Towards Personalized AI-Based Diabetes Therapy: A Review

Sara Campanella[®][,](https://orcid.org/0000-0003-3580-9232) Student Member, IEEE, Giovanni Paragliola[®], Valentino Cherubini, Paola Pierleoni, and Lorenzo Palma[®][,](https://orcid.org/0000-0003-2851-3310) Member, IEEE

*Abstract***—Insulin pumps and other smart devices have recently made significant advancements in the treatment of diabetes, a disorder that affects people all over the world. The development of medical AI has been influenced by AI methods designed to help physicians make diagnoses, choose a course of therapy, and predict outcomes. In this article, we thoroughly analyse how AI is being used to enhance and personalize diabetes treatment. The search turned up 77 original research papers, from which we've selected the most crucial information regarding the learning models employed, the data typology, the deployment stage, and the application domains. We identified two key trends, enabled mostly by AI: patient-based therapy personalization and therapeutic algorithm optimization. In the meanwhile, we point out various shortcomings in the existing literature, like a lack of multimodal database analysis or a lack of interpretability. The rapid improvements in AI and the expansion of the amount of data already available offer the possibility to overcome these difficulties shortly and enable a wider deployment of this technology in clinical settings.**

*Index Terms***—Artificial intelligence, deep learning, diabetes, machine learning, treatment optimization, patient-specific, wearable devices, personalization of care.**

I. INTRODUCTION

T HE impairment of insulin secretion or action is used to define diabetes as a long-term metabolic disorder. Diagnosis of diabetes occurs when glucose homeostasis is disrupted, resulting in hyperglycemia [\[1\].](#page-11-0) Around 387 million people worldwide are affected by the diabetes epidemic and its prevalence is expected to double over the next 20 years, impacting more than half a billion people [\[2\].](#page-11-0) Diabetes is distinguished by the clinical phenotype, historical precedent, genotype, and specific environmental causes, which has resulted in the classification of type 1 diabetes (T1D), type 2 diabetes (T2D), gestational

Received 30 August 2023; revised 22 July 2024; accepted 9 August 2024. Date of publication 13 August 2024; date of current version 7 November 2024. *(Corresponding author: Lorenzo Palma.)*

Sara Campanella, Paola Pierleoni, and Lorenzo Palma are with the Department of Information Engineering, Università Politecnica delle Marche, 60131 Ancona, Italy (e-mail: [s.campanella@pm.univpm.it;](mailto:s.campanella@pm.univpm.it) [p.pierleoni@staff.univpm.it;](mailto:p.pierleoni@staff.univpm.it) [l.palma@staff.univpm.it\)](mailto:l.palma@staff.univpm.it).

Giovanni Paragliola is with the ICAR-CNR, 80131 Naples, Italy (e-mail: [giovanni.paragliola@icar.cnr.it\)](mailto:giovanni.paragliola@icar.cnr.it).

Valentino Cherubini is with the Department of Women's and Children's Health, G. Salesi Hospital, 60123 Ancona, Italy (e-mail: [valentino.cherubini@gmail.com\)](mailto:valentino.cherubini@gmail.com).

Digital Object Identifier 10.1109/JBHI.2024.3443137

diabetes (GDM), and other disease types[\[3\].](#page-11-0) The manual testing of blood sugar levels followed by daily subcutaneous insulin injections is by far the most popular treatment method. Unfortunately, this routine makes it difficult to adhere to the therapy regimen, increasing the chances of the onset of acute and chronic diabetes-related complications such as cardiovascular disease or ketoacidosis and this is even more challenging when we consider youth and children [\[4\].](#page-11-0) Nearly 50 years ago, continuous subcutaneous insulin infusion (CSII), also known as insulin delivery with pumps, was developed. It only uses short- or rapid-acting insulin types, minimizing administration variability and lowering the possibility of glucose fluctuations. Pump technology has advanced to the point where it can accurately imitate physiological demands. To provide real-time, data-driven glycemic control and early identification of hypoglycemia, glucose biosensors, commonly referred to as continuous glucose monitoring (CGM), have been incorporated with controlled insulin administration in basal and bolus mode [\[5\].](#page-11-0) The combination of these devices is referred to as an artificial pancreas (AP), also known as a hybrid closed-loop system. It was demonstrated to be a valid substitute for the classic treatment, increasing the effectiveness of the therapy, especially in children and adolescents [\[6\],](#page-11-0) [\[7\].](#page-11-0) Nowadays, a person with diabetes can also receive decision support from a medical professional who makes recommendations via a mobile interface, or directly from the patient using a smartphone app that generates recommendations on its own [\[8\],](#page-11-0) [\[9\],](#page-11-0) [\[10\].](#page-11-0) Obtaining, interpreting, and applying the vast amount of knowledge required to address complicated medical issues is a challenge for modern medicine. Medical Artificial Intelligence (AI) has been connected to the development of AI programs that aid clinicians in formulating a diagnosis, choosing a course of therapy, and predicting outcomes [\[11\].](#page-11-0) The majority of its application in diabetology is linked with the forecasting of blood glucose levels [\[12\],](#page-11-0) [\[13\],](#page-11-0) diabetes prediction [\[14\],](#page-11-0) [\[15\],](#page-11-0) diabetes complications [\[16\],](#page-11-0) [\[17\]](#page-11-0) and meals or physical activity predictions [\[18\],](#page-11-0) [\[19\].](#page-11-0) However, youth and adults with diabetes face challenges in controlling pre-prandial blood sugar levels, counting the grams of carbohydrates, computing insulin sensitivity, or customizing the insulin-to-carbohydrate ratio, all of which can affect insulin dosing. People may also need to consider the day-to-day fluctuations in insulin, their glucose trend, and the context in which an insulin dose is taken, and adjust the therapy consequently. The burdens of the aforementioned difficulties are being reduced by AI-based systems (Fig. [1\)](#page-1-0) which are helping in generating patient-specific treatment by using not only clinical data but also considering personal variables like social and economic conditions.For example, managing therapy for diabetes can be particularly challenging when considering physical activity. Different levels of physical activity can

© 2024 The Authors. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 License. For more information, see https://creativecommons.org/licenses/by-nc-nd/4.0/

Fig. 1. Diabetes management along with the large amount of data produced by self-management and medical team visits. The data is processed to develop AI-based algorithms for new treatments and decision support.

significantly impact blood sugar levels. However, with real-time analysis and AI, it is possible to continuously monitor a patient's activity levels, through accelerometers or heart rate data, avoiding hypo or hypoglycaemia. Similarly, knowing the patient's socioeconomic status, like the family's annual income, or the parents' education, the therapy adherence can be predicted [\[20\].](#page-11-0) The same consideration can be made for pregnant women with type 1 diabetes since they are challenged in trying to maintain tight glycemic control [\[21\].](#page-11-0) Reviews in the literature primarily focus on analyzing various AI methods in well-established fields of diabetes research, like prevention [\[22\],](#page-11-0) [\[23\],](#page-11-0) the emergence of related illnesses [\[24\],](#page-11-0) [\[25\]](#page-11-0) or only technical reviews in diabetes management [\[26\],](#page-11-0) [\[27\].](#page-11-0) However, given the field's rapid advancements, a review that focuses solely on the diabetic patient and how researchers are attempting to personalize therapy is required. Furthermore, the data utilised in the previously stated research are primarily unimodal and usually come from a single category of data sources, such as clinical records or glucose readings. This restricted focus limits the capacity to comprehend and handle the complexities of diabetes treatment completely. None of this research aims to combine numerous data modalities to improve therapeutic outcomes, nor do they seek to approach the situation from a 360-degree viewpoint and, subsequentially, without exploiting the full potential of AI approaches. This disparity highlights the need for a more comprehensive strategy that uses a variety of data sources to improve the level of treatment personalisation for diabetes. Therefore, by examining the crosssectional association between diabetes and AI applications, the review aims to fill a gap in the literature, especially in light of the growing use of insulin pump therapy. We cover the difficulties people encounter in controlling their blood sugar levels and how this may affect insulin dosages, as well as the methods in which these problems are resolved by fine-tuning the algorithm and creating patient-centred strategies. The review evaluates the existing and prospective future of protocol patient-based care practices while emphasizing the significance of wearable technology as a therapeutic decision support system.

II. METHODOLOGY

To ensure adherence with the PRISMA statement [\[28\],](#page-11-0) a thorough investigation was conducted, from March 2023 to July 2023, utilizing the PubMed, Web of Science, IEEE Xplore, Scopus and Google Scholar databases. The selection of these databases facilitated the comprehensive exploration of both

Fig. 2. Selection process of the eligible articles.

medical and engineering publications. A complete overview of the selection process is presented in Fig. 2.

A. Search Strategy and inclusion/exclusion Criteria

The query search included using the truncation symbol * for the terms "diabetes", "type 1", "type 2", "gestational", "insulin pump", "hybrid closed-loop", "system*", "decision support", "personal*", "optimiz*", "child*", "adulescent*", "simulat*", "machine learning", "artificial intelligence", "insulin-tocarbohydrate ratio", "insulin sensitivity factor", "basal rate", "meal*", "physical activit*", "parameter*", "bolus*", "advisor*", and "artificial pancreas". Search terms were combined with the Boolean operators "OR" and "AND".

For duplicate removal, the studies were imported into the Mendeley Reference Manager program. We only considered research papers with titles, abstracts, and the full text (review papers were not included). Titles, abstracts, and full texts were all subject to exclusion standards: i) no English publications; ii) insufficient information about the study design and results; iii) comparative studies in the medical field. Therefore, the articles were included if i) present original research on the optimization and customization of diabetes treatment; ii) considered real data collected from diabetic patients or simulated data; and iii) applied at least an AI algorithm and similar techniques.

B. Information Extraction

We examined the full text of the selected articles and extracted crucial information to evaluate them. The data extraction was conducted independently by two authors, while the remaining three authors reviewed the results to ensure the accuracy of the information. Specifically: a) **Cases**: we classified the research

TABLE I SUMMARY OF SELECTED ARTICLES FROM THE LITERATURE DIVIDED BY THE APPLICATION FIELDS

Subcategories	Treatment Optimization	Therapy Personalization	Mixed Applications	
Blood Glucose Prediction	$[29]$, $[30]$, $[31]$, $[32]$ $[33]$, $[34]$	$[35]$, $[36]$, $[37]$	$[38]$, $[39]$, $[40]$	
Insulin or Bolus Dosing	$[41]$, $[42]$, $[43]$, $[44]$, $[45]$, $[46]$, $[47]$, $[48]$, $[49]$	$[50]$, $[51]$	$[52]$, $[53]$, $[54]$	
Meals	$[55]$, [56], [57], [58], [59]	$[60]$, $[61]$	$[62]$	
Glucose prediction and Meals	$[63]$, $[64]$, $[65]$, $[66]$, $[67]$	[68]		
Tailored device or algorithm	$[69]$, $[70]$, $[71]$	$[72]$, $[73]$, $[74]$	[75]	
Therapy recommendation system	$[76]$, $[77]$, $[78]$, $[79]$, $[80]$, $[81]$, $[82]$, $[83]$, $[84]$, $[85]$	$[86]$, $[87]$, $[88]$	$[89]$, $[90]$, $[91]$	
Patient Profiling/Pattern recognition	$[92]$	[93], [94], [95], [96], [97], [98], [99]		
		[100], [101], [102], [103], [104]		
GDM prediction	$[105]$, $[106]$			

based on the available information about the forms of diabetes into T1D, T2D, and GDM. b) **Data sources**: we extract information about the datasets used, such as sources, types, and formats. c) **Models**: we present an overview of model architectures, including various AI techniques and other models used with insight into the most used techniques for the intended use. d) **Applications**: we summarise the main field of applications of the examined works to demonstrate state-of-the-art AI for individualized diabetes monitoring and therapy. e) **Limitations**: this category gathers the studies' limitations, which could stimulate more research and enhance learning outcomes in each application area.

