Predicting Blood Glucose Levels with Machine Learning and IoT: A Meta-Analysis and Future Directions in IoMT Data Fusion for Healthcare Transformation

A Thesis Submitted
In Partial Fulfillment of the Requirements for the Degree of

MASTER OF TECHNOLOGY

in

BIOINFORMATICS

by

YAGYESH KAPOOR
(Roll No. 2K22/BIO/07)

Under the Supervision of
Prof. YASHA HASIJA

Department of Biotechnology

DELHI TECHNOLOGICAL UNIVERSITY
(Formerly Delhi College of Engineering)
Shahbad Daulatpur, Main Bawana Road, Delhi-110042. India

May, 2024

ACKNOWLEDGEMENTS

Completing my work would not be possible without acknowledging those who contributed to its success. Their guidance and encouragement were essential, serving as a beacon that guided my efforts to fruition.

I would like to express my profound gratitude to my guide, Prof. Yasha Hasija, for her continuous motivation and support in exploring new ventures. Her involvement, skilled assistance, and guidance throughout this project have been invaluable.

Additionally, I extend my thanks to Research Scholars Neha Kumari, Kushi Yadav, and Nakul Tanwar for their ongoing guidance, clarification of my doubts, and direction.

I am also grateful to everyone who directly or indirectly assisted me in completing my project and in writing and critically reviewing this report.

Yagyesh Kapoor

DELHI TECHNOLOGICAL UNIVERSITY
(Formerly Delhi College of Engineering)
Shahbad Daulatpur, Main Bawana Road, Delhi-42

CANDIDATE'S DECLARATION

I Yagyesh Kapoor hereby certify that the work which is being presented in the thesis entitled "Predicting Blood Glucose Levels with Machine Learning and IoT: A Meta-Analysis and Future Directions in IoMT Data Fusion for Healthcare Transformation" in partial fulfillment of the requirements for the award of the Degree of Master of Technology, submitted in the Department of Biotechnology , Delhi Technological University is an authentic record of my own work carried out during the period from May, 2023 to May, 2024 under the supervision of Prof. Yasha Hasija.

The matter presented in the thesis has not been submitted by me for the award of any other degree of this or any other Institute.

Candidate's Signature

This is to certify that the student has incorporated all the corrections suggested by the examiners in the thesis and the statement made by the candidate is correct to the best of our knowledge.

Signature of Supervisor **Signature of External Examiner**

DELHI TECHNOLOGICAL UNIVERSITY

(Formerly Delhi College of Engineering)

Shahbad Daulatpur, Main Bawana Road, Delhi-42

CERTIFICATE BY THE SUPERVISOR

Certified that **Yagyesh Kapoor (**Roll No. 2K22/BIO/07) has carried out their search work presented in this thesis entitled **"Predicting Blood Glucose Levels with Machine Learning and IoT: A Meta-Analysis and Future Directions in IoMT Data Fusion for Healthcare Transformation"** for the award of **Master of Technology** from Department of Biotechnology, Delhi Technological University, Delhi, under my supervision. The thesis embodies results of original work, and studies are carried out by the student himself and the contents of the thesis do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University/Institution.

Prof. Yasha Hasija

Head of Department,

Department of Biotechnology,

Delhi Technological University,

Shahbad Daulatpur, Main Bawana Road,

Delhi-110042, India

Place:

Date:

Predicting Blood Glucose Levels with Machine Learning and IoT: A Meta-Analysis and Future Directions in IoMT Data Fusion for Healthcare Transformation

Yagyesh Kapoor

ABSTRACT

The emergence of machine learning and medical IoT is changing healthcare, especially when it comes to managing diseases such as diabetes. Integration of machine learning algorithms and IoT device data offers a promising opportunity to improve glucose management models in context. At the same time, the Internet of Things is changing culture by enabling continuous monitoring, remote communication and increasing efficiency, thus changing delivery and service management. This comprehensive study aims to evaluate the effectiveness of machine learning models using IoT device data to predict blood sugar levels through a meta-analysis. It also examines recent developments, challenges, and future directions for data integration and management in the context of IoMT, highlighting its potential for healthcare reform. We searched electronic databases (such as Scopus, Springer, IEEE Xplore, PubMed, CINAHL, Embase, Web of Science, and Nature) for studies published between 2019 and 2023. Performance of machine learning models for predicting blood glucose. Studies that did not include machine learning models or performance measurements were excluded. The assessment was employed to assess study quality. Our primary outcomes included a comparison of ML models for BG-level prediction across different prediction horizons (PHs). Ten eligible studies were analyzed, focusing on BG prediction across PHs of 15, 30, 45, and 60 minutes. The ML models demonstrated mean absolute root mean square error (RMSE) values of 15.02 (SD 1.45), 21.488 (SD 2.92), 30.094 (SD 3.245), and 35.89 (SD 6.4) mg/dL, respectively. Among these, the Random Forest (RF) model exhibited superior performance across all prediction horizons. Alongside these findings, advancements in IoMT have shown significant benefits, such as enhanced disease monitoring, prevention, care, and diagnosis. However, challenges in managing and securely storing vast amounts of patient data and ensuring data privacy and security persist. The integration of blockchain technology and cloud computing is emerging as a promising solution to these challenges.

Yagyesh Kapoor

TABLE OF CONTENTS

List of Tables

List of Figures

List of Abbreviations

IoT	Internet of Things
IoMT	Internet of Medical Things
IIOT	Industrial Internet of Things
AI	Artificial Intelligence
ML	Machine Learning
DL	Deep Learning
CGMs	Continuous glucose monitors
EHR	Electronic Health Record
CAGR	Compound Annual Growth Rate
NFV	Network Function Virtualization
SDN	Software-Defined Networking
FHIR	Fast Healthcare Interoperability Resources
HL 7	Health Level Seven
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyography
CVD	Cardiovascular Diseases
SaaS	Software-as-a-Service
Q (1-4)	Fiscal Quarters
MCU	Microcontroller Unit
SoC	System-on-Chip
CSIRO	Commonwealth Scientific and Industrial Research Organization
GWAS	Genome-Wide Association Studies
API	Application Programming Interface
SQL	Structured Query Language
RDD	Resilient Distributed Dataset
DAG	Directed Acyclic Graph

UDFs	User Defined Functions
CSPM	Cloud Security Posture Management
ICs	Integrated Circuits
TPDs	Trust Platform Design Suite
MAC	Message Authentication Code
MPU	Microprocessor
EEPROM	Electrically Erasable Programmable Read-only memory
PIC	Peripheral Interface Controllers
TLS	Transport Layer Security
HTM	Healthcare Technology Management
FL	Federated Learning
LDP	Local Differential Privacy
IPFS	Interplanetary File System
FBS	Federated Blockchain System
QDPoS	Quantum Delegated Proof of Stake
BCT	Block Chain Technology

CHAPTER 1

INTRODUCTION

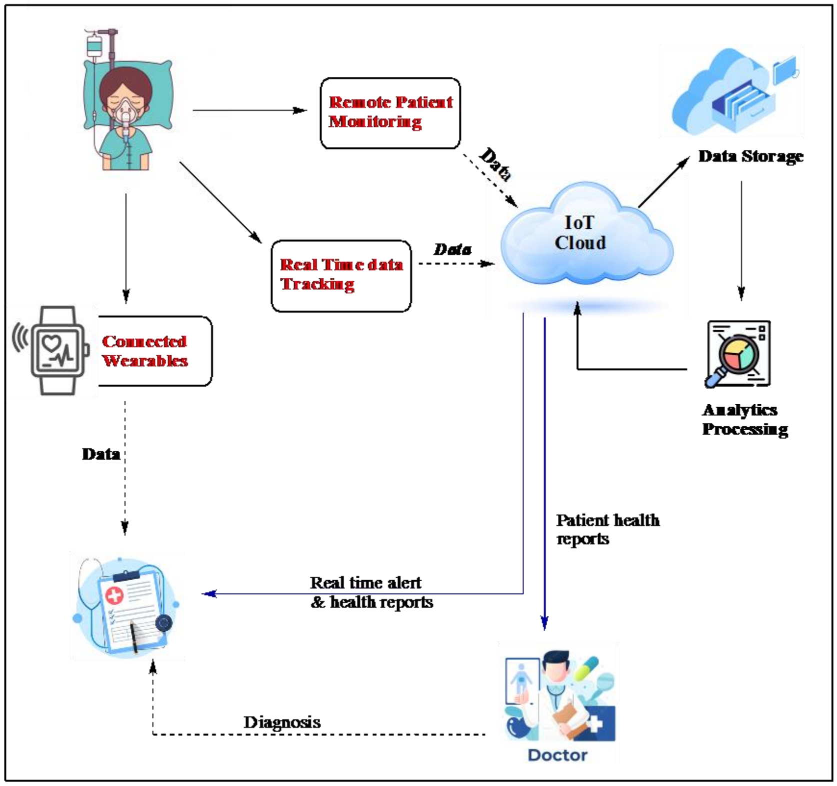
The medical sector has embraced the IoT for patient care and monitoring. IoT adoption in healthcare includes various applications such as remote tracking, integration of healthcare devices, wearable biometric sensors, and smart beds (Figure 1). For instance, tiny cameras attached to vitamin-sized tablets capture images of the patient's digestive tract, aiding specialists in disease diagnosis, such as colon cancer. Machine learning techniques enhance image processing, enabling more effective diagnosis and treatment. Continuous glucose monitors or CGMs provide real-time blood glucose monitoring through electrodes under the skin, transmitters, and receivers [1, 2]. IoT sensors placed near the windpipe collect cardiorespiratory signals, transmitting the data wirelessly for analysis [3]. Smart contact lenses with sensors and microcircuits can detect changes in eye fluid, assisting in the diagnosis of medical conditions [4]. Engineers have also developed hydrogel pills with attached sensors to monitor gastrointestinal temperatures and ulcers [5]. IoT has the potential to enable personalized medicine based on lifestyle, environmental, and genetic factors. The future of IoT in healthcare looks promising as consumers show increasing interest in collecting and understanding their health data [6, 7].

Diabetes represents a pressing global health challenge, with a rising prevalence that is projected to continue escalating in the coming decades [8,9]. The impact of uncontrolled diabetes on individuals' health and healthcare systems is profound, underscoring the critical need for effective management strategies to prevent complications and improve outcomes [10, 11]. In particular, the management of blood glucose (BG) levels is paramount for reducing the risk of acute and chronic complications associated with diabetes. Machine learning (ML) technologies, when integrated with Internet of Things (IoT) applications, hold significant promise for transforming diabetes management [12]. Diabetes is a growing global health problem that is expected to increase in the next decade

[8,9]. The impact of uncontrolled diabetes on an individual's health and well-being is significant; this highlights the urgent need for effective management strategies to prevent identified problems and improve outcomes [10, 11]. In particular, controlling blood sugar (BG) levels is important in reducing the risk of acute and chronic diseases associated with diabetes. Machine learning (ML) technology holds great promise in revolutionizing diabetes management when combined with Internet of Things (IoT) applications [12] . By monitoring physical and continuous data, IoT devices such as continuous blood glucose monitors (CGM) can provide valuable information that can be used by machine learning algorithms for predictive modeling and personal impact. ML algorithms can analyze complex data provided by CGMs, electronic health records (EHRs), and lifestyle factors to predict blood glucose changes and improve glycemic control [13, 14]. Several machine learning (ML) algorithms, such as random forests (RF), support vector machines (SVM), neural networks, and autoregressive models, have been examined for their ability to predict blood glucose (BG) levels and related addresses. problems. However, the effectiveness of these models may vary between studies due to differences in data elements, designs, and patient populations [15–17].

As machine learning models continue to improve and IoT devices evolve rapidly, this meta-analysis examines trends and trends over the past five years. By reviewing research published between 2019 and 2023, we plan to provide a new assessment of the future of machine learning in the context of legacy urine glucose monitoring with IoT technology. This meta-analysis focused on evaluating the effectiveness of machine learning models in predicting glycemic outcomes and improving glycemic control in diabetic patients. By combining existing literature, this study aims to explore the progress, challenges, and trends in the integration of urinary machine learning and IoT technologies for diabetes control. Furthermore, the study will investigate specific ML algorithms and IoT architectures that have demonstrated promising results in diabetes prediction and control. This study will contribute valuable insights to inform future research directions and guide the implementation of ML-driven solutions in clinical practice, ultimately improving diabetes management and reducing the burden of diabetes-related complications.

Figure 1: IoT HealthCare Architecture



1.1. IoMT Market Dynamics: Emerging Trends

In 2022, the market for Internet of Medical Things reached a valuation of USD 61.56 billion, with North America contributing 41.36% of the total share and it is projected to reach USD 516.40 billion by 2032 [18], with a CAGR (compound annual growth rate) of 23.70% from 2023 to 2032 (Figure 2). The Asia-Pacific region is anticipated to witness the highest growth rate throughout the forecast period in the global market for IoMT due to changes in lifestyle, improving diagnostic facilities and increasing awareness causing the rise in number of private players in countries such as India, China, and Thailand. The analysis of various segments within the IoMT market reveals interesting insights. In the platform segment, which includes device, cloud, and application management, the device management segment emerged as the dominant player, capturing approximately 39.32% of the market share in 2022. This can be attributed to advancements in implanted, wearable sensor, and other stationary devices. In the component segment, which consists of hardware, software, and services, the hardware segment took the lead, accounting for around 41.25% of the market share. This progress can be credited to the growing utilization of IoT-enabled medical equipment. Among the application segments, the real-time monitoring segment dominated the market, generating a revenue of USD 17.94 billion in 2022, primarily driven by the growing adoption of cost-effective sensors and connected devices. The smart wearable devices segment led the market with a 41.25% market share, generating a revenue of USD 25.39 billion [18] in the same year. This growth can be attributed to the rising consumer adoption of smart wearable technology products. Looking ahead, it is likely that by 2032, the home-use healthcare devices segment will dominate the market due to the increasing burden of chronic illnesses and the growing geriatric population worldwide.

