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IoMT innovations in diabetes management: Predictive models using wearable data

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ABSTRACT

Diabetes Mellitus (DM) represents a metabolic disorder characterized by consistently elevated blood glucose levels due to inadequate pancreatic insulin production. Type 1 DM (DM1) constitutes the insulin-dependent manifestation from disease onset. Effective DM1 management necessitates daily blood glucose monitoring, pattern recognition, and cognitive prediction of future glycemic levels to ascertain the requisite exogenous insulin dosage. Nevertheless, this methodology may prove imprecise and perilous. The advent of groundbreaking developments in information and communication technologies (ICT), encompassing Big Data, the Internet of Medical Things (IoMT), Cloud Computing, and Machine Learning algorithms (ML), has facilitated continuous DM1 management monitoring. This investigation concentrates on IoMT-based methodologies for the unbroken observation of DM1 management, thereby enabling comprehensive characterization of diabetic individuals. Integrating machine learning techniques with wearable technology may yield dependable models for forecasting short-term blood glucose concentrations. The objective of this research is to devise precise person-specific short-term prediction models, utilizing an array of features. To accomplish this, inventive modeling strategies were employed on an extensive dataset comprising glycaemia-related biological attributes gathered from a large-scale passive monitoring initiative involving 40 DM1 patients. The models produced via the Random Forest approach can predict glucose levels within a 30-minute horizon with an average error of 18.60 mg/dL for six-hour data, and 26.21 mg/dL for a 45-minute prediction horizon. These findings have also been corroborated with data from 10 Type 2 DM patients as a proof of concept, thereby demonstrating the potential of IoMT-based methodologies for continuous DM monitoring and management. The integration of innovative biological signal sensors and the application of transformative trends in ICT can offer a novel perspective on DM treatment, ensuring precise and secure glucose level management.

1. Introduction

Characterized by an autoimmune response that devastates pancreatic cells integral for insulin production, Type 1 Diabetes Mellitus (DM1) results in abnormally high blood glucose levels, due to the body's incapacity to generate or exploit insulin (Haller, Atkinson, & Schatz, 2005). The task of blood glucose regulation is thus complex, prompting DM1 sufferers to depend on insulin injections or pumps, coupled with capillary glucometer checks for glucose management (Riddell et al., 2017). With Intelligent Data Analysis (IDA) on the horizon, there's potential for enhancing the modeling of blood glucose levels, thus augmenting the ability of DM1 patients to efficiently monitor their health conditions.

On the other hand, Type 2 diabetes mellitus (DM2) is a unique version of the disease, wherein insulin resistance coupled with a relative deficiency in insulin secretion defines its characteristics, unlike DM1, which primarily suffers from a total lack of insulin due to the autoimmune obliteration of pancreatic beta cells. While a propensity for obesity and a sedentary lifestyle significantly fuels the onset of DM2, genetic predispositions cannot be disregarded (Magliano et al., 2019). Early DM2 management generally calls for lifestyle transformations and oral drugs, designed to ameliorate insulin sensitivity and production.

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However, as the illness evolves, there may be a progressive deterioration in the capacity of pancreatic beta cells to secrete insulin, culminating in a profound insulin deficit. In such scenarios, long-affected DM2 patients may necessitate insulin-based treatment mirroring that employed for DM1 management (Wallia & Molitch, 2014). This convergence in therapeutic strategies underscores the significance of comprehending the foundational mechanisms of the disease and the requisite for tailored treatment blueprints for diabetes patients.

Ongoing research initiatives are directing their efforts towards the creation of artificial pancreases (APs). These devices encompass Continuous Glucose-Monitoring (CGM) systems that allow real-time tracking of blood sugar levels and insulin injections that are directed by a numerical model creating the optimal glycemic balance (Peyser, Dassau, Breton, & Skyler, 2014; Cobelli, Renard, & Kovatchev, 2011). Moreover, biometric researchers are evaluating the practicability of performing 24-hour uninterrupted monitoring of patients to collect important health metrics such as heart rate, body temperature, sleep quality, and physical activity using readily available smart watches (Rodríguez-Rodríguez et al., 2018). In the growing realm of the Internet of Medical Things (IoMT), this method finds a conducive environment, facilitating the accumulation of wide-ranging data through multiple biosensors attached to diabetes patients.

This investigation involved the continuous surveillance of 40 DM1 patients under everyday circumstances to predict the progression of their blood glucose levels, a critical aspect of effective DM1 management. The adoption of IoT demonstrates considerable potential for devising sophisticated and reliable models to enhance DM1 monitoring. The availability of cloud computing allows the execution of intensive intelligent data methodologies to identify glucose level variations. This all-encompassing data examination opens up opportunities to utilize the massive datasets generated by IoT connections for feature identification, accelerating the process of obtaining crucial information that can enrich the analysis of glucose fluctuations. To substantiate this notion, the study also incorporated 10 DM2 patients.

This manuscript intends to offer an exhaustive analysis of predictive algorithms used for estimating glycemia within the IoMT context. The introduction serves as a stage-setter for the research and underscores the significance of precise glycemia forecasting in diabetes management. The second section delves into the IoMT scenario, emphasizing the importance of medical equipment and the burgeoning availability of data they generate. In the third section, the paper assesses state-of-the-art algorithms used for predicting glycemia, comparing their characteristics and efficacy. The fourth section provides an outline of the methodologies employed for data acquisition, preprocessing, and machine learning model training. In section fifth, the paper evaluates the performance of the machine learning models, including Random Forest, Support Vector Regression, and Bayesian Regularized NN, and presents the results in terms of accuracy and other metrics. Finally, the paper draws conclusions on the effectiveness of different algorithms for glycemia prediction and discusses future research directions. The study contributes to the growing body of knowledge on glycemia prediction and provides insights for researchers and practitioners in the healthcare domain.

2. Risks factors and overcoming barriers

Overcoming the risk factors associated with DM requires a multifaceted approach that emphasizes early detection, education, and advanced technological interventions. Pivotal to this is understanding the genetic and environmental precursors of DM, as early identification can pave the way for preventive strategies or interventions (Michels et al., 2015). Continuous patient education plays a critical role, ensuring that patients are well-equipped to manage the disease, understand the implications of their lifestyle choices, and effectively use technological tools to monitor and manage their blood glucose levels (Polonsky & Fisher, 2015).

Technological advancements, particularly in the realm of continuous glucose monitoring and predictive algorithms, have shown promise in proactively managing DM and mitigating its associated complications (D'Antoni et al., 2023; Quan, Doike, Bui, Arata, Kobayashi, & Islam, 2019). While these tools offer significant potential benefits, it is imperative that they are accessible and integrated seamlessly into the healthcare infrastructure, emphasizing interoperability, data security, and affordability (Klonoff, 2015; Azbeg, Ouchetto, Andaloussi, Fetjah, & Sekkaki, 2018). Furthermore, personalizing these technological solutions to cater to individual patient needs can ensure a more holistic and effective management of DM (Berget et al., 2021).