III. RESULTS

A. Selection Process

In total, 893 articles were retrieved by the query, as shown in Fig. [2.](#page-1-0) After removing the duplicates, we obtained 727 articles eligible for the next steps. Firstly, we excluded the articles based on the titles, following the criteria explained in Section [II-A.](#page-1-0) So, 235 articles were examined in the second step. The abstract was evaluated here, and 135 articles were selected for the full-textreading procedure. We manually assessed the eligibility of the remaining papers by full-text inspection and included 77 papers in the final collection. Based on the application scenarios, we divided the final collection into different categories to better analyze them: patient-based therapy personalizing $(PT, n = 26)$, optimization of the treatment (OT, $n = 40$), and mixed (POT, n $= 12$). Moreover, we have individuated other subcategories that can define better the aim of the examined works: blood glucose prediction (BGP, $n = 18$), meals (M, $n = 15$), insulin/bolus dosing (IBD, $n = 14$), tailored device/algorithm (TD, $n = 6$), therapy recommendation (TR, $n = 13$), patter/patient profiling (PPT, $n = 12$), and GDM prediction (GDMP, $n = 2$). The details of the selected works are presented in Table I while in Table II, there is a summary of the content that is common to all the articles belonging to that category. Moreover, among the final 77 papers, 60 of them deal with T1D, 11 with T2D, and 5 with GDM, and only 2 are focused on both T1D and T2D. Because T1D mostly affects young patients, the increasing number of studies focusing on it indicates a bigger challenge in optimizing therapy. The ongoing rise in T1D incidence raises concerns about customizing effective treatments to the specific needs of pediatric patients, due to their dynamic physiological changes. Simulation software has long been the go-to tool for many works [\[82\],](#page-12-0) [\[83\],](#page-13-0) but there's a growing interest in using realworld data to enhance the accuracy of the proposed solutions,

TABLE II DESCRIPTION OF EACH SUBCATEGORY ARGUMENTS

Subcategories	Treatment Optimization	Therapy Personalization
Blood Glucose Prediction	Glucose prediction with increased time range to optimize therapy	Improving glucose prediction with increased time range with personal information such as weight or age
Insulin or Bolus Dosing	Development of bolus calculators or insulin initialization	Bolus calculator using past personal information of insulin basal rate or boluses
Meals	Techniques for identifying unannounced meals or counting carbohydrates	Techniques for identifying unannounced meals using dietary habits and ingested carbs
Glucose prediction and Meals	Glucose prediction with unannounced meals	Glucose prediction with unannounced meals and personal information such as age, weight and food intake
Tailored device or algorithm	AP algorithm for glucose prediction using multiple inputs	Model the insulin pump users' behavior using multiple inputs
Therapy recommendation system	Tools to generally support therapy	Tool to personalize therapy based on past insulin pump setting or past CGM trend
Patient Profiling/Pattern recognition	Patient profiling using past CGM data	Using past CGM data, create profiles to match the future trends and tailor the therapy
GDM prediction	Early detection and treatment of gestational diabetes	

as reported in the lower panel of Fig. [3.](#page-3-0) As more researchers recognize the importance of using actual data, the demand for public databases based on real data has increased. Similarly, it can be said that looking at the upper panel of Fig. [3,](#page-3-0) the desire to put the patient at the centre of care is growing, as interest in personalized therapy. Fig. [4](#page-3-0) illustrates that most of the chosen articles were recently published, indicating that the AI approach for diabetes treatment optimization and personalization is a relatively new issue and that interest in it has been growing. In addition, we calculated and showed the Scopus citation counts for the chosen works as of July 2023. The next subsections will explore the selected works from the applicable point of view to analyze them comprehensively.

B. Treatment Optimization

Treatment optimization refers to the process of improving algorithms to achieve better precision and accuracy in the therapy

Fig. 3. Databases and subcategories distribution through the years in the selected works divided among the three main application categories.

Fig. 4. Number of articles included in the collection grouped by the year of publication and application fields until 2022.

formulation. This involves working on various aspects such as calculating boluses, predicting meals without announcements, testing platforms for the medical staff, and so on. By refining these algorithms, the treatment's overall quality can improve and reduce the likelihood of errors. Treatment optimization is essential for patients with chronic conditions as it can significantly enhance their quality of life and overall health outcomes [\[107\].](#page-13-0) Furthermore, technological advancements have made developing and implementing these algorithms easier, making treatment optimization a crucial part of modern healthcare.

When defining the optimal technique for insulin dosage computation or developing decision support devices, blood glucose level prediction and control are still crucial tasks to deal with. The importance of glucose forecasting cannot be overstated: it not only helps in reducing hyperglycemia and hypoglycemia events, identifying the cause and minimizing their impact on overall health, but it also improves insulin and bolus administration. In the past few years, many researchers from several disciplines have contributed to closing gaps in glucose forecasting

focusing on the data collected from CGM sensors to increase the prediction horizon while minimizing adverse events and applying both machine and deep learning approaches [\[29\],](#page-11-0) [\[30\],](#page-11-0) [\[31\],](#page-11-0) [\[64\].](#page-12-0) When dealing with glucose forecasting, an important aspect to consider is food [\[58\],](#page-12-0) [\[66\].](#page-12-0) The management of meals for people with diabetes is crucial and it is important to consider meal planning as an integral part of diabetes management. For example, in the study conducted by Zheng and colleagues [\[55\]](#page-12-0) a meal detection algorithm that combines simulations with CGM, insulin pump, and heart rate monitor data is proposed and it is capable of distinguishing if the predicted and actual glucose levels differ because of a meal. Similarly, Samadi et al. [\[56\]](#page-12-0) proposed an AP system that can automatically avoid postprandial hyperglycemia by detecting a consumed meal or snack and administering insulin boluses using an estimate of carbohydrates, based on qualitative factors characterizing variance in CGM values. Making errors in carbohydrate counting can result in inaccurate bolus/insulin doses, leading to dangerous fluctuations in blood glucose levels. According to [\[57\],](#page-12-0) postprandial hypoglycemia risk is not greatly enhanced if a meal is accurately recognized within 25 to 30 minutes of the meal's occurrence and dosed with a portion of the nominal amount of required prandial insulin. Only 20 minutes after eating a meal is a noticeable glucose rise related to meal intake, and this delay is also based on the meal's content. One of the meals that the algorithm failed to recognize contained a lot of fat, which slowed down the rise of glucose and delayed the peak in glucose levels. This demonstrates that considering nutritional factors when working with glucose prediction is crucial, as demonstrated by [\[65\].](#page-12-0) Another key role is played, as already stated, in glucose fluctuations meal control balancing is computing the right dose of boluses as well as adjusting in real time the basal rate: while the amount of fast-acting bolus insulin is often determined by a bolus adviser, basal insulin parameters such as the pump infusion rate can be changed depending on past data [\[83\],](#page-13-0) [\[108\].](#page-13-0) In the past, a lot of work has been done and investigated the topic from a different perspective applying mainly model predictive control or compartmental models $[43]$, $[47]$, $[48]$, $[71]$. Recently, more complex

methodologies have been developed due to the difficulties in fully comprehending the glucose-insulin dynamic. For example, in the research proposed by Zhu et al. [\[42\],](#page-12-0) an insulin bolus advisor uses an actor-critic model based on deep deterministic policy gradient and CGM data to optimize insulin dosing at mealtime, significantly improving the average percentage time in the target range in both the adult and adolescent simulated cohort. Furthermore, Noaro et al. [\[46\]](#page-12-0) attempt to overcome the problem of effective estimation of the meal-insulin bolus amount to avoid post-prandial hypo/hyperglycemia obtaining a reduction in hypoglycemia duration and incidence even though the time spent in the hyperglycemia state slightly increased. Due to the difficulties in retrieving the optimal target of the learning task, designing a supervised learning framework in such a scenario is far from straightforward. Therefore, in 2023 Noaro et al. [\[41\]](#page-12-0) applied a double deep Q-learning method to develop a bolus calculator which improved the time in the target range from 68.35% to 70.08% and significantly reduced the time in hypoglycemia (from 8.78% to 4.17%). %). The insulin bolus calculator plays a crucial role not only for subjects undergoing AP treatment but also for MDIs patients. An iterative learning control is employed to update basal therapy including one longacting insulin injection per day, as demonstrated in the study conducted by [\[67\].](#page-12-0) Furthermore, the run-to-run strategy modifies meal bolus therapy based on infrequent SMBG measurements by updating the mealtime-specific insulin-to-carbohydrate ratio. This strategy was confirmed further in their following study [\[49\],](#page-12-0) which resulted in a significant weekly decrease in glycaemic levels and an increase in time spent in the target range. Despite the increasing use of insulin pumps and CGM, many people with type 1 diabetes still struggle to meet their glycemic goals. Because of the increased complexity of using these devices and the need to avoid unwanted consequences, AP is a recent innovation in diabetes care that necessitates thorough training for medical staff to properly set all the parameters [\[92\].](#page-13-0) To support healthcare providers, several tools have been developed to aid in correctly configuring insulin pumps and accurately addressing therapy [\[76\],](#page-12-0) [\[78\],](#page-12-0) [\[80\],](#page-12-0) [\[82\],](#page-12-0) [\[83\],](#page-13-0) [\[109\].](#page-13-0) Additionally, researchers have focused on identifying critical variables that may cause hypoglycemia during AP startup [\[33\]](#page-11-0) and predicting glucose fluctuations by considering factors such as basal and fast-acting insulin infusion, current glucose levels, food intake, and physical activity [\[77\].](#page-12-0) Creating tailored devices and algorithms that can somehow make easier their utilization could be helped by designing bio-inspired approaches, that can join the AI methodology with the physiological and pharmacological characteristics which allow the algorithm to learn an automated treatment[\[69\],\[70\].](#page-12-0) There are now several instruments available to aid in forecasting therapy adherence. Mohebbi and colleagues developed a novel deep-learning algorithm to detect adherence using simulated CGM signals for T2D patients. Comparing various algorithms, the best performance (77.5% accuracy) was achieved by CNN, highlighting their potential in adherence detection [\[84\].](#page-13-0)

Optimizing gestational diabetes therapy necessitates a significant emphasis on prevention, and AI can play an important part in this process. Early detection and treatment of gestational diabetes are critical in reducing the development of type 2 diabetes later in life [\[105\],](#page-13-0) [\[106\].](#page-13-0) Pregnant women with gestational diabetes can minimise potential complications and achieve better health outcomes for themselves and their unborn children by constantly monitoring blood glucose levels and

sticking to a well-designed treatment plan. To support this, Rigla et al. [\[79\]](#page-12-0) presented an AI-augmented telemedicine strategy, while Pustozerov et al. [\[63\]](#page-12-0) investigated post-prandial glucose monitoring. Early detection and comprehensive therapy during pregnancy help greatly to lower the long-term incidence of type 2 diabetes.

