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Quantum machine learning in diabetes and metabolism: Applications and translational challenges

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ABSTRACT

Background and objective: Quantum machine learning is emerging as a promising extension of artificial intelligence, with potential advantages over classical approaches in handling complex biomedical data. This review aims to evaluate quantum machine learning applications in the detection, prediction, and personalized management of metabolic syndrome and type 2 diabetes mellitus.
Methods: We reviewed literature published between 1994 and 6 July 2026, with peer-reviewed journal articles and conference proceedings as the principal evidence base, complemented by selected preprints and technical sources. Quantum machine learning approaches, including quantum support vector machines, quantum neural networks, and quantum echo state networks, were classified and compared with classical counterparts across obesity and early metabolic dysregulation, diabetes diagnosis and glycemic management, and chronic complications.
Results: Quantum machine learning and hybrid quantum-classical systems demonstrated potential benefits in small-sample and noisy environments typical of wearable and biomedical sensor data. Reported performance gains included improvements in accuracy, robustness, and scalability, though interpretability and reproducibility remain challenges. Hardware limitations associated with noisy intermediate-scale quantum devices, data encoding, and privacy considerations emerged as key barriers to clinical translation.
Conclusions: Preliminary studies highlight the promise of quantum machine learning for predictive and personalized management of metabolic syndrome and type 2 diabetes mellitus. However, successful clinical adoption will require robust validation pipelines, regulatory sandboxes, and harmonized compliance frameworks. Domain-specific evaluation metrics and transparent conformity assessments are essential to ensure trustworthy, scalable, and equitable deployment. A staged roadmap is proposed to bridge experimental progress with ethical and regulatory readiness.

1. Introduction

Quantum Machine Learning (QML) is an emerging interdisciplinary field that merges the computational power of quantum mechanics with machine learning techniques to address problems that are computationally intractable for classical systems [1,2]. As global data production continues to rise exponentially (particularly in areas such as genomics, medical imaging, electronic health records, and wearable sensors) the demand for more powerful data analysis tools is rapidly growing [3]. While classical machine learning (ML) has enabled major advances in pattern recognition and predictive modeling [4], the increasing volume and complexity of biomedical data are pushing conventional methods to their limits. Quantum computing offers a potential leap forward by processing information using qubits, which can exist in superposition and entanglement states. These properties allow quantum systems to perform certain types of computations much faster than classical

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computers [5]. In recent years, QML algorithms such as quantum support vector machines, quantum neural networks, and variational quantum classifiers have shown promise in accelerating data analysis and optimization tasks [6–8]. Within this context, exploring the role of QML in complex, multifactorial diseases such as Metabolic Syndrome (MetS) and Type 2 Diabetes Mellitus (T2DM) is particularly timely and relevant. These conditions require the integration of heterogeneous, high-dimensional, and longitudinal biomedical data, creating potential opportunities for QML in diagnosis, risk stratification, and personalized disease management.

1.1. QML applications in metabolic syndrome and related chronic diseases

MetS and T2DM represent two of the most pressing global health challenges of the 21st century. According to the World Health Organization and the International Diabetes Federation, >1 billion people worldwide are estimated to be affected by MetS, while approximately 830 million adults were living with diabetes in 2022 [9]. These conditions not only contribute significantly to morbidity and mortality, but also impose a substantial economic burden on healthcare systems. Metabolic Syndrome is defined as a cluster of interrelated metabolic abnormalities, including abdominal obesity, insulin resistance, elevated blood pressure, high triglyceride levels, and low HDL cholesterol [10]. While each component is a risk factor on its own, their combination exponentially increases the likelihood of developing T2D and cardiovascular disease. Once established, T2D leads to chronic hyperglycemia, triggering long-term complications such as retinopathy, nephropathy, neuropathy, cardiomyopathy, and diabetic foot ulcers, often progressing silently until irreversible damage occurs [11]. The combination of the increasing burden of metabolic disorders and the growing complexity of biomedical data makes a focused assessment of QML in metabolic medicine both timely and clinically relevant.

Given the multifactorial nature of these conditions, their prevention and management rely on the integration and analysis of heterogeneous, high-dimensional, and longitudinal data, including genetic variants, transcriptomic and metabolomic profiles, clinical parameters, and real-time physiological signals from wearable devices such as continuous glucose monitors (CGMs). Traditional machine learning techniques have shown promise in analyzing this complexity but face well-recognized limitations when applied to real-world metabolic data, including susceptibility to overfitting in small cohorts, limited robustness to noise and missing values, reliance on extensive feature engineering, and difficulty in capturing high-order nonlinear interactions among heterogeneous variables [12,13]. These constraints are especially critical in early-stage metabolic dysregulation and personalized risk stratification, where data scarcity and variability are structural rather than incidental.

In this context, Quantum Machine Learning (QML) is explored not as a general replacement for classical artificial intelligence, but as a problem-driven methodological extension aligned with the intrinsic computational challenges of metabolic disorders. By encoding classical data into high-dimensional quantum feature spaces, QML models may offer enhanced representational capacity for complex correlations, nonlinear dynamics, and temporal dependencies under conditions where classical models often require extensive feature engineering or suffer from instability. QML exploits principles of quantum computing, such as superposition and entanglement, to enable such representations, potentially improving robustness and expressivity in noisy and heterogeneous biomedical datasets [1,2]. However, these theoretical properties do not establish a general quantum advantage, which must instead be demonstrated through task-specific, reproducible comparisons with well-optimized classical models.

Quantum Support Vector Machines (QSVMs), for example, have shown competitive classification performance in selected studies involving genetic and clinical data, particularly in constrained experimental settings [14]. Quantum Neural Networks (QNNs) and hybrid quantum-classical architectures are being explored for personalized medicine, enabling treatment strategies tailored to individual biological and lifestyle profiles [15,16]. QML is also being explored in early detection and complication forecasting: while classical models have been applied to predict glycemic excursions using CGM data [17], quantum-enhanced nearest-neighbor and kernel-based algorithms may further improve accuracy and stability when dealing with complex temporal patterns and noisy biosignals [18].

Within appropriately validated hybrid quantum–classical pipelines, quantum-enhanced approaches may contribute to more adaptive and personalized strategies for metabolic disease modeling and risk assessment.

Taken together, these emerging applications highlight the growing interest in QML for metabolic health, while also showing that the literature has so far developed mainly around individual applications, such as obesity prediction, diabetes classification, glycemic monitoring, and complication detection. Previous reviews by Ullah et al. [19] and Maheshwari et al. [20] examined QML broadly across healthcare and biomedical applications. However, neither review was specifically designed to synthesize evidence across the metabolic-disease continuum. The present review addresses this gap through a focused assessment of three predefined clinical domains: (i) obesity and early metabolic dysregulation, (ii) T2DM diagnosis and glycemic management, and (iii) diabetes- and metabolic-disease-associated complications. It also extends previous descriptive surveys by providing a five-stage translational roadmap linking methodological validation, hardware readiness, regulatory requirements, prospective clinical evaluation, and post-deployment monitoring.

Although much of the available evidence concerns T2DM, obesity, and related complications, these conditions are clinically interconnected within the broader cardiometabolic continuum addressed in this review, with MetS serving as an organizing framework.

1.2. Research objectives

The aim of this review is to systematically explore the emerging role of QML in the diagnosis, prediction, and personalized management of MetS and T2DM. Given the increasing complexity of biomedical data and the growing prevalence of metabolic disorders worldwide, there is an urgent need for computational models capable of handling heterogeneous, high-dimensional, and temporally dynamic datasets.

This work specifically focuses on evaluating QML's contributions across three interconnected domains:

- Early metabolic dysregulation and obesity monitoring, where QML models can support anticipatory prevention strategies;
- Glycemic control and T2DM management, through patient stratification and dynamic blood glucose forecasting;
- Prediction and risk stratification of chronic complications, such as neuropathy and cardiovascular disease.

In addressing these topics, the review also considers key technical, clinical, and ethical challenges, including the limitations of current quantum hardware and the implications of integrating QML into digital healthcare systems.

To guide this exploration, the review addresses the following research questions:

- How can Quantum Machine Learning enhance the diagnosis, prediction, and personalized treatment of metabolic disorders, specifically Type 2 Diabetes and its systemic complications?
- What are the primary limitations (technical, clinical, and ethical) affecting the adoption of QML in healthcare, and how might these be addressed to enable real-world deployment?

By answering these questions, this review seeks to define the current

capabilities of QML, assess its potential to transform metabolic medicine, and outline future directions for research and clinical translation.

2. Methods

2.1. Review design and search strategy

This study was conducted as a structured literature review with a multivocal component to examine the applications, methodological characteristics, limitations, and translational challenges of quantum machine learning in diabetes and metabolic disorders. Peer-reviewed journal articles and conference proceedings constituted the principal evidence base, while selected preprints and technical sources were considered to capture emerging developments in this rapidly evolving field. The inclusion of gray literature was informed by the general methodological principles proposed by Garousi et al. [21], while Soldani et al. [22] was considered as an example of the structured use of gray-literature sources in an emerging technological domain. The 1994 lower bound was selected to capture the foundational development of quantum algorithms that later informed QML, beginning with Shor's algorithm. It does not imply that biomedical QML applications were already available at that time, as application-oriented QML research emerged mainly in the following decades.

The literature search covered publications from 1994 to 6 July 2026 and was conducted using PubMed, Scopus, IEEE Xplore, and Google Scholar. Reference lists of relevant primary studies and previous reviews were also examined to identify additional publications, particularly those addressing specific metabolic and diabetes-associated complications.

The search strategy combined terms related to quantum machine learning with terms related to diabetes, metabolic disorders, and their clinically relevant complications.

In PubMed, the following search string was used:

"("quantum machine learning"[Title/Abstract] OR "quantum neural network"[Title/Abstract] OR "quantum neural networks"[Title/Abstract] OR "quantum support vector machine"[Title/Abstract] OR "quantum support vector machines"[Title/Abstract] OR "quantum support vector classifier"[Title/Abstract] OR "variational quantum classifier"[Title/Abstract] OR "quantum kernel"[Title/Abstract] OR "quantum kernels"[Title/Abstract] OR "quantum deep learning"[Title/Abstract] OR "hybrid quantum-classical"[Title/Abstract] OR "quantum-enhanced machine learning"[Title/Abstract] OR "quantum-inspired machine learning"[Title/Abstract])

AND

(diabetes[Title/Abstract] OR "type 2 diabetes"[Title/Abstract] OR "diabetes mellitus"[Title/Abstract] OR "metabolic syndrome"[Title/Abstract] OR obesity[Title/Abstract] OR glycemic[Title/Abstract] OR glucose[Title/Abstract] OR HbA1c[Title/Abstract] OR "diabetic retinopathy"[Title/Abstract] OR "diabetic foot"[Title/Abstract] OR nephropathy[Title/Abstract] OR neuropathy[Title/Abstract] OR cardiovascular[Title/Abstract] OR "heart disease"[Title/Abstract] OR "chronic kidney disease"[Title/Abstract] OR Alzheimer[Title/Abstract] OR dementia[Title/Abstract])

AND

("1994/01/01"[Date - Publication]: "2026/07/06"[Date - Publication])."

The PubMed search retrieved 27 records.

In Scopus, the search was conducted in the article title, abstract, and keyword fields using the following two-field strategy:

"TITLE-ABS-KEY("quantum machine learning")

AND

TITLE-ABS-KEY(diabetes OR "type 2 diabetes" OR "diabetes mellitus" OR "metabolic syndrome" OR obesity)." The Scopus search retrieved 39 records.

In IEEE Xplore, the search strategy was expanded to improve sensitivity by including both general and algorithm-specific quantum machine-learning terminology, together with additional diabetes- and metabolism-related terms. The following query was used:

"("All Metadata":"quantum machine learning" OR "All Metadata":"quantum neural network" OR "All Metadata":"quantum support vector machine" OR "All Metadata":"quantum kernel" OR "All Metadata":"variational quantum classifier" OR "All Metadata":"hybrid quantum-classical")

AND

("All Metadata":diabetes OR "All Metadata":"type 2 diabetes" OR "All Metadata":"diabetes mellitus" OR "All Metadata":"diabetic retinopathy" OR "All Metadata":"metabolic syndrome" OR "All Metadata":obesity OR "All Metadata":"insulin resistance" OR "All Metadata":glycemic)."

The IEEE Xplore search retrieved 24 records.

Google Scholar was searched using:

""quantum machine learning" AND (diabetes OR "type 2 diabetes" OR "metabolic syndrome" OR obesity)."

Google Scholar returned approximately 1800 results; the first 100 records ranked by relevance were screened.Reference-list screening was also used to identify potentially relevant publications addressing specific clinical complications, including diabetic retinopathy, diabetic foot disease, nephropathy, neuropathy, cardiovascular disease, chronic kidney disease, Alzheimer disease, dementia, and cognitive impairment. Any additional records identified during the final search update were assessed using the same eligibility criteria and incorporated into the study-selection process.

The study-selection process followed a structured sequence of record identification, duplicate removal, title and abstract screening, and full-text assessment. Methodological quality was evaluated separately using the qualitative, domain-based approach described in Section 2.3.

No review protocol was prospectively registered. The absence of protocol registration is acknowledged as a methodological limitation.

2.2. Eligibility criteria, study selection, and data extraction

Studies were considered eligible when they investigated a quantum machine-learning, hybrid quantum-classical, or explicitly quantum-inspired machine-learning approach applied to diabetes, Type 2 Diabetes Mellitus, metabolic syndrome, obesity, glycemic prediction or management, or a clinically relevant metabolic or diabetes-associated complication.

Eligible studies were required to describe an evaluated biomedical, clinical, or healthcare-related application and to provide sufficient information on the dataset, model, implementation, validation procedure, or performance outcomes to permit interpretation of the findings. English-language publications issued between 1994 and 6 July 2026 were considered.

Peer-reviewed original research articles and conference proceedings constituted the principal evidence base. Preprints were not excluded categorically because some emerging QML applications may initially be available only before formal publication. Their publication status was considered during interpretation, and findings that had not undergone peer review were interpreted with greater caution.

When multiple versions of the same work were identified, including a preprint, conference contribution, repository version, or journal publication, the most complete version was preferentially retained. Multiple versions of the same investigation were not automatically counted as separate studies.

Technical sources such as GitHub repositories, Kaggle notebooks, dataset pages, software documentation, and institutional reports were used when relevant to clarify data provenance, implementation details, code availability, or technical developments. These sources were not treated as equivalent to peer-reviewed clinical evidence and were not automatically counted as independent primary studies.

Studies were excluded when they:

1. did not contain a machine-learning component;
2. were unrelated to metabolic disease or its clinically relevant complications;

3. lacked sufficient methodological, validation, or performance information;
4. duplicated a more complete version of the same work.

Reviews, books, clinical guidelines, policy documents, general methodological papers, dataset descriptions, and software documentation were used for background or contextual discussion but were not counted as original QML application studies.

All identified records were considered for duplicate removal before screening. Records were then evaluated sequentially by title, abstract, and full text. Potentially relevant publications identified through reference-list screening were assessed using the same eligibility criteria. Fig. 1 presents the PRISMA 2020 flow diagram describing record identification, duplicate removal, screening, full-text eligibility assessment, and final study inclusion. The completed PRISMA 2020 reporting checklist is provided as Supplementary File S1.