In terms of the mode of service delivery segment, the on-premises segment accounted for a significant market share of 57.25% in 2022, generating a revenue of USD 35.24 billion.

Adoption of 5G technology and investments in advanced 5G networks are anticipated to fuel market growth [19]. The rising public and private expenditure on healthcare automation and digitalization, aimed at cost reduction and efficiency enhancement, is contributing to market expansion. Additionally, the growing use of network function virtualization (NFV) and software-defined networking (SDN) within the industry is expected to further stimulate market growth during the forecast period [20].

EHR collaboration plays a key role in facilitating the sharing and interpretation of medical data in a user-friendly format, enabling improved healthcare and better decision-making [21, 22]. Interoperability enables seamless flow of medical data between healthcare providers and other healthcare managing systems, resulting in enhanced efficiency and cost savings. Government initiatives to promote interoperability serve as major catalysts for improving healthcare interoperability. Encouragingly, notable standard bodies like

Fast Healthcare Interoperability Resources (FHIR) and Health Level Seven (HL7) are making remarkable strides towards achieving interoperability, bringing positive developments in the field [23]. After achieving interoperability, systems will be able to effectively handle data from various sources, allowing organizations to use AI and conduct data analytics to enhance outcomes for end users. [21] With a seamless flow of accurate data between entities, organizations can then implement advancements like ML and predictive analytics to extract increased value from the data. We are approaching a time when the possibilities for innovation to improve health outcomes are becoming more tangible. Committing to interoperability beyond mere compliance will turn this into an exhilarating and transformative moment in the field of healthcare.

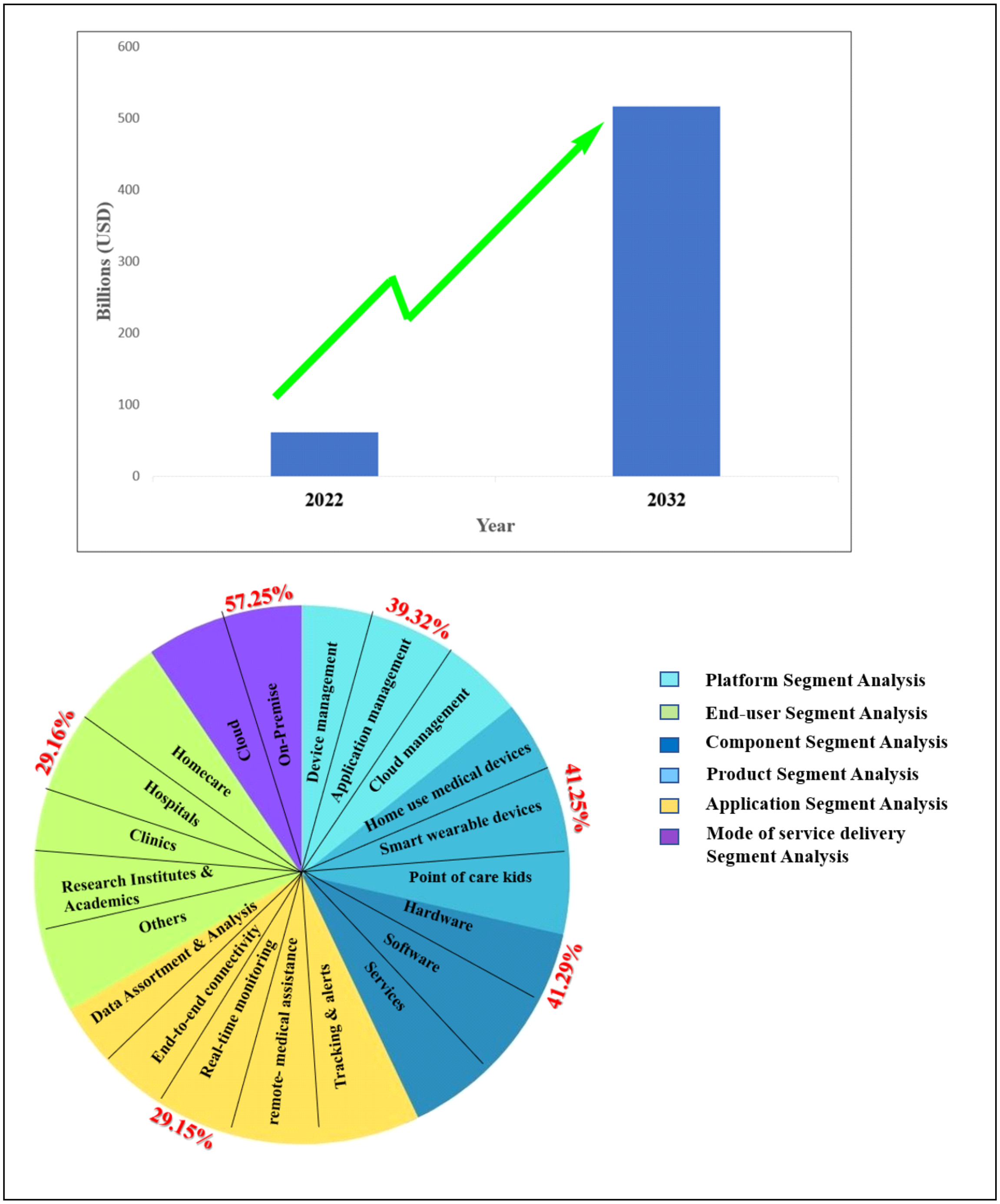


Figure 2: IoMT predicted market growth and segment analysis with market share of dominant sectors in Year 2022

1.2. Key Market Players: IoMT

The IoMT holds the potential to reduce healthcare expenses for both governments and patients [24]. Companies in MedTech sector are focused to transform the delivery of patient care via the IoMT. The pandemic has witnessed a significant rise in investments in this field, leading to projections of substantial growth in the global IoMT [25] market fueled by these increased investments. In the highly fragmented market, there are multiple prominent players, including Johnson & Johnson (J&J), Medtronic, Siemens Healthline, and Koninklijke Philips N.V., who hold significant market presence. Apple is making healthcare more accessible to everyone by offering convenient access to precise sensors and software [26]. This enables consumers to enhance their understanding of healthcare and gain insights into how their daily choices affect their well-being. These companies make substantial investments in research and development, technological advancements, patents, as well as collaborations, acquisitions, and mergers to enhance their revenue and fortify their market position. An example of this is the collaboration between Philips and Cognizant in July 2021, where they joined forces to create comprehensive digital solutions that expedite clinical trials and enhance patient care [27]. More recently J&J creates new IoT architecture with TCS as their digital transformation partner [28]. MedTech sector is now utilizing technologies such as analytics, AI, robotics, and many immersive technologies, among others. [29] In this many startups have joined the league and are involved in manufacturing wearables such as biopatches, ECG monitors, psychological monitoring devices, smart glasses etc. [30] For example, Aidmed a Polish startup developed a chest-worn wearable portable medical device Aidmed One [31]. This device using sensors collects various bio signals such as accelerometer (measurement of patient movement and position), bioimpedance (measuring changes in chest volume), Pressure sensor for measuring airflow through the mouth/nose, thermometer for skin surface temperature, microphone for volume level such as coughing, ECG (electrocardiogram), and SpO_2 sensor for pulse rate and blood oxygen saturation. The data is sent to a cell phone and subsequently to a server, which is accessible by a doctor or healthcare provider. By analyzing the collected data, the doctor can evaluate the patient’s condition and track their progress in treatment. Further, Gate Science a US based startup developed a wearable device called RELAY, designed to manage pain [32]. This innovative product combines pharmacological blockade and neuromodulation capabilities into a single multimodal device. Additionally, Gate Science offers a companion app that empowers patients to control these signaling mechanisms. By offering an alternative to post-surgery pain relieving narcotics, the startup's solution presents doctors and patients with a new approach to pain management. Orbicor Technologies, a startup based in Costa Rica, develops UnnoMed, a platform for cardiovascular management. [33] This platform utilizes IoMT medical devices to generate unique clinical data. The data provided by UnnoMed complements existing information available to cardiovascular patients and facilitates continuous monitoring and optimization of their treatment. By enabling healthcare providers to sense the early stages and advancement of cardiovascular diseases (CVD), the platform aids in proactive healthcare management. EloCare, a startup based in Singapore, specializes in the development of a connected device for menopause care [34]. Their wearable device, Elo, provides continuous monitoring of symptoms and collects essential health data. Clinicians with this data create personalized health profiles, enabling more effective delivery of lifestyle adjustments or medical interventions for women experiencing menopause.

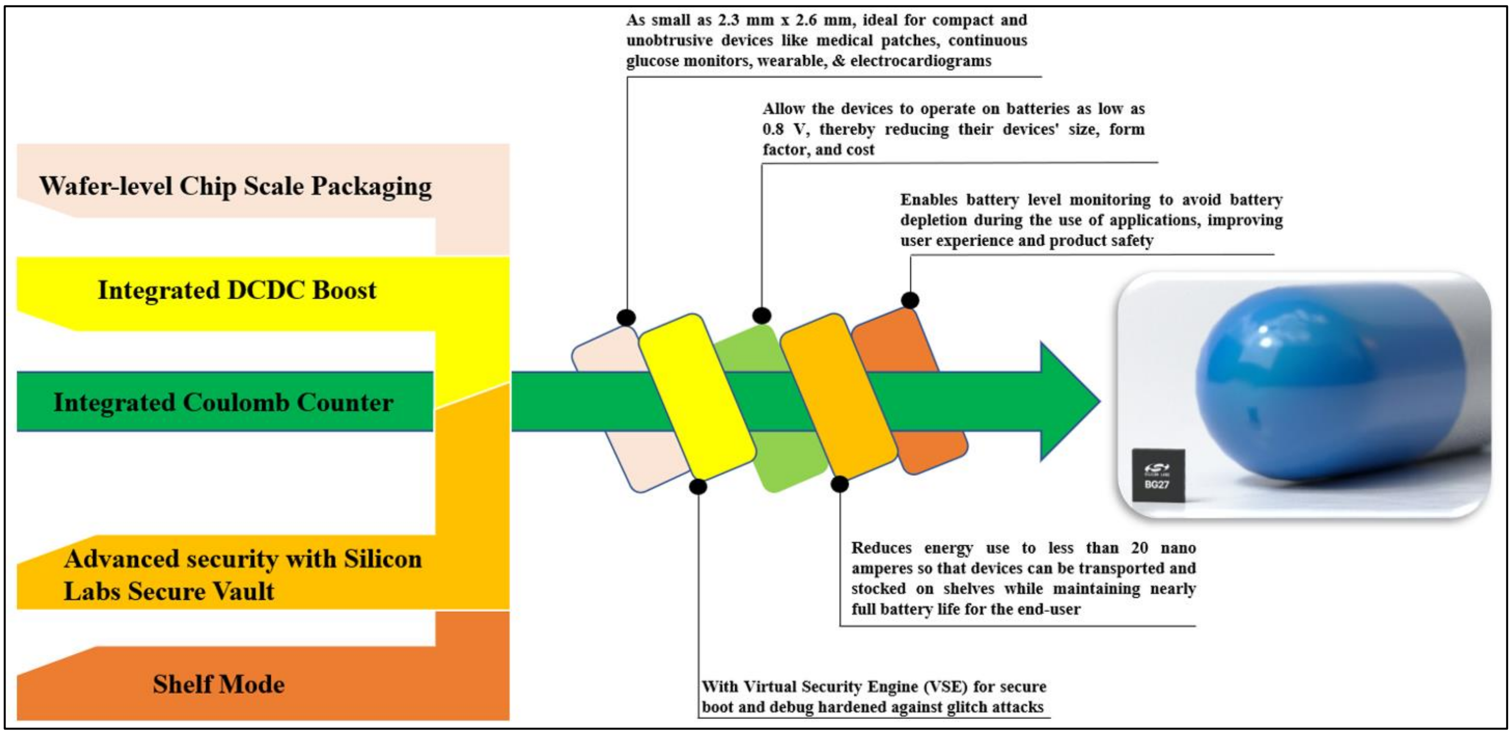
Many companies continue to prioritize the development of blood pressure and cardiac devices due to their significant importance. This strategic focus is understandable considering the existing availability of technology and sensors, which facilitates innovation and allows companies to make incremental improvements without starting from scratch. Furthermore, the presence of capable manufacturers simplifies the process of transforming an idea into a commercially viable product. Apple plans to enhance the cardiovascular measuring capabilities of the Apple Watch by implementing further improvements. The implementation of these updates is a complex process one crucial prerequisite is obtaining FDA approval, which is necessary for any significant improvement. The FDA approval can be time-consuming, often spanning several years before the desired enhancements can be incorporated. Established tech giants pose a significant challenge for traditional medical device companies in the wearable medical device market. While this might initially seem counterintuitive, it is clear given the prominence of companies like J&J MedTech and Medtronic. To safeguard and commercialize their ideas, companies need to obtain clearance from regulatory bodies and secure patents. However, the global medical industry witnessed a 20% decrease in IoT related patent applications in the first quarter of 2023 compared to the previous quarter as per GlobalData's Patent Analytics. They also revealed a 24% decline in the total number of grants for IoT related inventions during the same period. Specifically, the medical industry submitted 764 patent applications related to the IoT in Q1 2023, whereas the number was 957 in the preceding quarter. As competition intensifies and research and development investments soar, many companies are turning to collaboration through mergers and acquisitions (M&A). These strategic alliances allow for cost reduction while maximizing the overall impact and efficiency. Softheon, Inc., a US based company recently completed the acquisition of NextHealth Technologies, exemplifying the pursuit of growth and synergy in the industry. NextHealth is an AI based healthcare software-as-a-service (SaaS) analytics service. Its platform is built specifically to help healthcare professional by enabling users to monitor their daily readings, including metrics like heart rate and blood pressure. Through the merger Softheon go-to-strategy receives a substantial boost. This move will enhance the engineering process, leading to the development of more competitive and robust products. The shared objective of both companies is to provide more less expensive healthcare solutions to vulnerable class while improving the quality of care.