C. Personalizing Therapy

Personalization of therapy involves tailoring algorithms based on a patient's physical characteristics and habits. This means developing models that can understand and profile the patient, allowing for real-time adaptation of therapy without manual input from the patient or doctor. By incorporating data on a patient's lifestyle, such as exercise and dietary habits, algorithms can provide more accurate and effective treatment. Personalization is particularly important in chronic conditions, as it can improve psychophysical outcomes and quality of life [\[110\].](#page-13-0)With advances in AI, the potential for personalized therapy is growing rapidly.

As previously stated, it is challenging to infer patient-specific blood glucose trends from insulin units and carbohydrate content since the body's glucose kinetics is a complex, user-dependent process. Regarding the glucose-insulin relationship, several works have been proposed such as the [\[68\]](#page-12-0) where specific glucose and carbohydrate absorption curves for the patients have been derived or the work proposed by [\[36\],](#page-11-0) [\[37\]](#page-11-0) or Liu et al. [\[35\]](#page-11-0) where physical activities and precise meal information have been taken into account to increase the prediction horizon and consequentially improve adherence to the therapy, respectively. Another contribution to this topic is the one proposed by Amorim and colleagues [\[61\]:](#page-12-0) they suggested a method that makes use of individual patient characteristics to compute a safe range for the carbohydrate counting inaccuracy and then adapts this range to the patient's daily activities and eating habits. The proposed technique first computes a safe interval for the carbohydrate counting error using the insulin-to-carbohydrate ratio, insulin sensitivity factor, blood glucose limits, and blood glucose target, so the patient can train to accomplish this objective. The software then adapts the initial safe interval for the carbohydrate counting error based on the patient's demands using the acquired daily life data (such as blood glucose, meal carbohydrate content, and insulin bolus). There are also efforts to overcome the difficulties posed by inter- and intra-patient differences and personalize insulin treatment. Sun et al. [\[50\]](#page-12-0) suggested an adaptive basalbolus algorithm (ABBA) that accepts inputs from either SMBG or CGM devices and uses those inputs to offer individualized recommendations for the daily basal rate and prandial insulin dosages based on the patient's blood glucose levels of the day before, reducing hypoglycaemias gradually and keeping blood sugar levels in the desired range, even in the face of extreme circumstances involving doubt, variability, and skipped main meals. Also in the context of gestational diabetes, personalized therapy has been introduced to prevent complications and the onset of type 2 diabetes. For example, in the work [\[60\]](#page-12-0) a method that makes use of individual patient characteristics to compute a safe range for the carbohydrate counting inaccuracy and then adapts this range to the patient's daily activities and eating habits is proposed.

Personal health data is now more readily available thanks to the rising popularity of wearable devices for continuous sensing, although techniques for data interpretation are still under development. For example, Bartolome and colleagues [\[87\]](#page-13-0) create and test the GlucoMine algorithm to assist analysis of extended periods of CGM data to find patterns of poor management that are concealed and can be used to inform treatment strategies. They discovered that when extended periods of wearable device data are not examined or analyzed, hidden patterns of adverse glycemic events (high/low blood glucose episodes) are currently missing and that these repeated patterns of poor management cannot be found. Another therapy recommendation system is the one suggested by Alina et al.[\[86\]](#page-13-0) where they propose a proactive diabetes self-care recommendation system for American Indians, based on AI. By integrating the AI users' ontological profile with general clinical diabetes recommendations and guidelines, the system can make personalized recommendations (e.g., food intake and physical workout) based on special socioeconomic, cultural, and geographical status, and the correctness of the recommendations are also approved, in the majority of the cases, by the medical experts.

Clinical decision support systems utilizing pattern recognition can aid patients with their therapies by considering their medical conditions and the specific scenarios they encounter. The work carried out by Contreras and colleagues [\[94\]](#page-13-0) presents a clinical decision support system that combines a predictor of blood sugar levels with a classifier of glycaemic profiles. To forecast blood glucose levels, the system aims to discover data profiles by a given situation and to produce prediction models based on these scenarios. In 2018, using CGM data, Hall et al.[\[96\]](#page-13-0) assessed how frequently people experience postprandial glucose increases, the kinds of patterns they exhibit, and how patterns differ amongst people who had the same nutritional challenge. They also constructed a web tool for visualizing a user's uploaded CGM profile and classifying unique glucose patterns into glucotypes, as well as a model for discovering putative reasons for individual glucose dysregulation through comprehensive phenotyping. A clustering technique that extracts hidden information from T2D CGM data might offer a workable way to recognize patients with various characteristics of diabetes is presented in [\[111\].](#page-13-0) The findings, in particular, demonstrated that the four novel type 2 diabetes patient subgroups had unique clinical characteristics based on the evolutions of C-peptide values, insulin sensitivity and resistance as well as glucose level factor. Another work on this topic was conducted by Lobo et al. [\[93\]:](#page-13-0) they developed a data-driven strategy for identifying a limited number of typical daily profiles (motifs, Ω) so that nearly any daily T1D CGM profile produced by a patient can be matched to one of the motifs. A larger dataset the next year was used [\[98\]](#page-13-0) to evaluate Ω 's robustness after it successfully classified 99.0% of the 42595 daily CGM profiles in the testing data set. A further step forward was made by Kahkoska and colleagues when they tried to individuate dysglycaemia phenotypes and correlate them with glycated haemoglobin and pump use [\[104\].](#page-13-0) Three dysglycemia clusters were identified with significant variations across all CGM parameters and the most dysglycemic cluster was found to be the one linked with high HbA1c, which was associated with lower pump utilization, higher insulin dosages, and more frequent blood glucose readings.

The key obstacles in reporting and altering daily exercise routines are the reliance on error-prone self-reporting and the use of default settings in bolus calculators and insulin pumps. These devices are intended to recommend meal-related insulin doses based on predetermined insulin-to-carbohydrate ratios and insulin sensitivity variables, which may result in mistakes.

Changes in every day habits can also occur over time without being noticed, making self-management even more difficult. To address these concerns, the research proposed by [\[97\]](#page-13-0) suggests a data-driven approach that utilizes self-monitoring data to identify diurnal trends in diabetes management. The proposed model enhances time-block settings' accuracy, gives context to data, and increases engagement and adherence to the bolus advisor. A digital twin is also important to support in tailoring and customizing the therapy [\[112\].](#page-13-0) It is a virtual representation of a physical entity, living or not, such as a person or even a complex system connected to a physical part, with which it can exchange data and information both synchronously and asynchronously. It is an important tool in the development of personalized therapy recommendation systems as Thamotharan and colleagues [\[103\]](#page-13-0) demonstrate. They deal with the creation of several modules for forecasting, predicting food nutrient information, analyzing time-series trends, and other functions required for effectively managing elderly T2D. Moreover, an adaptive patient model, that personalizes insulin infusion based on geriatric factors, is proposed to deliver precise insulin doses. Similarly, Haidar and colleagues proposed a new method, "stochastic e-cloning," that generates virtual populations for metabolic simulators from routine data. Using a Bayesian approach and Markov chain Monte Carlo, it estimates parameters for a nonlinear glucose regulation model. This method reflects population variability and uncertainty, demonstrated with data from 12 young type 1 diabetes patients [\[85\].](#page-13-0)

D. Mixed Applications

We shall discuss mixed applications in this paragraph since they fall outside the two main categories. We will thus focus on publications that address both issues above, tailoring the therapy to the patient's needs and characteristics while making the best use of the available technology. Due to their flexibility and variety, mixed applications make interesting research and development topics since they offer a special opportunity for interdisciplinary collaboration and novel use cases. For example, the research by De Paula et al. [\[75\]](#page-12-0) proposed an online selective reinforcement learning system for real-time adaptation of a control strategy based on continuing interactions with the patient to tune the artificial pancreas. The suggested approach modifies the support data dictionary for online learning by determining whether there is unique information in the arriving data stream that should be added to the dictionary to personalize the treatment. Because of the high level of subject-specific glycemic variability, the regimen of care must be constantly adjusted to accommodate daily variations in the patient's metabolism and lifestyle. In two works proposed by Nimri and colleagues [\[89\],](#page-13-0) [\[90\],](#page-13-0) the AI-DSS is a tool designed to help people manage their diabetes more effectively. It collects data from various sources such as CGM readings, capillary blood glucose measurements, insulin doses, and carbohydrate intake from insulin pump data and the pump bolus calculator. This data is collected over at least 12 days during routine diabetes care. Using AI, the AI-DSS analyzes the data and identifies patterns in glucose levels and insulin dosing events. It applies a similar approach to that of a healthcare provider who relies on expert knowledge and recommendations based on data from clinical studies. The AI-DSS generates personalized recommendations, which may include specific adjustments for insulin pump settings (such as basal rates, correction ratios, and carbohydrate factors). It

Fig. 5. Trend of the adopted approaches in diabetes therapy through the years.

also offers diabetes management tips related to insulin delivery, like advice on missed boluses, timing of pre-meal boluses, and addressing hypoglycemia. These insights are based on an individual's insulin dosing and delivery behaviours, aiming to provide more tailored and effective diabetes management strategies. Similarly, Guzman Gomez et al. [\[54\]](#page-12-0) try to calculate the basal insulin dose in patients with T1D using subcutaneous insulin infusion pumps and considering several patient-based information such as weight, sex, age, and height. Moreover, the work proposed by Godoy and colleagues [\[62\]](#page-12-0) focuses on an offline carbohydrate intake signal reconstruction. The unknown input estimation is based on a feedback scheme where the measured blood glucose is compared with the predicted ones using the patient's functional insulin therapy parameters defined by the treating physician. As the problem to solve increases in difficulty, so do the techniques required to tackle it, growing in robustness and complexity. An example is the [\[40\],](#page-12-0) where they proposed a Fast-adaptive and Confidence Neural Network (FCNN) to learn representations from CGM input aiming to compute personalized blood glucose predictions aiming to solve the cold-start issue. They have also implemented the models in a smartphone app to provide real-time decision support and configured the system to be fed with other data generated by a wristband or a smartwatch.