After duplicate removal and application of the eligibility criteria, 33 unique original QML application studies were included in the narrative synthesis.

For each included study, information was extracted on the clinical domain, dataset source, sample size when reported, QML method, classical comparator, validation procedure, performance metrics, implementation platform, use of a simulator or real quantum hardware, and principal findings. The extracted information was subsequently organized according to clinical domain and methodological characteristics to support the narrative synthesis. The studies were grouped into the following principal clinical domains: obesity, metabolic syndrome, and early metabolic dysregulation; diabetes diagnosis and classification; glycemic prediction, monitoring, and personalized management; and metabolic or diabetes-associated complications. Because of substantial heterogeneity in the datasets, clinical populations, QML architectures, comparator models, validation strategies, and reported outcomes, the evidence was synthesized narratively rather than through quantitative meta-analysis. Quantitative pooling was not considered methodologically appropriate because the included studies reported heterogeneous outcomes and performance measures, including accuracy, AUC, precision, recall, F1-score, sensitivity, specificity, and computational metrics, often derived from different datasets, validation procedures, and experimental settings. These results were therefore summarized descriptively and interpreted within the methodological context of each study.

2.3. *Methodological quality and reference verification*

The methodological quality of the included studies was appraised qualitatively during data extraction and narrative synthesis. The appraisal domains were informed by methodological considerations reported in previous QML reviews, including Ullah et al. [19]. No numerical point-based or aggregate quality score was calculated. No inter-rater agreement assessment was performed; the use of a single reviewer is acknowledged as a methodological limitation.

Particular attention was given to:

1. dataset size and representativeness;
2. transparency of preprocessing and feature-selection procedures;
3. appropriateness of training, validation, and test-set separation;
4. potential data leakage or overfitting;
5. adequacy of the classical machine-learning comparator;
6. use of simulators or real quantum hardware;

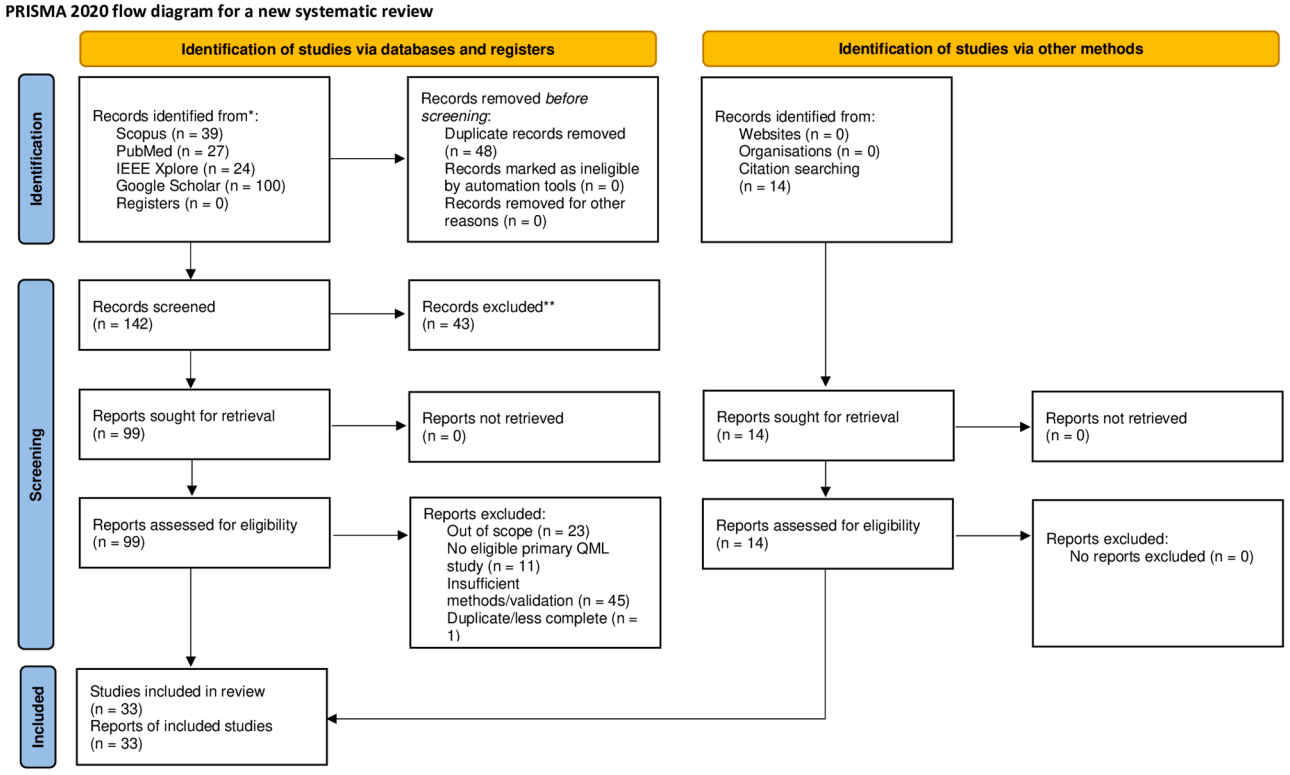

Fig. 1. PRISMA 2020 flow diagram of study identification, duplicate removal, title and abstract screening, full-text eligibility assessment, and final inclusion in the narrative synthesis.

7. reporting of repeated experiments, performance variability, or uncertainty;

When reported, statistical controls and data-handling procedures used in the individual studies, including normalization, feature selection, class-balancing strategies, and, where applicable, adjustment for clinical covariates, were considered during the methodological appraisal. Their inconsistent reporting and substantial heterogeneity prevented a formal comparative or quantitative synthesis. Studies reporting very high or near-perfect predictive performance were interpreted with particular caution, especially when independent testing or external validation, repeated experiments, uncertainty estimates, and sufficiently transparent preprocessing and data-splitting procedures were absent or incompletely reported.

This methodological appraisal was used to contextualize the reliability and strength of the evidence rather than as an automatic exclusion criterion. The study-level methodological appraisal was reported in the evidence tables and integrated into the narrative synthesis. Because of the heterogeneity of study designs, datasets, validation procedures, and implementation settings, no aggregate risk-of-bias score or numerical quality ranking was calculated. Recurrent methodological limitations identified during the appraisal are discussed in the Results and Discussion sections. The reference list was systematically rechecked during manuscript revision to identify duplicate citations, repeated versions of the same publication, incomplete or malformed entries, incorrect publication years, and inconsistencies between in-text citations and bibliography records. When the same work was available in several forms, the most complete publication was preferentially retained, with priority given to the peer-reviewed version. This verification process was also used to prevent the same study from being counted more than once in the review.

3. Background concepts

Classical computing has been the dominant paradigm for decades, forming the foundation of most current technologies, including machine learning systems applied in healthcare. These systems process data using binary bits, which can exist in only one of two states, 0 or 1, and are manipulated through deterministic logic gates based on Boolean algebra [5]. This model is well-suited for tasks involving structured data and linear relationships but struggles with scalability and efficiency when confronted with high-dimensional, non-linear datasets, such as those commonly found in genomics, electronic health records, or sensor-derived time series in chronic disease monitoring [23–25]. In contrast, quantum computing introduces a fundamentally different approach by leveraging the principles of quantum mechanics, notably superposition, entanglement, and quantum interference, to represent and process information. The basic unit of quantum computing is the qubit, which differs from the classical bit by existing in a superposition of states $|0\rangle$ and $|1\rangle$ simultaneously. This enables quantum systems to explore multiple computational paths at once, dramatically increasing processing power for certain tasks [26]. The state of a single qubit can be mathematically expressed as:

$$|\psi\rangle = \alpha|0\rangle + \beta|1\rangle$$

where α and β are complex probability amplitudes such that $|\alpha|^2 + |\beta|^2 = 1$

When visualized on a Bloch sphere, a qubit's state is represented as a vector in three-dimensional space, defined by spherical angles θ and φ, as shown in Fig. 2. This richer representation allows for a more nuanced encoding of information than classical binary logic.

Furthermore, quantum systems can exploit entanglement, a non-classical correlation between qubits in which the state of one directly influences the state of another, regardless of physical distance. This phenomenon enables highly coordinated, parallel computations across entangled qubit systems, particularly useful in data-rich environments such as healthcare. Quantum algorithms manipulate qubit states through quantum gates, such as the Hadamard (which creates superpositions), Pauli-X (quantum equivalent of a NOT operation), and CNOT (used to create entanglement). Unlike classical logic gates, quantum gates are represented by unitary matrices and are inherently reversible, preserving the full quantum information throughout computation [27]. Quantum computation concludes with measurement, during which the qubit collapses into one of its basis states ($|0\rangle$ or $|1\rangle$) with a probability determined by the square of the corresponding amplitude. This process introduces probabilistic elements absent in classical computing but also opens up powerful sampling strategies and optimization heuristics [28, 29]. A concise comparison between classical and quantum computing paradigms is presented in Table 1, highlighting differences in data representation, processing logic, scalability, and application domains.

The relevance of quantum computing to machine learning arises from the representation, encoding, and optimization of data. A quantum feature map encodes a classical input vector x into an n-qubit state $|\phi(x)\rangle = U_\phi(x)|0\rangle^{\otimes n}$, and the similarity between two inputs can be evaluated through a quantum kernel, commonly defined as $K(x, x') = |\langle\phi(x)|\phi(x')\rangle|^2$; the resulting kernel matrix can then be used by a classical algorithm such as a support vector machine [7,30]. One commonly used encoding strategy is angle encoding, in which each normalized feature x_j controls a single-qubit rotation, for example:

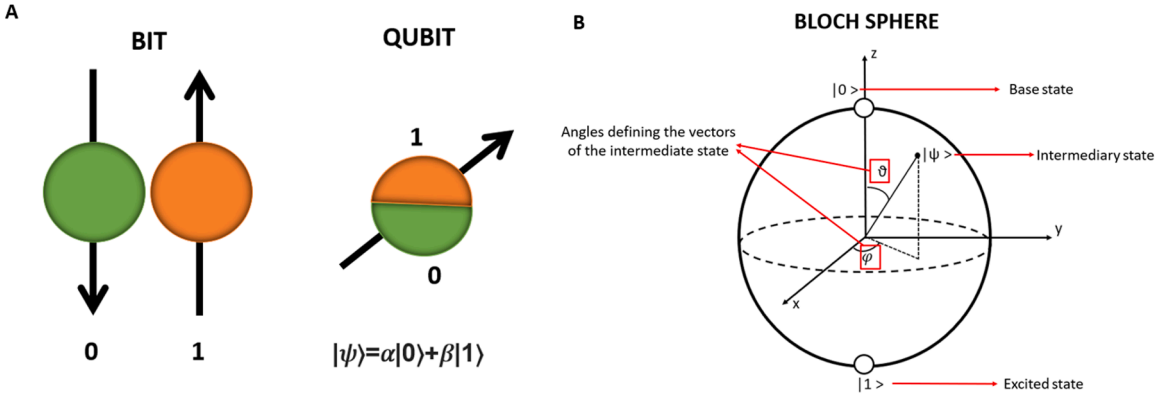

Fig. 2. Comparison between classical bit and quantum qubit representation (A) Classical bits can exist in one of two states, 0 or 1, represented by distinct orientations. In contrast, quantum bits (qubits) can exist in a superposition of both 0 and 1 states, shown here as a combination of the two. (B) The Bloch sphere visualizes the state of a qubit, where the qubit's state is defined by two angles, θ and ϕ, representing the superposition between the base state $|0\rangle$ and the excited state $|1\rangle$.

Table 1
Key differences between classical and quantum computing. This table summarizes the main distinctions between classical and quantum computing, focusing on information units, data processing, principles, error correction, and application areas.

Key aspect	Classical computing	Quantum computing
Basic unit	Bits (0 or 1)	Qubits (0, 1, or both simultaneously)
Data representation	Deterministic (binary states)	Probabilistic (superposition and entanglement)
Underlying principle	Boolean logic, Turing machine	Quantum mechanics
Error correction	Well-established techniques	Challenges in error correction (Quantum error codes)
Efficiency in problem solving	Efficient for general-purpose tasks	Exponential speedup in specific problems (e.g., factorization, optimization)
Scalability	Highly scalable	Limited by current technology and error rates

$$\left|\phi(x)\right\rangle = \bigotimes_{j=1}^{n} R_y\left(x_j\right)\left|0\right\rangle \tag{1}$$

Encoding n features in this form generally requires n qubits and $O(n)$ rotation gates per encoding layer, while repeated data-reuploading layers increase circuit depth and execution cost; therefore, dimensionality reduction is often required when biomedical datasets contain more variables than the available number of qubits [31,32]. In variational quantum models, the encoded state is processed by a parameterized circuit $U(\theta)$, and training seeks parameters that minimize a cost function such as:

$$C(\theta) = N^{-1}\sum_{i=1}^{N} L[y_i, f_\theta(x_i)] \tag{2}$$

where $f_\theta(x_i) = \langle\psi_\theta(x_i)|O|\psi_\theta(x_i)\rangle$ is obtained from quantum measurements as the expectation value of a problem-specific observable O (the measurement operator whose expectation encodes the model output), and L is a task-dependent loss function. The circuit parameters are updated by a classical optimizer, but repeated circuit measurements, hardware noise, increasing circuit depth, and barren plateaus can substantially increase the computational cost and impair trainability [33–35]. These limitations mean that the usefulness of quantum kernels and variational models must be evaluated through end-to-end comparisons that include data preparation, encoding, training, measurement, and hardware overheads.

4. From classical to quantum: the evolution of machine learning

4.1. Classical machine learning paradigms

ML has become central in modern data analysis, with applications ranging from finance to medicine [4,36]. It enables systems to learn patterns from data and generate predictions or decisions without being explicitly programmed. The main learning paradigms include:

- **Supervised learning**, where models are trained on labeled datasets (e.g., disease presence based on lab parameters), using algorithms like logistic regression, support vector machines (SVM), or decision trees [37].
- **Unsupervised learning,** which extracts patterns from unlabeled data (e.g., clustering metabolic phenotypes), using methods such as k-means or principal component analysis (PCA) [38].
- **Reinforcement learning,** where an agent learns optimal behaviors through feedback from the environment. This paradigm is increasingly applied in adaptive systems such as nutritional planning or insulin titration [39].

Despite their success, classical ML models remain challenged by high-dimensional, noisy, heterogeneous, and temporally dynamic data [23,24]. The growing scale and multimodality of healthcare, genomic, and behavioral data increase the need for more expressive and efficient methods [3,40]. QML is therefore being explored as a complementary approach to selected limitations of classical models, rather than as their general replacement [1,2].

