# Quantum Machine Learning for Digital Health? A Systematic Review

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#### Abstract

With the digitization of health data, the growth of electronic health and medical records lowers barriers for using algorithmic techniques for data analysis. While classical machine learning (ML) techniques for health data approach commercialization and incorporation into clinical workflows, there is not yet clear evidence whether quantum machine learning (QML) will actually provide any empirical advantage for digital health data processing tasks. In this systematic literature review we assess whether, in light of developing digital health technologies, quantum machine learning algorithms have the potential to outperform existing classical methods in efficacy or efficiency. We include digital electronic health/medical records (EH/MRs) and data considered to be a reasonable proxy to EH/MRs. Eligible QML algorithms must be designed for quantum computing hardware, as opposed to quantum-inspired techniques. PubMed, Embase, IEEE, Scopus and a physics preprint server arXiv yielded 4915 studies between 2015 to 10 June 2024. After screening 169 eligible studies, most studies contained widespread technical misconceptions about QML and we excluded 123 studies for insufficient rigor in analysis. Of the remaining 46 studies, only 16 studies consider realistic QML operating conditions, either by testing algorithms on quantum hardware, or using noisy quantum circuits when assessing QML algorithms. We find QML applications in digital health focus primarily on clinical decision support rather than health service delivery or public health. Nearly all QML models are linear quantum models, and therefore represent a subset of general quantum algorithm structures. Meanwhile, novel data-encoding strategies do not address scalibility issues, except in regimes requiring restrictive assumptions about quantum hardware, rendering these protocols inefficient for the general encoding of large health datasets. Our work establishes the current state of evidence for QML-based health applications, paving the way for meaningful QML use-case discovery in digital health.

Keywords: quantum machine learning, quantum computing algorithms, digital health, electronic health records, electronic medical records, medical imaging, machine learning, routinely collected health data

# 1 Introduction

Recent years have seen a proliferation of research proclaiming the utility of quantum machine learning (QML) algorithms for analyzing classical data in many sectors, e.g. finance, cybersecurity, logistics, pharmaceuticals, energy, minerals, and healthcare. With the increasing digitization of health data, the growth of electronic health and medical records [1] paves the way for the use of algorithmic techniques – quantum or classical – for analyzing this data. Potential digital health applications could include clinical decision support, clinical predictive health and health monitoring, public health applications and improving health services delivery and data fusion [2–5]. The potential for use-case discovery for QML in healthcare [6], biomedical [7] and clinical medicine applications [8] is found to be compelling in previous reviews. However, quantum technologies and classical machine learning are often grouped as interchangeable tools for information processing, creating widespread confusion about regimes in which quantum methods should be applied in lieu of classical methods to solve information processing tasks. Clarifying the algorithmic structure of quantum technologies and how these quantum algorithms are being used in a classical information processing pipeline is thus critical for meaningful dialogue about digital health applications.

Characterizing the role of QML algorithms applied to real-world classical data is nuanced and a challenging question in applications development but also in fundamental QML theory [9, 10]. Quantum advantage refers to asymptotic reduction in computational resources (or some other metric [11]) required by quantum algorithms when compared to classical counterparts, i.e. resources are saved as problem size scales to infinity. Empirical quantum advantage [12] colloquially refers to finite-sized simulations or experiments using quantum over classical algorithms to perform a task, where one assumes any desired resource-savings will scale to larger problems, e.g. in qubit number, high-dimensional or highly structured datasets. However, for classical datasets of arbitrary structure such as those encountered in healthcare settings, there is no known theoretically provable quantum advantage [11]. Instead, the field relies on mostly empirical analysis of QML performance for a variety of pseudo-real-world data, where performance differentials between quantum and classical methods on these smaller problems constitute evidence for testing empirical quantum advantage. In certain mathematical regimes, the role of quantum algorithms for solving inference tasks has been replaced by equivalent classical capability, in a process known as dequantization (e.g. [13, 14]). Meanwhile, most computational analysis of scaling behavior assumes ideal operating conditions and it is unknown if QML methods will retain any benefits in realistic operating settings, such as on near-term noisy quantum hardware.

As typical in medical research settings, a systematic literature review is a standard approach for assessing the strength of evidence for proposed interventions in clinical contexts and public health [15]. In this work, we undertake a systematic literature review of QML applications in digital health between 2015 and 2024. Based on existing evidence in literature, we ask whether quantum machine learning algorithms potentially outperform existing classical methods in efficacy or efficiency for digital health. We analyze the role quantum computing and quantum machine learning algorithms play in processing digital health data. Our objective is to assess the strength of the evidence and dominant trends associated with using QML algorithms for digital health. Our review synthesizes and assesses the current-state evidence including any empirical trends, but by design, the medium of a systematic review cannot speculate on the general future potential for use-case discovery of QML in digital health.

Our current-state analysis reveals that the empirical evidence for QML in digital health cannot conclusively address our research question. We find that numerous studies had to be excluded due to a lack of technical rigor in their analysis of QML algorithms. The majority of eligible studies use only ideal simulations of QML algorithms, thereby excluding the resource overhead incurred for error-mitigated or error-corrected algorithms required for noisy quantum hardware. Of high quality studies, nearly all QML algorithms are found to linear quantum models, and therefore represent a small subset of general QML. Most use-cases in digital health focussed on providing clinical support, and no studies considered health service delivery or public health applications. Only two synthesized studies used electronic health records for quantum machine learning applications, while the remaining studies repeatedly gravitated towards a handful of open-source health databases. Finally, 13 studies used quantum hardware demonstrations and separated into two classes: either algorithms for a gate-based, universal quantum computer using up to 20 qubits, or quantum annealers using O(100) qubits. Whether potential advantages of QML can be retained in the presence of noise is largely unaddressed in all studies.

The structure of this document is as follows. We begin by providing an overview of quantum machine learning in Section 2. In Section 3, we outline our approach in accordance with systematic review procedures and guidelines documenting database selection, screening procedures and inclusion criteria for articles. We tabulate key research themes and conduct meta-analysis of our final set of articles in Section 4. Finally, we return to address the research questions of our review, and comment on research opportunities, gaps, limitations and future work in Section 5 before providing concluding remarks in Section 6.

# 2 Overview of quantum machine learning (QML)

Quantum computing refers to a broad category of algorithms, for which it is desired that quantum computing hardware will be required to perform some of the computations. Quantum machine learning algorithms are a subset of quantum computation. For the scope of this review, the input of a quantum algorithm is associated with a classical dataset, and an inference problem is defined on the classical dataset. Quantum computational advantage accrues when a quantum algorithm can reduce the number of operations required to solve this inference problem as the size of the problem becomes asymptotically large. Here, the problem size is typically associated with features of the input data e.g. with input data dimension.

In this section, we provide background to common families of QML algorithms. Quantum algorithms separate into two different categories in this review: gate-based quantum models, or quantum annealing. This categorization can broadly reflect the difference between digital and universal vs. analogue and non-universal quantum computing. Background quantum notation and a fuller discussion is provided in Appendix A. We conclude this section by outlining the role of classical data in quantum machine learning.

## 2.1 Algorithms for universal, gate-based quantum computers

A large subset of quantum algorithms are designed for gate-based universal quantum computers. These algorithms include quantum kernel methods (including quantum support vector machines), quantum neural networks, quantum convolutional neural networks, and quantum deep learning. We summarize these quantum models by considering how outputs are generated from inputs.

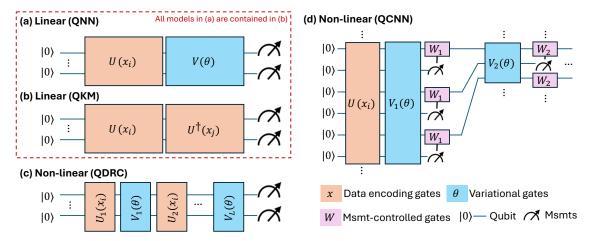


Fig. 1 Quantum circuit depictions of linear vs. non linear quantum models. Horizontal wires represent qubits where input states are shown as ket  $|\cdot\rangle$  symbols; temporal order of computations progresses from left to right. Boxed quantum gates (blue, orange) are reversible rotations, or 'unitary gates', of quantum states, i.e.  $U^{\dagger} = U^{-1}$ . If data encoding (blue) is separable from variational gates (orange), then the quantum model is linear. 'Circuit size' refers to the number of qubits, while 'circuit depth' represents the number of time-steps required to run the full circuit assuming that quantum operations on disjoint qubits have been parallelized. (a)-(c) Measurements (msmts.) are pushed to the end; quantum circuit can be summarized by a unitary operation. (d) Mid-circuit measurement outcomes change quantum operations 'on the fly' (pink). Circuits with tunable  $\theta$  (blue gates) can be broadly referred to as variational (VQC) or parameterized (PQC) quantum circuits.