E. Impact of AI in Diabetes Therapy

This segment provides an overarching perspective on the use of artificial intelligence methods in diabetes therapy, intending to facilitate the formulation and implementation of innovative interventions. First, a comprehensive delineation of the role of AI in diabetes therapy is presented, followed by an in-depth examination of its specific applications within various domains of diabetes care. This section focuses on the AI approaches found in the original 77 articles. Specifically, it will look at a subset of 58 papers that use AI models for our analysis [\[14\],](#page-11-0) [\[113\].](#page-13-0)

Fig. 5 shows a view of the types of technologies being used to manage diabetes therapies. The graph shows two trends: one related to *No AI-based* and one related to *AI-based* approaches. The first trend includes all articles in which the proposed solutions do not use model-based methods or AI-based algorithms. In contrast, the second trend shows solutions that use AI models, regardless of the learning paradigm or technique used. The figure shows that from the late 2000 s, non-AI-based solutions were in the majority. Specifically, the approaches used were mainly based on statistical [\[55\],](#page-12-0) [\[114\]](#page-13-0) or deterministic [\[48\],](#page-12-0) [\[115\]](#page-13-0) models. In the early 2010 s, AI-based solutions began to see

Fig. 6. State-of-the-art distribution between learning paradigm and AI sub-fields.

limited adoption. However, a significant increase in the use of AI was observed, eventually reaching a balance with non-AI approaches by the end of 2019. Subsequently, starting in 2020, a noticeable and pronounced increase in AI-based solutions took center stage, establishing it as the dominant methodology for diabetes therapies.

Given the importance of AI-based models, it is appropriate to provide an overview of the main learning approaches and techniques used. Fig. 6 and Table [IV,](#page-7-0) respectively, describe the distribution of state-of-the-art paradigms and learning techniques. Fig. 6 shows how the state-of-the-art spreads along two AI-based dimensions: 1) Learning Paradigms and 2) AI sub-fields approaches.

Concerning the learning paradigms dimension, this survey explores the relevance of different learning paradigms following the following classification $[116]$:

– *Supervised Paradigm;* which is the process of learning a set of rules to map an input to an output based on labelled datasets. These learned rules can be generalized to make predictions for unseen inputs.

– *Unsupervised Paradigm;* which is the process of finding previously unknown patterns based on unlabeled datasets.

– *Reinforcement Paradigm:* in which an agent interacts with an environment over several discrete time steps to achieve a specific goal.

– *Knowledge-Representation* (KR): in which an inference process is performed, via automated reasoning, on a represented knowledge [\[117\].](#page-13-0)

Concerning the AI sub-fields approaches dimension, the analysis of the state-of-the-art focus in terms of three main fields: *machine learning (ML)*, *Deep learning (DL), and reinforcement learning (RL)*. ML, DL and RL are integral components of artificial intelligence, each with distinct yet related characteristics. Machine Learning (ML) is a branch of artificial intelligence focused on developing algorithms that enable computers to learn from and make data-based decisions. It encompasses a range of techniques that allow systems to automatically discover patterns

Application	AI Subfields	Learning Paradigm	Papers
	Deep Learning	Supervised	$[29]$, $[65]$, $[30]$, $[31]$, $[66]$, $[69]$, $[57]$
Optimization		Knowledge Representation	[78], [76], [56]
	Machine Learning	Supervised	[63], [64], [92], [46], [33], [105], [106], [118], [59], [34]
		Unsupervised	[45]
	Reinforcement Learning	Reinforcement	$[77]$, $[42]$, $[41]$, $[44]$, $[80]$, $[49]$, $[70]$
Personalization	Deep Learning	Supervised	$[35]$, $[103]$, $[68]$
		Unsupervised	[102]
	Machine Learning	Knowledge Representation	[86]
		Supervised	$[60]$, $[61]$, $[100]$, $[37]$, $[36]$
		Unsupervised	$[99]$, $[72]$, $[93]$, $[94]$, $[87]$, $[96]$, $[104]$, $[97]$
	Reinforcement Learning	Reinforcement	[88], [50], [74], [51]
Mixed application	Deep Learning	Supervised	[52], [32], [40], [91]
	Machine Learning	Supervised	54
		Unsupervised	[39
	Reinforcement Learning	Reinforcement	1531, [75]

TABLE III DISTRIBUTION OF AI AMONG THE THREE APPLICATION FIELDS

TABLE IV OVERVIEW OF QUANTITATIVE DISTRIBUTION OF AI-BASED APPROACHES

and make predictions or decisions without explicit program-ming [\[119\].](#page-13-0) Deep learning (DL) is a subset of machine learning that uses layered neural networks to model complex patterns in data. These neural networks, inspired by the human brain, consist of interconnected neurons organized into layers. DL excels at tasks such as image and speech recognition, natural language processing, and game playing by automatically learning feature representations from raw data. Training requires large data sets and high computational power, often GPUs, to adjust network weights through backpropagation and gradient descent. Key architectures include convolutional neural networks (CNNs) for image data, recurrent neural networks (RNNs) for sequential data, and transformers for handling long-range dependencies in data [\[120\].](#page-13-0) Reinforcement Learning (RL) is a machine learning approach in which an agent learns to make decisions by interacting with the environment to maximize cumulative rewards. The agent observes the current state, takes action and receives rewards to develop a policy that optimizes long-term rewards. Key elements are states (current situations), actions (possible moves), and rewards (feedback signals). RL involves a cycle in which the agent acts, receives rewards, and updates its policy based on new experiences. Algorithms include Q-learning and policy gradients. RL applications range from games (e.g. AlphaGo) and robotics to autonomous vehicles and healthcare, highlighting its versatility in enabling adaptive decision-making in complex environments [\[121\].](#page-13-0) Fig. [6](#page-6-0) shows the state of the art, revealing distinct clusters concerning two dimensions. Each data point is presented using the adopted *Class of AI approach*. In particular, three densely populated clusters can be observed. The first cluster appears at the intersection of *(Deep Learning, Supervised Learning)*, where the dominant class of AI relies on *Neural Network* models. Here, *Neural Network* encompasses

a broad category of solutions whose models are based on algorithms such as recurrent networks (LSTM/RNN) [\[29\],](#page-11-0) [\[65\],](#page-12-0) convolutional networks (CNN[\)\[35\],](#page-11-0) and multi-layer perceptrons (DNN)[\[91\].](#page-13-0) The second cluster is at the intersection of*(Machine Learning, Supervised Learning)*. The cited papers propose various ML models in this cluster, such as support vector machines (SVM) [\[37\],](#page-11-0) Decision Trees (DT) [\[54\],](#page-12-0) and more. Moreover, the agent-based points are predominantly concentrated at the intersection of *(Reinforcement Learning, Reinforcement Paradigm)*, indicating a strong emphasis on agent-based methods [\[41\],](#page-12-0) [\[77\].](#page-12-0) Finally, a fourth cluster, less dense than the previous three, becomes apparent, primarily emerging at the intersection of *(Machine Learning, Unsupervised Learning)*. In this region, the predominant class of AI is anchored in clustering models [\[37\].](#page-11-0)

F. Review of the Application of AI by Diabetes Application

Table IV reveals that 51,8% of the adopted solutions are based on the Supervised Learning Paradigm (SP), which happens to be the most widely used approach. Additionally, Reinforce Paradigm (RP) and Unsupervised Paradigm (UP) are utilized to a lesser extent, accounting for 22,4% and 19% of the solutions, respectively. Conversely, a smaller fraction of solutions employ approaches based on Knowledge Representation (KR). The distribution of papers across various AI sub-fields is notably well-balanced, exhibiting a diverse range of proposed solutions.

Table III offers a comprehensive analysis overview, indicating that 48,3% of the papers in focus revolves around treatment optimization, which reveals a clear predilection for supervised approaches, which account for approximately 29,3% of the articles. In contrast, other methodologies, such as RL, are also considerably adopted, with about 12,1% of the papers demonstrating effective utilization of such models. Conversely, using unsupervised learning approaches remains limited, accounting for only a marginal portion of the proposed solutions.

Regarding personalization applications, approximately 38% of the selected papers fall into this category. Unlike the treatment optimization aspect, personalization applications exhibit a fair distribution of papers. Notably, there is a noteworthy increase in the adoption of unsupervised learning paradigms based on ML techniques, accounting for 13,8% of the solutions employed for

Fig. 7. Distribution of subcategories application among AI classes.

Fig. 8. Distribution of subcategories application among learning paradigms.

personalization applications. This combination emerges as the most popular choice in this context.

In summary, the findings reinforce the efficacy of solutions based on supervised learning paradigms in diabetes treatment applications. Such supervised learning approaches are validated in approximately 51,8% of the papers. On the other hand, RL-based approaches for personalization applications are in the minority, with only 7% of the papers exploring such methods. Lastly, the number of solutions addressing optimization and personalization applications appears small and insignificant.

G. Review of the Application of AI by Diabetes Subcategories Applications

To provide an in-depth analysis of the impact of AI models on diabetes care, we offer a comprehensive comparison across different application subcategories, as outlined in Tables [I](#page-2-0) and [V.](#page-9-0) Figs. 7 and 8 provide a comprehensive and detailed distribution of the state-of-the-art methodologies, offering valuable insights into two fundamental dimensions of analysis: AI subfields approaches and learning paradigms, as explicitly defined in Fig. 8. An in-depth examination of Fig. 8 highlights the continued preeminence of supervised learning approaches as the favoured learning model in diabetes care. Particularly noteworthy is their prominent utilization in the subcategories *Blood Glucose Prediction, Glucose Prediction and Meal*, and *Meal*. This aspect underscores the effectiveness of supervised learning techniques in addressing the specific challenges posed by these subcategories. Equally compelling is the

conspicuous dominance of reinforcement-based paradigms, which find extensive application in subcategories related to *Insulin/Bolus Dosing*. The strategic implementation of RL models in this context suggests their efficacy in optimizing insulin dosing and bolus adjustments, thus enhancing diabetes management. Simultaneously, learning approaches founded on unsupervised models witness significant usage, particularly within the *Patient Profiling/pattern recognition* subcategory. The ability of unsupervised models to discern patterns and profile patients underscores their relevance in facilitating personalized treatment strategies for individuals with diabetes. On the other hand, approaches based on KR remain a minority presence, primarily limited to the *Therapy recommendation system* subcategory. Although less prevalent, applying KR techniques in therapy recommendations signifies their potential to support healthcare decision-making processes. Furthermore, the remaining high-frequency subcategories demonstrate a well-balanced distribution across various learning models. This diversity of AI techniques indicates a tailored and adaptive approach to address the intricacies of diabetes care across different application subcategories. However, it is intriguing to note that algorithms based on RL models emerge as the dominant choice in specific subcategories, such as *Insulin/Bolus Dosing*. This suggests the efficacy of RL paradigms in tackling challenges related to insulin dosing and bolus adjustments for diabetic patients. The comprehensive analysis presented in Fig. 8 further substantiates these trends, underscoring the importance of choosing appropriate AI subfields and models to address the unique requirements of each subcategory in diabetes care. The widespread adoption of ML applications and the selective prominence of RL models signify the ever-expanding role of AI in revolutionizing diabetes care, offering personalized and effective solutions for patients and healthcare providers alike. A meticulous analysis of the state-of-the-art and the insights presented in Figs. 7 and 8 underscore the diverse array of models and algorithms employed in the discussed applications related to diabetic management. The comprehensive insights from this analysis and the informative table contribute significantly to understanding the current landscape of AI algorithms in diabetic management. To offer a more precise indication of the specific application of AI algorithms in supporting diabetic care, Table [III](#page-7-0) meticulously outlines, for each application subcategory, the most adopted algorithm serving as the baseline. The primary objective of this table is to serve as a valuable reference for developing future solutions tailored to address the unique requirements of each specific subcategory. The values in the *Algorithm Baseline* column provide a concise and consolidated representation of the most frequently utilized algorithm types within the respective subcategories. Concerning the value of the column *Algorithm Baseline:*

– *LSTM-based:* This value indicates that the analyzed papers utilized AI models based on DL techniques, specifically employing Long Short-Term Memory (LSTM) recurrent networks as a crucial data processing step. Subsequently, these solutions were complemented by other models more focused on the learning phase.