The widespread prevalence of diabetes mellitus necessitates innovative technological solutions for effective management. However, the path to integrating these advancements into patient care is fraught with challenges. One of the primary issues is the lack of data integration and interoperability, with devices from various manufacturers often operating in isolation, preventing a comprehensive view of the patient's condition (Klonoff & Kerr, 2016).

Moreover, the prohibitive costs of these technologies, such as Continuous Glucose Monitors and artificial pancreas systems, limit their accessibility and adoption, especially in resource-constrained settings (Funnell & Anderson, 2008). Beyond the hardware, the intricate nature of diabetes management demands continuous patient education to ensure the proper use and maintenance of these tools (Polonsky & Fisher, 2015).

Data security remains a pivotal concern. As the reliance on digital tools increases, apprehensions about potential breaches and unauthorized access to sensitive patient data can deter individuals from embracing these technologies (Azbeg et al., 2018). Furthermore, the risk of technological overreliance can impede proactive patient engagement in their health, emphasizing the importance of a balanced approach to care (Tanenbaum et al., 2017). Lastly, the overarching challenge is to provide personalized solutions within the standardized frameworks that many of these technologies offer, ensuring that individual patient needs are adequately addressed (Berget et al., 2021).

3. Internet of medical things context

The IoMT encompasses interconnected medical equipment facilitating remote patient health monitoring through automated interface sensors and machine learning. IoMT technology enables the gathering, assessment, and transmission of medical data via wearable and in-home devices, potentially reducing superfluous hospital visits and healthcare expenses. Numerous studies have explored IoMT utilization in diverse healthcare applications (Karagiannis, Mitsis, & Nikita, 2022), such as chronic disease monitoring, depression diagnosis, Parkinson's disease, heart attack detection, posture monitoring, and cancer therapy (Movassaghi, Abolhasan, Lipman, Smith, & Jamalipour, 2014; Talpur, Bhuiyan, & Wang, 2015; Ali, Kibria, Jarwar, Kumar, & Chong, 2017). These investigations have proposed various solutions addressing concerns like end-to-end security, energy optimization, authentication, privacy, and data transmission/exchange. The amalgamation of IoMT with 5G and cloud-based systems has been examined to augment healthcare diagnosis and treatment. Ultimately, IoMT holds significant potential to transform healthcare delivery and enhance patient outcomes.

Diabetes management entails selecting a CGM device capable of recording glucose fluctuations in diabetic patients with higher frequency and precision compared to conventional methods (Cappon, Acciaroli, Vettoretti, Facchinetti, & Sparacino, 2017). However, CGM devices exhibit shortcomings, such as random noise and delayed readings due to interstitial fluid sensing. To improve accuracy, the Mean Absolute Relative Difference (MARD) and Clarke error grid are employed to evaluate CGM devices (Cox et al., 1985). Notable CGM devices include Dexcom G6, Medtronic Guardian Sensor 3, and Abbott Freestyle Libre Pro (Leelarathna & Wilmot, 2018), with MARD values ranging from 8.7

to 10.5 % to 9.9 %. CGM devices utilize diverse algorithms to minimize delays and noise, but challenges persist in denoising, reducing rectification latency, and enhancing raw data accuracy. Adaptive self-tunable Bayesian smoother, denoising methods, stochastic deconvolution-based recalibration, autoregressive models, and other refinement techniques (Facchinetti, Sparacino, & Cobelli, 2011; Mahmoudi, Dencker Johansen, Christiansen, & Hejlesen, 2013) have been suggested to address these challenges.

The prediction of glucose values in type 1 diabetic patients necessitates accurate and consistent monitoring systems. In a recent study (Hu et al., 2023), they highlighted the challenges in developing CGM systems that maintain high linearity and superior glucose-responsive ability over an expansive detection range. Their groundbreaking research presented a silver-doped Concanavalin A (Con A) hydrogel sensor, which stands out in its precision and simplicity among existing enzyme-free glucose sensors. With its capabilities demonstrated by an impressive linearity of $R^2 = 0.97$, this sensor holds significant promise for enhancing the efficacy and reliability of CGM devices in the management of type 1 diabetes.

Contemporary advancements within the healthcare sector have prompted substantial technical improvements in monitoring systems, predominantly propelled by the emergence of novel technologies in the market. Among these, smartphones have surfaced as a crucial component, offering unparalleled versatility and facilitating numerous functions, such as maintaining software responsible for system dynamics, performing CGM, gathering insulin pump data, transmitting data to the cloud, initiating emergency calls, and updating software (Rigla, 2011). Besides smartphones, wearable devices like smart bands and health and sports wearables have contributed to the biometrics domain, enabling continuous vital signal measurements, such as heart rate and physical activity, which can impact blood glucose balance (Ding & Schumacher, 2016; Rodríguez-Rodríguez, Rodríguez, & Zamora-Izquierdo, 2018). Although these devices may present limitations regarding battery life, size, and professional usage, they furnish sufficiently accurate data and can supply valuable information for health monitoring. While several standalone trials have employed innovative devices, such as accelerometers, electrocardiograms, and thermistors, to investigate the relationship between blood glycaemia and other attributes or predict blood sugar levels, their integration into DM1 management systems remains unexplored.

The integration of innovative biological signal sensors has undeniably transformed the landscape of real-time patient monitoring and decision-making in healthcare. However, several real-time issues arise with their implementation. Primarily, there's the concern of data accuracy and precision. The sensors, while advanced, can still be prone to noise, artifacts, or other forms of interference, which could lead to misleading information being captured and communicated (Ling et al., 2020). Furthermore, the continuous influx of data can lead to information overload for healthcare professionals, complicating real-time decision-making processes.

Data security and privacy also emerge as significant challenges. With sensors continuously transmitting health data, there's a heightened risk of data breaches or unauthorized access. Protecting this sensitive information, while ensuring seamless transmission and integration with healthcare systems, becomes crucial (Klonoff & Kerr, 2016). Additionally, real-time processing demands robust computational infrastructure, especially when implementing AI-driven analyses, potentially leading to latency issues. Efficient algorithms and scalable computing solutions need to be in place to ensure timely responses. Finally, the wearability, battery longevity, and patient comfort associated with these sensors can't be overlooked, as these factors directly influence patient compliance and the reliability of real-time data acquisition (Koydemir & Ozcan, 2018).

Fig. 1 illustrates a conventional schematic representation of the Internet of Medical Things (IoMT) applied to Diabetes Mellitus management. The sensorization layer is responsible for gathering patient biosignals and transmitting them to the subsequent layer using established communication technologies, such as Zigbee, Bluetooth, or mobile communication systems. An intermediate layer serves to consolidate and preprocess the collected data, while the computation layer employs artificial intelligence techniques to extract valuable insights (Rodríguez-Rodríguez, Zamora-Izquierdo, & Rodríguez, 2018). The resulting information is then presented to either the patients or caregivers through visualization devices.