1.3. Booming Chip Industry for IoMT

With advancing knowledge companies are now focusing on designing chips that are secure, flexible, and cost-effective. More recently Silicon lab has decided to leave from any business other than IoT devices and wireless connectivity signifying the commencement of their transformation into a specialized IoT chip designer, focusing solely on this field. By 2022, they aimed to transform into a complete IoT chip designer, and they have achieved significant growth, doubling its revenue in just two years. In addition, silicon Labs has emerged as a pioneering force in harmonizing diverse standards utilized in IoT devices. They have introduced specialized silicon that supports the Matter standard and previous standards like Zigbee and Zwave. Companies seeking to develop products that seamlessly connect a wide range of smart home devices, are likely to consider Silicon Labs as their provider. They are facing competition from established and prominent companies such as MediaTek, Infineon, Broadcom, STMicroelectronics, and Qualcomm. For example, Taiwan-based MediaTek which specializes in chip design for smart speakers of Amazon Alexa achieved approximately $1.9 billion USD revenue from IoT connected devices in the Q2 2022. In contrast, Silicon Labs accomplished outstanding outcomes by achieving record revenue of $263 million in the second quarter (Q2) of that same year. Despite the competition it has proved its ability to thrive and achieve significant financial success. Although the IoT chip industry is experiencing growth, numerous end-user devices remain susceptible to hacking. They address this concern by implementing hardware-level security measures during the final stage of chip production. On 14 March 2023, Silicon Labs introduced system-on-chip family (xG27) and the BB50 microcontroller unit (MCU) which has sparked the development of various innovative products. They are designed for the smallest IoT devices. One such example is a wearable in-mouth sensor that harnesses the capabilities of silicon Lab’s system-on-chip (SoC), enabling data capture and transmission via Bluetooth and Zigbee. Companies have begun to build small, portable medical devices, asset trackers, home sensors, and wearable electronics that utilizes Silicon Lab recently introduced family of Internet of Things (IoT) wireless device SoC products. The xG27 family includes BG27 and MG27, BG27 comes with Bluetooth functionality and MG27 offers Bluetooth, Zigbee and proprietary wireless connectivity. They aim to empower companies in expanding their product portfolio by offering enhanced flexibility. Such as selling one version of device offering Zigbee or Bluetooth, and an unconnected version that could be more cost-effective, all utilizing the same SoC and microcontroller unit (MCU). An SoC is a unified chip that incorporates both an MCU and other components. The MCU delivers the necessary processing power to capture and manage data on the chip, allowing users to select the desired wireless functionality if required. Consider an advanced toothbrush designed to monitor an individual's brushing time. In one version, the toothbrush could utilize the MCU to display the brushing results directly to the user. Alternatively, with the incorporation of the BG27 chip, the toothbrush could establish a connectivity with the user smartphone via Bluetooth enabling the seamless transfer of data regarding the toothbrush usage to the Cloud, facilitating more comprehensive management and analysis. SoC products are meticulously designed to operate on low power, allowing them to maintain battery life even when left idle on a shelf for extended periods. Moreover, these chips come in a compact package measuring 2.3mm × 2.6mm (0.09-0.1 inch), making them ideal for integration into compact medical patches, continuous glucose monitors, wearable electrocardiograms, and asset tags across diverse settings. The BG27 &MG27 SoCs are centered around the ARM cortex M33 processor and offer a range of shared features (figure 3) carefully crafted to make them the perfect choice for small form-factor devices. The BG27 incorporates an integrated DCDC Boost, enabling its operation at voltages as low as 0.8 volts. This feature allows the utilization of single-cell alkaline, silver oxide, and 1.55v button cell batteries commonly found in healthcare utilities like wearable ECG, glucose monitors, and battery-operated patches. Earlier this year Lura Health, a medical device manufacture has chosen the new SoC as the foundation for their upcoming smart wearable. Unlike typical wrist-worn or external skin wearables this innovative Laura Health monitor is designed to be placed inside a person's mouth. To be more precise, the device is small enough to be securely attached to a tooth using adhesive. The sensor is worn continuously for months transmitting data to a smartphone through Bluetooth connectivity. The device will enable healthcare professionals and dentist to gather significant data from saliva that can be utilized for assessing health conditions such as pH levels that can contribute to tooth decay, as well as monitoring chronic kidney disease and glucose levels.

Looking into the IoT market today power consumption is becoming more vital since there is often no way for users to change batteries on a regular basis. To ensure robust security, both SoCs incorporate Silicon Lab's secure vault, which provides secure boot and debugging functionalities. This helps prevent glitch attacks, safeguard against tampering, and protect against remote cyber-threats. As wearable and other IoT devices continue to enhance their functionality, including the collection and transmission of larger amounts of sensor data, the challenges of size and energy efficiency become more pronounced for both the technology itself and its users.

Figure 3: Common features of BG27 and MG27 designed to make them the ideal SoC for small form-factor devices.



New advancements in technology have brought about impressive accomplishments not just in the identification and diagnosis of diseases, but also in predicting their occurrence [35]. Healthcare prediction systems strive to ascertain the likelihood of a future disease or the early identification of an existing one. These predictions draw upon various sources, including electronic medical records, data from wearable healthcare devices, and healthcare reports. Bracelets, smartwatches, and other devices equipped with accelerometers and heart rate trackers are extensively employed as wearable biosensors in a variety of settings, including hospitals, sports, and fitness applications [36-39]. Wearable devices equipped with medical sensors to gather measurements. These measurements, combined with existing medical data, are employed to provide medical recommendations, and monitor the individual’s health status. During real-time streaming, the health status data being streamed undergoes abnormality filtration to eliminate any irregularities. Following that, the extracted health data is input into a machine learning model to forecast the individual's health status [40].

CHAPTER 2

DATA FUSION

2. Fusion of Multimodal Data in Healthcare: Advancing Precision medicine with AI and ML

The field of healthcare data is inherently multimodal [41], encompassing various types of information such as medical images, multi-omics data, and EHRs. By integrating a wide range of different data, we can deepen our understanding of human health and deliver personalized treatments. Researchers are actively exploring ways to integrate multimodal data (so-called data fusion) to obtain a better view [42]. Advances in technology, especially machine learning, allow us to integrate these disparate data and provide useful capabilities [42]. Integrating disparate data is important in many medical applications by leveraging the power of different models to provide better diagnosis, treatment, prediction, and decision-making. This approach brings us closer to the goal of precision medicine, where treatment can be personalized to the individual [42].

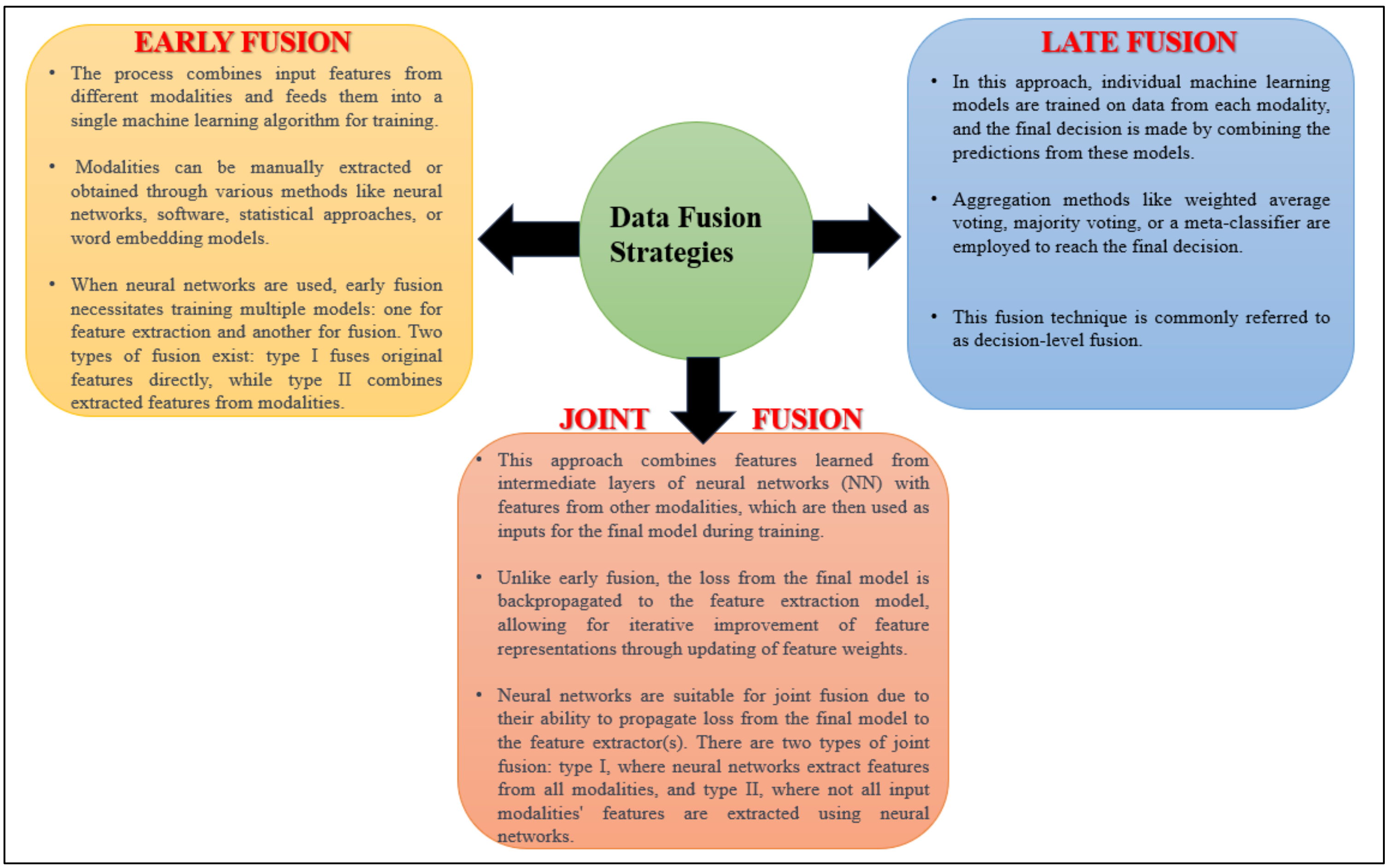
Data fusion refers to the combination of multiple data variables to provide different views of shared events to solve inference problems. Fusion technology focuses on using the coordination and integration of various adaptations to facilitate effective decision-making. For example, the fusion of medical data often plays an important role in the interpretation of medical images. Significant advances in artificial intelligence (AI) and machine learning (ML) models in recent years have made it possible to effectively integrate large amounts of data into small, large numbers of statistical and nonvariational models [43]. Multimodal machine learning is specific research that focuses on the combination of different information modalities [43]. There is clinical interest in combining multimodal data to automate clinical outcome prediction and diagnosis, as exemplified by research on Alzheimer's disease [44, 45].

Researchers have found that combining imaging data, specific lab test results, and demographic information as inputs to ML models yields enhanced performance compared to using single-source models [44, 45]. In a similar vein, the integration of pathological images with patient demographic data has shown improved performance in breast cancer diagnosis compared to models utilizing a single modality. These advantages have also been observed in various medical imaging applications such as predicting diabetic retinopathy, detecting COVID-19, and diagnosing glaucoma. Several studies have explored the utilization of artificial intelligence (AI) for the fusion of multimodal medical data [41-44].

However, previous reviews differ from our study in terms of their focus and coverage. Some studies have concentrated on fusing different medical imaging modalities without considering electronic health records (EHR) alongside imaging modalities. Others have specifically examined the fusion of omics data with other modalities using deep learning (DL) models [45]. Additionally, there has been research on the fusion of various Internet of Medical Things (IoMT) data for smart healthcare applications [46]. Liu *et al.* [47] investigated the integration of multimodal EHR data, considering both unstructured and structured data free texts within the electronic records, using a combination of conventional machine learning (ML) and deep learning (DL). Huang *et al.* [48] explored fusion strategies that concentrate on combining structured electronic health records (EHR) data with medical imaging. Their study specifically emphasized fusion techniques and methods for extracting features using deep learning (DL) models. Machine learning models can categorize fusion approaches based on when the features are combined, leading to different strategies such as late fusion, early fusion, and joint fusion [48] (Figure 4).

Multimodal machine learning (ML) has emerged as a prominent research area in the medical field, attracting significant attention. Our focus was to survey the existing literature in multimodal medical ML, particularly the fusion of EHR with medical imaging data. However, many studies have employed relatively simple fusion strategies, which, while effective, may not fully leverage the wealth of information embedded within these modalities. Given the rapid developments in the field and the continuous advancement of new AI models for multimodal data, it is important to acknowledge the possibility of studies existing beyond the scope of the reviewed fusion strategies or employing a combination of these strategies. We maintain optimism that the advancements in this field will foster more inclusive investigations of multimodal medical data, offering valuable assistance in the clinical decision-making process.

Figure 4: Fusion approaches can be classified as early, late, or joint fusion, based on when the features are combined within the machine learning model. These categorizations depend on the specific stage of fusion in the ML model.



CHAPTER 3

METHODS

The study was carried out in accordance with the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Liberati et al., 2009) [49, 50]. PRISMA provides a standardized and reproducible approach for literature identification, article selection, appraisal, and analysis. A pre-defined protocol was established to document the analysis methodology and criteria for inclusion.

3.1.Study Design

This section outlines the research design and methodology utilized in this study. It covers the eligibility criteria, information sources, research inquiries, study selection procedures, data collection methods, and the article selection process for publication.

3.2.Research Questions:

General Questions (GQ):

1. What advancements and trends have emerged in diabetes management with the integration of machine learning and IoT technologies over the past five years?
2. What are the key challenges and gaps identified in the literature regarding the practical implementation of machine learning and IoT solutions in diabetes management during this period?