4.2. Historical and methodological background of quantum machine learning

Quantum machine learning emerged from the convergence of advances in quantum computation and the growing use of machine learning for complex data-analysis tasks. Its conceptual foundations can be traced to the development of quantum algorithms in the 1990s. Shor's algorithm demonstrated that quantum computation could offer substantial advantages for selected mathematical problems, while Grover's algorithm introduced a quadratic speed-up for unstructured search [41,42]. These algorithms were not machine-learning methods, but they established the computational principles on which later quantum approaches were built. A further milestone was the quantum algorithm for solving linear systems proposed by Harrow, Hassidim, and Lloyd, which provided an important mathematical basis for several subsequent QML proposals [43]. QML began to develop as a distinct methodological field during the following decade. The proposal of a quantum support vector machine introduced quantum procedures for classification and linear-algebra operations relevant to supervised learning [6]. This was followed by the development of parameterized quantum circuits and hybrid quantum–classical learning frameworks suitable for near-term devices [33], as well as quantum-enhanced feature maps and kernel methods that embed classical data into high-dimensional quantum state spaces [7,30].

The methodological evolution of QML can be organized into three partially overlapping trajectories. The first concerns quantum kernels and feature Hilbert spaces, in which quantum circuits are used to construct representations for classification and pattern recognition. The second involves variational and hybrid quantum–classical models, where parameterized circuits are trained through classical optimization. Although these models are compatible with noisy intermediate-scale quantum devices, their scalability may be limited by trainability problems such as barren plateaus and noise-induced vanishing gradients [34,44]. The third trajectory concerns quantum data encoding. The way classical variables are mapped into quantum states or circuit parameters directly affects model expressivity, circuit depth, and the computational resources required for implementation [31]. Encoding choices are therefore particularly important in biomedical applications, where datasets may combine clinical variables, images, molecular profiles, and longitudinal signals.

Together, these developments shifted QML from foundational algorithmic proposals toward hybrid and NISQ-compatible implementations. However, most healthcare applications remain based on simulations, small-scale hardware experiments, or proof-of-concept models. The historical and methodological progression summarized in Fig. 3 provides the context for the applications in diabetes and metabolic disorders discussed in the following section.

4.3. Quantum machine learning: an emerging paradigm

Building upon the limitations of classical approaches, QML introduces a novel computational framework by integrating principles of quantum computing (such as superposition, entanglement, and quantum interference) into machine learning algorithms. Rather than replacing classical ML, QML augments it by enabling the construction of quantum-enhanced feature spaces, where complex patterns and correlations can be modeled more efficiently and with potentially exponential speedups in specific tasks [35,45].

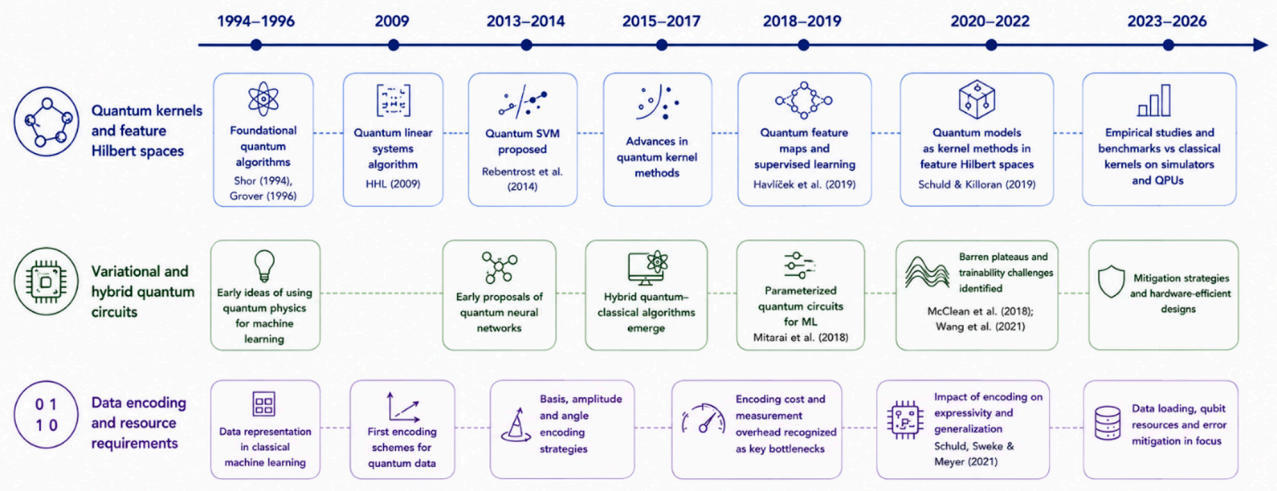

Fig. 3. Historical and methodological evolution of quantum machine learning. The timeline highlights key developments in quantum kernels, variational and hybrid circuits, data encoding, and the progression toward healthcare applications.

Several QML models have been proposed and explored across supervised, unsupervised, and hybrid learning paradigms. Among the most promising:

- **Quantum Support Vector Machines (QSVM):** extend classical SVMs by using quantum kernels for non-linear classification in high-dimensional spaces [6].
- **Quantum Neural Networks (QNN):** built using parameterized quantum circuits, these networks perform tasks similar to deep learning models with potentially lower computational cost [15,46].
- **Quantum k-Means and qPCA:** quantum versions of unsupervised learning algorithms that offer faster clustering and dimensionality reduction, useful for omics data and clinical subgrouping [47].
- **Hybrid quantum-classical models:** rather than a distinct learning paradigm, integrate quantum circuits with classical optimization loops (e.g., variational quantum algorithms and quantum GANs) and can be applied across supervised, unsupervised, and semi-supervised tasks, currently representing the most practical approach under existing hardware limitations [35].

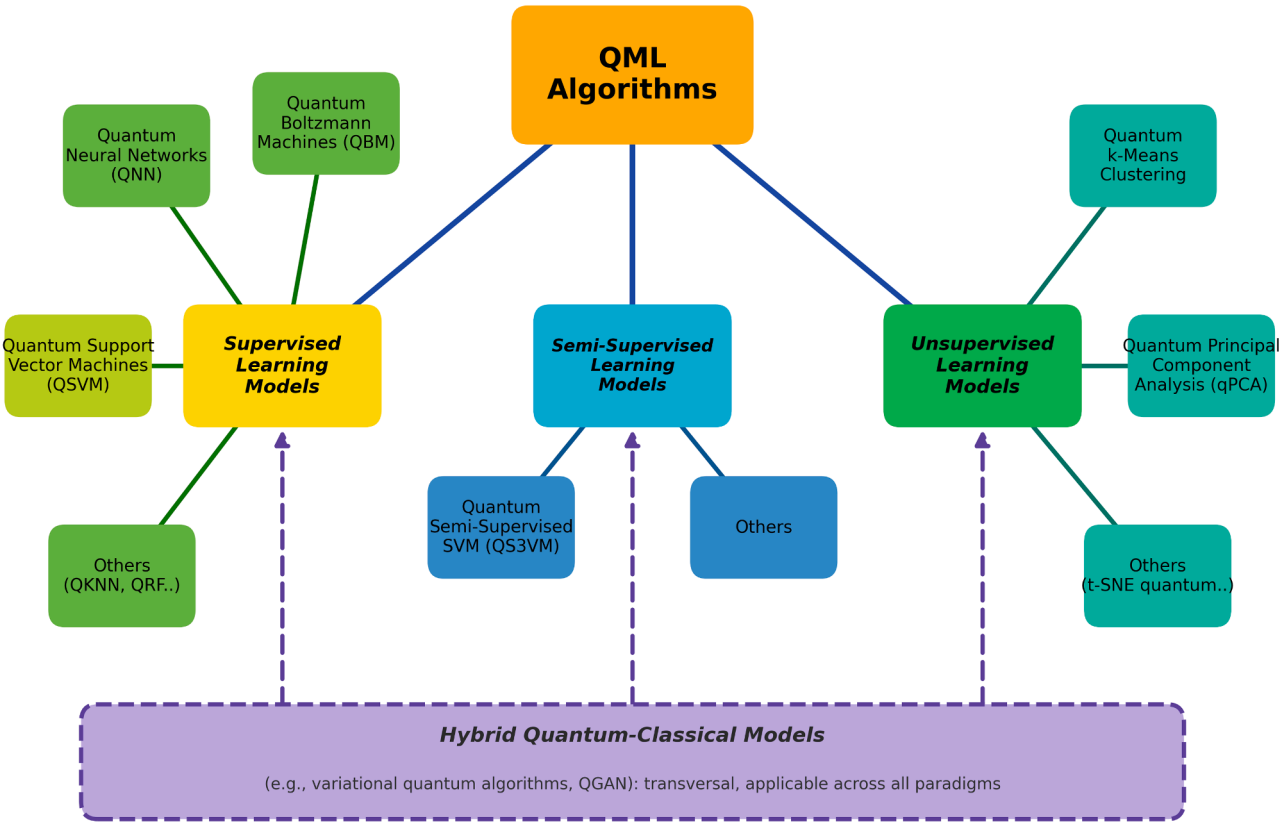

Fig. 4. Overview of QML algorithms. The diagram organizes QML methods along three learning paradigms (supervised, unsupervised, and semi-supervised), with hybrid quantum-classical approaches shown as a transversal category that cuts across all paradigms; key representative algorithms are listed under each.

- **Semi-supervised models:** exploit both limited labeled data and abundant unlabeled samples, a situation common in biomedical datasets; representative quantum approaches include quantum semi-supervised support vector machines (QS3VM), which propagate label information from labeled to unlabeled samples [48].

These algorithms can be organized along three learning paradigms (supervised, unsupervised, and semi-supervised), while hybrid quantum-classical implementations cut across all of them. Fig. 4 provides a visual summary of QML algorithm classes, illustrating their internal structure and key representatives.

5. QML in metabolic disorders: prediction, complication management, and glycemic control

QML is gaining momentum as a promising approach to tackle the complexity of metabolic disorders by enabling the analysis of nonlinear, heterogeneous, and temporally dynamic health data [2]. Among these disorders, MetS represents a critical clinical construct (characterized by the co-occurrence of central obesity, insulin resistance, dyslipidemia, hypertension, and impaired glucose metabolism) that substantially increases the risk of developing type 2 diabetes and cardiovascular complications [49]. Unlike discrete disease entities, MetS reflects a dynamic and multifactorial physiological state, shaped by interactions between genetic, environmental, and behavioral factors [50]. These interactions often follow non-linear and time-dependent trajectories that are difficult to capture using traditional statistical or machine learning approaches, especially when data are sparse, multimodal, or longitudinal [13]. QML algorithms, with their ability to encode information into quantum states and operate in exponentially large Hilbert spaces, offer a compelling alternative, particularly in scenarios where classical models struggle with scalability, generalization, or integration across data modalities [1].

This section explores QML applications across three core dimensions of metabolic health:

- Early metabolic dysregulation and obesity monitoring: where models such as quantum echo state networks (qESNs) are employed to detect early signs of metabolic imbalance and predict weight trajectories or behavioral risks.
- Glycemic control and type 2 diabetes management: focusing on the use of QML in dynamic glucose forecasting, early diagnosis, and individualized treatment planning through hybrid quantum-classical models and real-time data from wearable sensors.
- Prediction of chronic complications and risk stratification: leveraging quantum-enhanced algorithms to anticipate long-term risks like neuropathy, cardiomyopathy, and nephropathy, enabling timely intervention and precision prevention.

5.1. Quantum machine learning in obesity and metabolic dysregulation

Obesity is not only the most prevalent manifestation of metabolic imbalance but also a key early predictor of downstream cardiometabolic complications, including insulin resistance, type 2 diabetes, and cardiovascular disease [51]. As a core component of Metabolic Syndrome, its progression reflects a complex interplay of biological, behavioral, and environmental drivers, whose dynamic, nonlinear interactions are difficult to capture using traditional statistical or classical machine learning approaches, especially in the presence of data sparsity and noise.

To address these challenges, recent works have begun exploring QML for personalized prediction and risk modeling in the context of early metabolic dysregulation. One of the most innovative examples is the Quantum Metabolic Avatar (QMA), a system proposed by Abeltino and Serantoni et al. [52] that leverages a quantum echo state network (qESN) to forecast individual weight trajectories from multimodal time-series data (including energy balance, body weight, and macronutrient intake) collected via wearable devices. Unlike classical recurrent models, the qESN uses a virtual quantum reservoir to encode temporal dynamics into entangled state representations without requiring iterative circuit training. This architecture enhances both memory capacity and resilience to data imperfections. Experimental evaluations of the QMA demonstrated a 31.8% reduction in root mean squared error (RMSE) compared to classical echo state networks, as well as a 76% improvement in tolerance to missing or corrupted inputs, performance gains that are particularly relevant for real-world deployment in digital health ecosystems. Additionally, the model is compatible with current noisy intermediate-scale quantum (NISQ) hardware, supporting low-latency inference suitable for wearable or edge computing environments. Conceptually, the QMA serves as an early prototype of a quantum-enhanced digital twin, capable of emulating personal metabolic dynamics and issuing early warnings when deviations from homeostasis are detected. Several authors of the present review are also co-authors of the QMA study [52]. This authorship overlap is disclosed to ensure transparency, and the QMA study was assessed using the same eligibility and methodological appraisal criteria applied to the other included studies. Relevant institutional and industry co-funding is reported in the Funding statement.

Another contribution in this field is the study by Ozpolat [53], who developed a QML-based diagnostic framework for obesity classification using a publicly available dataset on physical condition and dietary habits. Their approach involved the integration of classical dimensionality reduction techniques like Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA) with Quantum Support Vector Machines (QSVMs) operating over multiple quantum feature maps (Z, ZZ, and Pauli X). The dataset, drawn from real and synthetic clinical records, included over 2000 individuals and aimed to stratify obesity into more precise categories (e.g., Overweight I, Obesity Type II). The study's results were particularly noteworthy. When the LDA method was used in combination with Z and Pauli X feature maps, the QSVM achieved 100% accuracy and 100% precision across all obesity classes matching the classical SVM combined with LDA, while outperforming the other QSVM configurationsThe authors attributed this success to LDA's capacity to enhance class separability and the effectiveness of quantum encoding via single-qubit transformations. Even compared to more advanced classical methods (e.g., Random Forests, Gradient Boosting, or ensemble deep learning), their model surpassed reported benchmarks, many of which achieved accuracies between 86% and 97% on the same dataset. In contrast, configurations using PCA or the ZZ feature map yielded lower accuracy and longer runtime, highlighting the sensitivity of QML performance to both preprocessing and encoding strategies. However, this gain came at a cost: while the classical SVM achieved 100% accuracy in just 0.01–0.04 s, the LDA-QSVM configurations required ~64–107 s to reach perfect performance. These perfect results should nevertheless be interpreted cautiously because the evaluation relied on a single 60/40 train–test split on a dataset containing synthetic records, without repeated cross-validation or external validation. The paper does not clearly state whether supervised LDA was fitted exclusively on the training partition; therefore, potential data leakage cannot be excluded. In contrast, PCA-based reductions or the ZZ feature map produced lower accuracy (60–75%) and even longer runtimes (up to ~200 s), underscoring the sensitivity of QML performance to both preprocessing and encoding strategies.

Together, these studies represent the first wave of QML applications in obesity and early metabolic imbalance. Despite their novelty and proof-of-concept nature, they highlight how quantum-enhanced architectures can begin to address the limitations of classical modeling by capturing complex physiological signals, managing uncertainty, and simulating disease trajectories in real time.