The COVID-19 pandemic has significantly disrupted healthcare systems worldwide, prompting a rapid shift towards telemedicine in various fields, including diabetes care. The benefits of telemedicine for diabetes management have become particularly evident during the

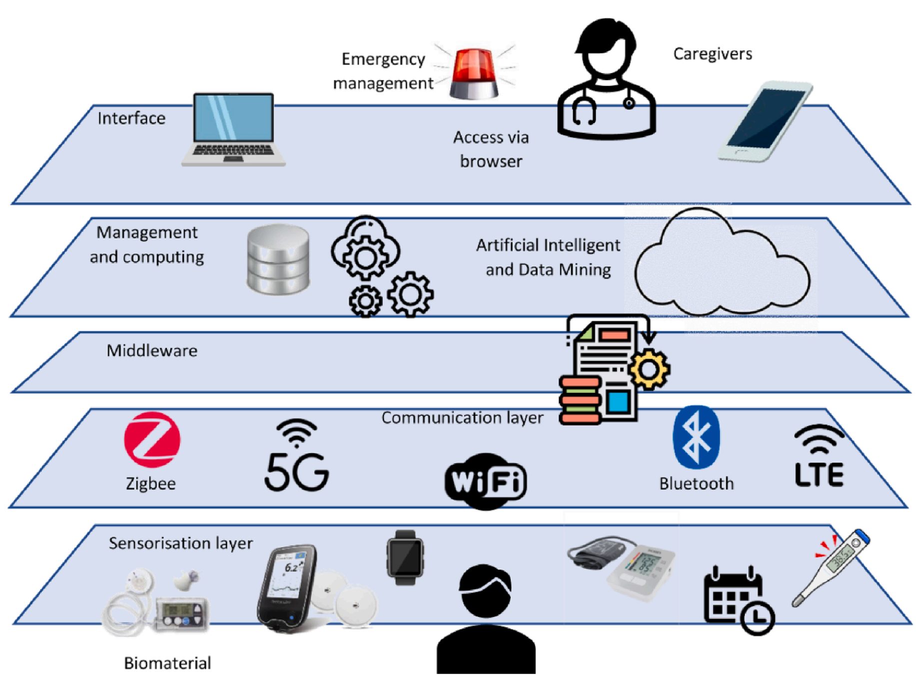

Fig. 1. Internet of Medical Things applied to Diabetes Mellitus.

pandemic, especially for adolescents and children (Umano et al., 2021).

In India, during the national lockdown period, telemedicine was employed to ensure continuity of care for patients with diabetes. Guidelines for effectively implementing telemedicine in diabetes care during pandemic times were presented by Ghosh, Gupta, and Misra (2020). The strategic adoption of telemedicine allowed remote consultations, constant monitoring of glucose levels, and necessary adjustments of insulin, maintaining vital health services while significantly reducing the risk of viral transmission between patients and healthcare professionals.

In a related context, de Kreutzenberg (2022) dissected the influence and important aspects of telemedicine in managing diabetes, drawing on the lessons learned during the COVID-19 pandemic. The author emphasized that telemedicine significantly contributed to preserving the standard of care while mitigating the strain on health systems. It also proposed a safer, more reachable substitute to traditional face-to-face consultations, thereby boosting patient satisfaction and treatment adherence.

Telemedicine also displayed encouraging outcomes in managing pediatric obesity and diabetes mellitus amid the pandemic (Umano et al., 2021). It enabled remote monitoring and management, ensuring uninterrupted care and diminishing the necessity for hospital admissions. The deployment of telemedicine sessions coupled with diabetes technology has ensured that healthcare professionals could continue to provide essential services to pediatric patients during the pandemic (Nørgaard, 2020).

In the research carried out by Predieri et al. (2020), a noticeable improvement was found in the glycemic control of Italian children and adolescents with type 1 diabetes during the lockdown period, courtesy of telemedicine. The study proposed that telemedicine could serve as an impactful instrument to augment self-management and adherence to treatment plans, resulting in better glycemic control in this demographic. The hasty implementation of telemedicine during the pandemic has ensured the continuity of care, enhanced glycemic control, and decreased the chances of viral spread. As the world evolves, telemedicine is expected to become an indispensable component of diabetes management, offering more accessible and efficient care for patients.

Incorporating a comprehensive framework that integrates both edge computing and machine learning for predicting early warning scores pertaining to hypoglycemia is a recommendation that the authors might consider deeply. The synthesis of these advanced technologies can establish a critical platform for decision support in glycemic interventions. By doing so, the effectiveness of timely interventions can be substantially augmented, providing healthcare practitioners with a more precise and rapid mechanism to preempt hypoglycemic episodes, ensuring patient safety and improving overall care outcomes.

This research primarily aims to evaluate the use of Intelligent Data Analysis (IDA) and machine learning (ML) methodologies in the framework of Internet of Things (IoT) platforms for effectively managing and modeling diabetes management-specific biosensor data, particularly in the case of DM1. The study underscores the vital function of ML algorithms in data processing, offering a thorough examination of various ML techniques that show promise in estimating glycemia dynamics.

The research investigates approaches like Bayesian Regularized Neural Networks (BRNNs), Random Forest (RF), and Support Vector Machines (SVMs). By assessing these algorithms' adaptability and efficiency, the research intends to illuminate their appropriateness for predicting and monitoring DM1 patients' glycemic levels. This comprehensive scrutiny allows for a better grasp of each technique's complexities, offering valuable insights into their performance and application in diabetes management.

By systematically assessing these ML methodologies, the study suggests they hold the potential to serve as the Modeling Cores for systems estimating glycemia dynamics. By forming the groundwork for these systems, these ML algorithms can significantly aid in advancing diabetes management, thereby improving the life quality of those living with this chronic disease. The study's outcomes highlight the necessity for ongoing exploration and development of ML techniques and their amalgamation with IoT platforms to further streamline and optimize diabetes management strategies.

4. Forecasting algorithms for glycaemia prediction

Utilizing the FCBPSS architectural paradigm (Wang et al., 2016), we establish a meticulous framework to understand and analyze the complexities of predicting glycemia values in type 1 diabetic patients. This paradigm categorizes the interaction of different components such as Function (the predictive capacity to determine glucose levels using bio-signals), Context (the diabetic state affected by various internal and external factors), Behavior (physiological responses due to glucose fluctuations), Principle (biological mechanisms of glucose regulation), State (instantaneous glucose level and physiological markers), and Structure (the collection of bio-signals like cardiac rhythm and physical activity level).

In essence, this problem is rooted in classification paradigms, where the human body is seen as a complex system of bio-signals and physiological responses. To predict glucose levels, algorithms are designed to decipher the system's state from diverse signals or features, necessitating a progression from identifying signals to extracting features and establishing thresholds. Through the FCBPSS lens, a multidimensional approach allows for a more systematic and precise prediction of blood glucose levels from varied bio-signals.

The burgeoning application of machine learning algorithms has emerged as a revolutionary force in facilitating short-term blood glucose prediction in diabetic patients, addressing crucial needs in insulin adjustment and overall diabetes management (Cappon, Vettoretti, Marturano, Facchinetti, & Sparacino, 2018). The precision and timeliness of these predictions are imperative for optimizing insulin dosing in individuals with type 1 diabetes mellitus. However, despite the advancements in Continuous Glucose Monitoring (CGM) technology enabling real-time glucose observation, procuring precise glucose forecasts continues to pose considerable challenges.