QML algorithms are frequently represented as quantum circuits, with some examples in Fig. 1. In this visualization, a quantum algorithm is composed of input qubit states denoted with ket-notation  $|\cdot\rangle$  and boxed operations denote quantum gates. These gates are associated with reversible, logical operations performed on quantum states. The circuit is terminated with measurements of a quantum state which yield probabilistic outcomes, '0' or '1', where probabilities are determined by the quantum circuit. Suppose for some input quantum state,  $\rho_0$ , the average output of a quantum algorithm is given by  $f(x,\theta)$ where  $(x, \theta)$  define classical inputs to a quantum algorithm. Here,  $\rho_0$  represents an input state, such as all qubits in their ground (zero) state; x represents one sample of real data with dimension  $d, x \in \mathbb{R}^d$  for a dataset with N samples; and tunable free parameters,  $\theta$ , that parameterize the circuit. One encodes data x into quantum states using a parameterized quantum gate, denoted U(x). The choice of a data encoder, U(x), is discussed in Section 2.3. Meanwhile, free parameters,  $\theta$ , implement classically optimized or trained quantum gates,  $V(\theta)$ . With these assumptions, the desired output information required from the algorithm is typically given with reference to an observable quantity, O. This output information is inherently statistical, i.e. one must infer average information about O from a statistical ensemble of '0' or '1' measurements obtained by repeatedly preparing and measuring the same quantum circuit  $N_s$  number of times. Therefore to extract information about O, we build up an ensemble of quantum measurements by repeatedly running a quantum circuit  $N_s$  number of times for a single instance of x, and repeating for different choices of x.

A quantum machine learning algorithm typically consists of input data (x-dependent) and tunable ( $\theta$ -dependent) quantum operations. Using Appendix A, we can write the general output of a QML algorithm as,

$$f(x,\theta) := \text{Tr}\left[U(x,\theta)\rho_0 U^{\dagger}(x,\theta)\hat{O}\right] = \langle \rho_{x,\theta}, \hat{O}\rangle,$$
 (1)

where the data (x-dependent) and tunable ( $\theta$ -dependent) components of the quantum state  $\rho_{x,\theta}$  cannot be separated. In the above,  $U(x,\theta)$  represents a parameterized quantum gate which depends on data x and tunable parameters  $\theta$ . The output of a QML algorithm thus computes the overlap between information in the quantum state  $\rho_{x,\theta} = U(x,\theta)\rho_0 U^{\dagger}(x,\theta)$ , and the desired output  $\hat{O}$ , using an inner product.

In contrast, linear quantum models allow us to separate the x-dependent quantum operations and  $\theta$ -dependent quantum operations within the inner product [16]. In these models, we perform data encoding operations followed by tunable gates  $V(\theta)$ . As shown in Fig. 1(a), a linear quantum neural network (QNN) can be expressed by,

$$f(x,\theta) := \operatorname{Tr} \left[ V(\theta)U(x)\rho_0 U^{\dagger}(x)V^{\dagger}(\theta)\hat{O} \right] = \langle \rho_x, \hat{O}_{\theta} \rangle.$$
 (2)

In the above,  $\theta$  can take the form of any other classical parameters that are not x; data encoding is expressed by  $\rho_x := U(x)\rho_0 U^{\dagger}(x)$ , and the parameterized neural net is expressed as  $\hat{O}_{\theta} := V^{\dagger}(\theta)\hat{O}V(\theta)$ . We note that the embedding U(x) can be nonlinear transformation of the input data, x. However, the terminology 'linear' quantum model refers to the linearity of the model with respect to the embedding i.e. data-dependent and parameterized components of the quantum algorithm can be separated as shown above.

With this structure, we can additionally describe many other types of quantum machine learning algorithms. For example, we can omit  $\theta$  entirely, and recover sophisticated algorithms that focus on data encoding procedures. In quantum kernel methods (QKMs),  $\theta$  is replaced by training data, and the algorithm output f during prediction represents a linear combination of all training samples. Sometimes the action of  $\rho$ , U(x) or  $V(\theta)$  is non-trivially restricted to some subset of quantum states. Quantum convolutional neural networks (QCNNs), quantum generative adversarial networks, quantum causal modelling, quantum transformers, and quantum deep reinforcement learning all have regimes in which they reduce to linear quantum models as discussed in Appendix A.

#### 2.2 Algorithms for adiabatic quantum computers

Quantum annealing algorithms assume a very specific type of quantum computing hardware, namely adiabatic computers, (e.g. D-Wave) to solve specific learning tasks. Adiabatic quantum computers can

approximately solve computationally hard (i.e. 'NP-hard') problems [17] which are very relevant to classical machine learning. The main class of problems encountered in this review relates to quadratic unconstrained binary optimization (QUBO). Examples of QUBO optimization problems include regression, classification, and data compression tasks. Classical, quantum and hybrid annealers can all approximately solve QUBO optimization problems [18], or be used to draw samples from particular types of probability distributions (e.g. Boltzmann distributions) [19].

Quantum algorithms for QUBO formulations have provable advantage over classical counterparts in some regimes. Quantum QUBO algorithms for optimizing support vector machines (SVMs) and balanced k-means clustering have better computational complexities compared to classical counterparts; while quantum algorithms for QUBO formulations of regression have equivalent computational complexity to classical algorithms [17]. For this limited class of problems, quantum adiabatic computers, such as D-Wave 2X processors, can access  $\approx 1000$  qubits, which is an order of magnitude larger than O(100) qubit processors for universal non-annealing quantum computers developed by IBM and Google.

# 2.3 Data encoding and preprocessing

So far we have introduced quantum machine learning algorithms in generality without reference to the dataset under consideration. In this section, we study inputs for QML and distinguish between data encoding vs. data-preprocessing steps. Data encoding describes the process of representing classical data as quantum states. Data encoding is required for both annealing and non-annealing quantum algorithms. On the other hand, data pre-processing is concerned with using classical techniques to clean up, rescale, compress, or transform data prior to quantum data encoding, or using a classical algorithm. Both data encoding and pre-processing are discussed below.

Characteristics of classical data and the representation of this data in a quantum algorithm can affect potential attainability of computational advantage in solving inference tasks [20, 21]. Ideally, data encoders must be efficient in computational complexity in both circuit size (number of qubits) and circuit depth (number of parallel operations). There are a number of ways to embed classical data x in quantum states, as summarized in Fig. 2. For continuous variable inputs, one may use binary representation of data to finite precision  $\tau$  and encode using discrete methods such as basis encoding, as reported in Fig. 2. The growth of the number of computations required for encoding is mathematically expressed in  $\mathcal{O}(g(n))$ -notation to express an upper bound g(n) on the number of operations as the argument n goes to infinity, ignoring constant multiplicative or additive factors. As an example from Fig. 2, angle-encoding can be prepared in constant depth but scales linearly with number of qubits. The trade-off is switched for amplitude encoding, which in general scale linearly with runtime and logarithmically with qubit number.

Encoding	Circuit Size (# of Qubits)	Circuit Depth (Runtime)	Ref.
Angle encoding	O(d)	O(1)	[22]
Basis encoding	O(d au)	$O(1), O(Nd\tau)$	[22, 23]
Amplitude encoding	$O(\log_2(d\tau))$	$O(\log_2(Nd\tau)), O(Nd\tau)$	[22, 23]
QRAM	$O(d\tau + m)$	$O(\log(m))$	m=O(d au) [24, 25]
Parallel unary loader	$O(\sqrt{d})$	$O(\sqrt{d}\log_2(d))$	[26]

Fig. 2 Table of data encoding strategies with circuit size and depth scaling for a data vector  $x \in \mathbb{R}^d$  with dimensionality d, a total number of N samples in the database. Suppose the binary representation of a single element of x is of length  $\tau$  bits, with an additional bit for storing signs  $\pm 1$ . Then the binary representation b of x has length  $d(\tau+1)=O(d\tau)$ . Only amplitude encoding has sub-polynomial scaling of number of qubits with number of classical bits required to represent input data. Runtime complexity refers to the number of parallel quantum operations during encoding. For basis encoding, a single data vector can be encoded in constant time [27] but linear time is required to prepare a superposition over N samples [28]. For amplitude encoding, runtime is linear for general datasets but can be reduced to sub-polynomial scaling only for restricted datasets or by enabling an algorithm to access QRAM using an additional m ancillary qubits under idealized conditions [23, 25].

Hardware-specific considerations can change exact implementation details of a quantum algorithm, but generally do not change computational resource requirements reported in Fig. 2. The decomposition of required quantum operations to the native set of quantum gates available on hardware may change the number of operations, e.g. replacing one 2-qubit gate with a decomposition involving several single and 2-qubit gates. Similarly, hardware implementation of any continuous variable often also incurs finite precision. In most cases, these changes are multiplicative or additive with problem size. These multiplicative

or additive changes do not affect the overall asymptotic scaling behaviour of the encoder. Some data encoders are not intended as a near-term, implementable strategy. For example, quantum random access memories (QRAM) [24] use an additional  $m = O(d\tau)$  ancillary qubits to randomly access superpositions of basis-encoded states in favourable logarithmic  $O(\log(m))$  time. However, robust QRAMs remain extremely challenging to implement on hardware [29]. Finally, the parallel unary encoder assumes specific hardware capabilities that affect the complexity of data encoding, as discussed in Section 5.

Since data encoding is expensive in quantum resources, and may impact performance, raw data is often pre-processed before encoding. This pre-processing can have many goals, e.g. to compress raw data, identify key features, or address missing values. For most near-term demonstrations of QML, it is well known that dimensionality reduction of classical datasets is often required to encode data into small or intermediate scale quantum circuits.

## 3 Methods

Having discussed broad categories of QML algorithms, we now turn to the research question that determines the design of our systematic review. The use of QML algorithms in health settings encompasses a broad range of clinical applications. We use the SPICE framework [30] to ask:

In developing digital health technologies, could quantum machine learning algorithms potentially outperform existing classical methods in efficacy or efficiency?