5.2. QML in diabetes diagnosis and personalized prediction

Diabetes is one of the most widespread chronic conditions globally, with approximately 830 million adults affected in 2022 [54]. It arises from multifactorial causes (genetic predisposition, metabolic dysregulation, and behavioral influences) and often progresses silently until complications emerge. Accurate early diagnosis and personalized risk prediction are critical for timely intervention, yet traditional machine learning models often struggle with small sample sizes, high-dimensional feature spaces, and complex variable interactions. QML offers a novel approach by enabling more expressive feature representations and efficient learning in such challenging scenarios. Recent studies have begun to explore the potential of QML in this domain.

For instance, Monteiro et al. [55] investigated the use of quantum perceptrons for binary classification tasks based on the PIMA Indian Diabetes Dataset (PIDD), a well-known benchmark comprising 768 medical records of female patients over 21 years of age, with features such as glucose levels, BMI, insulin, and age. Their model, designed as a quantum-inspired neuron capable of simulating superposition and interference effects in decision boundaries, was compared against a traditional perceptron and several alternative quantum neuron variants. Results indicated that while the quantum perceptron achieved a classification accuracy of 76%, outperforming classical perceptrons (63%), it still fell short of the performance attained by deep neural networks, which reached an AUC-ROC of 80%. This work is particularly relevant for introducing the concept of quantum neurons, which integrate principles of quantum computing into neural network structures without relying on variational circuits. In a related study, Gupta et al. [56] employed a different quantum approach by implementing a VQC within a hybrid quantum-classical architecture. Like Monteiro, they relied on the PIDD dataset, but their focus was on the comparison between VQC and a deep learning model built using a multilayer perceptron. The VQC was optimized using gradient-based methods and trained on quantum simulators due to hardware constraints. Their findings showed that the DL model significantly outperformed the VQC, achieving 95% accuracy, with a precision of 0.90 and recall of 0.95, while the quantum model reached 86% accuracy, precision of 0.74, and recall of 0.85. Despite this performance gap, the authors noted that QML models showed advantages in memory handling and parameter space efficiency, and could offer faster inference in future quantum-native implementations. Similarly, Vimal et al. [57] explored multiple quantum models for diabetes prediction, with particular attention to the performance gap between the Quantum Support Vector Classifier (QSVC) and the VQC. Using the UCI Diabetes dataset, they benchmarked these quantum models against classical baselines such as SVM and Logistic Regression. Results showed that QSVC delivered robust performance across all metrics (Accuracy 0.74, Precision 0.75, Recall 0.73, F1-score 0.74), essentially matching Logistic Regression and only slightly below SVM (0.76). By contrast, the VQC obtained substantially weaker results (Accuracy 0.61, Precision 0.60, Recall 0.61, F1-score 0.59), underscoring the challenges of variational approaches in this context. This clear disparity highlights that kernel-based quantum models like QSVC are already competitive with established classical methods, whereas variational classifiers such as VQC remain underdeveloped and sensitive to optimization and noise. Although the study did not demonstrate a quantum advantage in accuracy, QSVC's kernel-based formulation is often regarded in QML literature as promising for feature mapping and handling high-dimensional data [30]. Expanding on these insights, Genc et al. [58] conducted a comparative study evaluating both classical and quantum machine learning approaches on the Diabetes Health Indicators dataset, which includes 253,680 records and 22 features describing behavioral, physiological, and demographic aspects (e.g., BMI, general health status, blood pressure, cholesterol levels, age, physical activity, and smoking habits). Using Lasso regression for feature selection, they identified the five most predictive features (GenHlth, BMI, HighBP, HighChol, and Age) and employed them in both traditional and quantum models. Their quantum approach, based on Quantum Feature Mapping (QFM) and implemented using Quantum Support Vector Machines (QSVM) achieved a classification accuracy of 84.33%, comparable to or exceeding several classical models. This result emphasizes the promise of quantum-enhanced feature encoding and optimization in complex medical classification tasks. Hancco-Quispe et al. [14] investigated the integration of dimensionality reduction techniques with hybrid quantum-classical models for diabetes classification using the Pima Indians dataset. Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA) were employed as preprocessing steps to improve class separability and encoding efficiency before applying quantum classifiers specifically, QSVC and VQC. Their findings indicate that the combination of LDA with QSVC yielded better classification performance compared to the same models with PCA, and in some cases surpassed classical classifiers such as Logistic Regression and K-Nearest Neighbors. For instance, QSVC with LDA achieved an accuracy of approximately 83%, while VQC remained less competitive (~73%). The study underscores the potential of quantum models when paired with supervised dimensionality reduction, while also highlighting current hardware limitations, such as limited qubit availability and simulation constraints, that continue to restrict their scalability in practical healthcare settings. Maheshwari et al. [59] applied classical and quantum machine learning models to electronic health records (EHRs) from the Basque Health Service (Osakidetza) in order to address a binary classification task: distinguishing diabetes patients with acute diseases from those without. The study evaluated several classical classifiers, including Decision Tree, Random Forest, XGBoost, AdaBoost, and ensemble voting models, and compared them with quantum-based counterparts such as QBoost, QBoost Plus, and hybrid ensembles (New Model 1 and New Model 2). Results showed that the best-performing quantum ensemble (New Model 1) achieved an accuracy, precision, recall, F1-score, and specificity of about 69%, comparable to the classical approaches. However, the quantum implementation yielded a computational speed-up of approximately 55x, underscoring the potential of quantum computing to accelerate medical data processing without loss of predictive performance.

Complementing these efforts, other researchers have explored how classical medical datasets can be transformed to better exploit quantum computing capabilities through novel data encoding strategies. For example, Sierra-Sosa et al. [60] proposed a data preprocessing pipeline to enhance the applicability of VQC to real-world medical datasets. Their method combined feature selection, ellipsoidal coordinate mapping, and Stokes parameter representation within the Poincaré sphere to improve quantum state preparation. Using a dataset of 149,015 Type 2 Diabetes Mellitus patients from the Basque Health Service (Osakidetza), they applied the pipeline to predict the incidence of acute comorbidities. Implemented in IBM's Qiskit framework, the VQC achieved 70% accuracy with 2 qubits and 72% with 3 qubits, demonstrating clear improvements over standard normalization approaches. The study highlighted that the proposed preprocessing allowed comparable performance with fewer quantum resources, though scalability remains limited by current NISQ hardware constraints. In a related comparative effort, Prakash et al. [61] evaluated multiple classical classifiers (including SVM, KPCA, Decision Trees, and Bayesian Networks) against a quantum-enhanced QBoost classifier using a diabetes dataset. Their pipeline included standard preprocessing, a 70/30 train-test split, and binary labeling for patients with critical vs. non-critical diabetes. The QBoost model achieved the highest overall performance among all tested algorithms, with an accuracy of 73.4%, sensitivity of 78.1%, F1-score of 80.3%, and specificity of 85.7%, surpassing Bayesian (accuracy: 70%) and Decision Trees (accuracy: 57.3%). Notably, the quantum model required significantly less computation time (0.0428 s), highlighting both the predictive power and computational advantage of quantum classifiers when used with optimized preprocessing and ensemble techniques. Building on this line of research, Jha et al. [62] explored ensemble-based quantum models for diabetes prediction using

a dataset from the CDC public health repository. The study's goal was to classify patients as either diabetic or non-diabetic. Classical ensemble classifiers (Voting, AdaBoost, XGBoost, CatBoost) were benchmarked against the quantum boosting algorithm QBoost executed on a QPU. While QBoost demonstrated clear computational speed-ups, its predictive performance lagged behind the best classical models. Specifically, the proposed hybrid quantum–classical ensemble model achieved an accuracy of 0.89, precision 0.85, recall 0.95, F1-score 0.90, and AUC 0.96, compared to AdaBoost's higher performance (accuracy 0.94, precision 0.91, recall 0.98, F1-score 0.94, AUC 0.98). The authors conclude that quantum approaches can already accelerate computation but still incur a small reduction in classification quality (~5% accuracy and 0.186 AUC lower than AdaBoost). They suggest that continued hardware improvements will be crucial to close this gap and make hybrid quantum ML a viable tool for healthcare diagnostics. In a more recent study, Sridevi et al. [63] investigated the application of quantum machine learning for the noninvasive estimation of blood glucose and HbA1c levels using fingertip videos. The authors collected ten-second near-infrared spectroscopy recordings from 136 participants (81 healthy and 55 diabetic), extracting 45 photoplethysmography (PPG) features based on the Beer–Lambert law and applying feature selection to retain the most relevant predictors. They benchmarked two quantum models (QSVM and QNN) against seven classical machine learning algorithms, including SVM, Decision Tree, Logistic Regression, KNN,

Table 2
Key results of using QML algorithms for diabetes dataset.

Study	QML model / implementation	Study Aim	Results	Main strengths	Methodological limitations
Monteiro et al. [55].	quantum simulator (IBM Qiskit)	Compare quantum vs classical perceptrons and ANNs on PIDD dataset	76% (QP) vs 63% (classical); varying results across QN variants	Outperforms classical perceptron	Simulator-based evaluation on a single benchmark dataset; no execution on real quantum hardware; no external clinical validation.
Gupta et al. [56].	Variational Quantum Circuit (VQC), quantum simulator, 3 qubits; quantum framework/ backend not clearly reported	Compare VQC vs DL model on PIDD	VQC: 86% accuracy; DL model: 95% accuracy, precision 0.90, recall 0.95	Hybrid architecture; efficient parameter space	Simulator-based evaluation on a single benchmark dataset; lower predictive performance than the deep-learning comparator; real-hardware scalability was not demonstrated.
Vimal et al. [57].	QSVC and VQC, Qiskit implementation; execution backend not clearly reported; 8-qubit VQC circuit	Compare quantum vs classical models (UCI Diabetes dataset)	SVM: 76% accuracy, LR: 74% accuracy, QSVC: 74% accuracy, VQC: 61% accuracy	QSVC competitive with classical baselines	Evaluation restricted to a single public dataset; VQC performance was substantially lower than that of QSVC and classical SVM; results remain sensitive to model and optimization choices.
Genc et al. [58].	QSVM with quantum feature mapping, Cirq simulator, 5 qubits	Evaluate QML on large-scale Diabetes Health Indicators dataset	QSVM: 84.33% accuracy	Scales to large dataset; competitive with classical models	Evaluation based on a single public dataset; quantum implementation remained simulation-based; scalability on real quantum hardware was not demonstrated.
Hancco-Quispe et al. [14]	QSVC and VQC, quantum simulators (Qiskit Aer and PennyLane); qubit count not explicitly reported	Compare classical vs quantum classifiers on diabetes prediction, assessing effect of PCA and LDA	QSVC+LDA: ~83% Balanced Accuracy; VQC+LDA: ~73%	Shows benefit of LDA; QSVC competitive with classical models	Evaluation restricted to the Pima Indians dataset; performance was strongly dependent on the dimensionality-reduction method; limited qubit availability and simulation constraints restrict scalability.
Maheshwari et al. [59].	QBoost, QBoost Plus, New Model 1, and New Model 2, real D-Wave QPU using quantum annealing; qubit count not reported	Compare classical (DT, RF, XGBoost, AdaBoost, Voting) vs quantum ensemble models on EHRs from Osakidetza	New Model 1: ~69% accuracy, precision, recall, F1, specificity; ~55x computational speed-up vs classical	Significant computational efficiency gain	Evaluation based on data from a single healthcare system; predictive performance remained modest; the reported computational speed-up may depend on the specific implementation and hardware setting.
Sierra-Sosa et al. [60].	Variational Quantum Classifier (VQC) with Poincaré/Stokes-parameter preprocessing, Qiskit Aer simulator, 2–3 qubits	Predict acute comorbidities in T2DM using EHRs with Poincaré-based preprocessing	70% (2q), 72% (3q) accuracy	Better state prep; fewer qubits needed	Evaluation limited to two- and three-qubit configurations; predictive accuracy remained moderate; scalability to larger feature spaces and hardware configurations was not demonstrated.
Prakash et al. [61].	QBoost and enhanced hybrid QBoost models, real D-Wave QPU accessed through an API; qubit count not reported	Diabetes Severity Classification	QBoost: Accuracy 73.4%, Sens. 78.1%, F1 80.3%, Spec. 85.7%, Time 0.0428s	Best performance; large computational speed-up	Evaluation based on a single dataset and a single train–test split; limited information on repeated experiments and performance variability; computation-time comparisons may be platform-dependent.
Jha et al. [62].	QBoost and hybrid quantum–classical boosting model, real D-Wave 2000Q quantum annealer; number of qubits actually used not reporte	Classify patients as diabetic vs non-diabetic (CDC dataset)	Hybrid: Acc. 0.89, Prec. 0.85, Rec. 0.95, F1 0.90, AUC 0.96; AdaBoost best (Acc. 0.94, AUC 0.98)	Quantum speed-up; hybrid improves metrics vs pure QBoost	Preprint evidence based on a single public dataset; the hybrid quantum model underperformed the best classical ensemble; reported computational gains may depend on the QPU and implementation setting.
Sridevi et al. [63].	QSVM and QNN, quantum simulators (PennyLane default. qubit for QSVM; Qiskit QasmSimulator for QNN); QNN implemented with 10 qubits reported	Noninvasive glucose & HbA1c prediction from fingertip videos (136 participants)	QSVM best: Glucose Acc. 89.3%, HbA1c Acc. 96.3%, CV 92.5%	Demonstrated QML potential for noninvasive monitoring	Relatively small sample of 136 participants; lack of evaluation in an independent clinical cohort; longer training and inference times than classical models.

Random Forest, and XGBoost. Results demonstrated that QSVM outperformed all other models, achieving 89.3% accuracy and 92.5% average k-fold cross-validation score for blood glucose prediction, and 96.3% accuracy with the same CV score for HbA1c prediction. While the study highlighted longer training and inference times for quantum models compared to classical baselines, it underscored the potential of QML to advance noninvasive monitoring techniques for diabetes management.

A comprehensive summary of key studies applying QML techniques to diabetes prediction and classification, highlighting their objectives, outcomes, and comparative advantages, is provided in Table 2.

5.3. QML for diabetes- and metabolic-disease-associated complications

Chronic complications of metabolic syndromes are a major cause of long-term morbidity, with effects extending beyond glycemic imbalance. These conditions often lead to progressive macrovascular damage, neurological deterioration, and microvascular complications, through mechanisms such as chronic inflammation, endothelial dysfunction, and impaired perfusion [49,64]. In this section, we review recent studies that apply QML techniques to these complications, focusing on three main domains: microvascular conditions such as diabetic retinopathy and foot ulcer classification, cardiovascular disease and neurological impairment. A summary of these studies, including models, aims, and performance outcomes, is presented in Table 3.

5.3.1. Microvascular complications: retinopathy and diabetic foot ulcers

Recent applications of QML have demonstrated a growing potential in enhancing diagnostic precision for microvascular complications commonly associated with diabetes and metabolic syndrome, especially in the domains of diabetic retinopathy (DR) and diabetic foot ulcers (DFU) [65]. These pathologies are both prevalent and clinically elusive in early stages, making timely, accurate classification critical.