– *Q-Learning-based:* This score signifies the adoption of agent-based learning models, predominantly relying on the Q-Learning algorithm.

– *K-Means-Based:* This score indicates the application of the K-means clustering algorithm as the primary analysis algorithm. The papers in this category predominantly employed unsupervised learning approaches.

TABLE V MOST ADOPTED ALGORITHM BY SUBCATEGORIES

Subcategories	Baseline Algorithm	Papers
Blood glucose prediction	LSTM-based	$[29]$, $[31]$, $[40]$
Glucose prediction and Meals	LSTM-based	$[65]$, $[68]$, $[66]$, $[59]$
Insulin/Bolus Dosing	O-Learning-based	$[42]$, $[41]$, $[44]$, $[53]$
Meal	LSTM-based	$[32]$, $[57]$
Patient Profiling/ pattern recognition	K-Means-based	[93], [94], [97], [99]
GDM prediction	Multi-Algorithms	[99], [106]
Tailored device/algorithm	Multi-Algorithms	[72], [73], [74], $[75]$, [69], [70]
Therapy recommendation system	Fuzzy rules-based	$[78]$, $[86]$, $[76]$

Fig. 9. Distribution of AI categories among the final deployment groups.

– *Multi-Algorithms:* This value represents papers in which no single algorithm dominates the solution. Examining the papers within this category reveals a balanced use of algorithms, including SVM, K-Nearest Neighbors (KNN), and DT.

– *Fuzzy-rules-based:* This score denotes the prevalence of an algorithm based on fuzzy rule reasoning, representing the dominant approach in the adopted solutions.

These descriptive explanations within the *Algorithm Baseline* column offer valuable insights into the underlying AI techniques more frequently utilized in the respective subcategories, providing a clearer understanding of the methodologies employed in diabetic management applications and guiding the development of innovative and practical solutions to enhance patient care and optimize diabetes management strategies.

After conducting a comprehensive analysis of the application of AI in the treatment of diabetes, it is crucial to emphasize the final application targets of the solutions developed concerning the state of the art. Fig. 9 presents two vital dimensions of analysis: *AI subfields* and *Application Target*. The latter dimension defines four distinct types of applications:

– *Clinical Decision Support Systems (DSS):* This category encompasses clinical decision support systems, and standalone or web-based applications designed to integrate the generated AI models.

– *Insulin Pump:* The value associated with this category denotes solutions intended explicitly for seamless integration and embedding into infusion pumps and the subject's on-body control systems.

– *Mobile App:* This value pertains to solutions predominantly intended for integration into mobile devices.

– *Prototype:* The value assigned to this category indicates solutions that remain in the prototype stage without being integrated or deployed in commercial devices or systems.

Several observations can be derived from Fig. 9. Approximately 64% of the developed models are integrated into three main application typologies: *DSS, Insulin Pump*, and *Mobile App*. Among these, the primary application target is *DSS*, accounting for about 33% of the models, followed by *Insulin Pump* with 24%, and *Mobile App* with approximately 9%. Within the *DSS* category, most of the models are based on ML techniques, mainly focusing on clustering and generic AI models like SVM, KNN, and DT. In the context of *Insulin Pump* applications, the dominant algorithms are agent-based, relying on RL approaches and neural networks based on DL methodologies. Mobile solutions represent a minority among the application targets, with fewer models developed for this category. Techniques based on RL algorithms find primary usage in the *DSS* and *Insulin Pump* application targets, indicating their suitability for decision-making and control in these domains. The *Prototype* category comprises models not integrated into real-world applications. Approximately 34% of the produced models fall into this category, displaying a wellbalanced distribution across both the *AI Sub-Field* dimension and the class of algorithms employed. Analyzing the models within this category, some aspects can be highlighted: 65% of the reference papers related to the *Prototype* category were published between 2021 and 2023. Furthermore, it is interesting that only 23% of these projects use simulated data, while the remaining 77% utilize real data. This aspect contrasts to *DSS* and *Insulin Pump* targets, where the percentage of projects using simulated data is close to 50%. By highlighting the diverse application targets of the state-of-the-art solutions, stakeholders in the medical and technological domains gain a comprehensive understanding of the breadth and significance of AI in diabetes management.

IV. DISCUSSION

In this section, a deep explanation of the limitations found in the analyzed papers and possible future challenges are addressed. Specifically, among the limitations we discuss:

– Data availability and how it affects the AI model development.

– Lack of multimodal dataset.

– Model interpretability.

Similarly, for future challenges, we have:

– Development of a fully closed-loop system with multimodal data acquisition.

– New metrics to evaluate the AI model results in the medical fields.

– Trustworthy, explainability and ethics of AI in medicine.

A. Limitations

Even if AI has advanced state of the art in several diabetesrelated fields, applications in healthcare systems still need to be strong, trustworthy, and compelling to prevent safety concerns and offer useful therapeutic tools. Several restrictions and difficulties in this situation still prevent the wider introduction in actual therapeutic settings. The majority of the study makes use of publicly available datasets or simulated glycemic data, as was discussed in earlier sections. About 40% of the training data are simulated instances, which is indicative of this issue. The explanation is related to the difficulties faced by diabetes patients in precisely recording their routines or activities, uploading continuous data to the various storage platforms, and some concerns

with sensor artefacts. Since data protection rules make it difficult for research teams to share data sets, real data collection can be expensive and time-consuming. These factors cause many researchers to use a small, perhaps insufficient amount of data or modelling software, which can lead to biased predictions, as the AI model tends to favour the majority class while neglecting the minority class. Simulated data can be used to train and test AI-based models, however using them exclusively can result in a lack of data variability, which is essential for improving the generalization of AI algorithms. The variability among diabetics is high due to complex glucose dynamics, and it gets worse when we take into account various age groups going through various life stages. In general, patient participation is necessary for individualized diabetes treatment. Regular recording of pertinent events and adherence to the therapy goals are necessary for the development of elements for personalization. Another drawback of these studies is the insufficient consideration given to other factors and variables that can influence glucose evolution, such as information gathered from other wearable devices (smartwatches, wristbands, etc.), limiting the studies to use single-modal databases and inadvertently missing the opportunity to leverage different data sources and gain more comprehensive insights. The accuracy of currently accessible less intrusive sensor systems, however, is the issue and to avoid mistakes in the formulation of the therapy, sensors must be extremely precise. Socioeconomic variables and mental health measures have a big impact on diabetes management. Financial constraints, access to high-quality healthcare, and resources can prevent constant treatment and monitoring. Diabetes and mental health conditions like stress and depression frequently interact, which affects how well people take their medications, eat, and exercise. Stress can increase blood sugar levels and make it harder to care for oneself. Struggles with mental health may also sap motivation for good diabetes management. Addressing and considering these issues while optimizing algorithms would further personalize the therapy.

Addressing the interpretability of AI models in pediatric diabetes is critical due to the challenges posed by black-box models that often lack transparency in their results. The lack of explanation can introduce negative biases and reduce trust among patients and clinicians. From a clinical perspective, interpretability not only supports the adoption of these systems by clarifying the logic of the model but also supports clinical decision-making, monitoring, and verification of the reliability of AI models. This may help to identify and address potential errors, thereby improving patient safety and quality of care.

Despite groundbreaking advances in AI, susceptibility to black-box problems remains a significant shortcoming. To increase confidence in AI-generated results, it is important to augment outputs with comprehensive explanations that clarify the rationale behind specific decisions. Current methods often provide generic explanations that do not take into account the diverse backgrounds and knowledge levels of users.

Another issue concerning the balancing model of interpretability with predictive accuracy is a significant challenge. Indeed, hybrid methods attempt to achieve this balance by using post-hoc interpretability techniques or by designing new model architectures. However, post hoc techniques can be computationally expensive and may not fully capture the nuances of the model, while new models may struggle with complex interactions. The choice of approach depends on specific application requirements and acceptable trade-offs. Indeed, there are many more challenges worth addressing. However, these are the ones that, in our opinion, are particularly significant as they affect the medium- to long-term development vision of AI models in the context of pediatric diabetes [\[122\].](#page-13-0)

B. Future Works

The open problems described until now are common challenges in all medical fields since AI is still quite new support that the medical teams can adopt to predict, monitor and treat several diseases. Hence, there is the possibility to improve their applications, especially for diabetes treatment. Initializing and optimizing personalized therapy is a difficult undertaking due to the variety of variables impacting the therapy and the available therapeutic choices. To initiate and optimize therapy with a lower risk of safety-critical events like hypoglycemia, continuous monitoring with on-body sensors (blood glucose, dietary intake, physical activity, and health status) is recommended. Therefore, multi-modal systems using wearable and smartphone applications can help in recording digital records and vital signs. Researchers and practitioners should prioritize exploring and incorporating multi-modal approaches also to fully realize the potential of AI methods and to create a comprehensive and diverse dataset encompassing multiple data types, enabling the development and evaluation of more effective multi-modal AI models. In this way, we can overcome some of the limitations previously described since it will positively affect the data volume and variability. This means that many low-quality data samples can be filtered out and significantly lower measurement errors, training robust AI algorithms that can capture the interand intra-variability of the glucose evolution. The creation of a fully closed-loop artificial pancreas system is the ultimate objective of technical development in the field of diabetes therapy. Developing such a system requires considering several factors, such as socioeconomic, cultural, and mental status, that can be used to initialize and optimize the therapy from the very beginning. It has been demonstrated that, mainly for children and adolescents, these factors play a crucial role in adhering to and accepting the therapy [\[123\],](#page-13-0) [\[124\],](#page-13-0) [\[125\]](#page-13-0) and a first attempt in this direction has been made by [\[86\]](#page-13-0) demonstrating to be a piece of important information to add. Additionally, rather than just being saturated with performance metrics that may not be relevant to the adoption of medical technology, clinicians and practitioners should be given the chance to fairly evaluate the utilities of the proposed interpretability approaches. Although providing a visual and written explanation provided by an algorithm may seem like the logical solution, the specifics of how algorithms like DNNs make decisions are still not fully known. To address this, a specialized education combining medical knowledge, applied mathematics, data science, etc. may be required [\[126\].](#page-13-0) The imperative is to embrace the development of explainable AI systems that shed light on the decision-making process, thereby fostering trust and confidence in the results of these cutting-edge algorithms through various methodologies, such as incorporating attention mechanisms [\[127\].](#page-13-0) Furthermore, research in this area must focus on trustworthy AI and the ethical implications of its application. Reliable AI in medical devices needs to be strong, open, and egalitarian to guarantee both safety and effectiveness while maintaining patient privacy and accountability. Regulatory agencies must ensure that the aforementioned open problems meet high standards of safety and efficacy.