A systematic review was conducted in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [31] (Appendix B) and was registered on PROSPERO (ID: CRD42024562024) [32]. Screening and data extraction were performed in Covidence [33]. Commonly used nomenclature encountered in this review is summarized in Appendix C.

Search strategy: Our search strategy is formed by decomposing our research question into elements of the SPICE framework [30], as summarized in Fig. 3. Only articles published after 2015 were included, as the first commercially-available quantum computer was made accessible in 2016 [34] and digitization of health information into electronic records [1] is relatively recent. Hence both factors prohibit meaningful applications development prior to this date. Search syntax was refined by trial and error on PubMed (Fig. 3) in consultation with a health research librarian, and adapted to other databases (Embase, Scopus, arXiv and IEEE, refer Appendix D). Key articles were identified as litmus tests to sense check database-specific search term strategies. Searches were conducted from 10 May to 10 June 2024.

Inclusion/exclusion criteria: The eligibility criteria for the screening process is summarized in Fig. 4. Our study setting prioritized digital health data sources that consist of electronic medical records (EMRs) or electronic health records (EHRs). EMRs represent a real-time patient health record that collects, stores, and displays clinical information as the foundation of a digital hospital as opposed to an EHR which displays summarized patient information to the consumer in the community and across multiple health care providers. The terms "EMR" and "EHR" may be used interchangeably in some countries. Since health data is subject to strict privacy and security legislation, we also consider data that could be reasonably considered to be in an EHR or EMR, thereby permitting the inclusion of open source and published health datasets that are typically used for proof-of-principle results in both classical and quantum ML. While EHR/EMR data typically includes medical imaging, laboratory data, time-varying signals and patient information, we also include genomics data and biomarkers when used in a context where they supplement a patient's EHR or EMR for diagnosis or predictive health applications. A notable exclusion is textual search or analysis of digital or handwritten clinical notes, as these would imply looking at an entirely different class of algorithms that have little or no overlap with unstructured data analysis of non-textual health datasets listed above.

Our criteria also prioritized QML algorithms that were genuinely intended to be run on quantum computing hardware, and at least aspired to demonstrate some kind of advantageous scaling property as the number of qubits is increased. In Fig. 4, we list the sheer number of algorithms that are classical computations with a nominal usage of the word 'quantum'. This list was added to throughout screening as new

Setting	Intervention	Comparison*	Evaluation
In developing digital health analytics	could QC & QML	potentially outperform existing classical	in efficacy or
	algorithms	methods	efficiency?
"medical records"[MeSH Terms]	"quantum machine	(machine learning[MeSH Terms])	("2015"[Date -
OR "electronic health records"[MeSH Terms]	learning"[All Fields]	OR "machine learning"	Publication] :
OR "electronic health record*"[All Fields]	OR "quantum	OR algorithm[MeSH Terms]	"3000"[Date -
OR "health record*" [All Fields]	comput*"[All Fields]	OR "algorithm*" [All Fields]	Publication])
OR "medical record*"[All Fields]	OR "quantum	OR "Bayes*" [All Fields]	
OR "clinical record*"[All Fields]	inform*"[All Fields]	OR "kernel*"[All Fields]	NOT ("systematic
OR ("hospital"[All Fields] AND "data*"[All Fields])	OR quantum[Title/Abs]	OR "classif*" [All Fields]	review"[pt] OR "meta-
OR ("clinical"[All Fields] AND "data*"[All Fields])		OR "neural networks, computer"[MeSH Terms]	analysis"[pt] OR
OR ("medical"[All Fields] AND "data*"[All Fields])		OR "deep learning"[MeSH Terms]	"review"[pt] OR "clinical
OR ("health"[All Fields] AND "data*"[All Fields])		OR (cnn)	trial protocol"[pt] OR
OR ("patient*"[All Fields] AND "data*"[All Fields])		OR (svm)	"clinical conference"[pt]
DR "medical history"		OR (svd)	OR "case reports"[pt])
OR "Routinely Collected Health Data"[Mesh]		OR "pca" [Title/Abstract]	
OR "Routinely Collected Health Data"[All Fields]		OR "principal component analysis" [All Fields]	
OR "Administrative Data"[All Fields]		OR "reinforcement learning" [All Fields]	
OR "Administrative Health Data" [All Fields]		OR "k-means" [All Fields]	
OR "health information systems"[MeSH Terms]		OR "wavelet" [All Fields]	
OR "health services administration"[MeSH Terms]		OR "genetic algorithm*" [All Fields]	
OR "medical informatics computing"[MeSH Terms]		OR "neural net*" [All Fields]	
OR "medical informatics computing [Me311 Terms]  OR "medical inform*"[All Fields]		OR "support vector*"[All Fields]	
OR "radiography"[MeSH Terms]		OR "random forest*" [All Fields]	
OR "radiography"[All Fields]		OR "Boltzmann mach*"[All Fields]	
OR ("medical"[All Fields] AND "imaging"[All Fields])		OR "adversarial net*"[All Fields]	
OR "medical imaging"[All Fields]		OR "random walk*"[All Fields]	
OR "diagnostic imaging"[MeSH Terms]		OR "linear regression" [All Fields]	
OR ("diagnostic"[All Fields] AND "imaging"[All Fields])		OR "nonlinear regression" [All Fields]	
OR "diagnostic imaging"[All Fields]		OR "monte carlo method"[MeSH Terms]	
OR "radiography"[MeSH Terms]		OR "Markov chain"[All Fields]	
- · · · ·			
OR "electrocardiography"[MeSH Terms]		OR "gaussian process regression" [All Fields] OR "ChatGPT"	
OR "ecg"[All Fields]			
OR "electrocardiography"[MeSH Terms]		OR "large language models" [All Fields]	
OR "ekg"[All Fields]		OR "artificial intelligence" [All Fields]	
OR "radiograph*"		OR "big data" [All Fields]	
OR "magnetic resonance imaging"[MeSH Terms]		OR "data pre-processing" [All Fields]	
OR ("magnetic"[All Fields] AND "resonance"[All Fields])		OR "data post-processing" [All Fields]	
OR "magnetic resonance imaging"[All Fields]		OR "feature selection" [All Fields]	
OR "mri"[All Fields]		OR "feature extraction" [All Fields]	
OR " nuclear magnetic resonance imaging"		OR "predictive model*"[All Fields]	
OR "coherence tomography"			
OR "optical coherence tomography"			
OR "computer assisted tomography"			
OR "uss"[All Fields]			
OR "ct"[All Fields]			
OR "computed tomography"[All Fields]			
OR "ultrasound*"			
OR "echography"			
OR "x rays"[MeSH Terms] OR "x rays"[All Fields] OR			
'xray"[All Fields]			
OR "mammogra*"			
OR "holography"			
OR "electroencephalography"[MeSH Terms]			
OR "electroencephalography"[All Fields]			
OR "eeg"[All Fields]			
OR "radiology" [Title/Abstract]			
OR "laboratory data"			
OR "laboratory test*"			
OR "biostatistics" [Title/Abstract]			
OR epigenomics[Mesh] OR "epigenom*"			
OR metabolomics[Mesh] OR "metabolom*"			
OR biomarker[Mesh]			
OR transcriptomics[Mesh] OR "transcriptom*"			
OR proteomics[Mesh] OR "proteom*"			
OR genomics[Mesh] OR "genom*"			
OR "epiproteom*"			
OR "epiomic*"			
OR "vaccin*"			
OR "gene"			

Fig. 3 Search strategy in the SPICE framework [30]. Columns represent digital health setting and perspective (S,P), quantum intervention (I), classical comparator (C), and study characteristics for evidence evaluation (E). Search concepts within columns are combined with logical 'OR' statements, while independent columns are concatenated with logical 'AND' statements. Search concept performance differs by database e.g. PubMed, Embase (shown above) support reliable MESH explosion of health concepts; while Scopus, arXiv and IEEE instead rely on root word truncation. Complete search syntax modifications by database are enclosed in Appendix D.