In this regard, Alavi et al. [66] tackled the problem of DFU classification by proposing a hybrid classical–quantum framework. Using the DFUC2021 dataset (>11,000 labeled images across four categories: infection, ischaemia, none, and both), they first employed a transfer learning approach with a modified Xception CNN, extracting deep features from an intermediate layer. These were then used to train a multi-class VQC, with a variational circuit dedicated to each ulcer class. On the blind test set, the hybrid model achieved a macro-AUC of 0.7133 and macro-F1 of 0.5587, outperforming the classical CNN baseline (macro-AUC 0.6867, macro-F1 0.5067). While performance gains varied by class, the study demonstrates the potential of quantum–classical systems to enhance image-based medical decision support, particularly in complex multi-class settings such as DFU diagnosis. Expanding on this hybrid approach, Bali et al. [67] proposed QuantumNet, a hybrid classical–quantum transfer-learning model for the detection of diabetic retinopathy using the APTOS 2019 Blindness Detection dataset. Deep features extracted by a classical ResNet backbone were mapped to quantum states through angle embedding and classified by a variational quantum classifier simulated in Google Cirq. The quantum-enhanced model reached 94.11% classification accuracy, an improvement of roughly 12 percentage points over the best classical deep-learning baselines. The authors attribute this gain to the quantum transfer-learning stage, which enriched the feature representation available to the classifier, consistent with the broader observation that quantum encoding may add value when annotated retinal data are scarce. A further step was taken by Jain et al. [68], who focused not just on detecting DR but on the more challenging task of grading its multiple severity stages. They proposed a hybrid model that combined the classical ResNet-18 architecture with a Variational Quantum Classifier, trained again on the APTOS dataset. Their goal was to leverage the VQC's potential to model complex decision boundaries in high-dimensional feature space, especially useful for differentiating subtle inter-class variations in DR stages. The resulting model achieved a striking 97.2% classification accuracy, surpassing the standalone ResNet-18 by nearly 12 percentage points. Moreover, their system supported lesion-level localization and was able to distinguish reliably between all five severity levels of DR, from no apparent retinopathy to proliferative stages. This performance makes the model not only diagnostically accurate but also practical for use in clinical settings where both disease presence and stage-specific treatment recommendations are essential. The application of QML to ophthalmic imaging was further advanced by Acuña et al. [69], who designed a quantum-assisted diagnostic pipeline for the early detection of DR. Using approximately 3000 fundus images from the EyePACS and APTOS 2019 datasets, the authors trained and evaluated two quantum classifiers (QSVM and VQC) and benchmarked them against classical CNN and SVM baselines. The results demonstrated the superiority of the quantum models both in accuracy and efficiency: the QSVM reached 94.6% accuracy (ROC-AUC = 0.961) with an inference time of 30 ms, while the VQC achieved 93.8% accuracy (ROC-AUC = 0.952) with the lowest inference latency of 25 ms. By contrast, the CNN obtained 89.9% accuracy (ROC-AUC = 0.912) with 140 ms inference time, and the SVM only 88.5% accuracy (ROC-AUC = 0.905) with 70 ms latency. These findings indicate that quantum-enhanced classifiers not only surpass conventional deep learning models in predictive performance but also deliver substantially reduced inference times, making them highly promising for real-time and resource-constrained DR screening scenarios. Parallel to these image-based approaches, Alsubai et al. [70] explored an optimized multi-qubit quantum convolutional neural network designed to perform both classification and lesion localization on DR images. Trained on the Indian Diabetic Retinopathy dataset, their model incorporated quantum circuit designs using Hadamard and coupling gates, optimized to handle the five severity levels of DR. Unlike other studies focusing primarily on accuracy, Alsubai et al. evaluated a comprehensive suite of metrics (including precision, recall, specificity, and F1-score) and reported perfect performance (100%) across all of them. These perfect results should be interpreted cautiously because they were obtained from a single 80/20 split of 516 IDRiD images, without repeated cross-validation or uncertainty estimates, and the available reporting does not allow overfitting or data leakage to be excluded. Although the model was also evaluated on the SUSTech-SYSU dataset, the quantum implementation platform was not clearly reported, limiting reproducibility.Another significant contribution comes from Kalkonde et al. [71], who introduced the VF-QCNN model (Volans Finch–optimized Quantum Convolutional Neural Network) for DR detection. Their model encoded retinal fundus images into quantum states, leveraging entanglement and superposition for advanced parallel feature extraction. Combined with Volans Finch optimization, a swarm intelligence method with memory-based learning features, the architecture achieved 96.47% accuracy, an F1-score of 96.33%, and a recall of 97.43%. The model was tested on fundus images subjected to preprocessing (Wiener filtering, histogram equalization) and segmentation (TransUNet) to extract blood vessels, microaneurysms, and exudates. The authors emphasize that the optimization component significantly improved the learning of feature-rich but noisy retinal data, and that the model was robust against variations in contrast and lesion scale, challenges that often limit DR classifiers in practice.

5.3.2. Cardiovascular complications

Macrovascular complications, such as cardiovascular disease, chronic kidney disease (CKD), and stroke, are primary contributors to mortality among patients with diabetes and metabolic syndrome [72]. Recent developments in QML offer powerful tools for early detection and stratification of these conditions by enabling enhanced pattern recognition, particularly in high-dimensional and heterogeneous clinical data.

Parthasarathi et al. [73] applied QML to the early detection of CKD, a frequent long-term complication of diabetes. Their approach followed a structured four-phase pipeline comprising signal smoothing,

Table 3
Overview of key studies applying QML to metabolic syndromes complications. This table summarizes major studies on QML applications across metabolic syndromes complications, categorized into microvascular (e.g., retinopathy, foot ulcers), macrovascular (e.g., heart and kidney disease), and neurodegenerative (e.g., Alzheimer's, cognitive decline). It highlights the QML models used, study aims, key results, strengths, and limitations, providing a comparative perspective on performance and clinical potential.

Field	Study	QML model / implementation	Study Aim	Results	Main strengths	Methodological limitations
Microvascular	Alavi et al. [66].	Hybrid Xception–variational quantum classifier, four one-vs-all QNodes with six-layer parameterized circuits; execution backend and qubit count not reported	DFU classification	Hybrid: Macro-AUC 0.7133, Macro-F1 0.5587 vs. Xception 0.6867/0.5067	Improved performance over CNN baseline; first DFU quantum–classical application	Limited improvement for ischaemia class; simple quantum circuits
	Bali et al. [67].	QuantumNet: hybrid classical–quantum transfer learning (ResNet feature extractor + variational quantum classifier via angle embedding); Google Cirq simulation, no real-QPU execution	DR detection (APTOS 2019)	94.11% accuracy (~+12 pp vs classical DL)	Quantum transfer learning (angle embedding); F1/AUC not reported	Simulator only (Google Cirq); no real QPU
	Jain et al. [68].	Hybrid ResNet/Inception V3 + VQC, PennyLane, 4 qubits; backend not reported	DR severity grading	97% accuracy	Superior to ResNet-only model	May overfit
	Acuña et al. [69].	QSVM and VQC, IBM Qiskit ibmq_qasm_simulator, 8 qubits	Early DR detection (EyePACS, APTOS)	QSVM: 94.6% acc., ROC-AUC 0.961, 30 ms latency; VQC: 93.8% acc., ROC-AUC 0.952, 25 ms latency	Higher accuracy; fast inference	Simulated hardware; low-res input
	Alsubai et al. [70].	Optimized multiple-qubit gate QNN + modified CNN, 5 qubits; execution backend not reported	DR classification + localization	100% accuracy	Very high accuracy; lesion-level grading	Single 80/20 split; no repeated validation or uncertainty estimates; insufficient reporting to exclude leakage; quantum implementation unclear.
	Kalkonde et al. [71].	VF-QCNN (Angle-encoded PQC + hybrid VFO-optimized TransUNet/CNN pipeline), 4 qubits; execution backend not reported (simulation only, Python/PyCharm)	Optimized DR detection	96.47% accuracy, F1 96.33%	Optimized learning, robust to noise	Complex preprocessing
Macrovascular	Parthasarathi et al. [73].	VQC with RawFeatureVector and RealAmplitudes ansatz, Qiskit simulator; qubit count not reported	CKD detection	98.2% accuracy, 97.9% F1, 97.6% AUC-ROC	Outperforms all classical baselines; robust to noise and multicollinearity	Tested only on small structured dataset; hardware constraint
	Alotaib et al. [74].	QML-QPSO (Variational quantum circuit: MLP-based encoder/decoder/evaluator + QPSO-optimized cost function), 13 qubits; execution backend not reported (simulation, Python)	Heart disease prediction	96.7% accuracy; FDR = 0.09; 135 ms latency	High accuracy; fast convergence	Small dataset, hardware not tested
	Maheshwari et al. [75].	Optimized QSVM and hybrid quantum MLP, Qiskit IBM Statevector simulator, 10-qubit circuit	Ischemic heart classification	94.2% accuracy, F1 93.5%	Higher-order feature interaction	Complex architecture
	Abdulsalam et al. [76].	QSVC, 5 qubits; execution backend not reported (Qiskit simulator) QNN, 2 qubits; execution backend not reported (Qiskit simulator) VQC, 2 qubits; execution backend not reported (Qiskit simulator) Bagging-QSVC, 5 qubits; execution backend not reported (Qiskit simulator)	Heart disease prediction	Bagging-QSVC: 90.16% (vs. SVM/ANN 85.24%)	QML outperforms classical; ensemble improves accuracy; SHAP adds interpretability	Small dataset; simulator only;
	Prabhu et al. [77].	QSVC, multiclass Pegasos QSVC, and 4-qubit quanvolutional QNN, Qiskit Aer and PennyLane simulators	ECG image-based classification	QSVC: +10.8% vs SVC (94.1%vs 83.3%); Pegasos-QSVC: similar gains; QNN: 97.3% acc., 97.4% prec., 97.3% rec., 99.1% spec. (+3.9% vs CNN)	QML > classical; QNN extracts subtle ECG patterns; robust across folds	Single ECG-image dataset; no external or clearly reported patient-level validation; simulator-based implementation.

(*continued on next page*)

Table 3 (*continued*)

Field	Study	QML model / implementation	Study Aim	Results	Main strengths	Methodological limitations
	Heidari et al. [78].	HQNN (3 qubits, 3 layers) and HQRF (2 qubits, 1 layer), simulation, backend not reported	Early heart disease prediction	HQNN: AUC 96.4% (Cleveland), 97.8% (Statlog); HQRF: AUC 94.3% / 95.5%	HQNN = high accuracy on complex/high-dim data; HQRF = robust to outliers & imbalance	Small datasets; simulator only; HQNN sensitive to noise
	Banday et al. [79].	Hybrid ensemble models (CNN/RF/KNN/DT/LR/AdaBoost), IBM Qiskit listed; quantum component, backend, and qubit count not reported	CHD prediction	Classical: KNN 99.99%, DT 99.97%, RF 98.6%, LR 98.8% Hybrid: KNN–RF 99.96% acc., 99.97% rec.; AdaBoost–RF 99.93% acc.	Quantum kernels improve feature space; more stable, fewer FN;	Unclear data splitting and cross-validation; no external validation; potential overfitting; quantum implementation insufficiently described.
Neurodegenerative	Shahwar et al. [86].	Hybrid ResNet34 + 4-qubit QVC, PennyLane default.qubit, Qiskit Aer, and BasicAer simulators	MRI-based Alzheimer detection	Hybrid QML 97%, classics algorithm 92%	Improved feature reduction & accuracy; cross-simulator robustness	Simulator only
	Kim et al. [87].	QCCNN (ResNet-18 feature extractor + variational quantum circuit, angle encoding + CNOT entanglement, depth 3), 4 qubits; execution backend: PennyLane-Qiskit Aer device (simulation)	AD classification	CNN: 91.5% test, 89.2% val to QCCNN: 97.5% test, 95.1% val;	Higher acc. across all metrics; fewer features; strong generalization	Simulator only
	Chen et al. [88].	CNN–PCA–QSVM (CompressedMediQ), 8 reduced features; qubit count and execution backend not reported	Classification of MRI neuroimaging for dementia staging	QSVM: 96.1% acc. vs. classical SVM 78.8%; prec. up to 99% (early stages)	Quantum kernels improve separability in high-dim data; strong performance on subtle stages	NISQ hardware limits; proof-of-concept only; computationally heavy preprocessing
	Choi et al. [89].	Hybrid 1D-CNN + QCNN, PennyLane/PyTorch, 4 qubits (amplitude encoding); classical simulation only, no real quantum hardware	rs-fMRI time-series analysis for early dementia detection	Baseline CNN: 52.3% bal. acc. to Hybrid up to 58.1% (reported $p < 0.05$)	Quantum layers improve temporal pattern extraction; attention maps consistent with neuropathology; fewer params (↓overfitting risk)	Small dataset; modest accuracy gains; simulator only
	Cappiello et al. [90].	Quantum SVCs with 6-, 8-, and 12-qubit PQCs, Qiskit Aer simulator; noise tested on 14-qubit Fake Melbourne backend, no real QPU	Early Alzheimer's screening via handwriting (DARWIN dataset)	12q Q-SVC: 88.3% ± 4.7 accuracy; Classical SVC: 85.3% ± 7.5; kNN & DT <75%	Higher accuracy & stability; Robust across tasks;	Simulated hardware; Noise tests only preliminary
	Belay et al. [91].	Ensemble VGG16–ResNet50 + QSVM, Qiskit, 5 qubits; hardware/simulator backend not clearly specified	Classify 4 CE stages from ADNI I+II MRI	QSVM ensemble: 99.89% acc., 99.13% F1; CNN baselines: VGG 90.1%, ResNet 75.0%, Ensemble DL 90.6%; Classical SVM: 82–87%	High reported accuracy; comparison with classical SVM baselines.	Unclear patient-level data separation; no repeated or external validation; potential overlap across merged longitudinal images; quantum backend unclear.
	Islam et al. [92].	Hybrid CQ-CNN with ZZFeatureMap PQCs, Qiskit simulation, 2- and 3-qubit configurations; no real-QPU execution	Binary AD detection (OASIS-2 MRI)	97.5% ± 0.8 acc., F1 ≈ 0.89; Comparable to ResNet-50 (97.1%, 25 M params)	High accuracy with minimal parameters; Efficient in memory/computation	CPU-only simulation; Longer training; Quantum convergence issues
	Aryan Singhal, Hursh Shah [93]	QViSTA hybrid quantum vision transformer with VQCs, TensorCircuit simulation on CPU; qubit count not explicitly reported	Multi-class AD staging with 40k MRI scans	AUC 86.7% (test) vs. Classical ViT 88.4%; Strongest for Moderate AD (AUC 0.96)	Fewer params than ViT; Efficient features; Proof of hybrid Q-Transformers	Slightly lower accuracy; Simulated qubits; Weaker on early stages

