to detect eating and drinking gestures and trigger hands-free bolus delivery. Study [45] evaluated machine-learning meal detection as an additional component of basal-bolus control, while [16] modeled the magnitude and temporal shape of intestinal carbohydrate absorption using triple-tracer meal data. Study [36] provided a different form of decision support by allowing the personalized model to simulate how changes in meal size, bolus dose, or basal insulin could alter the subsequent glucose trajectory. This counterfactual capability is particularly characteristic of digital-twin technology because it enables alternative therapeutic scenarios to be evaluated in the virtual representation before being applied to the patient.

Decision support was not limited to insulin dosing or short-term glycemic control. Study [35] used routinely collected clinical and CGM characteristics to predict severe diabetes distress, thereby extending machine-learning support to a psychosocial outcome. Multimodal systems in [18, 34] incorporated physical activity, cardiovascular telemetry, sleep, circadian information, or fasting periods to recognize changes in metabolic context and modify risk estimates or control decisions. However, these broader contextual capabilities remained less frequently represented than CGM-based prediction and insulin optimization.

Overall, the reviewed technologies demonstrated a progression from descriptive monitoring to predictive, prescriptive, and autonomous decision support. CGM-only models primarily forecasted future glucose values or classified risk, whereas systems integrating insulin, meal, physiological, and behavioral data were able to generate more individualized therapeutic recommendations. The most advanced hybrid and closed-loop frameworks translated these recommendations directly into adaptive insulin delivery. Nevertheless, the degree of autonomy and clinical validation varied substantially: some solutions were assessed only retrospectively or in silico, while others were evaluated in pilot, crossover, or randomized clinical studies. Consequently, algorithmic functionality should be interpreted separately from clinical readiness, particularly when decision-support capabilities were demonstrated exclusively in simulated environments.

4. Discussion

This systematic review shows that AI-driven digital twins in type 1 diabetes form a heterogeneous technological continuum, ranging from glucose forecasting and risk-classification models to physiological simulators, adaptive decision support systems, and autonomous insulin delivery controllers. The field has not yet adopted a uniform operational definition of a digital twin. Several reviewed systems incorporated patient-specific data, adaptive learning, or physiological simulation without being formally described as digital twins [10, 14, 16–18, 20, 41]. Only selected solutions combined individualized modeling, continuous data acquisition, simulation of alternative interventions, and feedback to therapeutic decisions [26, 32, 36, 44, 49]. The available evidence therefore reflects different levels of digital-twin maturity rather than a homogeneous technological category.

Data-driven and mechanistic architectures offered different capabilities. Recurrent neural networks, transformers, ensemble methods, and other machine-learning approaches were predominantly used to identify temporal patterns and predict glucose concentrations or glycemic risk [8–10, 14, 22, 33, 34, 38, 40–42, 47]. Mechanistic models enabled simulation of patient-specific glucose–insulin responses, whereas hybrid approaches combined physiological representations with adaptive learning or control algorithms [12, 18, 26,

32, 36, 39, 44, 49]. Prediction or personalization alone, however, does not constitute a complete digital twin. A more mature system should maintain an individualized virtual representation through which alternative therapeutic actions can be assessed.

CGM formed the foundation of almost all reviewed technologies. CGM-only models generally inferred future glucose states from historical patterns, whereas systems integrating insulin, carbohydrate intake, clinical characteristics, and wearable telemetry represented a broader metabolic context. Heart rate, energy expenditure, activity, sleep, circadian information, and fasting status were incorporated only in selected multimodal systems [18, 30, 34]. These additional data streams may support context-sensitive prediction and adaptation but also increase susceptibility to missing, inaccurate, or poorly synchronized inputs.

This creates a trade-off between physiological completeness and user burden. Detailed meal, insulin, and activity logging may improve personalization but requires sustained patient engagement. Automated meal detection, gesture recognition, and insulin calculation without explicit carbohydrate estimation were therefore investigated as methods of reducing manual interaction [17, 21, 30, 45, 48]. Although these approaches may simplify diabetes management, missed or delayed meal detection can affect subsequent insulin decisions. Their assessment should therefore include detection accuracy, latency, failure management, and safety constraints in addition to overall glycemic performance.

Decision-support capabilities progressed from predictive to prescriptive and autonomous functions. Predictive systems forecasted glucose or identified the risk of hypoglycemia and hyperglycemia [8–10, 14, 22, 33, 34, 38, 40–42, 47, 48]. Prescriptive systems generated warnings, rescue-carbohydrate recommendations, personalized insulin-to-carbohydrate ratios, or suggested boluses [12, 13, 19, 21, 29, 32, 46, 49]. More autonomous systems directly modified insulin delivery using model predictive control, reinforcement learning, neural networks, or adaptive controllers [10, 11, 17, 18, 20, 25, 27, 31, 37, 39, 43, 44, 48]. This distinction is clinically relevant because an erroneous advisory prediction has different consequences from an erroneous prediction that automatically initiates insulin delivery.