V. CONCLUSION

In this article, we provide an in-depth analysis of the current development of AI-based diabetic therapy. We conducted a thorough search, selected several articles, and synthesized the important data with a focus on two areas: therapy personalization and treatment optimization. Patient-focused systems and algorithms have drawn a lot of attention in recent years. This pattern emphasizes the significance of treating the person as a whole, which directs the creation of personalized and focused treatments. This strategy represents a shift towards wider-ranging and more flexible medical solutions, constituting a substantial advancement in the integration of patient requirements into the medical setting. As AI research in diabetic management continuously evolves, novel algorithms and cutting-edge techniques are frequently introduced and explored in the literature. Researchers and developers are encouraged to explore and experiment with a diverse range of AI models and methodologies to uncover innovative solutions and address specific challenges in diabetic care effectively. By continuously expanding the knowledge base and embracing advancements in AI, we can enhance the quality of care and outcomes for diabetics.

REFERENCES

- [1] World Health Organization, "Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: Report of a WHO/IDF consultation," 2006. [Online]. Available: [https://iris.who.int/bitstream/handle/](https://iris.who.int/bitstream/handle/10665/43588/924159{?}sequence$=$1) [10665/43588/924159?sequence=1](https://iris.who.int/bitstream/handle/10665/43588/924159{?}sequence$=$1)
- [2] F. Zaccardi, D. R. Webb, T. Yates, and M. J. Davies, "Pathophysiology of type 1 and type 2 diabetes mellitus: A 90-year perspective," *Postgraduate Med. J.*, vol. 92, no. 1084, pp. 63–69, 2016.
- [3] L. A. DiMeglio, C. Evans-Molina, and R. A. Oram, "Type 1 diabetes," *Lancet*, vol. 391, no. 10138, pp. 2449–2462, 2018.
- [4] R. Streisand and M. Monaghan, "Young children with type 1 diabetes: Challenges, research, and future directions," *Curr. Diabetes Rep.*, vol. 14, pp. 1–9, 2014.
- [5] B. H. McAdams and A. A. Rizvi, "An overview of insulin pumps and glucose sensors for the generalist," *J. Clin. Med.*, vol. 5, no. 1, p. 5, 2016, doi: [10.1038/s41746-023-00783-1.](https://dx.doi.org/10.1038/s41746-023-00783-1)
- [6] T. Danne et al., "Establishing glycaemic control with continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes: Experience of the pedpump study in 17 countries," *Diabetologia*, vol. 51, pp. 1594–1601, 2008.
- [7] M. Tauschmann and R. Hovorka, "Technology in the management of type 1 diabetes mellitus—current status and future prospects," *Nature Rev. Endocrinol.*, vol. 14, no. 8, pp. 464–475, 2018.
- [8] C. K. Boughton and R. Hovorka, "The role of automated insulin delivery technology in diabetes," *Diabetologia*, 2024, doi: [10.1007/s00125-024-06165-w.](https://dx.doi.org/10.1007/s00125-024-06165-w)
- [9] B. Jeffrey et al., "Mobile phone applications and their use in the selfmanagement of type 2 diabetes mellitus: A qualitative study among app users and non-app users," *Diabetol. Metabolic Syndrome*, vol. 11, no. 1, pp. 1–17, 2019.
- [10] S. Franc et al., "Diabeo system combining a mobile app software with and without telemonitoring versus standard care: A randomized controlled trial in diabetes patients poorly controlled with a basal-bolus insulin regimen," *Diabetes Technol. Therapeutics*, vol. 22, no. 12, pp. 904–911, 2020.
- [11] A. Ramesh, C. Kambhampati, J. R. Monson, and P. Drew, "Artificial intelligence in medicine," *Ann. Roy. College Surgeons England*, vol. 86, no. 5, 2004, Art. no. 334.
- [12] G. Cappon, A. Facchinetti, G. Sparacino, P. Georgiou, and P. Herrero, "Classification of postprandial glycemic status with application to insulin dosing in type 1 diabetes—an in silico proof-of-concept," *Sensors*, vol. 19, no. 14, 2019, Art. no. 3168.
- [13] R. Reddy, N. Resalat, L. M. Wilson, J. R. Castle, J. El Youssef, and P. G. Jacobs, "Prediction of hypoglycemia during aerobic exercise in adults with type 1 diabetes," *J. Diabetes Sci. Technol.*, vol. 13, no. 5, pp. 919–927, 2019.
- [14] M. K. Hasan, M. A. Alam, D. Das, E. Hossain, and M. Hasan, "Diabetes prediction using ensembling of different machine learning classifiers," *IEEE Access*, vol. 8, pp. 76516–76531, 2020.
- [15] V. Jackins, S. Vimal, M. Kaliappan, and M. Y. Lee, "AI-based smart prediction of clinical disease using random forest classifier and naive bayes," *J. Supercomputing*, vol. 77, pp. 5198–5219, 2021.
- [16] M. S. Islam, M. K. Qaraqe, S. B. Belhaouari, and M. A. Abdul-Ghani, "Advanced techniques for predicting the future progression of type 2 diabetes," *IEEE Access*, vol. 8, pp. 120537–120547, 2020.
- [17] V. Dremin et al., "Skin complications of diabetes mellitus revealed by polarized hyperspectral imaging and machine learning," *IEEE Trans. Med. Imag.*, vol. 40, no. 4, pp. 1207–1216, Apr. 2021.
- [18] G. Annuzzi et al., "Impact of nutritional factors in blood glucose prediction in type 1 diabetes through machine learning," *IEEE Access*, vol. 11, pp. 17104–17115, 2023.
- [19] M. Sevil, M. Rashid, I. Hajizadeh, M. Park, L. Quinn, and A. Cinar, "Physical activity and psychological stress detection and assessment of their effects on glucose concentration predictions in diabetes management," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 7, pp. 2251–2260, Jul. 2021.
- [20] K. D. Barnard et al., "Closing the loop overnight at home setting: Psychosocial impact for adolescents with type 1 diabetes and their parents,' *BMJ Open Diabetes Res. Care*, vol. 2, no. 1, 2014, Art. no. e000025.
- [21] Z. A. Stewart et al., "Closed-loop insulin delivery during pregnancy in women with type 1 diabetes," *New England J. Med.*, vol. 375, no. 7, pp. 644–654, 2016, doi: [10.1056/NEJMoa1602494.](https://dx.doi.org/10.1056/NEJMoa1602494)
- [22] F. A. Khan, K. Zeb, M. Al-Rakhami, A. Derhab, and S. A. C. Bukhari, "Detection and prediction of diabetes using data mining: A comprehensive review," *IEEE Access*, vol. 9, pp. 43711–43735, 2021.
- [23] T. Gautier, L. B. Ziegler, M. S. Gerber, E. Campos-Náñez, and S. D. Patek, "Artificial intelligence and diabetes technology: A review," *Metabolism*, vol. 124, 2021, Art. no. 154872.
- [24] M. Barrett et al., "Artificial intelligence supported patient self-care in chronic heart failure: A paradigm shift from reactive to predictive, preventive and personalised care," *Epma J.*, vol. 10, pp. 445–464, 2019.
- [25] L. Gosak, A. Svensek, M. Lorber, and G. Stiglic, "Artificial intelligence based prediction of diabetic foot risk in patients with diabetes: A literature review," *Appl. Sci.*, vol. 13, no. 5, 2023, Art. no. 2823.
- [26] M. A. Makroum, M. Adda, A. Bouzouane, and H. Ibrahim, "Machine learning and smart devices for diabetes management: Systematic review," *Sensors*, vol. 22, no. 5, 2022, Art. no. 1843.
- [27] T. Zhu, K. Li, P. Herrero, and P. Georgiou, "Deep learning for diabetes: A systematic review," *IEEE J. Biomed. Health Inform.*, vol. 25, no. 7, pp. 2744–2757, Jul. 2021.
- [28] M. J. Page et al., "The Prisma 2020 statement: An updated guideline for reporting systematic reviews," *Int. J. Surg.*, vol. 88, 2021, Art. no. 105906.
- [29] H. Nemat, H. Khadem, M. R. Eissa, J. Elliott, and M. Benaissa, "Blood glucose level prediction: Advanced deep-ensemble learning approach," *IEEE J. Biomed. Health Inform.*, vol. 26, no. 6, pp. 2758–2769, Jun. 2022.
- [30] S.-M. Lee, D.-Y. Kim, and J. Woo, "Glucose transformer: Forecasting glucose level and events of hyperglycemia and hypoglycemia," *IEEE J. Biomed. Health Inform.*, vol. 27, no. 3, pp. 1600–1611, Mar. 2023.
- [31] F. D'Antoni et al., "Layered meta-learning algorithm for predicting adverse events in type 1 diabetes," *IEEE Access*, vol. 11, pp. 9074–9094, 2023.
- [32] M. Athanasiou, K. Zarkogianni, K. Karytsas, and K. S. Nikita, "An LSTM-based approach towards automated meal detection from continuous glucose monitoring in type 1 diabetes mellitus," in *2021 IEEE 21st Int. Conf. Bioinf. Bioeng.*, 2021, pp. 1–5.
- [33] C. Mosquera-Lopez, K. L. Ramsey, V. Roquemen-Echeverri, and P. G. Jacobs, "Modeling risk of hypoglycemia during and following physical activity in people with type 1 diabetes using explainable mixed-effects machine learning," *Comput. Biol. Med.*, vol. 155, 2023, Art. no. 106670.
- [34] A. Güemes et al., "Predicting quality of overnight glycaemic control in type 1 diabetes using binary classifiers," *IEEE J. Biomed. Health Inform.*, vol. 24, no. 5, pp. 1439–1446, May 2020.
- [35] K. Li, C. Liu, T. Zhu, P. Herrero, and P. Georgiou, "GluNet: A deep learning framework for accurate glucose forecasting," *IEEE J. Biomed. Health Inform.*, vol. 24, no. 2, pp. 414–423, Feb. 2020.
- [36] N. S. Tyler, C. Mosquera-Lopez, G. M. Young, J. El Youssef, J. R. Castle, and P. G. Jacobs, "Quantifying the impact of physical activity on future glucose trends using machine learning," *Iscience*, vol. 25, no. 3, 2022, Art. no. 103888.
- [37] A. Şahin and A. Aydin, "Personalized advanced time blood glucose level prediction," *Arabian J. Sci. Eng.*, vol. 46, no. 10, pp. 9333–9344, 2021.
- [38] F. Simone et al., "Linear model identification for personalized prediction and control in diabetes," *IEEE Trans. Biomed. Eng.*, vol. 69, no. 2, pp. 558–568, Feb. 2020.