In managing type 1 diabetes, extracting predictions from bio-signals through deep learning algorithms like Convolutional Neural Networks (CNNs) is indispensable, with notable applications in medical tasks such as automatic polyp detection (Qian, Jing, Lv, & Zhang, 2022) and surface defect identification (Zhang et al., 2023). However, these algorithms are hampered by the need for extensive annotated datasets and intricate design of CNN layers, and the complex, expertise-demanding task of labeling data in medical domains.

Innovative approaches like those by Qian et al. (2022), who augmented training datasets using Conditional Generative Adversarial Networks, and by Zhang et al. (2023), employing deep random chains for defect detection in small datasets, illuminate potential pathways for overcoming these challenges in glucose prediction efforts. The use of machine learning, as seen in studies like that by Pustozerov et al. (2020) employing decision tree gradient boosting algorithms to predict postprandial glycemic responses in gestational diabetes mellitus, underscores the continuous exploration and refinement in predictive models focusing on diverse aspects of glycemic responses, emphasizing the importance of evolving methodologies for enhanced glucose prediction accuracy.

Modi et al. (2011) conceptualized a socially inspired framework, emphasizing the integration of diverse 'inference experts' or algorithms to infer human states, a methodology that could find parallel applications in the nuanced field of glucose value predictions in type 1 diabetes. Similarly, studies by Contreras and Vehi (2018) and Zecchin, Facchinetti, Sparacino, and Cobelli (2014) illustrated the efficacy of artificial neural networks (ANNs) and neural networks respectively in predicting blood glucose levels with notable accuracy, highlighting the potential of these networks in advancing glucose forecasting methodologies.

Li et al. (Li, Liu, Zhu, Herrero, & Georgiou, 2019) introduced GluNet, a personalized deep learning framework that optimizes glucose forecasting in type 1 diabetes patients by analyzing an array of historical data, setting a benchmark in predictive accuracy with a root mean square error (RMSE) of 37.83±3.49 mg/dL. Xie and Wang (2020) undertook a comparative analysis of various machine-learning models, with the ARX model demonstrating superior performance, underlining the necessity for determining universally acceptable prediction accuracy levels. In this regard, a standard RMSE below 30 mg/dL has been identified by several studies including Zecchin et al. (2014), as facilitating safe and reliable insulin dosing adjustments, serving as a guideline in the development of predictive models.

When deploying machine learning algorithms for time series data forecasting like in glucose prediction, the proven approaches include Support Vector Regression (SVR) (Deng, Jin, & Zhong, 2005), Random Forest (Demidova & Ivkina, 2020), and Bayesian Regularized Neural Networks (BRNNs) (Burden & Winkler, 2008). SVR transforms forecasting into a regression problem, optimizing a hyperplane within a multi-dimensional feature space to predict future data points based on historical ones. In contrast, Random Forest employs ensemble learning, amalgamating predictions from multiple decision trees to mitigate variance and overfitting issues, establishing relationships between past and future data points.

BRNNs, recognized for their robustness in diabetes management, employ Bayesian regularization, eliminating the need for cross-validation and providing criteria to halt training, minimizing overtraining risks, though overfitting can still occur (Nguyen, Ghevondian, & Jones, 2008). Given the constraints of limited data and the necessity for manageable models, BRNN and SVM stand out due to their computational efficiency and lesser overfitting concerns compared to standard Neural Networks. However, the choice of algorithm would essentially be dictated by factors like architecture, hyperparameter tuning, and the nature of the dataset, requiring careful consideration of model complexity and computational efficiency.

5. Methodology: Data sources and algorithms

5.1. Monitoring campaign

In validating our thesis, we launched an initial monitoring campaign focused on patients. This operation unfolded by implementing an interconnected system equipped with a portable Abbott Freestyle Libre and a smartphone that was configured to transmit collected data to a central hub for subsequent examination. This setup incorporated a CGM sensor with a local memory that can retain up to eight hours of past data. The acquisition of the most recent measurements from the CGM apparatus is facilitated through the use of a secure, NFC-enabled short-range wireless linkage, supported by software installed on the patient's personal electronic device, such as a smartphone or a tablet. Some devices, acting as NFC-Bluetooth transformers, can establish a connection with the Libre, ensuring a consistent data transfer to the smartphone. The information is subsequently dispatched securely to a central database for additional processing and generation of predictive models. Further insight into the Information and Communication Technology (ICT) system utilized for data collection can be found in (Rodríguez-Rodríguez et al., 2018).

Inserted beneath the skin, the CGM sensor exhibits the capability to evaluate blood glucose levels (reported in mg/dL) on a minute-to-minute basis (Fokkert et al., 2017). These readings, which display a Mean Absolute Relative Difference (MARD) of 11.4 % (Bailey, Bode, Christiansen, Klaff, & Alva, 2015), offer an estimated depiction of the authentic glucose concentrations in the blood, as per the manufacturer's disclosure. The sensor's sensitivity range is broad, extending from 40 mg/dL (at which point it indicates "low") to 500 mg/dL (beyond which it merely represents "high"). There exists a slight delay, approximately 5 to 10 min, between the CGM sensor data and the actual glucose levels in the patient's bloodstream (Wientjes & Schoonen, 2001). It is worth noting that this time discrepancy can be effectively minimized, potentially down to six minutes, using mathematical techniques (Basu et al., 2014). The calibration period for the CGM sensor is relatively brief, lasting only a few hours (Hoss & Budiman, 2017), and the sensor itself can function optimally for a period of fourteen days. The collection process culminated in a dataset consisting of 13,440 h of data.

This comprehensive dataset was complemented with information gathered via the Fitbit Charge 5 smart band. Each participant was outfitted with the device, which persistently recorded physical activity (step count), heart rate, and sleep duration. Despite the fact that these apparatuses do not constitute specialized medical tools, they supply valuable data inputs while exerting minimal energy consumption. An expanded overview of these devices is available on the manufacturer's website.

This advanced technology was trialed with a cohort of 40 DM1 diabetics in 2021, in collaboration with local hospitals. The study adhered to the guidelines of the Helsinki Declaration, with data privacy regulations strictly enforced to protect stored data. Clinical characteristics of the participating patients are presented in Table 1. All participants were properly briefed on the nature of the study, its implications, and data management, following which they provided their informed consent in accordance with national regulations.

In order to examine our proposal, it has been tested as a proof of concept with 10 recently monitored DM2 patients with the clinical characteristics shown in Table 2. All DM2 patients meet the CGM meter handling knowledge requirements and are in the insulin-dependent stage, with treatment based on a bolus-basal regimen, so that the results are comparable to those of DM1 patients.

The overall DM1 management of the patients was commendable. All reported maintaining a healthy lifestyle with regular exercise, at least three times per week. Additionally, they adhered to structured schedules, ensuring a largely consistent daily routine devoid of unexpected disruptions.