Specific Questions (SQ):

These questions aim to delve deeper into the ways in which specific health parameters and physiological data are monitored and analyzed using machine learning and IoT devices in the context of diabetes management. They focus on understanding: what are the outcomes and effectiveness observed from the application of machine learning and IoT techniques in the management and control of diabetes, particularly in predicting blood glucose levels and optimizing glycemic control? Which machine learning algorithms and IoT architectures are predominantly employed in the development and deployment of solutions for diabetes management?

The answers to these research questions will provide comprehensive insights into the current state of machine learning and IoT applications in diabetes management. They will help evaluate the impact, challenges, and opportunities associated with these technologies in improving diabetes care and patient outcomes.

3.3.Search Strategy:

To define the search string, we conducted searches in scientific databases and cross-referenced familiar terms, including synonyms, acronyms, and relevant word combinations. We refined our search string using the PICOS approach, which is recommended for structuring the elements outlined by PRISMA, such as defining objectives, research questions, and eligibility criteria. Each component of PICOS represents a specific element: Participants (P), Interventions (I), Comparisons (C), Outcomes (O), and Study Design (S). Participants: Adult individuals diagnosed with diabetes mellitus, including those with type 1 diabetes, type 2 diabetes, or gestational diabetes.

- Interventions: Utilization of machine learning algorithms and IoT technologies, including wearable devices and smart sensors, for monitoring, management, and prediction of blood glucose levels in diabetic patients.
- Comparisons: Comparison of the effectiveness and outcomes achieved through the integration of machine learning and IoT technologies with traditional methods of diabetes management.
- Outcomes: Assessment of outcomes related to glycemic control, blood glucose prediction accuracy, improvement in patient outcomes (such as quality of life, morbidity, and mortality rates), identification of challenges and gaps in the implementation of machine learning and IoT solutions in diabetes management.
- Study Design: Inclusion of research articles, clinical trials, observational studies, and feasibility studies that investigate the integration of machine learning and IoT technologies in diabetes management. Emphasis on studies reporting outcomes related

to the application of machine learning algorithms and IoT architectures in predicting blood glucose levels, optimizing glycemic control, and addressing challenges in diabetes management.

- Based on the search strategy, we demonstrated the search string defined to be used in querying the databases:

("machine learning" OR "artificial intelligence" OR "data mining" OR "predictive modeling") AND ("Internet of Medical Things" OR "IoMT" OR "healthcare IoT" OR "wearable devices" OR "smart sensors") AND ("diabetes" OR "diabetes mellitus" OR "diabetic patients" OR "blood glucose" OR "glycemic control") AND ("predict blood glucose" OR "blood glucose prediction" OR "diabetes management" OR "glycemic prediction")

3.4.Study Selection:

For article selection, we retrieved studies published within the last five years (2019–2023) from electronic databases using our predefined search string. The databases surveyed included Scopus, Springer, IEEE Xplore, PubMed, CINAHL, Embase, Web of Science, and Nature. These databases were selected due to their comprehensive coverage of relevant articles in the field addressed in this paper. Moreover, they offer access to full-text journals and conference proceedings from prominent health conferences focusing on patient self-care, IoT, diabetes, wearable devices, and related topics. The last search was done on January 15th, 2024.

3.5.Exclusion Criteria:

- Articles focused on pediatric populations, including children and adolescents (up to 18 years of age), were excluded.
- Our meta-analysis specifically focuses on Continuous Glucose Monitoring (CGM) technologies used in diabetes management.
- Articles not reporting primary research studies, such as thesis, opinions, abstracts, dissertations, criticisms, books, protocols, posters, reviews, and oral presentations were excluded.

- Articles that do not specifically discuss the utilization of IoT techniques, including wearable electronic devices, for monitoring, self-care, and management during the treatment phase of diabetes patients were excluded.

3.6.Inclusion Criteria:

- Studies involving adult men and women diagnosed with diabetes mellitus, including type 1 diabetes, type 2 diabetes, or gestational diabetes.
- Studies published within the last 5 years to capture recent advancements and trends in the field of diabetes management.
- Articles written in English to ensure accessibility and comprehensibility for analysis and interpretation in the meta-analysis.

3.7.Data Extraction and Management:

Both reviewers independently conducted data extraction and quality assessment. Any disagreements were resolved by an impartial third reviewer. When a study reported multiple test results for the same ML model, the most favorable outcome was chosen for extraction. Similarly, if a study evaluated multiple ML models, performance metrics for each model were extracted individually. In studies focusing on blood glucose level prediction, root mean square errors (RMSEs) for different prediction horizons (PHs) were extracted. For studies not specifying PHs, performance metrics such as R-squared value and Accuracy of ML models were extracted.

3.8. Methodological Quality Assessment of Included Studies

The quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. This tool evaluates studies across four domains: patient selection (5 items), index test (3 items), reference standard (4 items), and flow and timing (4 items). All four domains were used to assess the risk of bias, while the first three domains were specifically used to evaluate concerns regarding applicability. Each domain consists of a set of questions (totaling 7) related to either risk of bias or applicability [52].

3.9. Data Synthesis and Statistical Analysis

The performance metrics of models used for blood glucose level prediction were evaluated independently based on their specified prediction horizons. Studies that did not specify prediction horizons were analyzed separately. The primary performance metric used was the root mean square error (RMSE) of ML models in predicting BG levels. For each study, effect sizes (Cohen's d) and standard errors were calculated. Study heterogeneity was assessed using I^2 values obtained from multivariate random-effects meta-regression, which accounted for within- and between-study correlations. Heterogeneity was categorized into quartiles based on these values: 0% to <25% for low heterogeneity, 25% to <50% for low-to-moderate heterogeneity, 50% to <75% for moderate-to-high heterogeneity, and >75% for high heterogeneity [53, 54]. Additionally, meta-regression was employed to explore the sources of heterogeneity. Publication bias was evaluated using regression testing for funnel plot asymmetry through Egger's test.

Furthermore, studies focusing on BG levels were divided into four subgroups based on different prediction horizons (15, 30, 45, 60, and 120 minutes). A two-sided P value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using JASP (Version 0.18.3), and we utilized guidelines from Cochrane Review Manager.

CHAPTER 4

RESULTS

From a total of 1,174 studies identified through a systematic search of predefined electronic databases, 1,067 (91%) remained after duplicates were removed. After screening titles and abstracts, 734 (68.79%) studies were excluded for irrelevant topics or a lack of predefined outcomes. The remaining 333 (31.2%) studies underwent full-text evaluation. Of these, 323 (97%) were excluded for various reasons, resulting in 10 (3%) studies being included in the final meta-analysis.

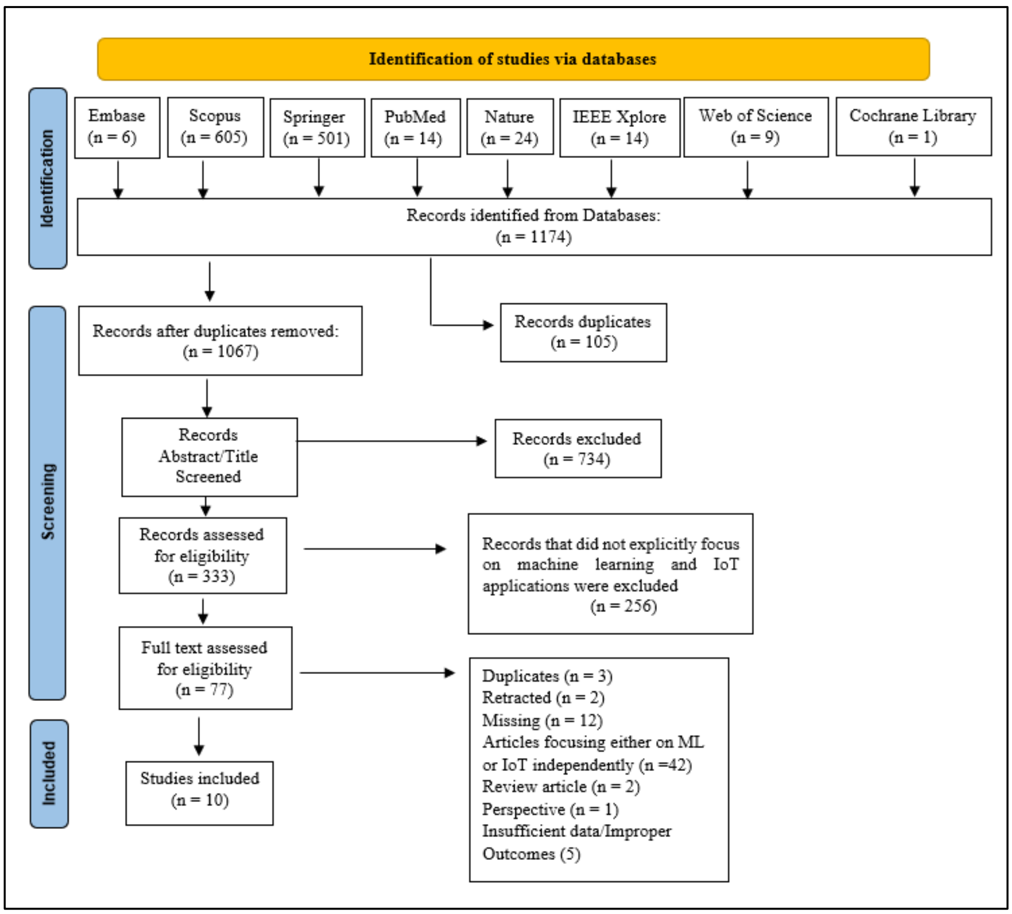


Figure 5: PRISMA Flow diagram of identifying and including studies.

4.1. Description of Included Studies

In total, the 10 studies included 8,776 participants with over 20 different ML models and different IoT devices (Table 1).

Study_ID	Sample Size (N)	Outcome Measure	ML model	IoT Devices	Demographic information
[55]	40 (DM1)	RMSE R-squared (R^2)	RF SVR	Abbott Freestyle Libre CGM System, Fitbit Charge 5 Smart Band	Age, sex, BMI, duration of diabetes, HbA1C (%)
[56]	40 (DM1)	RMSE, R squared (R2)	RF SVM BRNN	Abbott Freestyle Libre CGM System, Fitbit Charge 5 Smart Band	Age, sex, BMI, duration of diabetes, HbA1C (%)
[57]	3 different datasets: • 12-DM1 (OhioT1DM data set) • 25-DM1 (ABC4D data set) • 12 DM1 (ARISES data set)	RMSE MAE gRMSE	E3NN TCN [65] CRNN [66] LSTM [67] Bi-LSTM [68] SVR [69] ARIMA [70]	Medtronic Enlite CGM, Dexcom G5 CGM, Dexcom G6 CGM	-
[58]	40 DM1	RMSE	RF SVM BRNN	Abbott Freestyle Libre CGM sensor, Fitbit Charge 5 smart band	Sex, age, BMI, HbA1C %, insulin units per day, duration of diabetes
[59]	Six from the Ohio T1DM dataset and one study participant who is also an author of the study	RMSE, MRE	Ridge Regression	Dexcom G6 (CGM measurements to Apple Health), Empatica E4 wristband, Oura ring, Apple Watch	-
[60]	12 (T1DM)	RMSE, gRMSE,	Deep Learning	Clinically validated wearable sensor wristband	Age, gender, insulin regimen, HbA1c, glucose

		MAE, MAPE, Time Lag	algorithm embedded within the ARISES platform		level, daily risk range
[61]	Dataset 1 (768, Female) Dataset 2 (Excluded pediatric as well)	Precision, Accuracy, Specificity, Sensitivity, F1-Score, NPV, FNR, FPR, FDR, MCC	FMATSO-MDDTCN TSO-MDDTCN MAO-MDDTCN CSO-MDDTCN EOO-MDDTCN	IoT sensors-based diabetic data collection	Insulin level, Body Mass Index (BMI), age
[62]	2217 (T2D)	RMSE, MAPE	CGP Model (RNN based model)	Mobile-app (January AI), CGM (Freestyle Libre, Abbott), HR monitor (Apple Watch or Fitbit)	BMI, Weight, height, age
[63]	• Dataset1 (Pima Indians diabetes, 768) • Dataset2 (Hospital Frankfurt Germany diabetes dataset, 2000) • Dataset3 (merged dataset, 2768)	Confusion matrix; Accuracy	Adaptive random forest algorithm	IoT-enabled Blood Pressure Monitor, Glucose Monitor, Sleep Tracker, Heart Rate Monitor, Smart Scale (weight)	Age, BMI, Blood pressure, Diabetes Pedigree Function, Glucose, Insulin, Outcome, Pregnancies, and Skin Thickness
[64]	147 participants • 74 of 93 in waist-worn wearables arm	Area Under the Receiver Operating Characteristic (ROC)	LR LSR RR CART RF	Fitbit Zip or Fitbit Charge HR 2 wearable arm	age, gender, race/ ethnicity, education, marital status, and annual household income

	• 73 of 93 in wrist-worn wearables arm	Curve, R^2	GB EML		

Table 1: Baseline characteristics of predicting BG level-based studies.

RF, Random Forest; SVR, Support Vector Regression; SVM, Support Vector Machine; BRNN, Bayesian Regularized Neural Networks; RMSE, Root Mean Square Error; R^2, R squared; gRMSE, glucose specific RMSE; MAE, mean absolute error; MAPE, mean absolute percent error; One-Dimensional Convolutional Neural Network (1DCNN); Long Short-Term Memory (LSTM); Multi-scale Dilated Deep Temporal Convolutional Network (MDDTCN); CGP, Continuous glucose prediction; DirecNet, Diabetes research in children Network; LR, Linear Regression; LSR, Lasso regression, RR, Ridge regression; CART, Classification and regression trees; GB, Gradient boosting; EML, Ensemble machine learning, E3NN, embedded edge evidential neural network; TCN, temporal convolutional network; CRNN, convolutional RNN; ARIMA, autoregressive integrated moving average.