Counterfactual simulation was among the most distinctive digital-twin capabilities. Personalized models were used to replay glucose responses after modifications in meal size, bolus dose, or basal insulin [36] and to support bolus optimization in adult and pediatric populations [32, 49]. These applications move beyond predicting what is likely to happen and instead estimate how the glucose trajectory may change following a specific intervention. Their reliability nevertheless depends on whether the virtual model accurately reproduces responses outside the conditions used for its development and calibration.

A substantial gap remains between technological feasibility and clinical readiness. Many systems were evaluated retrospectively or in silico using public datasets or physiological simulators [11, 12, 17, 19–21, 36, 37, 39, 42, 43, 45, 48, 49]. Such environments are valuable for algorithm development and preliminary safety testing but cannot fully reproduce sensor failures, inaccurate meal reporting, illness, adherence problems, or other sources of real-world variability. Favorable in silico outcomes should therefore be interpreted as evidence of feasibility rather than direct evidence of clinical effectiveness.

Prospective findings were not uniformly positive. A randomized study of a digital-twin-enhanced decision support system demonstrated improved time in range compared with a conventional bolus calculator [32]. A randomized crossover study found broadly comparable glycemic outcomes between a neural-network artificial pancreas and a model-predictive controller [44]. In contrast, an adaptive bolus calculator did not significantly improve daytime time in range [46], while a short-term evaluation of hands-free meal bolusing found no significant differences in the principal glycemic outcomes [30]. Greater algorithmic sophistication therefore does not necessarily translate into superior clinical effects. Effectiveness may also depend on usability, adherence, duration of use, comparator performance, and adaptation to real-world behavior.

The evidence is further limited by small samples, repeated use of selected datasets, limited external validation, and inconsistent reporting of model updating, missing-data management, adverse events, and real-time integration. Public datasets such as OhioT1DM were used across several studies [9, 10, 14, 42, 45], facilitating technological benchmarking but potentially increasing dependence on dataset-specific patterns. Population-specific modeling, transfer learning, and domain-generalization approaches may improve transportability [10, 40], but they require prospective validation across different age groups, treatment modalities, devices, and clinical settings.

Future studies should define explicitly how a digital twin is individualized, updated, and connected to therapeutic decisions. Evaluation should extend beyond prediction accuracy and include calibration, robustness to missing or erroneous inputs, computational latency, interoperability, interpretability, cybersecurity, user burden, and the safety of autonomous actions. Most importantly, promising findings

obtained retrospectively or in silico require confirmation in adequately powered prospective studies conducted under everyday conditions.

Overall, AI-driven digital twins may connect continuous patient data with individualized prediction, simulation, and therapeutic action. Their principal value lies not merely in forecasting glucose but in testing alternative interventions and adapting decisions to changing metabolic conditions [26, 32, 36, 44, 49]. However, clearer terminology, standardized reporting, external validation, and evidence of sustained real-world benefit are required before these systems can be considered a mature component of routine T1D management.

5. Conclusions

AI-driven digital twins in type 1 diabetes comprise a heterogeneous group of technologies, including data-driven prediction models, mechanistic physiological simulators, hybrid architectures, adaptive decision support systems, and automated insulin delivery controllers. CGM was the principal data source, while the integration of insulin, carbohydrate, clinical, and wearable data enabled a more comprehensive representation of individual metabolic conditions. However, multimodal systems also introduced greater technical complexity, dependence on data quality, and additional challenges related to synchronization, interoperability, and user burden.

The reviewed systems supported glucose forecasting, detection of hypoglycemia and hyperglycemia, personalization of insulin parameters, bolus optimization, simulation of alternative interventions, and automated adaptation of insulin delivery. Although selected prospective studies demonstrated improvements in glycemic outcomes, other clinical evaluations reported comparable or nonsignificant effects, indicating that technological sophistication alone does not ensure clinical benefit. Moreover, much of the available evidence was derived from retrospective analyses, small cohorts, public datasets, or in silico experiments.

Digital twins therefore have the potential to extend diabetes technology beyond glucose prediction toward individualized simulation and adaptive therapeutic decision-making. Nevertheless, their clinical implementation requires clearer definitions, standardized reporting, robust external validation, and prospective assessment under real-world conditions. Future studies should evaluate not only glycemic effectiveness but also safety, interpretability, usability, resilience to incomplete data, and the consequences of increasing system autonomy.

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