- [39] N. Kim et al., "Toward personalized hemoglobin a1c estimation for type 2 diabetes," *IEEE Sensors J.*, vol. 22, no. 23, pp. 23023–23032, Dec. 2022.
- [40] T. Zhu, K. Li, P. Herrero, and P. Georgiou, "Personalized blood glucose prediction for type 1 diabetes using evidential deep learning and meta-learning," *IEEE Trans. Biomed. Eng.*, vol. 70, no. 1, pp. 193–204, Jan. 2023.
- [41] G. Noaro, T. Zhu, G. Cappon, A. Facchinetti, and P. Georgiou, "A personalized and adaptive insulin bolus calculator based on double deep q-learning to improve type 1 diabetes management," *IEEE J. Biomed. Health Inform.*, vol. 27, no. 5, pp. 2536–2544, May 2023.
- [42] T. Zhu, K. Li, L. Kuang, P. Herrero, and P. Georgiou, "An insulin bolus advisor for type 1 diabetes using deep reinforcement learning," *Sensors*, vol. 20, no. 18, 2020, Art. no. 5058.
- [43] P. Herrero, J. Bondia, M. Giménez, N. Oliver, and P. Georgiou, "Automatic adaptation of basal insulin using sensor-augmented pump therapy," *J. Diabetes Sci. Technol.*, vol. 12, no. 2, pp. 282–294, 2018.
- [44] S. Ahmad, A. Beneyto, I. Contreras, and J. Vehi, "Bolus insulin calculation without meal information. a reinforcement learning approach," *Artif. Intell. Med.*, vol. 134, 2022, Art. no. 102436.
- [45] I. Hajizadeh, M. R. Askari, R. Kumar, V. M. Zavala, and A. Cinar, "Integrating MPC with learning-based and adaptive methods to enhance safety, performance and reliability in automated insulin delivery," *IFAC-PapersOnLine*, vol. 53, no. 2, pp. 16149–16154, 2020.
- [46] G. Noaro, G. Cappon, M. Vettoretti, G. Sparacino, S. Del Favero, and A. Facchinetti, "Machine-learning based model to improve insulin bolus calculation in type 1 diabetes therapy," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 1, pp. 247–255, Jan. 2021.
- [47] I. Hajizadeh, M. Rashid, and A. Cinar, "Considering plasma insulin concentrations in adaptive model predictive control for artificial pancreas systems," in *2018 40th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2018, pp. 4452–4455.
- [48] J. Tuo, H. Sun, D. Shen, H. Wang, and Y. Wang, "Optimization of insulin pump therapy based on high order run-to-run control scheme," *Comput. Methods Programs Biomed.*, vol. 120, no. 3, pp. 123–134, 2015.
- [49] M. Jaloli and M. Cescon, "Reinforcement learning for multiple daily injection (MDI) therapy in type 1 diabetes (T1D)," *BioMedInform.*, vol. 3, no. 2, pp. 422–433, 2023.
- [50] Q. Sun et al., "A dual mode adaptive basal-bolus advisor based on reinforcement learning," *IEEE J. Biomed. Health Inform.*, vol. 23, no. 6, pp. 2633–2641, Nov. 2019.
- [51] E. Daskalaki, P. Diem, and S. G. Mougiakakou, "Model-free machine learning in biomedicine: Feasibility study in type 1 diabetes," *PLoS One*, vol. 11, no. 7, 2016, Art. no. e0158722.
- [52] M. M. Rashid, M. R. Askari, C. Chen, Y. Liang, K. Shu, and A. Cinar, "Artificial intelligence algorithms for treatment of diabetes," *Algorithms*, vol. 15, no. 9, 2022, Art. no. 299.
- [53] M. Shifrin and H. Siegelmann, "Near-optimal insulin treatment for diabetes patients: A machine learning approach," *Artif. Intell. Med.*, vol. 107, 2020, Art. no. 101917.
- [54] G. E. G. Gómez et al., "Application of artificial intelligence techniques for the estimation of basal insulin in patients with type I diabetes," *Int. J. Endocrinol.*, vol. 2020, 2020, Art. no. 7326073.
- [55] M. Zheng, B. Ni, and S. Kleinberg, "Automated meal detection from continuous glucose monitor data through simulation and explanation," *J. Amer. Med. Inform. Assoc.*, vol. 26, no. 12, pp. 1592–1599, 2019.
- [56] S. Samadi et al., "Automatic detection and estimation of unannounced meals for multivariable artificial pancreas system," *Diabetes Technol. Therapeutics*, vol. 20, no. 3, pp. 235–246, 2018.
- [57] C. Mosquera-Lopez et al., "Enabling fully automated insulin delivery through meal detection and size estimation using artificial intelligence," *NPJ Digit. Med.*, vol. 6, p. 39, 2023, doi: [10.1038/s41746-023-00783-1.](https://dx.doi.org/10.1038/s41746-023-00783-1)
- [58] Z. Mahmoudi, F. Cameron, N. K. Poulsen, H. Madsen, B. W. Bequette, and J. B. Jørgensen, "Sensor-based detection and estimation of meal carbohydrates for people with diabetes," *Biomed. Signal Process. Control*, vol. 48, pp. 12–25, 2019.
- [59] M. R. Askari et al., "Detection of meals and physical activity events from free-living data of people with diabetes," *J. Diabetes Sci. Technol.*, vol. 17, no. 6, pp. 1482–1492, 2023, doi: [10.1177/19322968221102183.](https://dx.doi.org/10.1177/19322968221102183)
- [60] H. T. Huynh and T. M. Hoang, "A novel approach for determining meal plan for gestational diabetes mellitus using artificial intelligence,' *Comput. J.*, vol. 65, no. 5, pp. 1088–1097, 2022.
- [61] D. Amorim, F. Miranda, L. Ferreira, and C. Abreu, "Data-driven carbohydrate counting accuracy monitoring: A personalized approach," *Procedia Comput. Sci.*, vol. 204, pp. 900–906, 2022.
- [62] J. L. Godoy, J. Sereno, and P. S. Rivadeneira, "Meal detection and carbohydrate estimation based on a feedback scheme with application to the artificial pancreas," *Biomed. Signal Process. Control*, vol. 68, 2021, Art. no. 102715.
- [63] E. A. Pustozerov et al., "Machine learning approach for postprandial blood glucose prediction in gestational diabetes mellitus," *IEEE Access*, vol. 8, pp. 219308–219321, 2020.
- [64] S. Oviedo et al., "Minimizing postprandial hypoglycemia in type 1 diabetes patients using multiple insulin injections and capillary blood glucose self-monitoring with machine learning techniques," *Comput. Methods Programs Biomed.*, vol. 178, pp. 175–180, 2019.
- [65] L. Angrisani et al., "Neural network-based prediction and monitoring of blood glucose response to nutritional factors in type-1 diabetes," in *2022 IEEE Int. Instrum. Meas. Technol. Conf.*, 2022, pp. 1–6.
- [66] L. Martínez-Delgado, M. Munoz-Organero, and P. Queipo-Alvarez, "Using absorption models for insulin and carbohydrates and deep leaning to improve glucose level predictions," *Sensors*, vol. 21, no. 16, 2021, Art. no. 5273.
- [67] M. Cescon, S. Deshpande, R. Nimri, F. J. Doyle III, and E. Dassau, "Using iterative learning for insulin dosage optimization in multipledaily-injections therapy for people with type 1 diabetes," *IEEE Trans. Biomed. Eng.*, vol. 68, no. 2, pp. 482–491, Feb. 2021.
- [68] M. Muñoz-Organero, P. Queipo-álvarez, and B. G. Gutiérrez, "Learning carbohydrate digestion and insulin absorption curves using blood glucose level prediction and deep learning models," *Sensors*, vol. 21, no. 14, 2021, Art. no. 4926.
- [69] S. K. Almulla et al., "Smart artificial-intelligence based self-care-device for diabetic patients," in *2022 Adv. Sci. Eng. Technol. Int. Conf.*, 2022, pp. 1–5.
- [70] S. Lee, J. Kim, S. W. Park, S.-M. Jin, and S.-M. Park, "Toward a fully automated artificial pancreas system using a bioinspired reinforcement learning design: In silico validation," *IEEE J. Biomed. Health Inform.*, vol. 25, no. 2, pp. 536–546, Feb. 2021.
- [71] C. Toffanin, R. Visentin, M. Messori, F. Di Palma, L. Magni, and C. Cobelli, "Toward a run-to-run adaptive artificial pancreas: In silico results," *IEEE Trans. Biomed. Eng.*, vol. 65, no. 3, pp. 479–488, Mar. 2018.
- [72] S. Chen, L. Feng, M. R. Rickels, A. Peleckis, O. Sokolsky, and I. Lee, "A data-driven behavior modeling and analysis framework for diabetic patients on insulin pumps," in *2015 Int. Conf. Healthcare Inform.*, 2015, pp. 213–222.
- [73] X. Sun, M. Rashid, M. R. Askari, and A. Cinar, "Adaptive personalized prior-knowledge-informed model predictive control for type 1 diabetes," *Control Eng. Pract.*, vol. 131, 2023, Art. no. 105386.
- [74] A. Mackey and E. Furey, "Artificial pancreas control for diabetes using TD3 deep reinforcement learning," in *2022 33rd Ir. Signals Syst. Conf.*, 2022, pp. 1–6.
- [75] M. De Paula, G. G. Acosta, and E. C. Martínez, "On-line policy learning and adaptation for real-time personalization of an artificial pancreas,' *Expert Syst. Appl.*, vol. 42, no. 4, pp. 2234–2255, 2015.
- [76] M. R. Smaoui and A. Lafi, "Leeno: Type 1 diabetes management training environment using smart algorithms," *Plos One*, vol. 17, no. 9, 2022, Art. no. e0274534.
- [77] J. P. A. Pereira, A. A. F. Brandão, J. d. S. Bevilacqua, and M. L. C. Côrrea-Giannella, "A multi-agent approach used to predict long-term glucose oscillation in individuals with type 1 diabetes," *Appl. Sci.*, vol. 12, no. 19, 2022, Art. no. 9641.
- [78] C.-S. Lee and M.-H. Wang, "A fuzzy expert system for diabetes decision support application," *IEEE Trans. Syst., Man, Cybern., Part B.*, vol. 41, no. 1, pp. 139–153, Feb. 2011.
- [79] M. Rigla, I. Martínez-Sarriegui, G. García-Sáez, B. Pons, and M. E. Hernando, "Gestational diabetes management using smart mobile telemedicine," *J. Diabetes Sci. Technol.*, vol. 12, no. 2, pp. 260–264, 2018.
- [80] Z. Ying, Y. Zhang, S. Cao, S. Xu, and X. Liu, "Oidpr: Optimized insulin dosage based on privacy-preserving reinforcement learning," in *2020 IFIP Netw. Conf.*, 2020, pp. 655–657.
- [81] N. S. Tyler and P. G. Jacobs, "Artificial intelligence in decision support systems for type 1 diabetes," *Sensors*, vol. 20, no. 11, 2020, Art. no. 3214.
- [82] R. Visentin et al., "The UVA/PADOVA type 1 diabetes simulator goes from single meal to single day," *J. Diabetes Sci. Technol.*, vol. 12, no. 2, pp. 273–281, 2018.