feature-space expansion via sparse autoencoders, dimensionality reduction through LASSO regularization, and final classification using a VQC. The model was trained and evaluated on the UCI Chronic Kidney Disease dataset, which contains 400 patient records with 25 clinical attributes (e.g., age, blood pressure, albumin). Experimental results demonstrated that the proposed VQC-based hybrid model achieved 98.2% accuracy, 97.9% F1-score, and 97.6% AUC-ROC, outperforming all conventional baselines. In comparison, classical classifiers such as Random Forest (89.3%), SVM (91.5%), Logistic Regression (92.7%), and MLP (93.6%) showed significantly lower accuracy, while even advanced RBF networks (95.9%) and a Quantum SVM (96.7%) remained behind the proposed architecture. Beyond raw accuracy, the VQC exhibited increased robustness to noise and multicollinearity, attributed to quantum superposition and entanglement effects that enhance exploration of the clinical feature space. This work highlights how QML can extend beyond image analysis to structured medical datasets, offering high-performance predictive modeling for early detection of chronic diseases. In the realm of cardiovascular complications, Alotaib et al. [74] implemented a Quantum Particle Swarm Optimization (QPSO)–optimized QSVM for heart disease prediction. Trained on a UCI heart disease dataset (14 features, 304 instances), their QML system achieved an accuracy of 96.7%, a low false detection rate of 0.09, and a fast computation time of 135 milliseconds. This performance outpaced the classical multilayer perceptron (MLP) baseline. Notably, the integration of QPSO facilitated superior hyperparameter tuning and kernel optimization, exploiting quantum parallelism to enhance boundary precision in complex feature spaces. The model's ability to converge faster and more accurately highlighted the utility of QML in real-time or

embedded medical systems. Maheshwari et al. [75] proposed two quantum machine learning models, an Optimized Quantum Support Vector Machine (OQSVM) and a Hybrid Quantum Multi-Layer Perceptron (HQMLP), for the prediction of cardiovascular disease using an electronic health record dataset collected at Basurto Hospital (Spain). After feature selection, the dataset was reduced to the ten most informative clinical variables, which were used to benchmark both quantum and classical algorithms. The OQSVM achieved 94% accuracy with balanced precision, recall, and F1-scores (all 94%), while the HQMLP obtained ~93% accuracy with precision of 95%, recall of 93%, and F1 of 92%. In comparison, the classical MLP reached ~93% accuracy, whereas a conventional SVM achieved 97%, representing the best-performing baseline. These results indicate that quantum models are already competitive with established machine learning methods, outperforming neural baselines such as MLP, though they have not yet surpassed the strongest classical techniques. Nevertheless, the study highlighted the computational efficiency of the proposed QML approaches, reinforcing their potential for real-time healthcare decision support. Abdulsalam et al. [76] proposed a novel heart disease prediction framework that integrates quantum and ensemble learning with explainability. Using the well-known Cleveland dataset, they benchmarked classical models (SVM and ANN) against quantum classifiers, namely QSVC, QNN, and VQC. The quantum approaches consistently outperformed their classical counterparts: SVM and ANN reached 85.24% accuracy, while QSVC, QNN, and VQC achieved 88.52%, 86.84%, and 85.25%, respectively. To further boost performance, they introduced a bagging ensemble of QSVCs, which obtained the highest accuracy of 90.16% with balanced precision, recall, and F1-score. Finally, to ensure transparency, they applied SHAP (SHapley Additive exPlanations), a game-theoretic method that quantifies the contribution of each feature to the model's decision, showing that variables such as the number of major vessels, thallium heart scan, and ST-slope were the most influential predictors. This combination of improved predictive power and interpretability highlights the promise of quantum machine learning for clinically relevant decision support. Prabhu et al. [77] introduced QuCardio, a quantum framework for multi-class cardiovascular disease classification using ECG images. They compared classical SVC and CNN with quantum-enhanced models, namely QSVC, Pegasos QSVC, and a novel QNN. The QSVC outperformed the classical SVC with a + 10.76% increase in accuracy (94.09%vs. 83.33%), alongside gains in precision (+9.73%), recall (+10.76%), F1-score (+10.79%), and specificity (+3.73%). Their multiclass Pegasos QSVC achieved similar improvements, showing improved performance over the classical SVC within this simulator-based experimental setting. The best results were obtained with the QNN architecture, which integrated quantum layers into a CNN pipeline, reaching 97.31% accuracy, 97.41% precision, 97.31% recall, 97.30% F1, and 99.10% specificity, outperforming the baseline CNN by +3.88% accuracy. Crucially, their quanvolutional layers enhanced spatial feature extraction, particularly capturing subtle ECG waveform deviations linked to arrhythmias and myocardial infarction. The QNN showed consistent performance across the five validation folds, although the evaluation remained limited to a single ECG-image dataset and simulator-based quantum implementations, without external or clearly reported patient-level validation. Heidari et al. [78] compared two hybrid quantum classifiers, Hybrid Quantum Neural Network (HQNN) and Hybrid Quantum Random Forest (HQRF), on the Cleveland and Statlog datasets to evaluate their suitability for early heart disease detection. HQNN delivered the highest discrimination power, reaching AUC values of 96.43% on Cleveland and 97.78% on Statlog, thanks to its ability to model complex, non-linear interactions through multi-layer entangled circuits. HQRF, while achieving slightly lower AUC scores (94.31% on Cleveland and 95.52% on Statlog), demonstrated greater robustness to outliers and class imbalance, often outperforming HQNN under noisy conditions. This head-to-head analysis suggests a practical trade-off: HQNN is preferable when accuracy on clean, high-dimensional data is paramount, whereas HQRF is better suited for real-world clinical datasets where imperfections and imbalance are unavoidable. In contrast, Banday et al. [79] introduced a quantum-assisted hybrid ensemble framework for coronary heart disease prediction, tested on a large cohort of 20,000 records with 14 reported attributes. Classical baselines such as KNN, Decision Trees, Random Forest, and Logistic Regression already delivered strong results, e.g., KNN and DT approached near-perfect accuracy (99.99% and 99.97%), while RF and LR trailed slightly at 98.60% and 98.79%, respectively. The ensemble models also reported near-perfect performance.The KNN–RF ensemble reached 99.96% accuracy with 99.95% precision, 99.97% recall, and 99.96% F1-score, while the AdaBoost–RF ensemble closely followed with 99.93% accuracy. These marginal but consistent gains are significant in a clinical context: quantum kernels improved feature space exploration and reduced the impact of noise, ensuring fewer false negatives and more reliable generalization across heterogeneous data sources. However, these near-perfect results should be interpreted cautiously because the study did not clearly report the data-splitting procedure or the cross-validation configuration, and no external validation or uncertainty estimates were provided. Moreover, the specific quantum component and execution backend were insufficiently described, limiting interpretation of these findings as evidence of quantum advantage. Coupled with deployment on an energy-efficient Raspberry Pi 5 GPU platform for real-time integration of EHRs, IoT signals, and imaging, the framework demonstrates how quantum assistance can refine already strong classical learners into clinically robust decision-support systems.

5.3.3. *Neurological complications*

In recent years, T2DM and metabolic syndrome have been increasingly linked not only with well-known microvascular and macrovascular complications, but also with early cognitive decline and neurodegeneration, commonly described in the literature as "Type 3 diabetes." [80]. Epidemiological and mechanistic studies indicate that brain insulin resistance, oxidative stress, and inflammation, pathways shared with T2DM, play a crucial role in Alzheimer's disease pathology and cognitive impairment [81]. Large cohort studies have found that individuals with T2DM face significantly elevated risk of dementia, including Alzheimer's, with one meta-analysis estimating up to 65% higher risk relative to nondiabetic counterparts [82,83]. Despite this strong association, early detection of cognitive decline secondary to metabolic dysfunction remains problematic using conventional tools. Standard cognitive screenings exhibit limited sensitivity in detecting subtle deficits during the initial stages, while neuroimaging markers often appear after irreversible damage has occurred [84,85]. In this context, QML emerges as a promising approach. Several studies have recently explored the integration of quantum-enhanced architectures to improve detection and classification of cognitive decline, particularly in Alzheimer's disease (AD).

One of the earliest and most cited efforts is by Shahwar et al. [86], who developed a hybrid model combining a ResNet-34 feature extractor trained on structural MRI images with a six-layer VQC. The quantum component compressed a 512-dimensional feature vector into a 4-dimensional quantum embedding using amplitude encoding. Trained on 6400 MRI scans from the ADNI dataset, the hybrid model achieved a 97.2% test accuracy and 99.1% training accuracy, outperforming the classical baseline (92%) in both performance and convergence, and highlighting the value of VQCs for dimensionality reduction and enhanced decision boundaries. Expanding on this foundation, Kim et al. [87] proposed QCCNN, a hybrid CNN–VQC model for AD classification using the same dataset. The VQC was integrated after a dense layer, enabling quantum feature interaction at a deeper level. QCCNN achieved a 97.5% test accuracy and 95.1% validation accuracy, while the classical CNN reached only 91.5% and 89.2%, respectively. Notably, the model displayed balanced accuracy across demented (95%) and non-demented (98%) classes, suggesting that QML can improve robustness in clinically diverse populations. Addressing the challenge of

high-dimensional neuroimaging data, Chen et al. [88] proposed CompressedMediQ, a hybrid quantum-classical pipeline that combines CNN-based feature extraction and PCA-based dimensionality reduction with a QSVM for final classification. Applied to the ADNI and NIFD datasets, the pipeline achieved high multiclass classification accuracy across six dementia stages, including precision rates of 98% (normal controls), 99% (questionable cognitive impairment), and 91% (very mild dementia). Overall, the quantum model reached an accuracy of 96.1%, outperforming the classical SVM baseline at 78.8%, particularly in distinguishing intermediate dementia stages where traditional models tend to misclassify. These results validate the efficacy and scalability of quantum-enhanced pipelines for complex neuroimaging applications under NISQ constraints, highlighting their potential utility in clinical diagnostics for neurodegenerative diseases. From a temporal perspective, Choi et al. [89] analyzed resting-state fMRI time series from nine brain regions strongly implicated in early cognitive decline, such as the hippocampus, medial frontal gyrus, and parahippocampal cortex. They proposed a hybrid pipeline where 1D convolutional layers extracted local temporal features, while QCNNs modeled higher-order non-linear dependencies across time. Classical CNN baselines achieved a balanced accuracy of 52.3%, whereas the model with four QCNN blocks reached 58.1%; this difference was reported as statistically significant in the original study ($p < 0.05$).Notably, the quantum-enhanced models required fewer parameters (~4k vs. ~11k), reducing the risk of overfitting while maintaining robustness across test folds. Attention maps further revealed that the model focused on clinically relevant structures (particularly the hippocampus and parahippocampal cortex) mirroring established neuropathological findings in early dementia. These results, while modest in raw accuracy, highlight the unique advantage of quantum layers in capturing subtle temporal signatures from rs-fMRI that classical CNNs fail to disentangle, pointing toward scalable quantum-enhanced temporal modeling in neuroimaging-based dementia research. In a novel shift from traditional neuroimaging approaches, Cappiello et al. [90] explored quantum machine learning for non-invasive cognitive screening based on handwriting biometrics. Utilizing the DARWIN (Diagnosis AlzheimeR WIth haNdwriting) dataset, they compared classical models (SVC, kNN, and DT) with quantum kernel methods implemented via variational quantum circuits. Among the classical baselines, SVC achieved the best accuracy (85.3% ± 7.5), while kNN and DT performed significantly worse (69.6% ± 8.2 and 73.6% ± 5.3, respectively). Quantum classifiers with 6 and 8 qubits reached accuracies comparable to classical SVC (≈83%), but with improved stability across folds. The 12-qubit quantum SVC outperformed all models, reaching 88.3% ± 4.7 accuracy, combining both higher predictive power and lower variance. Additional analyses on feature subsets (copy, graphic, memory/dictation tasks) and per-task evaluations confirmed the robustness of the quantum approach, which consistently matched or exceeded classical baselines. These findings demonstrate the feasibility of deploying quantum-enhanced models as scalable, cost-effective preclinical screening tools, particularly in contexts where imaging resources are limited. Building further on hybrid quantum-classical pipelines, Belay et al. [91] proposed an ensemble architecture combining customized VGG16 and ResNet50 networks for feature extraction with a QSVM classifier. Using merged Alzheimer's disease Neuroimaging Initiative I and II (ADNI I and II) datasets, the model was trained to discriminate among four Alzheimer's stages: non-demented, very mild, mild, and moderate. The proposed VGG16+ResNet50+QSVM ensemble achieved 99.89% accuracy, 99.25% precision, 99.23% recall, and 99.13% F1-score, substantially surpassing both individual CNN baselines (VGGNet: 90.1%, ResNet: 75.0%, Ensemble DL: 90.6%) and classical SVM classifiers applied to deep features (VGG+SVM: 85.2%, ResNet+SVM: 82.2%, Ensemble+SVM: 86.8%). Compared to its classical counterpart, the QSVM provided gains of +8.5% over the best end-to-end ensemble DL and +12.2% over the ensemble+SVM baseline, showing higher performance than the reported classical baselines within this experimental setting.. However, this near-perfect performance should be interpreted cautiously because the study did not clearly report the train–validation–test proportions or confirm patient-level data separation. Given that merged ADNI1 and ADNI2 images included scans acquired at different time points, overlap between related images across data partitions cannot be excluded. No repeated cross-validation, external validation, or uncertainty estimates were reported. Islam et al. [92] proposed CQ-CNN, a hybrid framework for Alzheimer's detection from 3D MRI that integrates three key components: a U-Net–based segmentation model (SkullNet) for brain tissue extraction, a probabilistic diffusion module for minority-class augmentation, and a lightweight 3-qubit variational quantum circuit (≈13 K parameters) as the final classifier. Evaluated on the OASIS-2 dataset (binary task: non-demented vs. moderate AD), the model achieved 97.5% ± 0.8 accuracy and an F1-score of 0.89, surpassing parameter-matched classical CNNs and approaching or exceeding the performance of much larger state-of-the-art deep learning models. For instance, while AlexNet reported 92.9% accuracy with 60 M parameters and ResNet-50 reached 97.1% with 25.6 M parameters, the proposed CQ-CNN achieved comparable accuracy with over 99.99% fewer parameters (0.48 MB vs. tens or hundreds of MBs). This highlights the model's efficiency in both memory and computation, underscoring its potential suitability for resource-constrained clinical environments. However, training remained restricted to CPU-based quantum simulations, resulting in longer runtimes than GPU-accelerated CNNs, and convergence issues in the quantum circuits occasionally limited training stability. Lastly, some authors [93] introduced QViSTA, a hybrid quantum vision transformer model designed for multi-stage Alzheimer's diagnosis using structural MRI. Unlike classical vision transformers (ViTs) that rely on self-attention, QViSTA replaces these components with VQC blocks embedded into the transformer encoder. Trained on a large, balanced dataset of 40,000 preprocessed MRI slices spanning four Alzheimer's stages, QViSTA achieved a test AUC of 86.67% and a validation AUC of 87.86%, closely matching the performance of a classical ViT (88.39% AUC) while reducing feature space by 3.18%. Notably, QViSTA showed the highest true positive rate for Moderate Demented cases (861/900 correctly classified) and the lowest for Very Mild Demented cases (483/900). While simulated quantum circuits may have limited its full potential, QViSTA exhibited faster convergence and lighter computational overhead, indicating its potential for deployment on edge devices or hospital systems with limited hardware resources. Together, these studies provide robust and converging evidence that QML, particularly in hybrid configurations, can enhance classification accuracy, training efficiency, and interpretability across a range of input modalities, including structural MRI, fMRI, and even behavioral time series. The consistent outperformance of classical baselines across various experimental setups reinforces the promise of QML for early detection of neurodegenerative disease, especially in populations affected by T2DM and metabolic syndrome, where such conditions may manifest earlier and progress more rapidly.