	Inclusion	Exclusion
Setting	electronic medical records, electronic health records, medical records, health records diagnostic or medical imaging or tomography or radiology, (MRI, PET, CET, CT, USS, XRAY) time-varying signals (EEC, EEG, EKG) data associated with EHR (biomarkers, genomics, laboratory tests, medical demographic data) digital health, healthcare delivery	<ul> <li>textual or handwritten data in EHRs</li> <li>raw data from physical sensors (e.g. raw data prior to image reconstruction for MRI)</li> <li>data not used as part of EMRs / EHRs (e.g. raw biofield / bio-signal data, biomarkers, genomics, motor imagery, head movement, facial expression detection)</li> <li>datasets for non-digital health applications (e.g. drug delivery; drug design, drug/vaccine development, nanomaterials analysis, computational biology or chemistry calculation; smart buildings, smart devices, smart healthcare infrastructure or systems management; data mining, intrusion detection, watermarking, encryption, authentication, transmission, storage or retrieval of health data, data anonymization or privacy; or medical imaging hardware, wearable health devices, scanning devices)</li> <li>text-based analysis of handwritten or digital textual data</li> </ul>
Persp.	<ul> <li>healthcare delivery (public, private), hospital and medical centers (administration, data, service delivery), clinical service delivery, patient flow</li> <li>health-specific data sharing for ML / QML</li> </ul>	<ul> <li>health suppliers</li> <li>public service delivery unrelated to health</li> <li>financial sustainability of public health</li> </ul>
Intervention	quantum machine learning, quantum computing, quantum computers     quantum algorithm, quantum-enhanced algorithms, hybrid quantum classical algorithms     quantum circuits, variational quantum circuits, parametrized quantum circuits, variational quantum algorithms, variational quantum eigensolvers     Quantum Approximate Optimization Algorithm (QAOA)     quantum neural nets QNN, quantum convolutional neural nets QCNN, quanvolutional quantum algorithm     quantum generative (adversarial) networks QGANs, quantum genetic algorithms, quantum evolutionary algorithms     dequantization     quantum Monte Carlo, Markov chain techniques     quantum kernel methods     quantum kernel methods     quantum SVM     quantum SVM     quantum tensor network states, QNNs based on tensor networks     quantum transfer learning, quantum reinforcement learning     Quantum Long Short Term Memory     quantum integer wavelet transforms, quantum wavelet transforms	<ul> <li>quantum-inspired algorithms, quantum-inspired clustering (quantum grey wolf, quantum fruit fly, quantum particle swarm, quantum ant lion, quantum squirrel search, quantum bat, quantum whale, quantum grasshopper, quantum artificial bee colony, quantum avian navigation, quantum marine predator, quantum seagull algorithms)</li> <li>quantum algorithms for textual search, sequence search, or sequence alignment</li> <li>quantum iterative reconstruction algorithm</li> <li>quantum particle swarm optimization</li> <li>quantum inspired evolutionary algorithm</li> <li>quantum inspired genetic algorithm</li> <li>quantum key distribution, quantum cryptography, quantum-safe classical algorithms, quantum communication, steganography</li> <li>quantum dots or nano materials, quantum yield, quantum efficiency metrics</li> <li>quantum noise in medical imaging, photon counting in medical imaging</li> <li>quantum sensing, quantum metrology, quantum magnetometers, ptychography</li> <li>quantum mechanics for computational biology or chemistry calculations</li> <li>quantum mechanical calculations or simulations, quantum chemical calculations or simulations</li> <li>generic quantum physics, consciousness, psychosomatic, quantum consciousness quantum-inspired algorithms</li> <li>quantum security, encryption, block chain, authentication</li> <li>colloquial use of "quantum" e.g. 'quantum leap', 'quantum step', 'quantum of'</li> </ul>
Comparison	Only apply this at extraction  classical machine learning inc. deep, reinforcement & unsupervised learning  classifiers, classification, kernel methods, neural networks, SVM, PCA, tensor networks  generative algorithms, genetic algorithms, Monte Carlo, Markov chain techniques, random walks, random forests regression, filtering, Bayesian analysis, Long Short Term Memory  wavelets, Hadamard transforms, Fourier analysis	Only apply this at extraction  image reconstruction algorithms  image denoising algorithms  speckle reduction  federated learning applications for security, data privacy and authentication  methods/algorithms/computational analysis for non-digital health applications (see Setting)
/ Eval.	Only apply this at extraction  High quality articles  Peer reviewed articles, research papers after 2015	Only apply this at extraction  Low quality articles  Reviews or technical reports; irrelevant modes (e.g. conference)
Study	Publication date 2015 – present	abstracts, book chapters, lecture notes, clinical trials, patents, observational studies) or publication before 2015

Fig. 4 Eligibility criteria for title and abstract screening and full text review. Columns represent inclusion/exclusion criteria, while rows are elements of SPICE framework aligned with search strategy in Fig. 3. Criteria for digital health setting, quantum interventions, and study characteristics were applied during title and abstract screen and full text review. Meanwhile, criteria for classical comparators and evaluating technical robustness were only applied after data extraction and prior to synthesis.

terms were encountered. Many studies technically obfuscated the distinction between QML algorithms and classical computations that use quantum mechanical theory or other insights. For instance, in medical imaging we exclude quantum mechanical corrections to classical algorithms which help to reduce noise in reconstructing images from raw sensor data. Finally, we exclude quantum algorithms unlikely to arise in the context of analyzing classical digital health data, for example: quantum sensing, quantum cryptography, and quantum algorithms for genome pattern matching, genomic sequence alignment, or molecular and chemistry simulations.

**Screening:** Two independent researchers conducted title and abstract screening of all search results: one reviewer had a health background, while the other had a physics background. Full text review was performed by a total of three reviewers. For consistency, one reviewer participated for all screening stages including both abstract and full text screening. Conflicts were resolved through internal discussion or by involving a third reviewer's opinion.

Data extraction and study quality appraisal: Study characteristics were extracted for all included studies. Additionally, a study quality appraisal was performed to form consensus-based decisions about including or excluding particular studies based on robustness [35]. These appraisals are typically implemented during data extraction and prior to narrative synthesis [35]. Our study quality assessment criteria analyses the rigor with which QML algorithms were investigated [9] and we do not include a myriad of other potential benchmarks, e.g. for clinical robustness. At least two reviewers independently scored eligible studies, and the maximum score over both reviewers was selected during consensus formation. Attributes of low vs. high quality studies with were compared with respect to our criteria. Full data extraction template is enclosed in Appendix E and extracted data as well as underlying analysis code for data extraction is available online [36].

### 4 Results

In this section, we present results data from our systematic review in two stages. Firstly, we depict results of the screening process and the study quality appraisal, which has led to a focus on 16 studies for final synthesis. Secondly, we summarize synthesized evidence and discuss the extent to which our original research question is addressed.

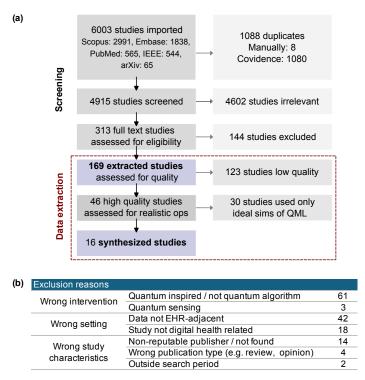


Fig. 5 PRISMA diagram. (a) Overview of systematic review from screening to synthesis. Of 4915 studies returned from search in 5 databases, 93.6% of abstracts are deemed ineligible based on digital health setting and quantum intervention criteria. During full text review, 144 studies are excluded, and exclusion reasons are given in (b). Data is extracted (red box) for 169 eligible studies; additional quality assessment and selection criteria is applied to yield a total of 16 studies for final synthesis.

Study Quality Appraisal	Counts
Q1: Explains quantum algorithm selection by referencing learning problem class or dataset structure	
o : No theory or empirical rationale for quantum algorithm selection discussed or cited	32
1: Quantum algorithm selection is empirical or mostly cites empirical literature	115
2 : Quantum algorithm selection is linked to underlying class of learning problem or data structure	21
3 : Quantum algorithm has provable advantage with respect to class of learning problem or data structure	1
Q2: Identifies/discusses impact of data encoding on quantum algorithm performance	
o : Encoding methodology omitted or incomplete	38
o : Impact of different encoding strategies on overall performance is not analyzed	85
1: Performance impact is discussed with incomplete analysis (e.g. compares at least 2 methods)	37
2 : Performance impact is well characterized empirically or theoretically	7
Not applicable	2
Q3: Identifies/discusses impact of classical input data processing on quantum algorithm performance	
o : Data pre-processing methodology is omitted or incomplete	18
o : Impact of different data pre-processing strategies on overall performance is not analyzed	96
1 : Performance impact is discussed with incomplete analysis (e.g. compares at least 2 methods)	45
2 : Performance impact is well characterized empirically or theoretically	7
Not applicable (no classical input data processing)	3
Q4: (EMPIRICAL ONLY) Dimensionality of data input for quantum algorithm	
o : Not reported or discussed; or unclear	31
o : Negligible i.e. O(1)	102
1 : Small i.e. O(10)	30
2 : Intermediate i.e. $O(10^2)$	3
3 : Large i.e. $O(10^3)$ or greater	2
Not applicable (theory study)	1

Fig. 6 Resulting score distribution for study quality assessment applied to 169 eligible studies at extraction. Each study was scored independently by two reviewers. Consensus scores reflect agreed values formed by discussion with a view to taking the maximum possible of two scores where differences in interpretation were trivial.

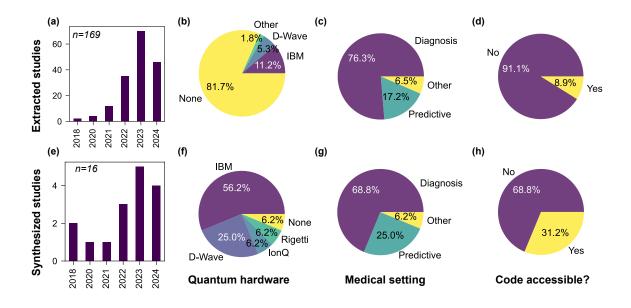


Fig. 7 Data extraction for eligible studies in Fig. 5, with n=169,16 for number of studies extracted ((a)-(d)) or synthesized ((e)-(h)) respectively. Synthesized studies exclude eligible studies that do not meet our quality criteria or rely solely on ideal simulations. (a), (e) Histogram of number of studies by publication year; eligible studies show rapid increase in number by year in (a) while synthesized studies appear more uniformly distributed in (e). (b),(f) Percentage of studies that mentioned using quantum hardware using either health or non-health datasets. 'None' in (b) indicates usage of both ideal and noisy simulations, while 'None' in (f) indicates only noisy simulations of quantum computers. (c),(g) Percentage of studies summarized by digital health setting, broadly characterized as aiding clinical diagnosis ('Diagnosis'), enabling predictive health ('Predictive'), and 'Other'. (d), (h) Number of studies providing open access to software code and input datasets. The absence of code/data availability statements; statements 'upon reasonable request'; broken links or unusable repositories are all categorized as 'No' above.