4.2. Quality Assessment of Included Studies

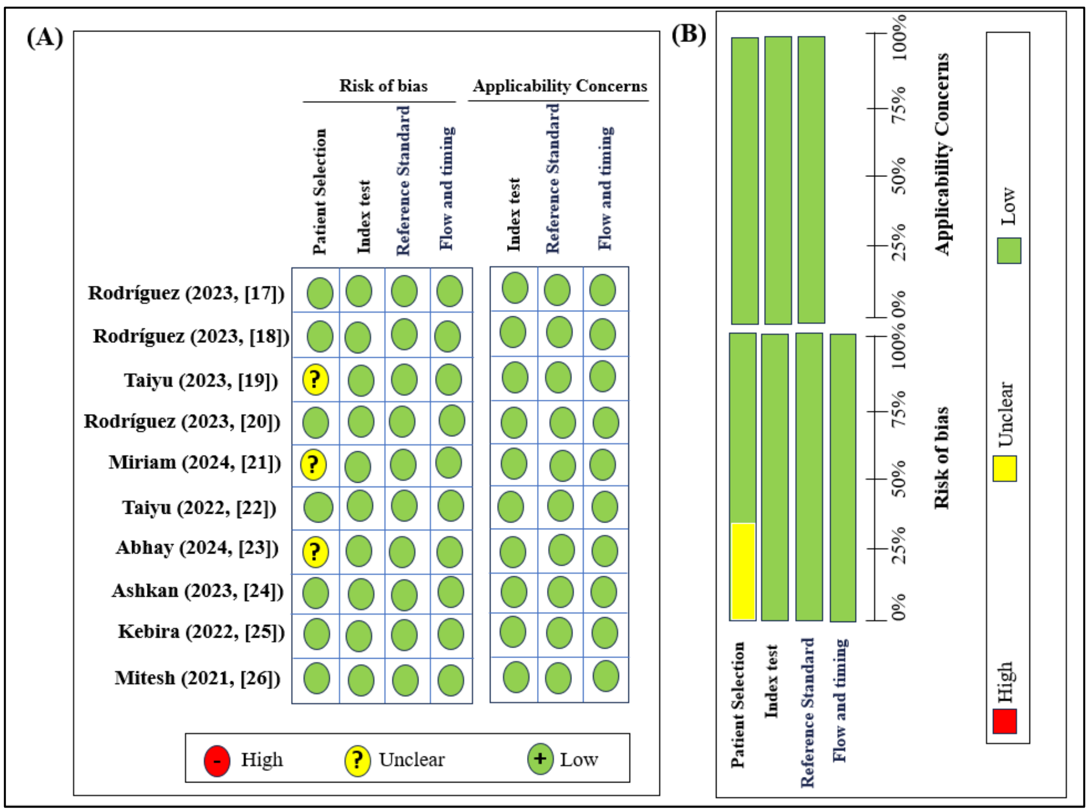


Figure 6: Assessment of study quality. Graph (A) depicting risk of bias and concerns about applicability, and Summary (B) showing risk of bias and applicability concerns.

The evaluation findings using the QUADAS-2 tool indicated that 30% of the studies included did not provide detailed reporting of patient selection criteria, resulting in substandard patient selection quality.

4.3.Statistical Analysis

4.3.1. Machine Learning Models for Predicting Blood Glucose Levels

In our meta-analysis evaluating the performance of machine learning (ML) models at a 15-minute prediction horizon, we observed significant heterogeneity across the included studies. This analysis incorporated data from 4 studies [55, 56, 58, 60], collectively examining 5 distinct ML models. The mean RMSE was 15.02 (SD 1.45) mg/dL. The omnibus test of model coefficients yielded a statistically significant result ($Q = 15.651$, $df = 1$, $p < 0.001$), indicating that the choice of ML model significantly influenced the outcome variable. Similarly, the test of residual heterogeneity revealed substantial residual heterogeneity across studies ($Q = 191.880$, $df = 7$, $p < 0.001$), underscoring significant variability in effect sizes not explained by the ML models alone. Residual heterogeneity estimates further confirmed the extent of variability, with an estimated τ^2 (Tau-squared) of 4.435 and τ (Tau) of approximately 2.106 as shown in the Forest Plot (Figure 7). The I^2 statistic (97.345%) indicated that a large proportion of the total variability in effect sizes was due to heterogeneity rather than sampling error, emphasizing considerable differences in study outcomes among the included ML models. Additionally, the H^2 value (37.668%) reflected the ratio of true heterogeneity to total observed variability, highlighting the impact of heterogeneity on the meta-analysis results. Furthermore, regression testing for funnel plot asymmetry using Egger's test detected significant asymmetry ($z = -5.707$, $p < 0.001$), suggesting the presence of publication bias. This finding underscores the need for cautious interpretation of the meta-analytic results and consideration of potential bias in the synthesized evidence.

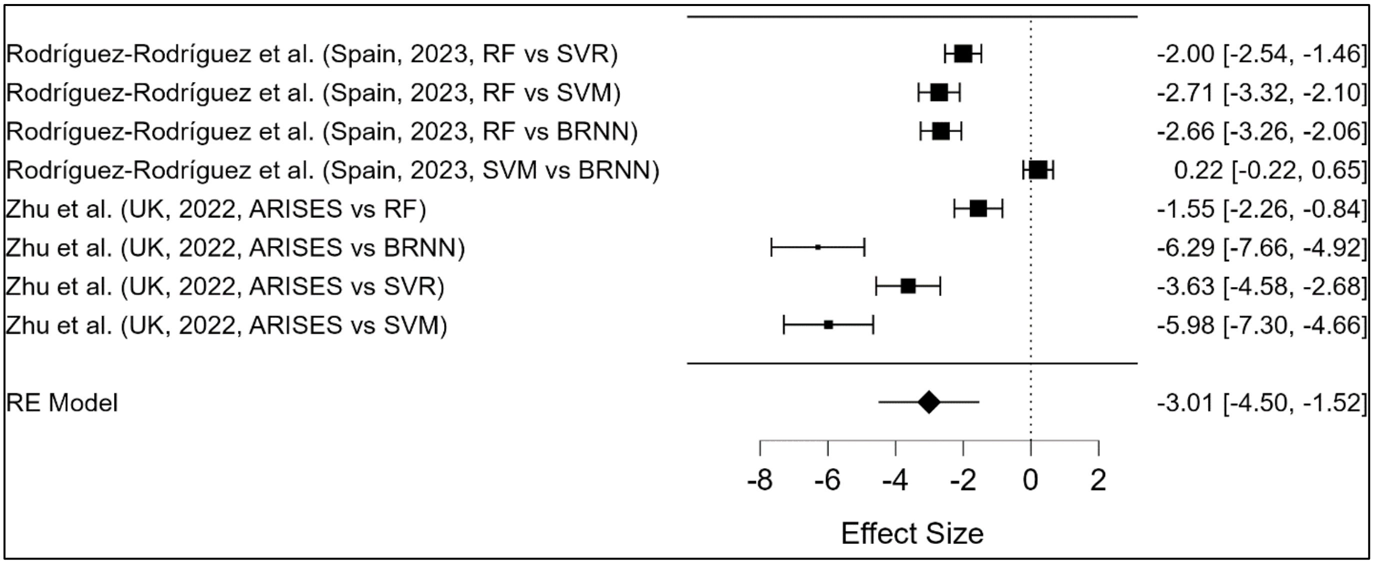
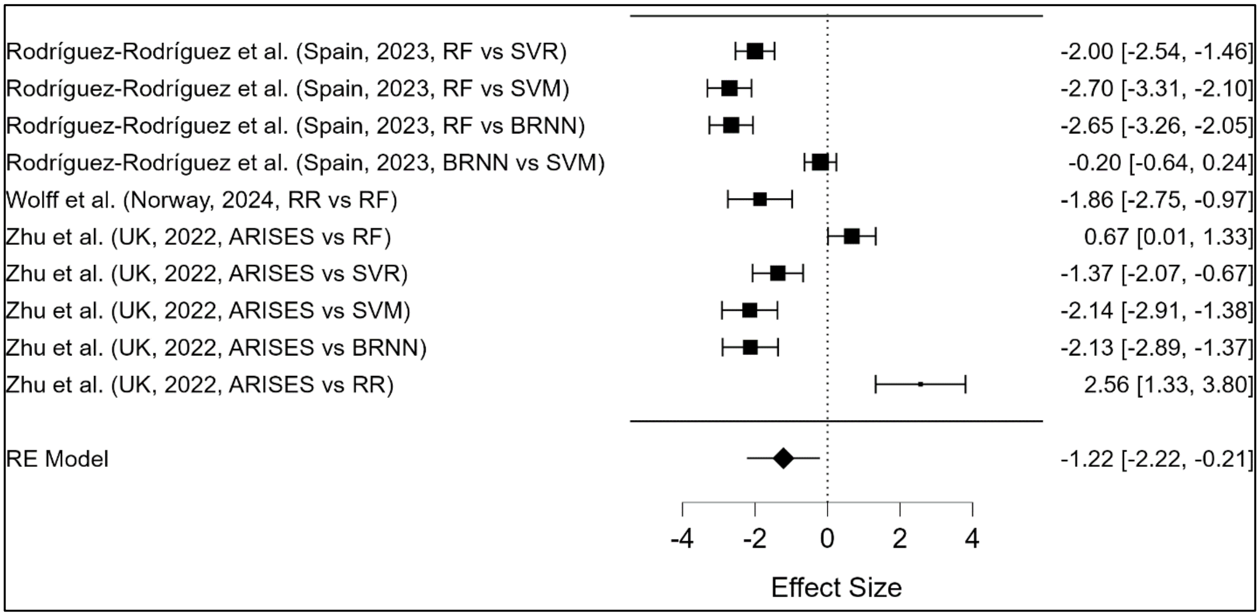


Figure 7: Forest Plot for comparing ML models at a PH = 15 mins

For PH = 30 minutes, 3 studies [57, 58, 60] with 11 different ML models. The mean RMSE was 21.488 (SD 2.92) mg/dL. The omnibus test of model coefficients revealed a statistically significant effect (Q = 6.895, df = 1, p = 0.009), indicating that the choice of ML model significantly influenced the outcome variable within the selected studies. Similarly, the test of residual heterogeneity showed substantial residual heterogeneity across studies (Q = 306.266, df = 71, p < 0.001), highlighting significant variability in effect sizes not explained by the ML models alone. Residual heterogeneity estimates further quantified the variability, with an estimated τ^2 of 0.384 and τ of approximately 0.620 as shown in the Forest Plot. The I^2 statistic (75.595%) indicated a moderate to high level of heterogeneity among the included studies, suggesting considerable differences in effect sizes across ML models. Additionally, the H^2 value (4.098%) reflected the ratio of true heterogeneity to total observed variability, emphasizing the impact of heterogeneity on the meta-analysis results. Furthermore, regression testing for funnel plot asymmetry using Egger's test did not detect significant asymmetry (z = 0.427, p = 0.669), suggesting no substantial publication bias among the included studies.

For PH = 45 minutes, 5 studies [55, 56, 58, 59, 60] with 7 different ML models. The mean RMSE was 30.094 (SD 3.245) mg/dL. The omnibus test of model coefficients yielded a statistically significant result ($Q = 5.580$, $df = 1$, $p = 0.018$), indicating that the choice of ML model significantly influenced the outcome variable within the selected studies. Similarly, the test of residual heterogeneity revealed substantial residual heterogeneity across studies ($Q = 153.332$, $df = 9$, $p < 0.001$), highlighting significant variability in effect sizes not explained solely by the ML models. Residual heterogeneity estimates further quantified the extent of variability, with an estimated τ^2 of 2.505 and τ of approximately 1.583 as shown in the Forest Plot (Figure 8). The I^2 statistic (95.709%) indicated a high level of heterogeneity among the included studies, suggesting considerable differences in effect sizes across ML models. Additionally, the H^2 value (23.304%) reflected the ratio of true heterogeneity to total observed variability, emphasizing the impact of heterogeneity on the meta-analysis results. Furthermore, regression testing for funnel plot asymmetry using Egger's test did not detect significant asymmetry ($z = 1.700$, $p = 0.089$), suggesting no substantial publication bias among the included studies at this prediction horizon. These findings highlight the challenges associated with assessing ML model performance at the 45-minute prediction horizon, characterized by notable residual heterogeneity and variability across studies. Future research efforts should aim to address heterogeneity and consider the implications of different ML model choices within this timeframe, enhancing the reliability and applicability of ML-based predictive modeling in relevant healthcare contexts.