During the passive monitoring period, patients were encouraged to maintain their regular routines and consume a balanced diet. Throughout the monitoring phase, all patients were advised to abide strictly by their doctors' recommendations. All participants adopted a basal-bolus regimen, utilizing insulins with a flat action curve, such as Levemir or Tresiba, along with fast-acting insulins like Humalog Lispro. The former supplies a basal dose for over 24 h, while the latter serves to counteract any spikes in blood glucose levels resulting from meal consumption or other hyperglycemic triggers.

In this paper, we will critically evaluate and compare various methods of modeling glycemic oscillations. The following parameters, gathered during our experimental phase, will be considered: Blood sugar levels, administration of insulin, meals, physical activity, cardiac rhythm, and slumber duration. These parameters encapsulate historical and current values, ranging from past glycemia measurements, insulin dosages, meals consumed, steps taken, heart rate values, and sleep status ("asleep" or "awake"). These values were carefully collected from selected T1DM patients with sufficient experience in carbohydrate

Table 1
Information on the DM1 People Included in the Trial.

Features	Value		
Number of patients	40		
Sex	24 men – 16 women		
Population Characteristics	Median	Min	Max
Age (years)	22.53	18	56
Body Mass Index (BMI, kg/m2)	21.30	18.25	23.71
Duration of diabetes (years)	12	4	29
HbA1C (%)	6.7	6.1	7.8

Table 2
Information on the DM2 People Included in the Trial.

Features	Value		
Number of patients	10		
Sex	5 men – 5 women		
Population Characteristics	Median	Min	Max
Age (years)	58.31	51	67
Body Mass Index (BMI, kg/m2)	26.42	24.75	33.48
Duration of diabetes (years)	16	3	26
HbA1C (%)	7.1	6.9	8.9

estimation.

5.2. Steps for time series forecasting

In machine learning, the prediction of time series data involves a sequence of customary steps to derive insights and prognostications from the data. Our investigation zeroes in on predicting the blood glucose levels of 40 patients with type 1 diabetes. We have gathered a variety of time series attributes during our experimental phase for this purpose, including glycemia, insulin injections, meal intake, physical activity, heart rate, and sleep patterns. An outline of the methodological steps can be found in Fig. 2.

The inaugural step in predicting time series data is data preprocessing. This procedure includes cleaning, transforming, and prepping the data for model formation. It consists of the management of missing values, outlier control, data normalization or scaling, and feature engineering. Throughout our study, we adopted various preprocessing techniques to manage missing values such as interpolation and imputation. Also, we ensured normalization and scaling of the data so that every attribute equally contributes to the model.

The subsequent step is the partitioning of data into training, validation, and testing sets. The training set is employed to tailor the model to the data. The validation set is used during the training phase to assess model performance and determine the best hyperparameters. Lastly, the testing set helps evaluate the model's final performance.

The third phase is cross-validation of the time series, which splits the data into folds chronologically. Each fold encompasses a subset of the data. This method is used to gauge the model's performance on unseen data by educating the model on one fold and testing it on another, subsequently repeating this process for all the folds. In our research, we employed this cross-validation method to ensure the model is assessed on data that possesses the same temporal attributes as the training data.

The fourth phase of our methodology involves hyperparameter optimization, designed to select the most optimal hyperparameters for the model, thereby refining its performance. For this study, we implemented three distinct machine learning algorithms: RF, SVM, and BRNN. We engaged in hyperparameter tuning for each of these algorithms using a grid search, adhering to the specific hyperparameters and ranges indicated in Table 3. This phase entails fitting the model to the training data through various hyperparameter combinations and selecting the combination that yields the best results on the validation set.

Subsequently, we proceed to the fifth and concluding phase, where the performance of the model is assessed on the testing set. This is achieved by computing various measures, such as the root mean squared error (RMSE), which permits a comparison of the predicted values with the actual ones. For this study, we gauged the performance of each algorithm using this metric and designated the algorithm generating the least error as the superior performer. This entire process was iterated for all possible combinations of the Past Sliding Window (PSW) and Predictive Horizon (PH).

Table 3
Hyper-Tuning Parameters.

Algorithm	Parameter	Range
Random Forest (RF)	Max depth	10 to 70
	Min samples leaf	1 to 4
	Min samples split	2 to 10
	n estimators	200 to 1200
Support Vector Machines (SVM)	C	0.1 to 1000
	gamma	1 to 0.0001
	kernel	'rbf'
Bayesian Regularized	Hidden layers	1
Neural Networks (BRNN)	Dense layer size	50–350
	Optimizer	'adam'
	Learning rate	0.1 to 0.001

To carry out this process, we employed several Python libraries: Pandas, for managing and preprocessing the data, and Scikit-learn, for implementing the machine learning algorithms and cross-validation techniques.

5.3. Statistical analysis across algorithms and past sliding windows

To contrast the results obtained through different machine learning algorithms and past sliding windows in predicting blood glucose levels in type 1 diabetes patients, we executed two statistical procedures: the Shapiro-Wilk test and a two-way ANOVA examination. The Shapiro-Wilk test's role was to verify the normal distribution of the predicted blood glucose values yielded by each algorithm and window, an essential precondition for undertaking a multivariate ANOVA comparison, which stipulates normality for the dependent variable.

Upon validating the data's adherence to a normal distribution, we initiated a two-way ANOVA comparison to evaluate the discrepancies in predicted blood glucose values across the varying algorithms and sliding windows. This form of ANOVA analysis is appropriate when we are dealing with several independent variables (here, the algorithms and sliding windows) and a single dependent variable (the predicted blood glucose values). The ANOVA test scrutinizes whether any significant differences exist among the data groups, and if confirmed, identifies which groups show significant variances. A significance level of 0.05 was applied to distinguish whether any significant differences were present among the groups.

The post-hoc Tukey test is a statistical method used to compare all possible pairwise comparisons between means in a dataset after a significant difference has been detected in the ANOVA test. In other words, it allows us to determine which groups or levels within a factor are significantly different from one another. The test uses a critical value based on the studentized range distribution to calculate confidence intervals for each comparison. If the intervals do not overlap, it means that

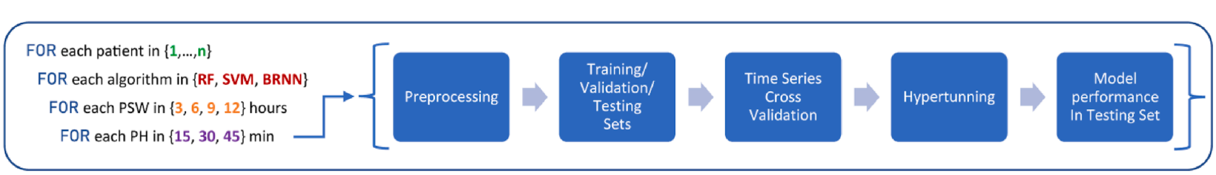

Fig. 2. Time Series forecasting schema.

the groups are significantly different from one another. The Tukey test is considered one of the most powerful and reliable post-hoc tests, and it is widely used in many fields, including psychology, medicine, and engineering. The results of the test are usually reported in a table that includes the mean difference, the standard error, and the p-value for each comparison, as well as a graphical representation of the intervals.