## 4.1 Characterization of synthesized studies

Our systematic review is summarized by a PRISMA diagram in Fig. 5(a). Our searches identified 4915 distinct studies. A total of 313 studies passed title and abstract screening and went through full-text screening, of which 169 met eligibility criteria. Inter-rater reliability as measured by Cohen's kappa was substantial for title and abstract screening (0.72) and moderate for full text screening (0.48). According to the distribution of exclusion reasons shown in Fig. 5(b), the most frequent cause for full-text exclusion during screening was distinguishing between genuinely quantum algorithms designed to run on quantum hardware, vs. classical computation invoking ideas, insights or jargon from quantum physics.

To address issues of technical rigor, we approach data extraction in two steps: first, the application of the quality assessment criteria, and secondly, narrowing the focus to studies that investigated realistic operating conditions either via noisy simulations or by testing algorithms on real quantum hardware. The distribution of quality scores after consensus is reported in Fig. 6. Only 6 of 169 studies led to non-trivial and unresolvable differences in scoring criteria between two independent reviewers, indicating 96.4% consensus rate for quality assessment scoring. Borderline studies arise when a quality score for two of the following three concerns remains unresolved by reviewers: insufficient performance analysis of classical pre-processing before data input to quantum algorithm, insufficient performance analysis of scalability using qubit numbers > O(1), and/or insufficient performance analysis of choice of data encoding strategy.

The resulting metadata for extracted (synthesized) studies is shown in the top (bottom) row of Fig. 7. Of all eligible studies in Fig. 7 (top row), 138 of 169 (81.7%) use only simulations of quantum machine learning applications for digital health without testing on hardware. Where simulations are the only evidence base in a study, only 7 out of 138 studies use some form of noisy simulations, while the remaining 131 studies use only ideal simulations. When restricting to synthesized studies in Fig. 7 (bottom row), a greater proportion of studies do appear to test quantum algorithms on actual quantum hardware (refer Fig. 7 (b) vs. (f)).

The growth in the number of eligible articles on quantum algorithms for digital health seems almost exponential in Fig. 7(a). These applications are broadly categorized into diagnosis, predictive health, and 'other' in Fig. 7(c), where an example of the latter could include synthetic health data generation for classical machine learning. Despite this growth, the majority of studies did not enable code and data accessibility.

### 4.2 Empirical evidence from synthesized studies

Nearly all of our synthesized studies were concerned with a learning task of performing a clinical diagnosis or a clinical prediction based on classical datasets. From a clinical perspective, all studies rationalized quantum algorithm design by citing other empirical literature. Any empirical rationale for the choice of quantum intervention did not necessarily refer back to comparable clinical settings: in most cases, it appeared that the matching between health datasets and quantum interventions was either ad-hoc, or one tried all possible quantum interventions in order to empirically discover the best performing models for a fixed health dataset. No QML applications were focussed on health service delivery, public health, and consumer health monitoring applications. Only one study, Qu (2023) [37], focussed on health-data analytics applications, namely, that QGANs may be beneficial in ameliorating issues of model collapse for synthetic data generation in digital health applications but these are untested at scale in both simulations and quantum hardware. No studies were related to improving efficacy or efficiency of health service delivery, e.g. optimization problems for patient flow, or operational cost-down in hospitals.

We find that quantum kernel methods and quantum annealing techniques dominate our synthesized evidence in Fig. 8 (top). The choice of quantum intervention typically then informs the choice of classical comparator (middle) within each study, and hence the distributions of quantum and classical algorithms are correlated. Finally we note that datasets (bottom) are not particularly clinically diverse and factorize into private and open-source datasets. While EHR and hospital data are often private, the remaining datasets are all open-source. Most empirical evidence does not use electronic health records, but gravitates

		Nyugen 2018	Piat 2018	Yano 2020	Niraula 2021	Krunic 2022	Landman 2022	Moradi 2022	Das 2023	Guddanti 2023	Kawaguchi 2023	Moradi 2023	Qu 2023	Asiwga 2024	Cherrat 2024	Kazdaghli 2024	Choi 2024	Total
	Quantum kernel methods, QSVMs, and other classifiers			Χ		Х		Χ			Χ	Χ		Х				6
	Quantum annealing and RBMs	Х	Х							Х							Χ	4
	Quantum neural networks, VQCs, PQCs						Χ					Χ						2
Quantum	Quantum deep reinforcement learning				Χ													1
ant	Quantum sampling algorithms															Х		1
ő	Quantum generative adversarial networks												Х					1
	Quantum causal models										Χ							1
	Quantum transformers														Х			1
	Other (pattern recognition)								Χ									1
	Kernel methods, SVMs, and other classifiers					Х		Χ				Χ		Χ				4
	Classical annealing, classical QUBO solvers, and RBMs	Х	Х							Χ								3
	Neural networks (NN) (not inc. convolutional)						Χ					Χ						2
न्न	K-Nearest Neighbours							Χ				Χ						2
Classical	No comparator			Χ					Χ									2
las	Deep reinforcement learning				Х													1
ပ	Sampling algorithms															Х		1
	Classical adversarial networks												Χ					1
	Classical transformers														Х			1
	Signal processing techniques																Χ	1
	Private		Х		Х	Х			Х								Χ	5
	Wisconsin Breast Cancer			Х				Χ						Х				3
	MedMNIST						Χ								Х			2
	Synthetic	X														Х		2
	Stanford Chest X-Rays	X																1
ţ	ECG MIT BIH Arrhythmia and ST Change												Χ					1
Data sets	ECG European ST-T												Χ					1
ata	ECG Sudden Cardiac Death												Χ					1
Δ	PET Radiomic cancer cohorts (multiple)											Χ						1
	Heart Failure							Χ										1
	Paediatric Bone Marrow							Χ										1
	EHR MIMIC-III															Х		1
	Pima Indian Diabetes										Χ							1
	UCI Heart Disease										Χ							1

Fig. 8 Overview of setting, interventions, and comparators for all 16 synthesized studies (columns), including studies with borderline or weak consensus (shaded gray columns). For each study, we indicate primary quantum interventions (top), classical comparators (middle), and digital health datasets (bottom). Quantum interventions deployed on non-digital health datasets are excluded. Interventions or comparators (rows) combine similar multiple-choice data extraction entries. QNNs exclude QCNNs and no VQCs / PQCs were found to contain mid-circuit measurements (MCM) or adaptive gates.

to a handful of open-source health databases. We thus find that the diversity of applications investigated empirically is limited.

In Fig. 9, we report performance metrics from synthesized studies comparing quantum interventions with classical machine learning counterparts for different digital health applications. The choice of quantum algorithms again separates into two groups: annealing vs. gate-based techniques. Indeed, quantum annealing studies focus on digital health tasks that can be mapped to a QUBO problem, and are able to scale to problem sizes at least an order of magnitude larger than non-annealing quantum hardware in qubit number. On the other hand, gate-based non-annealing quantum hardware accommodates a broader range of QML algorithms, as shown by the remaining rows in Fig. 9, and a broader range of hardware platforms, such as trapped ions (IonQ) and superconducting qubits (Rigetti, IBM). However, hardware experiments in many instances are almost outdated e.g. IBM quantum processors (56.2% of synthesized studies) are Falcon models or older despite the availability of processors with 100+ qubits since 2022.