- [83] T. B. Aradóttir, D. Boiroux, H. Bengtsson, J. B. Jørgensen, and N. K. Poulsen, "Model predictive control with sub-frequency actuation for long acting insulin treatment in type 2 diabetes," in *2019 IEEE Conf. Control Technol. Appl.*, 2019, pp. 914–919.
- [84] A. Mohebbi, T. B. Aradóttir, A. R. Johansen, H. Bengtsson, M. Fraccaro, and M. Mørup, "A deep learning approach to adherence detection for type 2 diabetics," in *2017 39th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2017, pp. 2896–2899.
- [85] A. Haidar, M. E. Wilinska, J. A. Graveston, and R. Hovorka, "Stochastic virtual population of subjects with type 1 diabetes for the assessment of closed-loop glucose controllers," *IEEE Trans. Biomed. Eng.*, vol. 60, no. 12, pp. 3524–3533, Dec. 2013.
- [86] S. Alian, J. Li, and V. Pandey, "A personalized recommendation system to support diabetes self-management for american indians," *IEEE Access*, vol. 6, pp. 73041–73051, 2018.
- [87] A. Bartolome, S. Shah, and T. Prioleau, "Glucomine: A case for improving the use of wearable device data in diabetes management," *Proc. ACM Interactive, Mobile, Wearable Ubiquitous Technol.*, vol. 5, no. 3, pp. 1–24, 2021.
- [88] S. H. Oh, S. J. Lee, and J. Park, "Effective data-driven precision medicine by cluster-applied deep reinforcement learning," *Knowl.-Based Syst.*, vol. 256, 2022, Art. no. 109877.
- [89] R. Nimri et al., "Adjustment of insulin pump settings in type 1 diabetes management: Advisor pro device compared to physicians' recommendations," *J. Diabetes Sci. Technol.*, vol. 16, no. 2, pp. 364–372, 2022.
- [90] R. Nimri et al., "Insulin dose optimization using an automated artificial intelligence-based decision support system in youths with type 1 diabetes," *Nature Med.*, vol. 26, no. 9, pp. 1380–1384, 2020.
- [91] R. M. Ansari, M. F. Harris, H. Hosseinzadeh, and N. Zwar, "Application of artificial intelligence in assessing the self-management practices of patients with type 2 diabetes," *Healthcare*, vol. 11, no. 6, 2023, Art. no. 903.
- [92] S. Campanella et al., "Machine learning approach for care improvement of children and youth with type 1 diabetes treated with hybrid closed-loop system," *Electronics*, vol. 11, no. 14, 2022, Art. no. 2227.
- [93] B. Lobo, L. Farhy, M. Shafiei, and B. Kovatchev, "A data-driven approach to classifying daily continuous glucose monitoring (CGM) time series," *IEEE Trans. Biomed. Eng.*, vol. 69, no. 2, pp. 654–665, Feb. 2022.
- [94] I. Contreras, J. Vehí, R. Visentin, and M. Vettoretti, "A hybrid clustering prediction for type 1 diabetes aid: Towards decision support systems based upon scenario profile analysis," in *2017 IEEE/ACM Int. Conf. Connected Health, Appl., Syst. Eng. Technol.*, 2017, pp. 64–69.
- M. Moscoso-Vasquez, P. Colmegna, N. Rosales, F. Garelli, and R. Sanchez-Pena, "Control-oriented model with intra-patient variations for an artificial pancreas," *IEEE J. Biomed. Health Inform.*, vol. 24, no. 9, pp. 2681–2689, Sep. 2020.
- [96] H. Hall et al., "Glucotypes reveal new patterns of glucose dysregulation," *PLoS Biol.*, vol. 16, no. 7, 2018, Art. no. e2005143.
- [97] M. R. Eissa, T. Good, J. Elliott, and M. Benaissa, "Intelligent data-driven model for diabetes diurnal patterns analysis," *IEEE J. Biomed. Health Inform.*, vol. 24, no. 10, pp. 2984–2992, Oct. 2020.
- [98] B. J. Lobo and B. P. Kovatchev, "External validation of a classifier of daily continuous glucose monitoring (CGM) profiles," *Comput. Biol. Med.*, vol. 143, 2022, Art. no. 105293.
- [99] R. Tao et al., "Multilevel clustering approach driven by continuous glucose monitoring data for further classification of type 2 diabetes," *BMJ Open Diabetes Res. Care*, vol. 9, no. 1, 2021, Art. no. e001869.
- [100] K. Kölle, T. Biester, S. Christiansen, A. L. Fougner, and Ø. Stavdahl, "Pattern recognition reveals characteristic postprandial glucose changes: Non-individualized meal detection in diabetes mellitus type 1," *IEEE J. Biomed. Health Inform.*, vol. 24, no. 2, pp. 594–602, Feb. 2020.
- [101] M. Vasquez-Muñoz et al., "Oscillatory pattern of glycemic control in patients with diabetes mellitus," *Sci. Rep.*, vol. 11, no. 1, pp. 1–12, 2021.
- [102] M. H. Lim, Y. M. Cho, and S. Kim, "Multi-task disentangled autoencoder for time-series data in glucose dynamics," *IEEE J. Biomed. Health Inform.*, vol. 26, no. 9, pp. 4702–4713, Sep. 2022.
- [103] P. Thamotharan et al., "Human digital twin for personalized elderly type 2 diabetes management," *J. Clin. Med.*, vol. 12, no. 6, 2023, Art. no. 2094.
- [104] A. R. Kahkoska et al., "Identification of clinically relevant dysglycemia phenotypes based on continuous glucose monitoring data from youth with type 1 diabetes and elevated hemoglobin A1C," *Pediatr. Diabetes*, vol. 20, no. 5, pp. 556–566, 2019.
- [105] J. Shen et al., "An innovative artificial intelligence-based app for the diagnosis of gestational diabetes mellitus (GDM-AI): Development study," *J. Med. Internet Res.*, vol. 22, no. 9, 2020, Art. no. e21573.
- [106] Y.-T. Wu et al., "Early prediction of gestational diabetes mellitus in the chinese population via advanced machine learning," *J. Clin. Endocrinol. Metab.*, vol. 106, no. 3, pp. e1191–e1205, 2021.
- [107] D. Rankin, B. Kimbell, R. Hovorka, and J. Lawton, "Adolescents' and their parents' experiences of using a closed-loop system to manage type 1 diabetes in everyday life: Qualitative study," *Chronic Illness*, vol. 18, no. 4, pp. 742–756, 2022.
- [108] D. Boiroux, T. B. Aradóttir, K. Nørgaard, N. K. Poulsen, H. Madsen, and J. B. Jørgensen, "An adaptive nonlinear basal-bolus calculator for patients with type 1 diabetes," *J. Diabetes Sci. Technol.*, vol. 11, no. 1, pp. 29–36, 2017.
- [109] E. Lehmann, T. Deutsch, E. Carson, and P. Sönksen, "Aida: An interactive diabetes advisor," *Comput. Methods Programs Biomed.*, vol. 41, no. 3/4, pp. 183–203, 1994.
- [110] C. De Beaufort et al., "Psychological well-being of parents of very young children with type 1 diabetes–baseline assessment," *Front. Endocrinol.*, vol. 12, 2021, Art. no. 721028.
- [111] K. R. Tan et al., "Evaluation of machine learning methods developed for prediction of diabetes complications: A systematic review," *J. Diabetes Sci. Technol.*, vol. 17, no. 2, pp. 474–489, 2023, doi: [10.1177/19322968211056917.](https://dx.doi.org/10.1177/19322968211056917)
- [112] R. Visentin, C. D. Man, and C. Cobelli, "One-day bayesian cloning of type 1 diabetes subjects: Toward a single-day UVA/PADOVA type 1 diabetes simulator," *IEEE Trans. Biomed. Eng.*, vol. 63, no. 11, pp. 2416–2424, Nov. 2016.
- [113] S. H. Park et al., "Methods for clinical evaluation of artificial intelligence algorithms for medical diagnosis," *Radiol.*, vol. 306, no. 1, pp. 20–31, 2023.
- [114] N. Chow et al., "Determining starting basal rates of insulin infusion for insulin pump users: A comparison between methods," *BMJ Open Diabetes Res. Care*, vol. 4, no. 1, 2016, Art. no. e000145.
- [115] C. C. Palerm, H. Zisser, L. Jovanovič, and F. J. Doyle III, "A run-to-run control strategy to adjust basal insulin infusion rates in type 1 diabetes," *J. Process Control*, vol. 18, no. 3/4, pp. 258–265, 2008.
- [116] N. Wu and Y. Xie, "A survey of machine learning for computer architecture and systems," *ACM Comput. Surv.*, vol. 55, no. 3, Feb. 2022, doi: [10.1145/3494523.](https://dx.doi.org/10.1145/3494523)
- [117] T. Schneider and M. Šimkus, "Ontologies and data management: A brief survey," *KI-Künstliche Intelligenz*, vol. 34, pp. 329–353, Aug. 2020, doi: [10.1007/s13218-020-00686-3.](https://dx.doi.org/10.1007/s13218-020-00686-3)
- [118] N. S. Tyler et al., "An artificial intelligence decision support system for the management of type 1 diabetes," *Nature Metab.*, vol. 2, no. 7, pp. 612–619, 2020.
- [119] T. M. Mitchell, "Machine learning," New York: McGraw-hill, vol. 1, no. 9, 1997.
- [120] Y. LeCun, Y. Bengio, and G. Hinton, "Deep learning," *Nature*, vol. 521, no. 7553, pp. 436–444, May 2015, doi: [10.1038/nature14539.](https://dx.doi.org/10.1038/nature14539)
- [121] V. Mnih et al., "Human-level control through deep reinforcement learning," *Nature*, vol. 518, no. 7540, pp. 529–533, 2015.
- [122] W. Yang et al., "Survey on explainable AI: From approaches, limitations and applications aspects," vol. 3, pp. 161–188, Aug. 2023, doi: [10.1007/s44230-023-00038-y.](https://dx.doi.org/10.1007/s44230-023-00038-y)
- [123] R. Gesuita et al., "The role of socio-economic and clinical factors on hba1c in children and adolescents with type 1 diabetes: An Italian multicentre survey," *Pediatr. Diabetes*, vol. 18, no. 3, pp. 241–248, 2017.
- [124] M. de Wit, P. Trief, J. Huber, and I. Willaing, "State of the art: Understanding and integration of the social context in diabetes care," *Diabetic Med.*, vol. 37, no. 3, pp. 473–482, 2020.
- [125] L. N. Jespersen, M. H. Vested, L. B. Johansen, and D. Grabowski, "Mirroring life of adolescents with type 1 diabetes—An outline of key aspects," *Diabetology*, vol. 2, no. 3, pp. 141–156, 2021.
- [126] E. Tjoa and C. Guan, "A survey on explainable artificial intelligence (XAI): Toward medical XAI," *IEEE Trans. Neural Netw. Learn. Syst.*, vol. 32, no. 11, pp. 4793–4813, Nov. 2021.
- [127] D. Bahdanau, K. Cho, and Y. Bengio, "Neural machine translation by jointly learning to align and translate," 2014, *arXiv: 1409.0473*

Open Access provided by 'Università Politecnica delle Marche' within the CRUI CARE Agreement