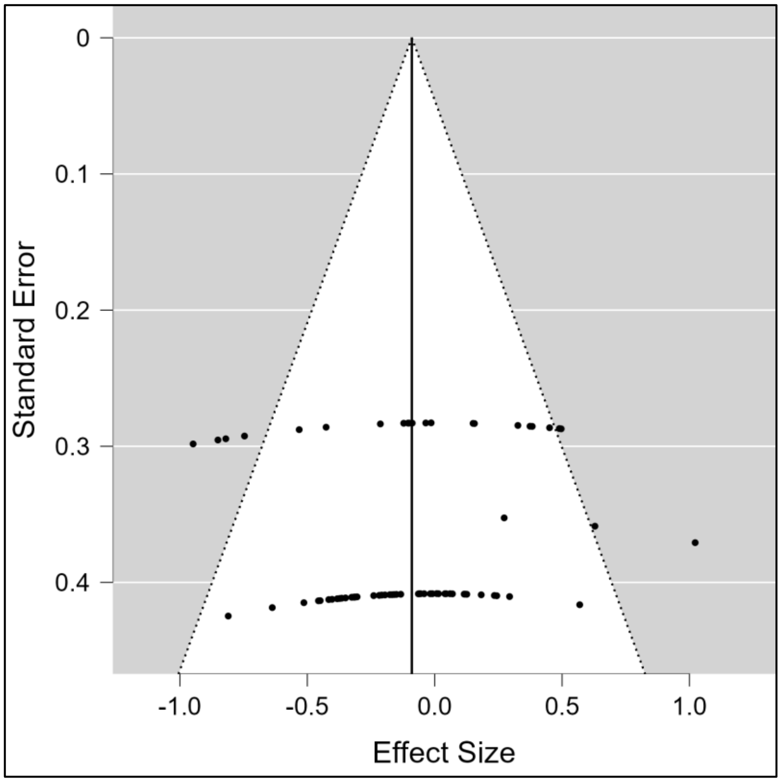
Figure 8: Forest Plot for comparing ML models at a PH = 45 mins



For PH = 60 minutes, 2 studies [57, 60] with 9 different ML models. The mean RMSE was 35.89 (SD 6.4) mg/dL. The omnibus test of model coefficients did not yield a statistically significant result (Q = 3.182, df = 1, p = 0.074), suggesting that the choice of ML model may have a relatively minor influence on the outcome variable within the selected studies. Similarly, the test of residual heterogeneity showed moderate residual heterogeneity across studies (Q = 83.888, df = 68, p = 0.093), indicating some variability in effect sizes not entirely explained by the ML models. Residual heterogeneity estimates quantified the extent of variability, with an estimated τ^2 of 0.044 and τ of approximately 0.210 as shown in the Forest Plot. The I^2 statistic (25.830%) indicated a relatively low level of heterogeneity among the included studies, suggesting moderate consistency in effect sizes across ML models. Additionally, the H^2 value (1.348%) reflected a low ratio of true heterogeneity to total observed variability, indicating less impact of heterogeneity on the meta-analysis results compared to other prediction horizons. Regression testing for funnel plot asymmetry using Egger's test did not detect significant asymmetry (z = -0.625, p = 0.532), suggesting no substantial publication bias among the included studies at this prediction horizon (Figure 9). These findings suggest that ML model performance at the

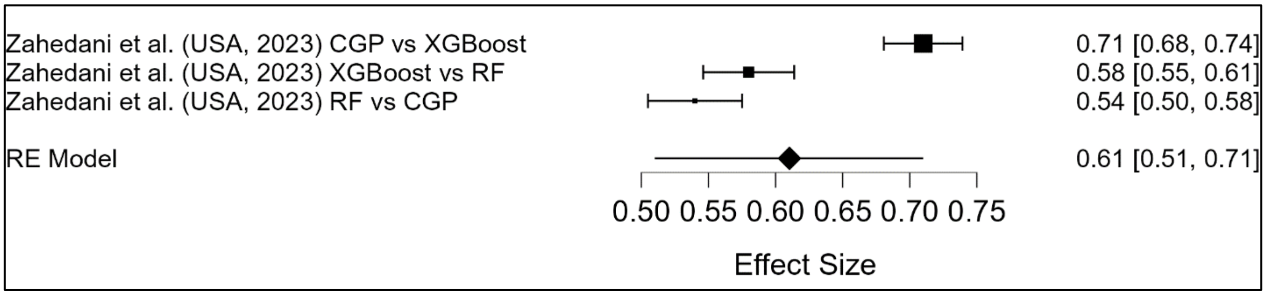
60-minute prediction horizon may be relatively consistent and less influenced by model choice compared to shorter prediction horizons.

Figure 9: Funnel Plot for studies comparing ML models at a PH = 60 mins



For PH = 2 hours, 1 study [62] with 3 different ML models. The omnibus test of model coefficients revealed a statistically significant result ($Q = 140.661$, $df = 1$, $p < .001$), indicating variability in model effects beyond chance. The test of residual heterogeneity also showed significant heterogeneity ($Q = 61.527$, $df = 2$, $p < .001$), suggesting substantial inconsistency among study outcomes. The estimate of residual heterogeneity ($\tau^2 = 0.008$, $\tau = 0.088$) indicated a high degree of variability between studies as shown in the Forest Plot (Figure 10), with an I^2 value of 96.501% and H^2 of 28.582%, classifying the heterogeneity as high. The regression test for funnel plot asymmetry (Egger's test) further confirmed asymmetry ($z = -7.839$, $p < .001$), suggesting potential publication bias or other sources of bias affecting the meta-analysis results.

Figure 10: Forest Plot for comparing ML models at a PH = 2 hours



Studies without a specific predictive horizon were included in the analysis to assess the performance of machine learning models in diabetes management irrespective of time-based forecasting; this includes 3 studies [61, 64, 63] with 13 different ML models. The omnibus test of model coefficients yielded a statistically significant result ($Q = 7.731$, $df = 1$, $p = 0.005$), suggesting that the choice of ML model significantly influenced the outcome variable within the selected studies. Similarly, the test of residual heterogeneity revealed substantial residual heterogeneity across studies ($Q = 898.036$, $df = 54$, $p < 0.001$), indicating significant variability in effect sizes not entirely explained by the ML models. Residual heterogeneity estimates quantified the extent of variability, with an estimated τ^2 of 0.102 and τ of approximately 0.320 as shown in the Forest Plot. The I^2 statistic (93.118%) indicated a high level of heterogeneity among the included studies, suggesting considerable differences in effect sizes across ML models. Additionally, the H^2 value (14.530%) reflected a moderate ratio of true heterogeneity to total observed variability, emphasizing the impact of heterogeneity on the meta-analysis results. Furthermore, regression testing for funnel plot asymmetry using Egger's test did not detect significant asymmetry ($z = -1.326$, $p = 0.185$), suggesting no substantial publication bias among the included studies without a specific predictive horizon. These findings underscore the complexity and variability in ML model performance across studies without a defined prediction horizon, highlighting the need for further investigation into specific model characteristics and contextual factors influencing performance.

5. DISCUSSION

5.1. Key Findings

This study evaluates the effectiveness of various ML models in improving blood glucose management among patients with diabetes mellitus (DM), from a selection of 10 eligible studies. Through a thorough and exhaustive literature searches, we obtained comprehensive evidence to assess the collective predictive capacity of ML models for BG level prediction in diabetes management.

5.2. Included Studies Comparison

Based on these findings, the Random Forest (RF) model consistently demonstrates superior performance compared to other models (SVR, SVM, ARISES) across different studies for a prediction horizon of 15 minutes. Therefore, RF may be considered the best-performing model for predicting BG levels at this specific prediction horizon based on the available data. In our research focusing on a 15-minute prediction horizon for blood glucose management in diabetes, we analyzed multiple studies with Cohen's d values ranging from -2 to -2.7119. These results indicate RF's superior ability to predict BG levels within a short time frame. Overall, our meta-analysis highlights Random Forest as the most effective ML model for BG prediction at a 15-minute horizon in diabetes management.

In the investigation of a 30-minute prediction horizon the results from Rodríguez-Rodríguez *et al.* consistently demonstrated that Random Forest exhibited superior performance compared to Support Vector Machine and Bidirectional Recurrent Neural Network models, with Cohen's d values ranging from -2.6358 to -2.7226. This indicates RF's effectiveness in predicting BG levels within a 30-minute window. Additionally, Zhu *et al.* [57] investigated multiple models using the OhioT1DM dataset, where diverse models such as TCN, CRNN, LSTM, Bi-LSTM, SVR, and ARIMA were compared, showcasing varying performance metrics. Our meta-analysis underscores Random Forest as the most effective ML model for BG prediction at a 30-minute horizon, aligned with findings from Rodríguez-Rodríguez et al.'s studies [55, 56, 58]. In examining the 45-

minute prediction horizon, the meta-analysis revealed several notable findings. Rodríguez-Rodríguez *et al.* [55, 56, 58] demonstrated that Random Forest outperformed Support Vector Regression (SVR) with a Cohen's d of -2.0, indicating substantial predictive capability. Similarly, it was reported RF's superiority over SVM and Bidirectional Recurrent Neural Network (BRNN) models, suggesting RF's efficacy in BG prediction within a 45-minute window. Notably, Zhu *et al.* [60] showcased the effectiveness of the ARISES model with RF, achieving a Cohen's d of 0.6691, suggesting positive performance in BG prediction at this timeframe. Additionally, Zhu *et al.* demonstrated contrasting results with SVM and BRNN models, underscoring the variability in model performance across different studies and datasets. These findings highlight the nuanced effectiveness of ML models in BG management within a 45-minute prediction horizon. Based on the provided data for the 45-minute prediction horizon in blood glucose management, the model with the highest Cohen's d value, indicating the best performance, is the ARISES model with Random Forest (RF) from Zhu *et al.* The Cohen's d value for this model is 0.6691, suggesting that it exhibited the most favorable predictive capability compared to the other models evaluated within this timeframe.

For PH = 60 min Across multiple comparisons, E3NN (OhioT1DM) consistently demonstrated superior performance compared to other models (TCN, CRNN, LSTM, Bi-LSTM, SVR, ARIMA). Negative Cohen's d values (ranging from -0.4562 to -0.8103) indicated that E3NN (OhioT1DM) outperformed these models in various contexts. The effect sizes, though moderate in magnitude, were consistently in favor of E3NN (OhioT1DM). The 95% confidence intervals around Cohen's d estimates provided additional context, indicating the precision and reliability of the effect size measurements. While some intervals were relatively wide due to the small sample size (N = 12), they generally supported the conclusion of E3NN (OhioT1DM) superiority.

In our comparative analysis of predictive models with no specific time frame, the Ensemble machine learning consistently emerged as the most effective model. This model demonstrated a substantial advantage over Linear Regression (LR), Random Forest (RF), and Gradient Boosting (GB), with Cohen's d effect sizes ranging from -0.665 to -0.7335, favoring EML. These results were statistically significant, as evidenced by the non-overlapping confidence intervals. The superior performance of EML underscores its potential as a robust predictive tool and highlights the importance of model selection in optimizing predictive accuracy.

For Zahedani *et al.* [62] study, among evaluated models (CGP, XGBoost, RF), CGP outperformed with the lowest RMSE (13.4), highest correlation (0.71), and lowest percent error (10.3%). These results highlight CGP's suitability for accurate predictions in similar datasets, underscoring the impact of advanced machine learning techniques on predictive accuracy.

5.3.Strengths and Limitations

The study is subject to several limitations. Despite utilizing a comprehensive search strategy, some relevant studies may have been missed. To improve literature retrieval, major medical databases like PubMed, CINAHL, and Embase were included, and baseline models from pertinent studies were screened to minimize omissions. Additionally, significant heterogeneity was observed across all subgroups due to various factors, including different types of diabetes mellitus, machine learning models, data sources, reference indices, and the timing and settings of data collection. To address this, meta-regression analyses were conducted within subgroups to explore potential sources of heterogeneity. Moreover, some studies lacked the required outcome measures or had inconsistent ones, necessitating the use of estimation methods for calculating indicators, which may have introduced some estimation error. However, this error was considered acceptable due to the use of appropriate estimation methods, enriching the study's findings. Nonetheless, future studies should report all relevant outcome measures for comprehensive evaluation.

CHAPTER 5

CONCLUSION AND FUTURE DIRECTIONS

The Internet of Things (IoT) plays a crucial role in remotely monitoring patients, proving to be a significant advantage. Its capabilities become particularly valuable during emergency situations, such as a pandemic, where it can aid in providing timely assistance. Several challenges arise in the context of remote patient monitoring in IoT:

- The transmission of data to the monitoring center introduces the risk of noise contamination, which can compromise the data quality.
- Monitoring generally requires the presence of experts, making it a supervised process that leads to additional costs.
- Live monitoring demands numerous sensors, which increases energy consumption and power leakage during data processing, posing significant challenges.
- Managing multiple users within the IoT ecosystem adds to the overall complexity and management requirements.
- Patient privacy is ultimately at risk as their data is stored in cloud environments, making the protection of patient privacy a critical concern.

The healthcare sector faces numerous challenges, including the diversity of devices, data security risks from breaches, flexible usage, compatibility issues, resource availability, real-time data processing, accurate correlation between measured attributes and disease diagnosis, thorough analysis of personnel vulnerability reports, rapid data growth, maintenance of patient vital records, digital watermarking of patient images, high infrastructure costs, and the lack of standardized protocols, among other obstacles.

Recent advancements in medical devices have introduced numerous benefits but have also heightened security and privacy concerns. As healthcare systems gather, store, and analyze sensitive medical data, there is increasing worry that vulnerabilities in IoMT tools could be exploited. Cybercriminals may use these weaknesses to gain unauthorized access to personal and medical information, jeopardizing hospital security. The interconnected nature of these devices makes them susceptible to attacks, which can result in serious consequences, including physical harm and loss of life. The use of IoT devices introduces common security threats and vulnerabilities, often due to insecure connections via Application Programming Interfaces (APIs). Communication between IoT devices frequently lacks strong security measures. Given that health data includes personally identifiable information, adhering to industry-standard regulations is essential to address data security concerns. Ensuring the integrity and confidentiality of data, as well as mitigating cybersecurity risks in IoT solutions, is critical for success. Incorporating digital security measures into the design of IoT devices from the beginning is vital to protect against data security risks. The complexity of modern IoT devices and the convergence of various technologies often lead to the neglect of security measures during device interconnection and data exchange. There is currently no universal solution to these security challenges, underscoring the importance of implementing risk mitigation protocols before widespread adoption. Besides research and development, medical device manufacturers have critical responsibilities, including designing user-friendly interfaces, performing rigorous verification and validation processes, and offering comprehensive life-cycle services. Production services face challenges such as achieving faster time-to-market, reducing costs, complying with medical regulations, and providing end-to-end product support. Security concerns also hold significant importance and should be addressed during the design phase to realize the anticipated benefits in the market.

The healthcare industry is currently experiencing a notable shift towards digitalization, necessitating a focus on privacy and security measures through case studies and technical tools. Within this context, the IoMT emerges as a key player, harnessing its potential to connect diverse devices and propel the advancements of Industry 4.0. While IoMT brings numerous benefits, it is vital to approach its implementation carefully to mitigate potential challenges that could undermine its positive outcomes. Achieving a delicate equilibrium is crucial as we navigate the ongoing technological revolution in the years to come.