						Strong Consensus	Weak consensus
Algorithm	Score Metric	Dataset	Device	Qubits	Quantum	Classical	Ref.
	Absolute squared error	Synthetic - Radiograph	D-Wave	21-47	0.54	0.1	Nguyen 2018
		Kaggle - Pneumonia X Ray (balanced)	D-Wave	NR. Est. O(100)	0.903	0.925 - 0.764	Guddanti 2023
Quantum annealing and RBMs	Accuracy	Private - MRI , Xrays, Medical images of tools	D-Wave	NR. Est. O(1000)	0.879-0.998	98.1-99.8	Piat 2018
	Balanced accuracy	Private / Commercial - survey data	D-Wave	NR. Est. O(100)	0.736-0.746	0.589-0.621	Choi 2024
Quantum deep reinforcement learning	Root mean square error	Private / Commercial - Oncology clinical trial	IBM Melbourne, Santiago	10	0.71	0.7	Niraula 2021
	Accuracy	Wisconsin breast cancer dataset	Rigetti	NR. Est. 2	0.828	0.6324-0.7856	Asiwga 2024
		Pediatric Bone Marrow Transplant 2-year survival	IBM Melbourne	4	0.66-0.69	0.64,0.71	Moradi 2022
	AUC	Wisconsin breast cancer dataset	IBM Melbourne	4	0.88-0.93	0.93,0.89	Moradi 2022
Quantum kernel methods, QSVMs, and other quantum classifiers		Heart Failure Mortality	IBM Melbourne	3	0.5-0.51	0.58,0.53	Moradi 2022
		Multiple - PET radiomic cancer cohorts (Glaucoma, Lung, Prostate)	IonQ Aria	3	(0.73 - 0.68) vs (0.59-0.63)	0.78-0.63	Moradi 2023
	Balanced accuracy	Multiple - PET radiomic cancer cohorts (Glaucoma, Lung, Prostate)	IonQ Aria	4	(0.83-0.68) vs (0.75 - 0.63)	0.8-0.61	Moradi 2023
	Relative balanced accuracy (Quantum - Classical)	Commerical - Optum - EHR data set	IBM Dublin	20	-0.0449 to - 0.0295	NA	Krunic 2022
	,	MedMINST - PneumoniaMNIST	IBM Guadalupe, Casablanca and Bogota	4	0.79	NR	Landman 2022
	Accuracy	MedMINST - RetinaMNIST	IBM Guadalupe, Casablanca and Bogota	4	0.6	NR	Landman 2022
Quantum neural networks, VQCs, PQCs (no MCM)		UCI Heart Disease Dataset	IBM Almaden	2	0.861	NR	Yano 2020
	ALIO	MedMINST - PneumoniaMNIST	IBM Guadalupe, Casablanca and Bogota	4	0.87	NR	Landman 2022
	AUC	MedMINST - RetinaMNIST	IBM Guadalupe, Casablanca and Bogota	4	0.65	NR	Landman 2022
Quantum sampling algorithms	AUC	MIMIC-III - Medical Information Mart for Intensive Care	IBM Hanoi	10	0.7675 ± .01545 MNAR , 0.7262 ± 0.0299 MCAR	0.7712 ± 0.0116 MNAR , 0.6968 ± 0.03 MCAR	Kazdaghli 2024
Quantum transformers	Accuracy	MedMINST - RetinaMNIST	IBM Hanoi, IBM Guadalupe	4,5	0.4575 to 0.55	0.531 to 0.5575	Cherrat 2024

Fig. 9 Selected test scores (accuracy, AUC and squared error  $\in [0,1]$ ) reported for quantum interventions deployed on quantum hardware using health data. Ranges reflected min and max test scores attained over different experimental configurations reported in each study; error bars for each test score are shown if originally reported. Synthesized studies with strong (weak) consensus are shaded in green (gray). Ideal scores for accuracy and AUC metrics (unity) differ from squared error metrics (zero). Performance benchmarks that cannot be easily compared or interpreted alongside other metrics, or are not consistently reported, e.g. F1 scores and precision, are excluded for readability. NA: Not applicable. NR: Not explicitly reported or unclear.

In facilitating a comparison between quantum vs. classical machine learning, Das (2023) [38], Kawaguchi (2023) [39] and Qu (2023) [37] studies are not represented in Fig. 9 due to the lack of reportable metrics for quantum hardware experiments, while Yano (2020) [40] and Landman (2022) [41] are represented in Fig. 9 but do not report a numerical classical benchmark. The remaining 11 studies reported in Fig. 9 reveal major issues in facilitating the comparison between quantum vs. classical interventions. There are three scientifically concerning flaws:

1. No empirical evidence of performance scaling: All quantum computing demonstrations, even in simulations, have not been carried out at scale. Leaving aside the issue of quantum advantage for classical datasets, empirical investigations on universal, gate-based quantum computers have not investigated performance as a function of increasing problem size or qubit number e.g. to O(100) qubits. Even for these small-scale experiments on universal, gate-based platforms, only Krunic (2022) [12] plotted trend lines of performance vs. problem size / qubit number to establish empirical scaling behavior. In all other cases, including annealing applications, algorithmic performance scaling was

not established in ideal or noisy simulations or prior to running on quantum hardware.

- 2. Limited reporting of statistical uncertainties: All studies provided limited or no discussion of how statistical fluctuations in test scores should be interpreted. Only Kazdaghli (2024) estimates and reports sample error bars for test score values [42], while Krunic (2022) proposed a technique to contextualize fluctuations in performance score to the underlying configuration of experiments using PTRI metrics [12] but in lieu of uncertainty analysis. In the absence of error bars, any differences in classical vs. quantum performance appeared to be statistically equivalent fluctuations for a range of configurations.
- 3. Lack of noise characterization and impact of quantum hardware: Most studies recognize the significantly large deterioration between ideal and actual quantum hardware performance due to the effect of noise. Despite this, studies compared quantum hardware performance mostly only with ideal simulations, rather than using noisy simulations or secondary data to provide insight into algorithm performance on hardware. Only two synthesized studies [38, 43] used noisy simulations to compare to hardware results in their analysis. When running algorithms on quantum hardware, only two studies [38, 44] explicitly considered error mitigation. Of these, only one study used an application-agnostic error mitigation technique and distinguished between raw vs. mitigated results to contextualize the impact of noise [44]. All studies failed to take data to characterize performance of the underlying quantum hardware while running QML experiments. Consequently, these studies offer almost no insight into whether fluctuations in classical vs. quantum QML performance are entirely dominated by drift in performance of underlying quantum hardware.

In all these studies, we conclude that the performance differentials between quantum and classical machine learning metrics for digital health reported in Fig. 9 are negligible. Not only is empirical evidence difficult to synthesize and interpret, but the tabulated performance scores show no clear, consistent, statistically significant trend to support any empirical claims of quantum utility in digital health across a range of hardware platforms.

#### 5 Discussion

We have discussed until this point why a meta-analysis of empirical evidence in synthesized studies is insufficient for claiming empirical quantum utility for quantum machine learning in digital health. This absence of empirical evidence may be understandable in a relatively new field where applications development may temporally lag new insights in quantum machine learning theory and new hardware capabilities. We now consider these observations on research methodology and themes below.

Even in a discipline that must rely on heuristics and empirical investigations, the majority of studies claim empirical quantum advantage but do not take into account realistic operating conditions in their analysis. The absence of noise characterization or noisy simulations to explain deviations of quantum hardware experiments from idealized conditions is particularly surprising. In 14 out of 16 studies, hardware results were compared to ideal simulations without any noise characterization or the use of noise simulations to contextualize results. Of the two studies that used noise simulations, these simulations were limited to simple noise models. For example, in Qu (2023) [37], QGANs are used for synthetic heartbeat data generation. Ideal QGANs converged to accuracies ranging from 87.7% - 90.9% for different types of heartbeat data. Standard noise simulations of bit-flip, phase-flip, amplitude damping and depolarizing noise at moderately strong levels reduced the range of accuracies to  $\approx 75\% - 90\%$ , where each noise model is individually considered. However, in realistic settings, these noise models are inadequate—at the very least, requiring a mixture of different error types. While similar noise simulations were used as evidence to show noise-robustness of QML methods, the limited nature of these noise models would not reflect realistic operating conditions.

Indeed the field appears to lack empirical comparisons of quantum annealing vs. gate-based QML in regimes where quantum annealing is anticipated to have provable quantum advantage, e.g. for specific learning tasks such as binary classification. Four studies formulated learning tasks as QUBO problems and used a quantum annealer. Two of these studies focussed on classification tasks using a support vector

machine [18, 19], which could be easily compared with a universal gate-based computer. The remaining two studies focussed on areas such as linear regression [45] and data compression [46] for which there does not appear to be provable computational advantage for quantum annealing. Since D-Wave architectures have been available for some time before newer quantum processors, two of these four studies represent our oldest publications dating back to 2018. All annealing studies are also subject to study considerations above, and our review did not find strong evidence of quantum annealers outperforming either newer gate-based, universal quantum computers or classical counterparts.

Only one synthesized study used electronic health records as opposed to generic digital health data. In Krunic (2022) [12], electronic health records were used to perform kernel-based prediction of six-month persistence of rheumatoid arthritis patients on biologic therapies. Both quantum and classical kernels were compared for different configurations of number of features and number of samples of training data. The study offers weak evidence of empirical quantum advantage when the configuration space is restricted to small dimensional datasets with a low number of features. Aside from directly using electronic health records, Kazdaghli (2024) [42] focussed on using quantum interventions for data imputation in clinical data, applicable to the analysis of electronic health records, but also other types of clinical data, such as those used in clinical trials. Meanwhile, some eligible but not synthesized studies discussed the use of quantum algorithms for securely pooling health data in federated learning applications [47].

Some of the quantum algorithms encountered in this review cited significant improvements in data-encoding compared to typical approaches in Section 2.3. Efficient image processing tasks are pursued using quantum transformers in Cherrat (2024) [48] and Landman (2022) [41], while data imputation is pursued in Kazdaghli (2024) [42]. While these applications in digital health differ, the underlying technologies in Landman (2022) [41], Cherrat (2024) [48], and Kazdaghli (2024) [42] all rely on methods in Ref. [49] and appear to inherit favourable resource scaling from assuming specific hardware capabilities that do not exist generally. The underlying data encoders assume hardware can implement entangling gates on overlapping sets of qubits in parallel (as opposed to sequentially). This hardware capability is so-far only shown for small-scale trapped ions [50] and it is not expected to scale to systems with large qubit number.

Meanwhile health data consists of both continuous and discrete data and Yano (2020) [40] fills an existing gap in literature by looking at encoding of discrete variable data into quantum VQCs using Quantum Random Access Coding (QRAC). The authors argue that  $O(\log_2(d\tau))/2$  improvement in circuit size complexity can be attained for discrete variable inputs, suggesting a two-fold improvement over amplitude scaling in Fig. 2. Nevertheless, the critical challenge for amplitude encoding strategies in QML is that linear runtime complexity can prohibit accessing super-polynomial advantage and this barrier is not addressed by the paper.