6. Performance evaluation of machine learning models for glycemia prediction

Fig. 3 shows an example of the prediction process. By choosing a PSW, the biomedical data contained in that time window are collected, and with them and by means of a model, future glycemia is predicted at a predictive horizon (PH). The figure, constructed with real data, shows a PSW = 6 h and a PH of 45 min.

In this study, the accuracy of predicting future glucose levels is investigated. The results, expressed as the root mean square error (RMSE) between predicted and actual measured values, are presented in Fig. 4. It is observed that the prediction error for all patient models increases as the prediction horizon (PH) lengthens, which is expected as the collected data travel further away from the prediction horizon. A 45-minute window appears to be adequate for evaluating glucose level trends.

Subsequently, the significance of the volume of previous data in accurately forecasting future glucose levels is examined. It is hypothesized that increasing the quantity of previous data would improve the overall precision of the forecast. The size of the preceding data window aids the model in capturing the temporal component of the time series. Utilizing previous window sizes (PSW), patient models are trained using data from the prior 3, 6, 9, and 12 h. In this experiment, samples are collected every five minutes, with prediction horizons set at 15, 30, and 45 min.

Considering the various PSW sizes and the volume of historical data necessary for accurate prediction, the results indicate that all person-centric models exhibit a minimum RMSE with a 6-hour window length. When the amount of historical data is initially increased from 3 to 6 h, prediction accuracy improves. However, further enlargement of the window size generally has a detrimental effect on performance. The RMSE is higher for a 9-hour window than for a 3-hour period. Consequently, any increase in the volume of previous data diminishes the attained precision.

The evidence gathered from experiments demonstrates that, irrespective of the method employed to create the models and for every forecast horizon, there exists a boundary (6 h) when considering past data to enhance forecast accuracy. Beyond this optimal value, earlier data become irrelevant and diminish forecast accuracy. Previous research has connected the concept of circadian cycles (Van Cauter, Polonsky, & Scheen, 1997) to the daily morning, afternoon, and evening time windows, thus establishing this essential hierarchy.

In terms of the performance of the three distinct methods used to construct person-centric models, the results indicate that the RF technique is the most accurate, providing high-quality forecasts for all investigated PSWs and PHs. Additionally, RF exhibits a smaller standard deviation, suggesting that it is less reliant on the unique characteristics of individual patients. It is important to acknowledge that the performance for each subject is influenced by their habits and personal attributes.

To analyze the differences between the different algorithms and past sliding windows, we conducted a multivariable ANOVA comparison. The ANOVA was performed to determine whether the mean glucose values of the different algorithms and past sliding windows were significantly different. First, we checked the normality of the distribution of the glucose values for each algorithm and past sliding window using the Shapiro-Wilk test. The results showed that the glucose values were normally distributed for all algorithms and past sliding windows ($p > 0.05$), which means that we met the assumption of normality for the ANOVA.

We then performed a two-way ANOVA to compare the mean glucose values of the different algorithms and past sliding windows. The results showed a significant difference between the different algorithms and past sliding windows, for all the PH used. We can observe in Table 4 as all the p-values are significantly < 0.05.

The post-hoc Tukey test is used to determine which groups have statistically significant differences after performing an ANOVA analysis. It compares the mean differences between all pairs of groups and calculates the standard error for each comparison.

In this case, it is optimal to use a PSW = 6 and RF as the algorithm because the minimum result (0.000044) is obtained when comparing the means of RF and the other algorithms at PSW = 6. This means that the difference in means between these groups is statistically significant. This result suggests that the algorithms perform differently at PSW = 6.

In order to assess the performance of the RF algorithm more accurately from the DM1 perspective, we present the prediction results according to the Parkes Grid (Pfützner, Klonoff, Pardo, & Parkes, 2013). The Parkes error grid was introduced in 2000, following a survey of 100 medical professionals who attended the American Diabetes Meeting in June 1994. The objective of this measurement tool is to evaluate the clinical accuracy of blood glucose meters utilized by patients for self-

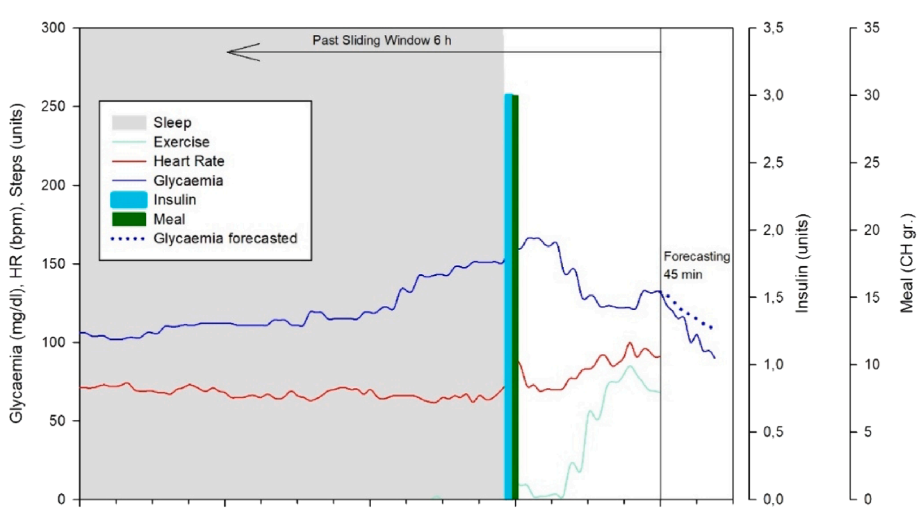

Fig. 3. Prediction process.