In the future, improved ML models will enhance BG management for patients with DM, reducing adverse BG events and improving quality of life. Future studies should prioritize enhancing ML model performance in longer prediction horizons (e.g., 60 minutes) and address imbalanced CGM data to improve model accuracy. Integrating factors like meal intake and exercise into ML models, optimizing ensemble structures, and validating models in clinical settings are crucial steps for advancing BG management to support real-time feedback and medical intervention. Additionally, leveraging IoT benefits such as continuous monitoring and data integration could further enhance the effectiveness of these ML models in managing blood glucose levels. In summary, as the prediction horizon (PH) extends, the RMSE for blood glucose level prediction models increases, with Random Forest (RF) demonstrating the most robust performance among the ML models assessed. Future research should prioritize improving predictive accuracy and implementing ML models effectively in clinical settings. Additionally, exploring enhanced approaches for integrating data from IoT devices could further optimize glucose management strategies.

REFERENCES

[1]. Z. Mian, K.L. Hermayer, A. Jenkins, Continuous Glucose Monitoring: Review of an Innovation in Diabetes Management, *Am. J. Med. Sci*. 358 (2019) 332-339. https://doi.org/10.1016/j.amjms.2019.07.003.

[2]. National Institute of Diabetes and Digestive and Kidney Diseases, Continuous Glucose Monitoring https://www.niddk.nih.gov/health-information/diabetes/overview/managing-diabetes/continuous-glucose-monitoring (accessed 20 May 2023).

[3]. J. Lin, R. Fu, X. Zhong, *et al.*, Wearable sensors and devices for real-time cardiovascular disease monitoring, Cell Rep. Phys. Sci. 2 (2021) 100541. https://doi.org/10.1016/j.xcrp.2021.100541.

[4]. X. Ma, S. Ahadian, *et al.*, Smart Contact Lenses for Biosensing Applications, Adv. Intell. Syst. 3 (2021) 2000263. https://doi.org/10.1002/aisy.202000263.

[5]. M. M. Mau, S. Sarker, B. S. Terry, Ingestible devices for long-term gastrointestinal residency: a review, *Prog. Biomed. Eng.* 3 (2021) 042001. 10.1088/2516-1091/ac1731.

[6]. M. Zhu, F. Zhu, O. G. Schmidt, Nano energy for miniaturized systems, Nano Materials Sci. 3 (2021) 107-112. https://doi.org/10.1016/j.nanoms.2020.10.001.

[7]. Is. Keshta, A. Odeh, Security, and privacy of electronic health records: Concerns and challenges, Egypt. Inform. J. 22 (2021) 177-183. https://doi.org/10.1016/j.eij.2020.07.003.

[8]. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, *et al.* IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9 edition. Diabetes Res Clin Pract. 2019; 157:107843.

[9]. Rowley WR, Bezold C, Arikan Y, Byrne E, Krohe S. Diabetes 2030: Insights from Yesterday, Today, and Future Trends. Popul Health Manag. 2017; 20(1):6-12. doi:10.1089/pop.2015.0181.

[10]. Chen D, Wang M, Shang X, Liu X, Liu X, Ge T, *et al.* Development and validation of an incidence risk prediction model for early foot ulcer in diabetes based on a high evidence systematic review and meta-analysis. Diabetes Res Clin Pract. 2021; 180:109040.

[11]. Li Y, Su X, Ye Q, Guo X, Xu B, Guan T, et al. The predictive value of diabetic retinopathy on subsequent diabetic nephropathy in patients with type 2 diabetes: a systematic review and meta-analysis of prospective studies. Ren Fail. Dec 2021;43(1):231-240.

[12]. Farooq MS, Riaz S, Tehseen R, Farooq U, Saleem K. Role of Internet of things in diabetes healthcare: Network infrastructure, taxonomy, challenges, and security model. Digit Health. 2023; 9:20552076231179056. doi:10.1177/20552076231179056

[13]. Bellemo V, Lim G, Rim TH, Tan GSW, Cheung CY, Sadda S, et al. Artificial intelligence screening for diabetic retinopathy: the real-world emerging application. Curr Diab Rep. Jul 31, 2019;19(9):72.

[14]. Wu B, Niu Z, Hu F. Study on risk factors of peripheral neuropathy in type 2 diabetes mellitus and establishment of prediction model. Diabetes Metab J. Jul 2021;45(4):526-538.

[15]. Afsaneh, E., Sharifdini, A., Ghazzaghi, H. *et al.* Recent applications of machine learning and deep learning models in the prediction, diagnosis, and management of diabetes: a comprehensive review. Diabetol Metab Syndr. 2022; 14, 196.

[16]. Contreras I, Vehi J. Artificial Intelligence for Diabetes Management and Decision Support: Literature Review. J Med Internet Res. 2018;20(5): e10775. doi:10.2196/10775.

[17]. Liu K, Li L, Ma Y, et al. Machine Learning Models for Blood Glucose Level Prediction in Patients With Diabetes Mellitus: Systematic Review and Network Meta-Analysis. JMIR Med Inform. 2023;11:e47833. doi:10.2196/47833.

[18]. Newark (GLOBE NEWSWIRE), The Brainy Insights, Internet of Medical Things [IoMT] Market (accessed April 18, 2023) https://www.thebrainyinsights.com/report/internet-of-medical-things-iomt-market-13410

[19]. M. Attaran, The impact of 5G on the evolution of intelligent automation and industry digitization, J. Ambient Intell. Human Comput. 14 (2023) 5977–5993. https://doi.org/10.1007/s12652-020-02521-x.

[20]. H. Boudlal, M. Serrhini, A. Tahiri, Towards an SDN/NFV based Network Infrastructure for Hospital Information Systems and Healthcare Services, *2022 5th International Conference on Networking, Information Systems and Security: Envisage Intelligent Systems in 5g//6G-based Interconnected Digital Worlds (NISS)*, Bandung, Indonesia, (2022) 1-5. 10.1109/NISS55057.2022.10085476.

[21]. M. Lehne, J. Sass, A. Essenwanger, *et al.*, Why digital medicine depends on interoperability, *npj Digit. Med.* 2, 79 (2019). https://doi.org/10.1038/s41746-019-0158-1.

[22]. E. Li, J. Clarke, H. Ashrafian, A. Darzi, AL Neves, The Impact of Electronic Health Record Interoperability on Safety and Quality of Care in High-Income Countries: Systematic Review, J. Med. Internet Res. 24(2022) e38144. 10.2196/38144.

[23]. C.N. Vorisek, M. Lehne, S.A.I. Klopfenstein, P.J. Mayer, *et al.*, Fast Healthcare Interoperability Resources (FHIR) for Interoperability in Health Research: Systematic Review, JMIR Med. Inform. 10(2022) e35724. 10.2196/35724.

[24]. R. Dwivedi, D. Mehrotra, S. Chandra, Potential of Internet of Medical Things (IoMT) applications in building a smart healthcare system: A systematic review, 12 (2022) 302-318. https://doi.org/10.1016/j.jobcr.2021.11.010.

[25]. M. Umair, M.A. Cheema, O. Cheema, H. Li, H. Lu, Impact of COVID-19 on IoT Adoption in Healthcare, Smart Homes, Smart Buildings, Smart Cities, Transportation and Industrial IoT, *Sensors* 21 (2021) 3838. https://doi.org/10.3390/s21113838.

[26]. Empowering people to live a healthier day Innovation using Apple technology to support personal health, research, and care July 2022. https://www.apple.com/newsroom/pdfs/Health-Report-July-2022.pdf.

[27]. Philips and Cognizant Collaborate to Introduce Digital Health Solutions to Providers, Researchers and Patients. https://news.cognizant.com/2021-07-08-Philips-and-Cognizant-Collaborate-to-Introduce-Digital-Health-Solutions-to-Providers,-Researchers-and-Patients (accessed Jan, 2023).

[28]. J&J creates new IoT architecture with TCS, https://www.tcs.com/what-we-do/industries/life-sciences/case-study/iot-platform-healthcare-digital-transformation-journey (accessed June 2023).

[29]. A. Bohr, K. Memarzadeh, MedTech sector is now utilizing technologies such as analytics, AI, robotics, and many immersive technologies, among others, Artificial Intelligence in Healthcare (2020) 25-60. 10.1016/B978-0-12-818438-7.00002-2.

[30]. Emerging Startups 2022: Top Wearable Technology Startups, Tracxn, https://tracxn.com/d/emerging-startups/top-wearable-technology-startups-2022 (accessed March 2023).

[31]. Aidmed – System to measure patient vital signs, https://www.aidmed.ai/ (accessed June 2023).

[32]. RELAY, Gate SCIENCE, https://gatescience.com/ (accessed May 2023). **I**

[33]. UNNOMED, Orbicor Technologies, https://www.unnomed.com/ (accessed May 2023).

[34]. EloCare, https://www.elo.care/ (accessed May, 2023).

[35]. Y. Kumar, A. Koul, R. Singla, *et al.*, Artificial intelligence in disease diagnosis: a systematic literature review, synthesizing framework and future research agenda, J. Ambient Intell. Human Comput. 14 (2023) 8459–8486. https://doi.org/10.1007/s12652-021-03612-z.

[36]. M. Javaid, A. Haleem, R. P. Singh, R. Suman, S. Rab, Significance of machine learning in healthcare: Features, pillars and applications, *Int. J. Intell. Net. 3 (2022) 58-73* https://doi.org/10.1016/j.ijin.2022.05.002.

[37]. A. Ometov, V. Shubina, *et al.*, A Survey on Wearable Technology: History, State-of-the-Art and Current Challenges, 193 (2021) 108074 https://doi.org/10.1016/j.comnet.2021.108074.

[38]. A. A. Smith, R. Li, Z. T. H. Tse, Reshaping healthcare with wearable biosensors, Sci. Rep. 13 (2023) 4998 https://doi.org/10.1038/s41598-022-26951-z.

[39]. J. V. Vaghasiya, C. C. Mayorga-Martinez, M. Pumera, Wearable sensors for telehealth based on emerging materials and nanoarchitectonics. npj Flex Electron 7,26 (2023). https://doi.org/10.1038/s41528-023-00261-4.

[40]. H. Habehh, S. Gohel, Machine Learning in Healthcare, Curr Genomics. 22 (2021) 291-300 10.2174/1389202922666210705124359.

[41]. J. N. Acosta, G. J. Falcone, P. Rajpurkar, *et al.*, Multimodal biomedical AI, Nat. Med. 28 (2022) 1773–1784. https://doi.org/10.1038/s41591-022-01981-2.

[42]. A. Kline, H. Wang, Y. Li, et al., Multimodal machine learning in precision health: A scoping review, npj Digit. Med. **5** (2022) 171. https://doi.org/10.1038/s41746-022-00712-8.

[43]. J. Lipkova, R. J. Chen, *et al.*, Artificial intelligence for multimodal data integration in oncology, Cancer Cell 40 (2022) 1095-1110. https://doi.org/10.1016/j.ccell.2022.09.012.

[44]. S. El-Sappagh, J. M. Alonso, S. M. R. Islam, *et al.*, A multilayer multimodal detection and prediction model based on explainable artificial intelligence for Alzheimer's disease, Sci. Rep. 11 (2021) 2660. https://doi.org/10.1038/s41598-021-82098-3.

[45]. S. Qiu, M. I. Miller, P. S. Joshi, *et al.*, Multimodal deep learning for Alzheimer's disease dementia assessment, Nat. Commun. 13 (2022) 3404. 10.1038/s41467-022-31037-5.

[46]. F. Mohsen, H. Ali, E. N. Hajj, *et al.*, Artificial intelligence-based methods for fusion of electronic health records and imaging data, Sci. Rep. 12 (2022) 17981. https://doi.org/10.1038/s41598-022-22514-4.

[47]. S. Liu, X. Wang, Y. Hou, *et al.*, Multimodal Data Matters: Language Model Pre-Training Over Structured and Unstructured Electronic Health Records, IEEE J. Biomed. Health Inform. 27 (2023) 504-514. 10.1109/JBHI.2022.3217810.

[48]. S. C. Huang, A. Pareek, S, Seyyedi, I. Banerjee, M. P. Lungren, Fusion of medical imaging and electronic health records using deep learning: a systematic review and implementation guidelines. npj Digit. Med. 3 (2020) 136. 10.1038/s41746-020-00341-z.

[49]. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. PLoS Med. 2009;6(7): e1000097.

[50]. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009; 339: b2700.

[51]. Huang X, Lin J, Demner-Fushman D. Evaluation of PICO as a knowledge representation for clinical questions. AMIA Annu Symp Proc. 2006; 359-363.

[52]. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529-536.

[53]. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-560.

[54]. White I. Multivariate random-effects meta-regression: updates to Mvmeta. Stata J. 2011;11(2):255-270.

[55]. Rodríguez-Rodríguez I, Campo-Valera M, Rodríguez JV, Frisa-Rubio A. Constrained IoT-Based Machine Learning for Accurate Glycemia Forecasting in Type 1 Diabetes Patients. Sensors (Basel). 2023; 23(7):3665. doi:10.3390/s23073665.

[56]. Rodríguez-Rodríguez I, Campo-Valera M, *et al*. IoMT innovations in diabetes management: Predictive models using wearable data. Expert Syst Appl. 2023;238(Part C) https://doi.org/10.1016/j.eswa.2023.121994.

[57]. Zhu T, Kuang L, Daniels J, *et al*. IoMT-Enabled Real-Time Blood Glucose Prediction with Deep Learning and Edge Computing. IEEE Internet of Things Journal. 2023; 10(5):3706-3719. doi: 10.1109/JIOT.2022.3143375.

[58]. Rodríguez-Rodríguez I, Campo-Valera M, *et al.* Forecasting glycaemia for type 1 diabetes mellitus patients by means of IoMT devices, Internet of Things 2023;24: 100945. https://doi.org/10.1016/j.iot.2023.100945.

[59]. Wolff MK, Schaathun HG *et al*. Mobile Software Development Kit for Real Time Multivariate Blood Glucose Prediction. IEEE Access, 2024; 12: 5910-5919. doi: 10.1109/ACCESS.2024.3349496.