Nearly all quantum algorithms were linear quantum models. Some theoretical evidence shows that linear quantum models will require exponentially more qubits than non-linear models [16], and heuristic evidence shows that certain types of linear quantum models will not be useful for the analysis of classical datasets [10]. Even broadening to a larger pool of 169 eligible studies, non-linear quantum models were not encountered. Of our synthesized studies, seven studies used linear quantum kernel methods including Moradi (2022, 2023) [43, 44], Yano (2020) [40], Aswiga (2024) [51], Krunic (2022) [12] and Kawaguchi (2023) [39]. For non-kernel methods, the underlying technologies for Nirula (2021) [52], Qu (2023) [37] and Das (2023) [38] can be recast in linear form. Finally, the quantum transformers and data encoding strategies that yield favourable scaling properties in Cherrat (2024) [48], Landman (2022) [41], and Kazdaghli (2024) [42] use methods developed in Ref. [49]. Aside from a variant proposed in Cherrat (2024), the data encoders and neural networks leveraged by these studies all appear to be described by the framework of linear quantum models. Indeed, the observed absence of clear, consistent performance trends in the empirical meta-analysis of the previous section could in part be explained by the underlying linear quantum models used for many of the studies.

Despite the fact that all quantum models were trained by a supervised learning problem, no study explicitly characterized their optimization landscape. It is well known that optimization of supervised QML algorithms can be plagued by exponentially vanishing gradients (barren plateaus)[53], exponential concentration of kernel values [54], or exponentially concentrated local minima [55]. However only two out of sixteen synthesized studies mentioned optimization challenges associated with their proposed methods for supervised quantum machine learning. Only Cherrat (2024) [48] and Landman (2022) [41]

pointed out that their proposed QML methods' structures may indeed avoid barren plateaus. Whether these circuits avoid exponential concentration remains open. Meanwhile no substantial improvements are found in reducing shot number requirements for QML methods.

Finally, classical data preprocessing tasks are highly discretionary and impact on QML is poorly understood. There are two areas where data preprocessing is frequently used in QML: feature selection for kernel methods, and dimensionality reduction for data encoding. In feature selection, both the number of features [43], and statistical significance of features were established using statistical tests [44] to aid kernel design. Meanwhile, dimensionality reduction is required to encode data on quantum hardware with limited qubit numbers, e.g. by cropping, PCA or LDA. However, the impact of dimensionality reduction on QML performance is unaddressed. For example, reducing images to  $2^n$  length, where the number of qubits n is small, risks creating duplication in training and testing datasets if two different full-sized images become identical after dimensionality reduction. Other preprocessing tasks include re-scaling, using statistical summaries, or transforming data, e.g. using Haralick features [56] or Fourier methods, but there has been no characterization of the impact of these methods on investigations of empirical quantum advantage.

We note that this review does not address the future state of QML in health applications. Many open questions remain in the use of quantum algorithms to solve classical inference problems. As examples: whether quantum kernels can offer an advantage in classifying real world data; the role of data vs. quantum model design for attaining quantum advantage, the effects of optimization protocols and noise on overall QML performance, or the existence of quantum sampling or optimization algorithms that could be of use in classical machine learning.

## 6 Conclusion

Digital health aims to transform access, affordability and quality of healthcare. While classical machine learning methods in health are approaching commercialization, we find an exponentially growing number of studies advocating the use of QML in health. While assessing the future potential of use-case discovery in digital health is out of scope for a systematic review, we assess current-state evidence consisting of 4915 studies. We find most applications are focussed on clinical decision support and little attention is given to health service delivery and public health use-cases. Of eligible studies, we appraise study quality yielding 16 robust studies which analyze QML applications in realistic operating environments. However, we find that this synthesized empirical evidence does not establish clear trends in performance scaling of QML algorithms, and does not contextualize statistical fluctuations in classical vs. quantum analysis. Most QML algorithms were restricted to linear quantum models. Efficient data encoding remains elusive unless very specific hardware capabilities are assumed, while the impacts of data preprocessing on QML study design are unaddressed. Enabling meaningful use-case discovery for QML in digital health thus requires improved guidelines for empirical investigations, rationalizing the choice of QML structures on classical datasets, and establishing performance scaling under realistic operating conditions.

**Author contributions:** R.S.G, T.E, S.S and J.D.P were involved in study design, formulating research question, defining scope considerations, and inclusion/exclusion criteria. R.S.G, T.E, S.S developed search strategy, data extraction and quality appraisal templates. R.S.G, C.E.W, T.E and S.S participated in screening, data extraction, and resolution of conflicts. R.S.G performed data analysis. All authors contributed to writing the manuscript.

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Data and code availability: The datasets generated by Covidence during data-extraction and underlying analysis code for the current study are freely available online via DOI: 10.6084/m9.figshare.27148386

[36]. A complete list of search are provided in Supplementary	strategies by database Materials.	, inclusion/exclusion of	criteria, and data extraction
	177		

# A Quantum background

We briefly introduce notation and terminology associated with quantum algorithms. Quantum states are represented by the notation of a ket  $|\cdot\rangle$ . We will consider a specific type of quantum state, called a qubit (or quantum bit). At the extremal points, a qubit occupies the state associated classical binary bit  $|0\rangle, |1\rangle$ . However, a qubit can also occupy values that are superposition states,

$$|\psi\rangle := \alpha|0\rangle + \beta|1\rangle,\tag{3}$$

where  $\alpha, \beta$  are complex amplitudes satisfying  $|\alpha|^2 + |\beta|^2 = 1$ , and the linear combination of  $|0\rangle, |1\rangle$  has a well-defined relative phase. Indeed, the relative phase relationships between quantum states in superposition allows quantum states to interfere, i.e. add or cancel out, in ways that may enhance computations. When measured, quantum systems are also inherently probabilistic, i.e. in the above example, the measured qubit will be associated with a binary outcome 0 (1) with probability  $|\alpha|^2$  ( $|\beta|^2$ ). For most applications, these quantum measurements are repeated for  $N_{shots}$  number of times in order to build a statistical distribution over measurement outcomes from which useful quantities are inferred.

We can demystify quantum computations by thinking of them as basic operations in linear algebra. Here, kets are represented as column vectors in a complex linear space, and quantum operations are represented by matrices, which act on states via matrix multiplication. For every quantum state ket, we associate a bra,  $\langle \psi |$ , which can be thought of as a row vector containing the complex conjugate of elements of  $|\psi\rangle$ . To compare any two quantum states,  $|\psi\rangle$  and  $|\phi\rangle$ , we compute their overlap as an inner product between  $\langle \phi |$  and  $|\psi\rangle$ , denoted  $\langle \phi | \psi\rangle$ . To summarize quantum algorithms, it is useful to represent quantum states with matrices as well as vectors. The matrix representation of a quantum state  $|\psi\rangle$  is the density matrix,  $\rho:=|\psi\rangle\langle\psi|$ , such that  $\rho$  is an outer product. The density operator is required to satisfy three mathematical properties: unit trace  $(\text{Tr}[\rho]=1)$ , hermicity  $(\rho=\rho^{\dagger})$  and positive semi-definiteness. These requirements ensure that measurement statistics can always be associated to quantum probability amplitudes (e.g.  $\alpha, \beta$ ) of an underlying quantum state. In the above, mathematical operations are denoted by the trace Tr,  $\langle \cdot \rangle$  denotes an inner product, and  $^{\dagger}$  denotes complex conjugation.

Nearly all transformations of a quantum state, including those within quantum machine learning algorithms in the presence of realistic noise, are called quantum channels. These channels, denoted  $\eta$ , can represent transformations such as quantum gates (rotations), quantum measurements, or the impact of noise on a quantum state interacting with its environment. For all these phenomena, we represent channels as,

$$\eta(\rho) := \sum_{i} K_{i} \rho K_{i}^{\dagger}, \tag{4}$$

where  $K_i$  represents a quantum gate, measurement, or noise process. For the transformation  $\eta(\rho)$  to output a physically valid quantum state,  $\eta$  must satisfy mathematical properties (completely positivity and  $0 \leq \text{Tr}[\eta(\rho)] \leq 1$ ) or alternatively,  $\sum_i K_i^{\dagger} K_i \leq 1$ .

Quantum circuits only represent a simple subset of all possible quantum channels. By placing restrictions on what  $\eta$  can represent, we can draw  $\eta$  as a quantum circuit. A quantum circuit contains horizontal wires representing qubits where input states are shown as ket symbols to the left of each wire and temporal order progresses from left to right. Boxed symbols represent quantum gates or quantum measurements on relevant wires. The main restriction is that boxed quantum gates must be reversible rotations of quantum states, i.e. unitary operations satisfying  $K^{\dagger} = K^{-1}$ . With measurements pushed to the end, a quantum circuit typically represents a unitary quantum channel with only one term in the sum in Eq. (4), i.e.  $i \in \{1\}$ , and therefore only an ensemble of quantum circuits can represent the collective action of noisy quantum circuits. The term 'circuit size' represents the number of qubits, while 'circuit depth' represents the number of time steps required to run the full circuit. Circuit depth assumes that quantum operations have been parallelized where possible and therefore refers to the minimum number of sequential steps, rather than a full tally of quantum gates in a circuit. While measurements are typically ignored until the very end, some measurements are performed 'mid-circuit'. If these mid-circuit measurement outcomes, or measured qubits, are not used in subsequent processing, then they can be safely pushed to the end of the circuit. In other cases, a double-wire may be used to visually represent how outcomes of mid-circuit measurements can be used to change quantum operations 'on the fly'.