6. Discussion

Quantum Machine Learning (QML) is progressively emerging as a viable analytical framework for addressing the intrinsic complexity of metabolic disorders such as Metabolic Syndrome and Type 2 Diabetes Mellitus [10]. These conditions are characterized by the convergence of genetic predisposition, behavioral patterns, metabolic fluctuations, and progressive organ dysfunction, generating data landscapes that are heterogeneous, nonlinear, and temporally evolving, spanning electronic health records, wearable sensor streams, multi-omics data, and patient-reported outcomes [94]. Across the studies reviewed, QML and hybrid quantum–classical models have been explored as tools to model these complex data structures under conditions where classical machine learning methods often encounter limitations, particularly in the presence of noise, missing values, and small-to-moderate cohort sizes [1,30,

45]. The available evidence does not indicate a uniform performance advantage of QML over state-of-the-art classical approaches. Instead, quantum-enhanced models appear most effective in constrained analytical regimes typical of metabolic research, where improvements are observed primarily in robustness, stability, and, in selected cases, computational efficiency [7,8]. Within this context, the present Discussion synthesizes QML applications across three interconnected domains (early metabolic dysregulation and obesity, glycemic control and diabetes management, and the prediction of chronic complications) highlighting both emerging strengths and persistent methodological and translational limitations.

Obesity, as the most prevalent and clinically impactful manifestation of metabolic imbalance, provides a particularly illustrative starting point. Recent proof-of-concept studies illustrate this potential in the context of obesity and early metabolic dysregulation. Abeltino et al. [52], through the QMA framework, explored the use of a quantum echo state network to model individual weight trajectories from longitudinal metabolic and behavioral data, with particular attention to the management of incomplete or noisy inputs. Ozpolat et al. [53],in contrast, investigated QSVM-based obesity classification using different dimensionality-reduction methods and quantum feature maps, showing how model performance may vary substantially according to preprocessing and encoding choices. Together, these studies suggest that QML may offer flexible approaches for representing complex temporal patterns and nonlinear metabolic phenotypes. However, the current evidence remains based on a limited number of proof-of-concept investigations, individual datasets, and constrained experimental settings. The lack of repeated or external validation, the dependence on supervised preprocessing, and the predominant use of simulated quantum environments limit the generalizability of the reported findings. These results should therefore be interpreted as preliminary evidence of methodological feasibility rather than as confirmation of established clinical utility or quantum advantage.

Building on this, several studies have investigated the application of QML to type 2 diabetes, motivated by the need to improve early diagnosis and personalized disease management. While classical models often struggle with small sample sizes, high-dimensional features, and nonlinear interactions, quantum approaches have begun to demonstrate competitive performance and unique computational benefits. Monteiro et al. [55] aimed to improve early diabetes classification using the well-known PIMA Indian Diabetes Dataset. By introducing a quantum perceptron, their goal was to test whether quantum-inspired neurons could enrich decision boundaries through superposition and interference. The model achieved 76% accuracy, outperforming classical perceptrons (63%), though still below deep neural networks (AUC-ROC 0.80). The main contribution here was conceptual, showing how quantum principles can be integrated into neural architectures, even without variational circuits. Subsequent studies focused more directly on diagnostic accuracy and scalability. Vimal et al. [57] benchmarked different quantum models for predicting diabetes status and found that a Quantum QSVC delivered 0.74 accuracy, essentially matching Logistic Regression and approaching SVM (0.76), while VQC performed poorly (0.61). Genc et al. [58] extended this line of work to the Diabetes Health Indicators dataset (>250,000 records), aiming to test whether quantum feature encodings could handle high-dimensional, real-world health data. Their QSVM with quantum feature mapping achieved 84.3% accuracy, confirming that quantum kernels can scale to large and heterogeneous datasets. Similarly, Hancco-Quispe et al. [14] explored dimensionality reduction before quantum classification, showing that LDA preprocessing with QSVC improved accuracy to ~83%, in some cases surpassing Logistic Regression and KNN, highlighting the importance of careful feature preparation in hybrid pipelines. A different research goal was accelerating large-scale medical data analysis. Maheshwari et al. [75] tested quantum boosting ensembles on EHRs to separate diabetes patients with and without acute diseases. While accuracy (~69%) was comparable to Random Forests and XGBoost, the quantum implementation achieved a ~55 × computational speed-up, underscoring efficiency gains. Prakash et al. [61] pursued a similar goal (reducing training time without losing predictive power) and showed that QBoost reached 73.4% accuracy and 85.7% specificity, outperforming Bayesian networks and decision trees with much faster runtimes. Jha et al. [62] refined this direction by developing a hybrid quantum–classical ensemble: performance was strong (Accuracy 0.89, AUC 0.96), only slightly below AdaBoost (0.94, AUC 0.98), while offering clear computational advantages. Finally, one of the most innovative directions is noninvasive diabetes monitoring. Sridevi et al. [63] collected fingertip near-infrared spectroscopy videos to estimate glucose and HbA1c levels. Their goal was to evaluate whether QML could handle noisy biosignals more effectively than classical ML. Results were striking: QSVM achieved 89.3% accuracy for glucose prediction and 96.3% for HbA1c, outperforming all seven classical baselines. This study demonstrates QML's ability to move beyond structured clinical datasets toward wearable and sensor-based applications. Beyond glycemic control, QML has also been applied to the study of chronic complications of metabolic syndrome, where the challenge lies in detecting subtle pathological changes across imaging, physiological, and neurological data streams. In the microvascular domain, Alavi et al. [66] targeted the classification of diabetic foot ulcers, integrating transfer learning from a CNN with a Variational Quantum Classifier; their hybrid approach improved diagnostic accuracy over the CNN baseline (macro-AUC 0.713 vs. 0.687), demonstrating the feasibility of quantum–classical pipelines for complex multi-class image recognition. More striking advances have been reported in diabetic retinopathy (DR): Bali et al. [67] proposed QuantumNet, a hybrid ResNet–variational quantum classifier that reached 94.11% accuracy on the APTOS 2019 dataset, roughly 12 percentage points above the best classical deep-learning baselines. Jain et al. [68] extended this to stage grading, where a ResNet18–VQC hybrid attained 97.2% accuracy, outperforming the classical backbone by nearly 12 percentage points and reliably distinguishing all five DR severity levels. Similarly, Acuña et al. [69] benchmarked QSVM and VQC against CNN and SVM baselines on 3000 fundus images, showing that QSVM reached 94.6% accuracy (AUC = 0.961) with only 30 ms inference time, markedly faster and more accurate than CNN (89.9%, AUC = 0.912, 140 ms), highlighting the promise of QML for real-time screening. Comparable progress is seen in cardiovascular complications. Parthasarathi et al. [73] designed a VQC-based hybrid model for early chronic kidney disease detection using structured clinical data; their pipeline achieved 98.2% accuracy and 97.9% F1-score, significantly surpassing Random Forests (89.3%) and even advanced kernels such as QSVM (96.7%), while demonstrating robustness to noise and multicollinearity. Prabhu et al. [77] focused on multi-class cardiovascular classification from ECG signals, where their QSVM improved accuracy by +10.8% over a classical SVC (94.1%vs. 83.3%) and a QNN–CNN hybrid achieved 97.3% accuracy with 99.1% specificity, underscoring the potential of quantum layers to capture subtle waveform variations linked to arrhythmias and myocardial infarction. Finally, in the neurological sphere, where T2DM is strongly associated with accelerated cognitive decline, quantum models have shown particular value in Alzheimer's disease detection. Shahwar et al. [86] demonstrated that embedding a VQC into a ResNet-34 trained on MRI scans improved accuracy from 92% to 97.2%, while Kim et al. [87] confirmed similar gains (97.5%vs. 91.5% for classical CNNs). Chen et al. [88] addressed the harder task of multi-stage dementia classification using CompressedMediQ, a CNN+QSVM pipeline that achieved 96.1% accuracy versus 78.8% for classical SVMs, with particular improvements in intermediate dementia stages often misclassified by traditional models.

Table 4 provides a structured comparison of the classical and quantum machine learning approaches reviewed across the main clinical domains.

While the comparative results summarized in Table 4 highlight several instances in which quantum-enhanced models match or surpass

Table 4

Comparative overview of classical versus quantum machine learning models across clinical domains. This table summarizes the main differences in performance, structure, and application of classical and QML approaches for obesity prediction, type 2 diabetes diagnosis and management, and the detection of chronic complications including retinopathy, cardiovascular disease, and cognitive decline. Quantum-enhanced models show advantages in accuracy, robustness to noise, inference speed, and early-stage detection, particularly in small-sample and high-dimensional scenarios.

Clinical Area	Task	Classical Models	QML Models	QML Key Advantages
Obesity / Early Metabolic Risk	Body weight prediction	Echo State Networks	Quantum Echo State Network (qESN – QMA)	31.8% lower RMSE; 76% greater robustness in case of outliers [52]
	Obesity classification (multiclass)	LDA & PCA + SVM	LDA & PCA + QSVM	LDA-QSVM (Z Feature Map & Pauli X); superior class separation [53]
Diabetes Diagnosis & Glycemic Control	T2DM prediction	SVM, LR, RF, KNN, XGBoost	QSVM, QNN	QSVM achieved state-of-the-art accuracy (HbA1c 96.3%); promising for non-invasive monitoring despite longer training times.
	Binary classification (diabetic vs. non-diabetic)	Perceptron, Deep Neural Networks	Quantum Perceptron	Exploits superposition/interference in decision boundaries; higher accuracy than classical perceptron; introduces quantum neuron concept.
	Binary classification	Multilayer Perceptron (DL)	Variational Quantum Classifier	Memory handling efficiency; compact parameterization; potential faster inference in native QPU implementations.
	Binary classification	Logistic Regression, SVM	QSVC, VQC	QSVC competitive with LR and SVM; kernel-based quantum mapping promising for high-dimensional features; VQC limited by noise/optimization issues.
	Binary classification	Logistic Regression, KNN	QSVC + LDA, VQC	LDA + QSVC outperforms PCA-based quantum pipelines; hybrid preprocessing enhances quantum classifier efficiency.
	Binary classification	Decision Tree, Random Forest, XGBoost, AdaBoost	QBoost, QBoost Plus, Hybrid Ensembles	Comparable accuracy but ~55x computational speed-up with quantum ensembles.
	Binary classification (critical vs. non-critical)	SVM, KPCA, DT, Bayesian Networks	QBoost	Higher accuracy and sensitivity than classical models; faster computation with optimized preprocessing.
	Binary classification	AdaBoost, XGBoost, CatBoost, Voting ensembles	Hybrid QBoost ensembles	Significant computational speed-ups; near-parity in accuracy/AUC with classical boosting.
Chronic Complications	Multi-class ulcer classification (infection, ischaemia, none, both)	Xception CNN (transfer learning)	Hybrid CNN + VQC	Improved macro-AUC (0.7133 vs. 0.6867); better F1 (0.5587 vs. 0.5067); demonstrates value of hybrid quantum–classical models in complex multi-class tasks.
	DR detection (APTOS 2019)	ResNet backbone	QuantumNet: quantum transfer learning with variational quantum classifier	94.11% accuracy (~+12 pp vs classical DL).
	Multi-class severity grading (5 DR stages)	ResNet-18	Hybrid ResNet-18 + VQC	97.2% accuracy (+12% vs ResNet-18); strong lesion-level localization; reliable discrimination across all DR stages.
	Multi-class DR classification	CNN, SVM	QSVM, VQC	Higher accuracy (QSVM 94.6%, VQC 93.8%) vs CNN (89.9%) and SVM (88.5); significantly reduced inference times (25–30 ms vs 70–140 ms).
	Early detection of CKD	RF, SVM, LR, MLP	VQC-based hybrid pipeline	Achieved 98.2% accuracy, 97.9% F1, 97.6% AUC; more robust to noise & multicollinearity; quantum superposition/entanglement enhances feature exploration.
	Binary classification of cardiovascular disease	MLP baseline	QPSO-optimized QSVM	Accuracy 96.7%, low false detection (0.09), 135 ms runtime; QPSO improved kernel tuning & convergence speed.
	Binary classification of cardiovascular disease	MLP, SVM	OQSVM, HQMLP	Competitive with strong classical models; better than MLP but below SVM; highlighted computational efficiency for real-time deployment.
	Binary classification of cardiovascular disease + explainability	SVM, ANN	QSVC, QNN, VQC, Ensemble QSVC	QSVC ensemble best performer (90.2% acc); SHAP explainability; interpretable feature importance for clinical decision support.
	Multi-class ECG classification	SVC, CNN baseline	QSVC, Pegasos-QSVC, QNN	QNN achieved best results (97.3% acc, 99.1% specificity); quanvolutional layers enhanced spatial feature extraction for subtle ECG patterns.
	Binary classification of cardiovascular disease	KNN, DT, RF, LR	Quantum-assisted hybrid ensembles	Marginal but consistent gains (KNN–RF ensemble 99.96% acc); improved generalization, reduced noise sensitivity; efficient deployment on Raspberry Pi 5 for IoT/EHR integration.
	Binary classification for Alzheimer's Detection	ResNet-34 baseline	Hybrid ResNet-34 + VQC	Accuracy 97.2%; superior convergence; dimensionality reduction (512 to 4 quantum embedding) enhances decision boundaries.
	Binary classification for Alzheimer's Detection	Classical CNN	QCCNN (CNN + VQC)	Accuracy 97.5%; balanced across classes (95% demented, 98% non-demented); improved robustness to clinical heterogeneity.
	Multiclass dementia staging	Classical SVM	CompressedMediQ (CNN + PCA + QSVM)	Accuracy 96.1%; precision up to 99% in early stages; excels at intermediate stages prone to misclassification in classical ML.

(*continued on next page*)

Table 4 (*continued*)

Clinical Area	Task	Classical Models	QML Models	QML Key Advantages
	Temporal signature modeling from brain regions for Early Cognitive Decline	1D CNN baseline	QCNN temporal blocks	Improved accuracy (58.1%); fewer parameters (~4k vs 11k); better generalization; attention maps aligned with clinical regions (hippocampus, PHC).
	Non-invasive cognitive screening via handwriting for Alzheimer's Screening	SVC, kNN, DT	Variational quantum kernel classifiers	Best performance with 12-qubit QSVC (88.3%); lower variance across folds; robust across handwriting subtasks.
	Multi-class classification for Alzheimer's Staging	VGG16, ResNet50, Ensemble DL, Ensemble+SVM	Hybrid Ensemble (VGG16+ResNet50+QSVM)	Accuracy 99.9%; +8.5% vs best ensemble DL; +12.2% vs ensemble+SVM; quantum kernel generalizes better on imbalanced classes.
	Binary classification for Alzheimer's Staging	AlexNet, ResNet-50	CQ-CNN (SkullNet + diffusion augmentation + 3-qubit VQC)	Accuracy 97.5% with 99.99% fewer parameters than SOTA CNNs; lightweight (0.48 MB) to suitable for resource-constrained clinical settings.
	Multi-class classification for Alzheimer's Staging	Vision Transformer (ViT) baseline	QViSTA (ViT + VQC self-attention)	AUC ~87%, close to ViT; reduced feature space (−3.2%); faster convergence & lower overhead to feasible for edge/hospital deployment.

classical machine learning approaches, these outcomes should be interpreted as emerging patterns rather than evidence of a universal quantum advantage. Across the reviewed studies, performance gains associated with QML consistently depend on the operational context, dataset characteristics, and clinical task under consideration. Classical AI approaches remain the preferred solution in large-scale, data-rich scenarios (such as population-level imaging or extensive electronic health record analyses) where deep learning models benefit from abundant labeled data, mature optimization strategies, and established validation pipelines (e.g., [56,62,75]). In several of these cases, QML models achieve performance parity but do not yet surpass state-of-the-art classical architectures. By contrast, QML and hybrid quantum–classical models demonstrate their most consistent advantages in constrained regimes typical of metabolic and chronic disease research, including small-to-moderate cohort sizes, heterogeneous and multimodal inputs, strong nonlinear dependencies, and noisy or incomplete longitudinal measurements. In these settings, multiple studies report improved robustness, reduced sensitivity to data corruption, or significant computational speed-ups without loss of predictive accuracy (e.g., [52,59,62]). From a practical perspective, and based on the comparative evidence presented in this review, QML should therefore be regarded as a specialized methodological extension addressing specific bottlenecks in metabolic research (such as early risk stratification, individualized trajectory modeling, and sensor-driven monitoring) rather than as a general replacement for classical AI frameworks.