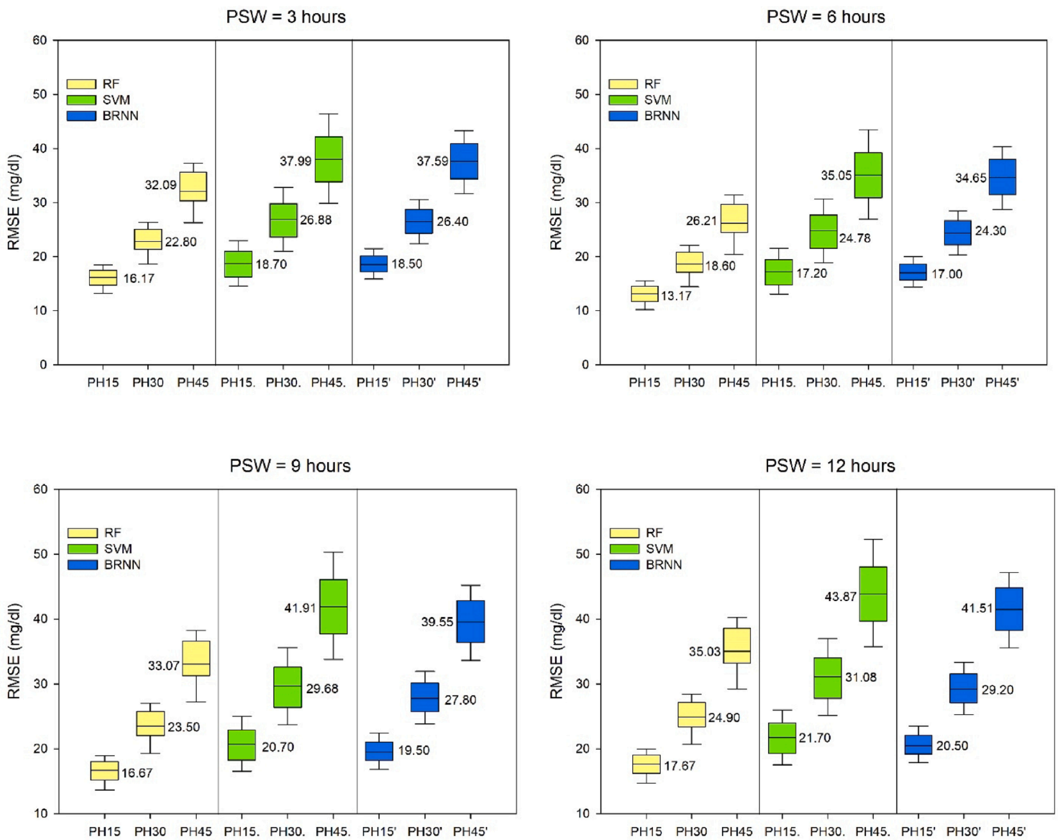

Fig. 4. RMSE expressed in mg/dL: random forest RF, SVM, and BRNN using past sliding window lengths (PSWs) of 3, 6, 9, 12 h; predictive horizons (PHs) in minutes, 15, 30, and 45. DM1 group.

Table 4
Two-Way ANOVA Results – DM1 Group.

PH = 15	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic	P-value
Factor Algorithms	2	844.6447	422.3224	82.3001	5.0869E-29
Factor PSW	3	720.8333	240.2778	46.8241	1.0679E-24
Error	294	1508.6592	5.1315		
Total	299	3074.1373			
PH = 30	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic	P-value
Factor Algorithms	2	1716.2685	858.1342	82.3142	5.3171E-29
Factor PSW	3	1412.8333	470.9444	45.1741	5.8994E-24
Error	294	3002.4277	10.4250		
Total	299	6194.8213			
PH = 45	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic	P-value
Factor Algorithms	2	3452.0093	1726.0046	81.5713	8.537E-29
Factor PSW	3	2769.1533	923.05111	43.6236	2.8601E-23
Error	294	6093.9184	21.15943		
Total	299	12439.1328			

measurement. The authors aimed to provide an alternative to the original Clarke error grid, which was initially developed as an educational tool rather than a clinical accuracy assessment instrument. The Clarke error grid has also faced criticism for its risk boundary placements. In our study, we will use it as a measure of prediction validity by comparing the forecast with the actual measurement obtained by the CGM for the predicted time.

Fig. 5 displays the results obtained for the different predictive horizons. We can observe that for 15 and 30 min, nearly all predictions are in zone A (clinically accurate measurements, no effect on clinical action). In the case of a 45-minute horizon, only a portion of the predictions falls in zone B (altered clinical action, little or no effect on clinical outcome). The incursion into zone C is minimal for this predictive horizon (altered clinical action, likely to affect clinical outcome), and there are no results in zones D and E (altered clinical action, potentially significant/dangerous clinical risk).

In order to validate our proposal also for type 2 diabetes, the entire process has been replicated with a preliminary sample of 10 patients with type 2 diabetes, as a proof of concept. All of them follow a bolus-basal regimen and have followed the same indications as the rest of the patients in the DM2 group. Fig. 6 expresses the prediction results for the 6-hour PSW, comparing the three PH and the three algorithms. It is clearly observed that again the optimal value is reached for RF.

Two-way ANOVA analysis again confirms that there are differences both in the predictive horizons, which is evident at first glance, and in the performance of the different algorithms. Table 5 shows the p-values obtained. The post-hoc Tukey test is again clear indicating differences that lead to the conclusion that RF obtains a lower result, as is natural for the 15-minute PH. Thus we can conclude that our proposal is consistent and supports the comparison with the proof of concept applied to the sample of DM2 patients.

Fig. 7 shows the results for the group of type 2 patients using RF and a 6-hour PSW, showing the Parkes grids for 15 and 45 min (30 min has been omitted for simplicity). It can be seen how the prediction at 15 min is still valid, and at 45 min also, with some incursions into zone C.

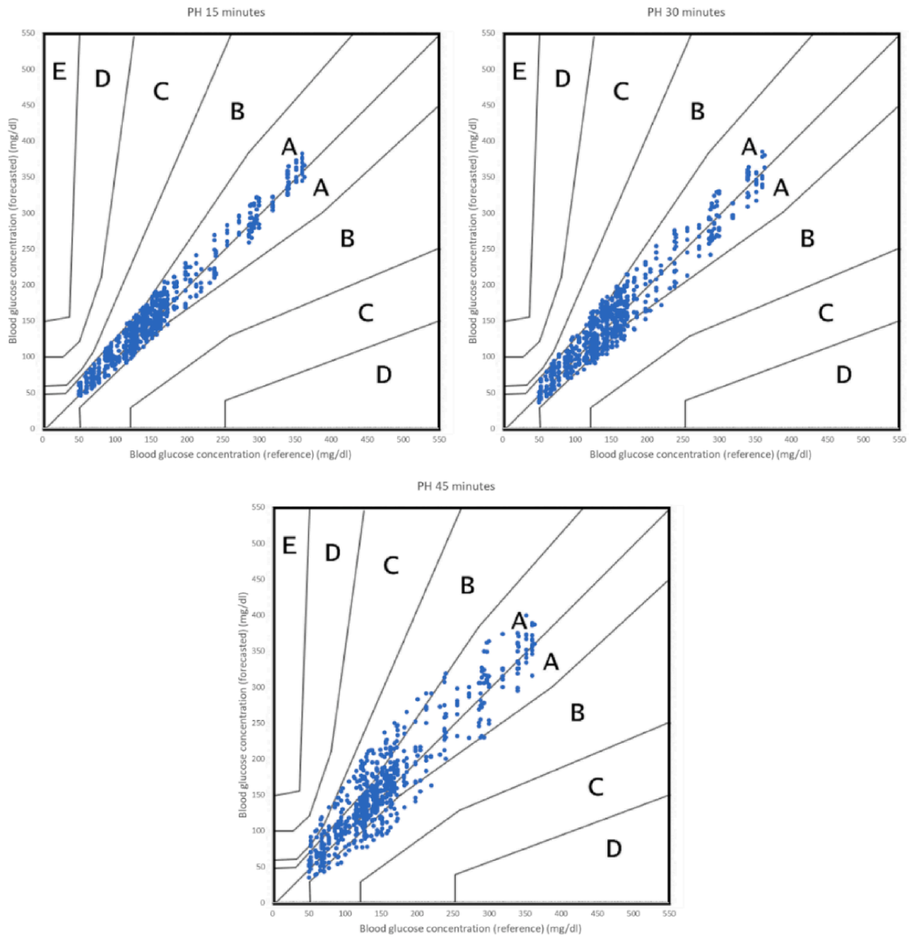

Fig. 5. Parkes grid forecasting performance. RF (algorithm), 6 h (PSW). DM1 group.