[60]. Zhu T, Uduku C, Li K, Herrero P, Oliver N, Georgiou P. Enhancing self-management in type 1 diabetes with wearables and deep learning. NPJ Digit Med. 2022;5(1):78. doi:10.1038/s41746-022-00626-5.

[61]. Tripathi AK, Mishra S, Vasudevan SK. Smart Diabetic Prediction: An Intelligent IoT-Based Diabetic Monitoring System with Stacked Spatio Temporal Features-Based Multiscale Dilated Deep Temporal Convolutional Network. Sens Imaging 2024; 25(2). https://doi.org/10.1007/s11220-023-00446-1.

[62]. Zahedani AD, McLaughlin T, Veluvali A. *et al*. Digital health application integrating wearable data and behavioral patterns improves metabolic health. npj Digit. Med. 2023; 216. https://doi.org/10.1038/s41746-023-00956-y.

[63]. Azbeg K, Boudhane M, Ouchetto O. *et al.* Diabetes emergency cases identification based on a statistical predictive model. J Big Data 2022; 31 (9). https://doi.org/10.1186/s40537-022-00582-7.

[64]. Patel MS, Polsky D, Small DS, *et al.* Predicting changes in glycemic control among adults with prediabetes from activity patterns collected by wearable devices. NPJ Digit Med. 2021;4(1):172. doi:10.1038/s41746-021-00541-1.

[65]. Li K, Liu C, Zhu T, *et al.* GluNet: A deep learning framework for accurate glucose forecasting. IEEE J. Biomed. Health Inform. 2020; 24(2): 414-423.

[66]. Li K, Daniels J, *et al*. Convolutional recurrent neural networks for glucose prediction. IEEE J. Biomed. Health Inform. 2020; 24(2): 603–613.

[67]. Martinsson J, Schliep A, Eliasson B, Mogren O. Blood glucose prediction with variance estimation using recurrent neural networks. J. Healthcare Informat. Res. 2020; 4(1):1-18.

[68]. Mohebbi A *et al.* Short term blood glucose prediction based on continuous glucose monitoring data. Proc. 42nd Annu. IEEE Int. Conf. Eng. Med. Biol. Soc. 2020; 5140-5145.

[69]. Georga EI et al. Multivariate prediction of subcutaneous glucose concentration in type 1 diabetes patients based on support vector regression. IEEE J. Biomed. Health Inform. 2013; 17(1): 71-81.

[70]. Plis K, Bunescu R, Marling C, et al. A machine learning approach to predicting blood glucose levels for diabetes management. Proc. Workshops 28th AAAI Conf. Artif. Intell. 2014; 35-39.

List of Publications

In Communication:

Reference#: BMS-MC-2024-63
Submission Title: Exploring Phytochemicals as Potential Inhibitors of Cancer Cell Metabolic Pathways: A Computational Study
Dear Dr. Hasija,
This is to update you about your manuscript titled "Exploring Phytochemicals as Potential Inhibitors of Cancer Cell Metabolic Pathways: A Computational Study" submitted to the journal "Medicinal Chemistry". Your manuscript has been passed through Initial scrutiny successfully. Currently the manuscript is at the peer review stage.

You may track all the stages of publication online until your manuscript is finalized and is ready for publication. Log onto JMS https://bentham.manuscriptpoint.com and click the article reference number from the available list of your submitted manuscripts to view the detailed status at every stage of the peer-review process and editorial decision.

Paper 1; Journal: Medicinal Chemistry, Publisher: Bentham Science; IF 2.3

Re: "Predicting Blood Glucose Using Machine Learning and IoT Data: A Meta-Analysis"
Full author list: Yagyesh Kapoor; Yasha Hasija

Dear Mr. Kapoor,

We have just received the submission entitled: "Predicting Blood Glucose Using Machine Learning and IoT Data: A Meta-Analysis" for possible publication in International Journal of Diabetes in Developing Countries, and you are listed as one of the co-authors.

The manuscript has been submitted to the journal by Dr. Prof. yasha hasija who will be able to track the status of the paper through his/her login.

Paper 2; Journal: Journal of Diabetes in Developing Countries, Publisher: Springer, IF: 0.9

Dear Dr Hasija,

Your manuscript entitled "Advancements, Challenges, and Future Directions in Data Fusion and Management for the Internet of Medical Things (IoMT): Transforming Healthcare in the Digital Era" has been successfully submitted online and will shortly be given full consideration for publication in Transactions on Emerging Telecommunications Technologies.

Your manuscript number is ETT-24-1078. Please mention this number in all future correspondence regarding this submission.

You can view the status of your manuscript at any time by checking your Author Center after logging into https://mc.manuscriptcentral.com/ett. If you have difficulty using this site, please click the 'Get Help Now' link at the top right corner of the site.

You paper will now be assigned to an Executive Editor. Prior to this, however, the EiC will check that all authors and emails are correctly registered in the system, as well as that the paper is of sufficient quality and aligned with the transaction's objectives. Finally, ETT uses the services of iThenticate.

This journal offers a number of license options for published papers; information about this is available here: https://authorservices.wiley.com/author-resources/Journal-Authors/licensing/index.html. The submitting author has confirmed that all co-authors have the necessary rights to grant in the submission, including in light of each co-author's funder policies. If any author's funder has a policy that restricts which kinds of license they can sign, for example if the funder is a member of Coalition S, please make sure the submitting author is aware.

Paper 3; Journal: Transactions on Emerging Telecommunications Technologies, Publisher: Wiley, IF: 3.6

DELHI TECHNOLOGICAL UNIVERSITY

(Formerly Delhi College of Engineering)
Shahbad Daulatpur, Main Bawana Road, Delhi-42

PLAGIARISM VERIFICATION

Title of the Thesis **"Predicting Blood Glucose Levels with Machine Learning and IoT: A Meta-Analysis and Future Dins in IoMT Data Fusion for Healthcare Transformation"** Total Pages 46 Name of the Scholar Yagyesh Kapoor

Supervisor

Prof. Yasha Hasija

Department of Biotechnology

This is to report that the above thesis was scanned for similarity detection. Process and outcome are given below:

Software used: **Turnitin** Similarity Index: 8%, Total Word Count: 10,282

Date:

Candidate's Signature **Signature of Supervisor**

Similarity Report

PAPER NAME

Thesis.docx

WORD COUNT	CHARACTER COUNT
10282 Words	**62965 Characters**
PAGE COUNT	FILE SIZE
46 Pages	**8.4MB**
SUBMISSION DATE	REPORT DATE
May 28, 2024 3:17 PM GMT+5:30	**May 28, 2024 3:19 PM GMT+5:30**

8% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

- 7% Internet database
- 3% Publications database
- Crossref database
- Crossref Posted Content database
- 2% Submitted Works database

Excluded from Similarity Report

- Bibliographic material
- Cited material
- Small Matches (Less then 10 words)

turnitin Page 2 of 48 - AI Writing Overview Submission ID trn:oid:::27535:60171437

How much of this submission has been generated by AI?

***3%**

of qualifying text in this submission has been determined to be generated by AI.

* Low scores have a higher likelihood of false positives.

Caution: Percentage may not indicate academic misconduct. Review required.

It is essential to understand the limitations of AI detection before making decisions about a student's work. We encourage you to learn more about Turnitin's AI detection capabilities before using the tool.

Yagyesh Kapoor
Flat 220, Navjeevan Apartments, Dwarka Sector-
1A NewDelhi-110045

+91-9910055273
yagyeshkapoor@gmail.com
www.linkedin.com/in/yagyesh-kapoor-
9757b5134

OBJECTIVE

To make optimum utilization of my knowledge and skills, utilize opportunities for professional growth and to contribute in the best possible way for the betterment of the organization and self.

ACADEMIC QUALIFICATIONS

YEAR	PROGRAMME	UNIVERSITY/BOARD	MARKS OBTAINED
2022-2024	M.Tech Bioinformatics	Delhi TechnologicalUniversity	9.0 (I Semester) 9.24(II Semester)
2016-2020	B. Pharmacy	Apeejay Stya University	94.65%
2015-2016	Higher Secondary Certificate	Jindal Public School/C.B.S.E	73%
2013-2014	Secondary School Certificate	Jindal Public School/C.B.S.E	9.0 (C.G.P.A)

WORK EXPERIENCE

1. 1 Year Internship at Stryker Global Technology Center R&D.
2. Industrial training at **Sun Pharmaceutical Industries Ltd.** in Product Development Research Department of Research & Development Centre; Gurugram, Haryana.
3. Completed 150 hours of Pharmacy Practice School as a part of curriculum in Final year and worked as a trainee in various hospitals and pharmacies.
4. Worked as a Pharmacist at the Healing Touch Eye and Maternity Centre (Vikas Pharmacy), Vikas Puri, New Delhi.

AWARDS & HONORS

1. Recipient of **Dr. Stya Paul Award for Human Values** by Apeejay Stya University for the academic year 2019-2020 for imbibing core human values and diligently practicing them in life through action, behavior, and work.
2. Qualified Graduate Aptitude Test in Engineering (GATE) – Life Science 2022.

PROJECT WORK

1. Structure Based Multitargeted Molecular Docking Analysis of Selected Furanocoumarins against Cancer Cell Metabolic Pathways.
2. Study of drugs that are under clinical investigation for various cancer cell metabolic checkpoints.

PUBLICATIONS

Review/General Articles

1. **Kapoor Y**, Kumar K. Structural and clinical impact of anti-allergy agents: An Overview. Bioorganic Chemistry 94 (2020). https://doi.org/10.1016/j.bioorg.2019.103351(**IMPACT FACTOR 5.3**)

2. **Kapoor Y**, Kumar K. Quantitative Structure Activity Relationship in Drug Design: An Overview. SF J Pharm Anal Chem. 2019; 2(2): 1017. https://scienceforecastoa.com/Articles/SJPAC-V2-E2-1017.pdf

3. **Yagyesh K** and Kapil K. Drug Design: An Overview. Med & Analy Chem Int J 2019, 3(2): 000136. https://medwinpublishers.com/MACIJ/MACIJ16000136.pdf

4. Kaur R, **Kapoor Y**, Manjal SK, Rawal RK, Kumar K. Diversity-Oriented Synthetic Approaches for Furoindoline: A Review. Curr Org Synth 2019; 16(0): 1-27.http://www.eurekaselect.com/node/171098 (**IMPACT FACTOR 2.157**)

5. **Kapoor Y**, Kumar K. Medicinal and Chemical Perspectives of Nitric Oxide: An Overview. SF J. Pharm. Anal. Chem. 2019; 2(1): 1015. https://scienceforecastoa.com/Articles/SJPAC-V2-E1-1015.pdf

6. **Kapoor Y**, Dubey S, Kar S, Kumar K. CAR T Cell: A Novel Treatment Regime for Cancer. SF J. Pharm. Anal. Chem. 2018; 1(1): 1008. https://scienceforecastoa.com/Articles/SJPAC-V1-E1-1008.pdf

7. **Yagyesh K**, Fatima SN and Kapil K. Synthesis and Structure Activity Relationship of Thiazolyl Hydrazones as Monoamine Oxidase Inhibitors: An Overview. Curr. Trends Med. Chem. 2018; 1(1): 1003. http://smjournals.com/medicinal-chemistry/download.php?file=fulltext/ctmc-v1-1003.pdf

8. **Kapoor Y**, Kumar K. Morita-Baylis-Hillman reaction: scope and significance. J. Pharm. Chem.Chem. Sci. 2018; 2(1):11-20. http://www.alliedacademies.org/articles/moritabaylishillman-reaction-scope-and- significance.pdf

9. Kaur R, Rani V, Abbot V, **Kapoor Y**, Konar D, Kumar K. Recent synthetic and medicinal perspectives of pyrroles: An overview. J. Pharm. Chem. Chem. Sci. 2017; 1(1):17-32. http://www.alliedacademies.org/articles/recent-synthetic-and-medicinal-perspectives-of-pyrroles-an-overview-9135.html

Seminar/Abstract

1. **Kapoor Y**, Kumar K (2018) Nanogel Based Delivery in CAR T cell Therapy for Treatment Regime of Cancer. National Seminar on Nanomedicine and Nanotechnology in Heath Care, Apeejay Stya University, Gurgaon.

EXTRA-CURRICULAR ACTIVITIES

1. Participated & Volunteered in Blood Donation Camp organized by Mission Jan Jagriti Blood Bank held on 03-01-2019 at Janakpuri, New Delhi.
2. Volunteer, S M Lok Kalyan India Foundation, New Delhi for a period of 45 days from 1 June – 15July, 2018.
3. Actively Volunteered during 11^{th} walk for life – stride against cancer-2018 at Raj Path, New Delhi.
4. Participated in Pharma Quiz organized during ELAAN tech fest- 2017 & 2018 at ApeejayStya University and secured **2^{nd} position**.
5. Volunteer, 2-Day: Health camp, organized by Apeejay Stya University during "National Pharmacy Week". 19 – 25 November, 2017.
6. Volunteer, Rotaract Club of Apeejay Stya University (RCASU) Sep. 2016 – Mar. 2017.
   - Delivered speech on the topic **"Dementia"** at mental health camp organized by RCASU.
7. Participated in Poster making and Tree plantation during National Pharmacy Week-2016.

SKILLS

- Intermediate Knowledge of Software includes: ChemDraw, Chimera, PyRx, LigPlus, SciFinder, Avogadro, AutoDock Vina
- Knowledge of Tablet Punching Machine, DT & Dissolution Apparatus, Tablet Coating Machine.
- Pharmaceutical Microbiology & Biochemistry
- Python (Beginners)
- Data Science for Biologist
- Drug Designing and Synthesis
- Pharmacovigilance
- Bioinformatics
- Scientific content writing
- RNA Biology
- Techniques – HPLC, Electrophoresis, Bacteria Culture/Media, DNA sequencing, Gene Cloning etc.
- Novel Drug Delivery System

INTERESTS

Data Science, Artificial Intelligence, Healthcare, Drug Designing

I hereby declare that all the information furnished above is true, complete and correct to the best of my knowledge.