Despite its transformative potential, QML still faces several critical limitations that must be addressed before it can be responsibly deployed in healthcare and nutrition. Most notably, current implementations depend on Noisy Intermediate-Scale Quantum devices, which are constrained by qubit instability, limited scalability, and the absence of robust error correction systems [19,20,29]. More specifically, restricted qubit connectivity, short coherence times, gate and readout errors, and limited circuit depth reduce the size and complexity of models that can be executed reliably on real quantum hardware [34,35]. Moreover, many healthcare-oriented QML studies still rely on quantum simulators rather than real quantum processing units, which complicates reproducibility across platforms and limits the validity of direct comparisons of runtime, scalability, and computational efficiency with classical hardware [95], translating high-dimensional clinical data into quantum representations, via encoding schemes or quantum feature maps, remains computationally expensive and error-prone, especially when dealing with heterogeneous data such as time-series, images, and molecular profiles [30]. On the ethical and regulatory front, QML raises significant challenges. The integration of sensitive patient data (especially from wearable, omics, or personal monitoring sources) escalates concerns around privacy, algorithmic transparency, and equitable access. Current regulatory frameworks remain insufficiently tailored to quantum-enhanced systems. Beyond privacy and transparency, the clinical use of QML also raises questions about how quantum-enhanced predictions can be explained, audited, and attributed when they contribute to high-stakes medical decisions, particularly in hybrid systems where responsibility is shared across developers, healthcare professionals, and institutions [96].

In the EU, the recently enacted AI Act (effective August 2024) imposes risk-based requirements, including stringent transparency, cybersecurity, and conformity assessment obligations for high-risk medical AI systems, potentially overlapping and clashing with existing MDR/IVDR provisions (EU AI Act, Article 6; [97]). In the US, the FDA's evolving AI/ML Software as a Medical Device (SaMD) Action Plan and the lifecycle-based Predetermined Change Control Plan address adaptive ML, but do not yet account for the distinct complexities of quantum models [98]. These challenges are compounded by the high cost and specialized expertise required to develop and deploy QML systems, risking a widening of health inequities if access to quantum-empowered diagnostics remains limited to well-resourced institutions.

Taken together with the hardware, regulatory, and scalability constraints discussed above, a further consideration concerns the current level of technological maturity of quantum computing and its translation into real-world applications. Despite decades of theoretical development and sustained investment, fully deployed quantum systems solving large-scale, real-world problems remain rare, particularly in regulated domains such as healthcare [99]. Most quantum and quantum-enhanced solutions reported to date, including those reviewed here, are best described as proof-of-concept or hybrid implementations that still rely heavily on classical computational infrastructures. Notably, a small number of recent studies have reported task-specific quantum utility in highly controlled settings, such as optimization and sampling problems on utility-scale devices [100]. However, these demonstrations remain narrowly scoped and do not yet translate into general-purpose or clinically deployable solutions. Consequently, the evidence discussed in this review should be interpreted primarily as an indication of feasibility and directional promise, rather than immediate clinical readiness. The interpretation of apparently high QML performance also requires rigorous benchmarking. Predictive accuracy alone should not be considered evidence of quantum advantage unless quantum models are compared with well-optimized classical baselines under equivalent validation conditions. Recent methodological work has emphasized that the usefulness of quantum models depends strongly on the structure of the data, the selected feature representation, and the strength of the classical comparator [101]. The broader dequantization literature cautions that some apparent quantum speed-ups may disappear when improved classical algorithms and equivalent data-access assumptions are considered [102]. Quantum-inspired classical methods have reproduced the performance of selected quantum algorithms, including recommendation-system and low-rank linear-algebra approaches, thereby narrowing some previously claimed advantages [102,103]. These findings do not exclude task-specific quantum utility, but indicate that claims of quantum advantage in biomedical QML

should be supported by end-to-end comparisons that include data encoding, training, inference, and hardware-related overheads.

A further aspect that warrants careful consideration is the comparison between quantum machine learning and traditional Von Neumann computing architectures, particularly from the perspective of sustainability and energy consumption. Most contemporary artificial intelligence systems are implemented on Von Neumann architectures, in which memory and computation are physically separated. This architectural design results in substantial data movement between processing units and memory, a well-known bottleneck that significantly contributes to the energy footprint of modern AI workloads, especially in large-scale deep learning applications [104]. Quantum computing follows a fundamentally different paradigm, where information storage and processing are intrinsically co-located within quantum states. In principle, this architectural distinction could reduce data movement and enable certain computations to be performed with fewer logical operations. However, at the current stage of technological development, quantum hardware does not offer a measurable advantage in terms of sustainability or energy efficiency compared to classical systems. Present-day quantum processors require energy-intensive cryogenic cooling, complex control electronics, and extensive error mitigation procedures, all of which dominate their overall energy footprint and offset any potential algorithmic gains [99,105]. As a consequence, existing demonstrations of QML (particularly those relying on hybrid quantum–classical pipelines or embedded classical co-processors) should be interpreted as proofs of feasibility rather than as evidence of improved sustainability. Meaningful comparisons between QML and classical AI in terms of energy efficiency therefore remain premature and will only become scientifically robust once fault-tolerant quantum hardware, standardized benchmarking methodologies, and full lifecycle energy assessments are available. At present, sustainability considerations should thus be framed as a long-term architectural hypothesis, rather than as a validated benefit of current quantum machine learning implementations [1].

Looking forward, the QMA proof-of-concept could evolve into a broader quantum-enabled Personalised Metabolic Avatar (PMA). Proposed by the present author group as a future research framework, the PMA would extend the QMA beyond weight trajectories and energy balance by integrating physiological, behavioral, clinical, and molecular information. The PMA should therefore be regarded as a prospective conceptual development rather than as an independently validated model.The rationale is clear: metabolic health is shaped by systemic interactions that extend well beyond glucose and body weight. For instance, red blood cell membrane fluidity, as emphasized by Pitocco et al. [106] reflects oxidative stress–driven lipid alterations and has been linked to the progression of type 2 diabetes, making it a potential early biomarker of systemic dysfunction. Similarly, gut microbiota composition, shown by Bianchetti et al. [107] and Abeltino et al. [108] to predict glycemic responses and metabolic phenotypes, represents another promising dimension. Embedding these non-traditional yet mechanistically relevant signals into hybrid quantum-classical models could substantially enhance early detection, fine-grained phenotyping, and precision intervention strategies. Recent work on quantum computing in precision medicine has similarly emphasized the potential of hybrid quantum–classical workflows for integrating genomic, multi-omic, and clinical data, while highlighting persistent challenges related to hardware maturity, scalable data encoding, clinical validation, privacy, and regulatory governance [109]. Against this background, in the short term, such hybrid pipelines (where classical preprocessing is combined with quantum-enhanced learning components) remain the most viable route [45,110]. However, the computational cost of encoding large and heterogeneous biomedical datasets into quantum representations remains a significant limitation and may reduce the practical benefit of the quantum component [111]. Variational quantum models may also be affected by optimization and trainability problems, including noise-induced barren plateaus and vanishing gradients [34]. Future investigations should therefore move beyond isolated technical demonstrations by including reproducible comparisons with optimized classical baselines, repeated experiments, external validation, and prospective evaluation in representative clinical populations. Privacy-preserving approaches may also become important for multicenter applications involving sensitive clinical data. Differentially private QML and quantum federated-learning frameworks represent possible directions for distributed analysis without the direct centralization of patient-level information [112,113].

In the longer term, however, true quantum advantage will depend on advances in hardware reliability and scalability [114], as well as the design of domain-specific quantum algorithms. If these technical and ethical barriers can be addressed in parallel, QML-enabled systems like the QMA may redefine the management of metabolic disorders, delivering not only individualized care but also scalable frameworks for population-level risk prediction and public health planning.

6.1. Roadmap for clinical adoption of quantum machine learning in healthcare

Bridging this outlined translational gap will require concerted regulatory innovation. While preliminary studies have demonstrated promising diagnostic and predictive performance in diabetes [55,56,63] and its complications [68,91], real-world deployment demands robust validation pipelines, regulatory sandboxes, and international harmonization of compliance criteria. As recent reviews suggest [14,58], the design of domain-specific evaluation metrics, transparent conformity pathways, and AI-aware medical standards will be essential to align QML advancements with clinical and legal acceptability. To translate QML from research into clinical impact, a structured, multi-phase roadmap is required, one that aligns technical feasibility with regulatory compliance, ethical acceptability, and clinical integration.

6.1.1. Phase 1: experimental validation and benchmarking

Early-stage QML models should undergo rigorous internal validation against classical baselines using publicly available biomedical datasets (e.g., PIDD, MIMIC-IV, ADNI). Emphasis should be placed on reproducibility, performance under noise, interpretability, and robustness on small-sample or heterogeneous data. Standardized metrics (AUC, F1-score, calibration curves) and uncertainty quantification must be reported transparently. This phase should also document hardware specifications (type of quantum processor, number of qubits, simulator vs. real chip) to ensure reproducibility.

6.1.2. Phase 2: hybrid deployment and clinical simulation

Given current NISQ limitations, hybrid classical-quantum pipelines should be tested in simulated clinical environments, including sandboxing or digital twins of hospital workflows. Integration with real-time data from wearables or EHRs should be explored in non-interventional settings. Here, explainability becomes critical: methods such as QSHAP or quantum kernel visualization may help bridge the interpretability gap. Concurrently, interaction with hospital IT infrastructures and medical devices (Software as a Medical Device – SaMD) must be assessed for feasibility.

6.1.3. Phase 3: ethical and regulatory readiness

As models approach clinical use, alignment with legal frameworks becomes essential. In the EU, QML-based systems may fall under the Medical Device Regulation (MDR) if they support diagnosis or prediction, and under the AI Act as high-risk systems. This entails the need for human oversight, risk classification, transparency documentation, and post-market monitoring plans. In the US, FDA guidance on AI/ML-enabled SaMD will likely apply, requiring a predetermined change control plan, clinical performance testing, and cybersecurity documentation. Since QML pipelines often rely on cloud-based or hybrid infrastructures, GDPR compliance (data minimization, lawful basis, data

subject rights) must also be integrated into system design from the outset.

6.1.4. Phase 4: clinical trials and regulatory certification

QML models intended for direct clinical use (e.g., risk scoring, decision support, diagnostic triage) will require prospective validation through clinical trials or real-world evidence studies, following Good Machine Learning Practice (GMLP) principles. Where applicable, submission to regulatory authorities (e.g., Notified Bodies in the EU, FDA De Novo or 510(k) pathway in the US) should include algorithmic transparency reports, training dataset provenance, risk-benefit analysis, and robust validation documentation. A possible intermediary step is regulatory "sandbox" programs (e.g., AI sandbox by the European Commission), which allow limited deployment under monitoring before full approval.

6.1.5. Phase 5: scalable integration and equity monitoring

Once validated and certified, QML solutions should be integrated into clinical decision workflows via interoperable platforms (e.g., FHIR standards, HL7 interfaces), with continuous post-deployment monitoring for bias, performance drift, and patient safety. Accessibility and equity must be explicitly addressed, especially given the concentration of quantum resources in high-income settings. Initiatives for open-access QML tools, federated training, and inclusive datasets are essential to avoid exacerbating digital divides.

QML's path to clinical relevance requires not only scientific innovation, but regulatory intelligence, ethical alignment, and system-level integration planning. Future efforts should foster collaboration between quantum scientists, clinical researchers, bioethicists, and regulators to build trustable, transparent, and effective quantum-enabled health systems.

7. Conclusions

QML is emerging as a promising experimental approach in metabolic medicine, with potential applications in the analysis of complex clinical, physiological, and behavioral data. The applications examined in this work illustrate how quantum and hybrid quantum–classical models may contribute to the analysis of chronic, multifactorial disorders such as Metabolic Syndrome and type 2 diabetes. Models including QSVM, VQC, and QBoost have reported competitive performance in selected applications, including blood glucose prediction, retinal image classification, and the assessment of cardiovascular and neurodegenerative complications. However, these findings were obtained across heterogeneous datasets, validation procedures, execution environments, and performance metrics, and were often reported without confidence intervals or measures of variability. Consequently, the current evidence does not yet support general claims of superior accuracy, faster processing, or established quantum advantage over well-optimized classical approaches. However, the widespread use of QML in healthcare remains hindered by technological challenges and systemic issues. The current limitations of quantum hardware (noise, instability, poor scalability) and the difficulties in integrating heterogeneous clinical data into quantum circuits remain significant obstacles. Added to this are significant ethical and regulatory issues related to personal data protection, model transparency, and equitable access to new technologies.

In light of these considerations, future developments must focus on improving quantum infrastructures, designing more efficient and resilient algorithms, and building regulatory and clinical ecosystems ready to accommodate these innovations. Hybrid quantum–classical models currently represent the most feasible near-term approach for integrating quantum components into healthcare applications. QML may contribute to the evolution of precision medicine by supporting more predictive, personalized, and timely approaches to chronic disease management. However, its impact on patient outcomes and healthcare-system efficiency will depend on rigorous clinical validation, technological maturity, and responsible implementation.

Ethics statement

According to the institutional and national guidelines, this research did not require formal ethical approval, as it did not involve human participants, animals, or identifiable personal data.

Statement about the use of artificial intelligence

During manuscript revision, the authors used OpenAI ChatGPT for language editing, consistency checking. The authors reviewed all outputs and take full responsibility for the final content

CRediT authorship contribution statement

Alessia Riente: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Cassandra Serantoni:** Validation, Methodology, Investigation. **Michele Maria De Giulio:** Validation, Methodology, Investigation. **Stefano Capezzone:** Validation, Methodology, Investigation. **Rosita Esposito:** Validation, Methodology, Investigation. **Marco De Spirito:** Validation, Methodology, Investigation. **Giuseppe Maulucci:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors have no relevant interests to declare.

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Supplementary materials

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