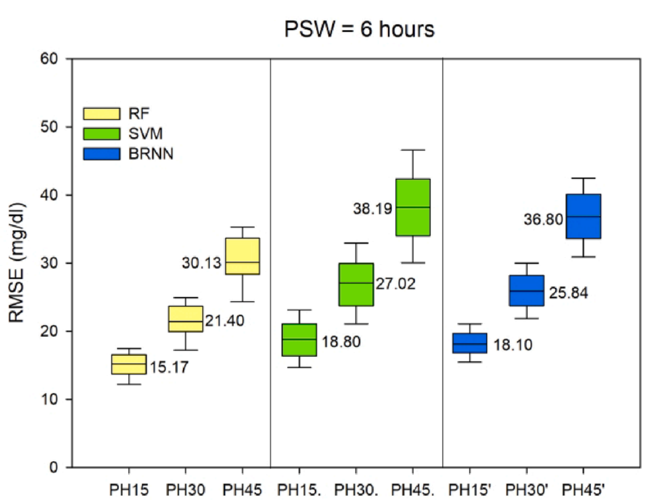

Fig. 6. RMSE expressed in mg/dL: random forest RF, SVM, and BRNN using past sliding window lengths (PSWs) of 6 h; predictive horizons (PHs) in minutes, 15, 30, and 45. DM2 group.

Overall, the prediction for the DM2 group is slightly worse, which makes sense as these are usually older patients, with poorer glycemic control, lack of regular exercise intensity and sometimes lack of knowledge about diabetes regulation.

In light of the findings presented, the RF algorithm emerges as a robust and reliable approach for predicting future glucose levels in DM1 management. The superior performance of RF can be attributed to its ensemble learning nature, which combines multiple decision trees to produce a more accurate and stable prediction. The RF's ability to effectively discern complex relationships and nonlinear patterns in glucose time series data, according to our research, makes it an ideal tool for addressing the intricacies involved in DM1 management.

Table 5
Two-way ANOVA results. DM2 group.

PSW = 6 h	DF	Sum of Square (SS)	Mean Square (MS)	F Statistic	P-value
Factor Algorithms	2	1373.0213	686.5106	56.1013	2,3858E-20
Factor PH	2	12076.8931	6038.4465	493.4595	2,8541E-81
Error	220	2643.1842	12.2369		
Total	224	16203.1589			

Furthermore, our research underscores the importance of an optimal Previous Sliding Window (PSW) size. In the context of precise predictions, a window of 6 h surfaced as the most appropriate choice. The PSW size is crucial for encapsulating the temporal aspect of the time series, and our results suggest that expanding data beyond the 6-hour window might not substantially enhance the accuracy of the predictions. It's plausible that the 6-hour window adequately embodies a patient's glucose dynamics information, including the impact of meals, insulin use, and physical activity, while limiting the inclusion of irrelevant or outdated data. This realization underscores the necessity for personalized, data-oriented strategies in DM1 management that strive to balance the inclusion of relevant historical data and the avoidance of

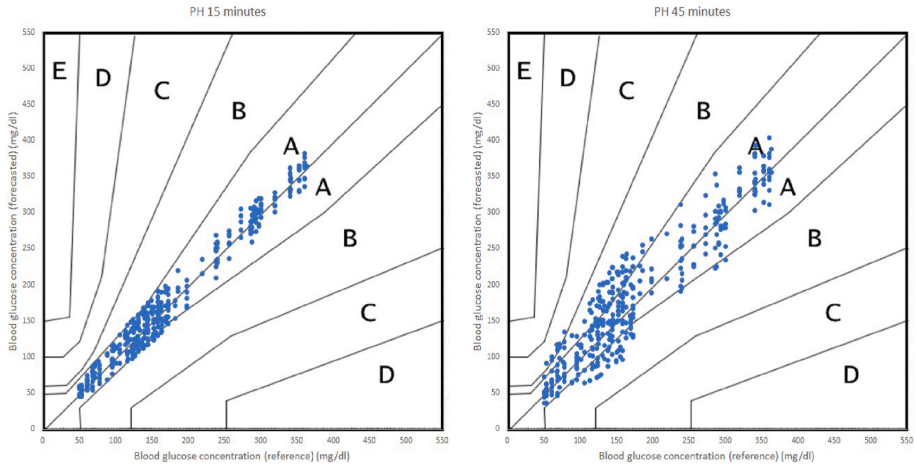

Fig. 7. Parkes grid forecasting performance. RF (algorithm), 6 h (PSW). DM2 group.

data saturation.

7. Conclusions

Technological advancements have significantly influenced quality of life across multiple sectors, with CGMs and insulin pumps emblematic of this transformative shift, especially in the realm of diabetes management. The dynamics of glucose in DM1 patients are multifaceted, influenced by variables such as insulin intake, diet, and lifestyle habits. The rise of the IoMT and the synergy of biosensors with machine learning have augmented our capability to discern patterns and insights from extensive datasets, particularly in DM1.

In this study, the focus was to discern the optimal data duration required for accurate prediction of blood glucose levels. By monitoring forty DM1 patients over a two-week span, the research generated an encompassing dataset that integrated CGM readings with other critical variables like insulin dosage, meal intake, exercise routines, heart rate, and sleep patterns. The findings underscored the Random Forest (RF) technique's efficacy in forecasting glucose levels within a 30-minute span, particularly when considering a six-hour historical data window. Extending this data window surprisingly did not amplify the prediction accuracy. In fact, model performance waned with the augmentation of historical data across various prediction scopes. The study thus elevates the RF technique as the pinnacle in glucose prediction modeling. It is imperative for subsequent research to extend monitoring durations and leverage cutting-edge algorithms to refine glucose level predictions. Given the burgeoning landscape of the IoMT, the horizon seems rife with possibilities for breakthroughs and innovations.

Future studies should consider extending the monitoring period beyond 14 days to assess the models' long-term validity. Moreover, state-of-the-art prediction algorithms can facilitate reliable blood glucose level forecasts for specific prediction horizons. With the expanding IoMT smart ecosystem, there is ample opportunity for further contributions and innovations in this field.

CRediT authorship contribution statement

Ignacio Rodríguez-Rodríguez: Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Visualization. **María Campo-Valera:** Validation, Formal analysis, Resources, Visualization. **José-Víctor Rodríguez:** Methodology, Validation, Formal analysis, Investigation, Writing – original draft, Visualization. **Wai Lok Woo:** Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Visualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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