Extracting information from a quantum computer is inherently statistical. In the case of qubits, all quantum measurements form a distribution of random '0' or '1' outcomes i.e. binary outcomes of a Bernoulli trial. Typically there is some desired physical quantity,  $\hat{O}$ , whose average value must be computed from this distribution of quantum measurements. The quantum state  $\rho$  is prepared, and the type (or basis) of quantum measurements is chosen according to  $\hat{O}$ . The statistical average (expectation value) of  $\langle \hat{O} \rangle$  is then represented by,

$$f := \text{Tr}[\rho \hat{O}], \tag{5}$$

where f is estimated empirically by collecting experimental data on a quantum computer using  $N_{shots}$ , and the right-hand side of the equation is a mathematical description of the information extraction process. Since  $\text{Tr}[A^{\dagger}B] = \langle B,A \rangle$  represents an inner product, f is some measure of the overlap between our quantum state  $\rho$  and the desired operation  $\hat{O}$ , analogous to the overlap of quantum states represented as vectors. Indeed if  $\rho = |\psi\rangle\langle\psi|$ , then  $\text{Tr}[\rho\hat{O}] = \text{Tr}[|\psi\rangle\langle\psi|\hat{O}] = \text{Tr}[\langle\psi|\hat{O}|\psi\rangle] = \langle\psi|\hat{O}|\psi\rangle$  which is a scalar number representing the average value of  $\hat{O}$  under  $|\psi\rangle$ . Computing this average requires repeatedly preparing  $|\psi\rangle$ , measuring this quantum circuit in the appropriate basis  $N_{shots}$  number of times, and using classical post-processing of distribution of measurement outcomes. All quantum algorithms in this review extract information from quantum computers in this manner.

Let  $f(x,\theta)$  be the average output of a quantum algorithm, and  $\rho_0$  be the input quantum state, e.g. where all qubits are in their ground (zero) state, and where  $(x,\theta)$  define classical inputs to a quantum algorithm. Here, x represents one sample of real data with dimension  $d, x \in \mathbb{R}^d$ , for a dataset containing a total of N data samples. Meanwhile, we also define tunable free parameters,  $\theta$ , that potentially could implement tunable quantum gates. The desired output information required from the algorithm is typically given by  $\hat{O}$ . We now discuss specific quantum algorithms that prepare quantum states, transform these states, and extract information from quantum computers in order to complete learning tasks.

**Quantum neural networks (QNNs)** consist of input data (x-dependent) and tunable ( $\theta$ -dependent) quantum operations. Generally, the output of a QNN is,

$$f(x,\theta) := \text{Tr}\left[U(x,\theta)\rho_0 U^{\dagger}(x,\theta)\hat{O}\right] = \langle \rho_{x,\theta}, \hat{O}\rangle, \tag{6}$$

where the data (x-dependent) and tunable ( $\theta$ -dependent) components of QNNs cannot be separated. In the above,  $U(x,\theta)$  represents a parameterized quantum gate which depends on data x and tunable parameters  $\theta$ . The equation above computes the overlap between information in the quantum state  $\rho_{x,\theta} = U(x,\theta)\rho_0 U^{\dagger}(x,\theta)$ , and the desired output  $\hat{O}$ , using an inner product.

In contrast, linear quantum models allow us to separate the x-dependent quantum operations and  $\theta$ -dependent quantum operations within the inner product [16]. In these models, we perform data encoding operations followed by tunable gates  $V(\theta)$ . As shown in Fig. 1(a), a linear QNN can be expressed by,

$$f(x,\theta) := \text{Tr} \left[ U(x)\rho_0 U^{\dagger}(x) V^{\dagger}(\theta) \hat{O}V(\theta) \right] = \langle \rho_x, \hat{O}_{\theta} \rangle$$
 (7)

In the above,  $\theta$  can take the form of any other classical parameters that are not x, data encoding is expressed by  $\rho_x := U(x)\rho_0 U^{\dagger}(x)$ , and the parameterized neural net is expressed as  $\hat{O}_{\theta} := V^{\dagger}(\theta)\hat{O}V(\theta)$ .

With this structure, we can describe many quantum machine learning algorithms. For example, we can omit  $\theta$  entirely, and recover sophisticated algorithms that focus on data encoding procedures. In kernel methods,  $\theta$  is replaced by training data, and the algorithm output f during prediction represents a linear combination of all training samples. Sometimes the action of  $\rho$ , U(x) or  $V(\theta)$  is non-trivially restricted to some subset of quantum states, yielding so-called quantum transformers. These choices are valid examples of linear quantum models, discussed below.

Quantum kernel methods (QKMs) are expressed as linear quantum models by replacing free tunable parameters  $\theta$  by optimized linear combinations of training data given by  $(\alpha, \mathcal{X}_T)$ . To see this, we redefine the second term in the inner product,  $\hat{O}_{\theta} \equiv \hat{O}_{\alpha,\mathcal{X}_T} := \sum_{t=1}^{T} \alpha_t \rho(x_t)$  for training data  $x_t \in \mathcal{X}_T, t = \sum_{t=1}^{T} \alpha_t \rho(x_t)$ 

 $1, \ldots, T$ . Substituting this expression into the inner product, the output of quantum kernel methods is

$$f(x, \alpha, x_t) := \sum_{t=1}^{T} \alpha_t \langle \rho_x, \rho_{x_t} \rangle, \tag{8}$$

where the inner product compares the overlap between two quantum states parameterized by two data points, x and training data sample,  $x_t$ , as in Fig. 1(b). The weights,  $\alpha$ , are optimized during training.

Quantum transformers, such as those of synthesized studies in Cherrat (2024) and Landman (2022), use sophisticated data encoders and neural network structures. Here, the data loaders ensure that the encoded state  $\rho_x$  consists of all possible combinations of states where all but one qubit is nonzero, i.e. states with Hamming weight-1 like '00010' or '10000' but not '10100'. The action of the quantum neural network is then chosen to ensure that output superpositions of quantum states are also of Hamming weight of one. In particular, let  $\rho_x$  denote the Hamming weight-1 inputs,  $\Lambda$  represents the restriction of linear algebra operations that preserve the weight of these states, and  $V_{\Lambda}$  the quantum operation which implements  $V_{\Lambda}|x\rangle = |\Lambda x\rangle$ . Here, some choice of weight matrix  $\Lambda$  enables one to compute linear multiplication  $\Lambda x$  using a quantum circuit. Choosing  $\hat{O}_{\Lambda} \equiv V_{\Lambda} \hat{O} V_{\Lambda}$  yields all the data loaders introduced in both Cherrat (2024) and Landman (2022). Similarly, one can add a trainable layer with parameters  $\theta$  such that a quantum operation implements a trainable matrix multiplication,  $V_W(\theta)|x\rangle = |W(\theta)x\rangle$ , where trainability of W is made explicit in notation. For one of the algorithms, the quantum orthogonal transformer discussed in Cherrat (2024), we find that the output function for computing the so-called attention mechanism  $A_{i,j}$  for two data patches  $x_i, x_j$ , is

$$A_{i,j} \equiv f(x_i, \theta, x_j) := \text{Tr} \left[ U^{\dagger}(x_j) V_W(\theta) U(x_i) \rho_0 U^{\dagger}(x_i) V_W^{\dagger}(\theta) U(x_j) \hat{O} \right] = \langle \rho_{x_i}, \hat{O}_{x_j, \theta} \rangle, \tag{9}$$

$$\hat{O}_{x_j,\theta} = V_W^{\dagger}(\theta)U(x_j)\hat{O}U^{\dagger}(x_j)V_W(\theta). \tag{10}$$

In the above, the term  $\hat{O}_{x_j,\theta}$  is reminiscent of a quantum kernel method since it depends on another data sample  $x_j \neq x_i$ , but also depends on a trainable matrix  $W(\theta)$  that affects parameterization of quantum gates. Assuming two different patches,  $x_i \neq x_j$ , one can factorize the inner product by grouping  $x_j, \theta$ , and argue that the inner product remains linear in  $x_i$ . Unlike kernel methods, however,  $x_j$  is not limited to the training dataset and consists of all pairwise combinations in the data. Indeed if  $x_i \equiv x_j$ , then the output function would be non-linear in  $x_i$  in a manner similar to non-linear quantum models [16] such as quantum data re-uploading classifiers (QDRCs) depicted for reference in Fig. 1(c)[57].

Quantum convolutional neural networks (QCNNs) can similarly be understood as a tunable quantum channel  $\tilde{\eta}_{\theta}$  that is composed of many smaller channels  $\eta_{\theta_i}$ , where quantum channels are introduced in Appendix A. For each *i*-th tunable layer, the algorithm's structure can be written as  $\tilde{\eta}_{\theta}(\rho) := \bigcirc_i \eta_{\theta_i}(\rho) = \dots \eta_{\theta_3}(\eta_{\theta_2}(\eta_{\theta_1}(\rho))) \dots$  In typical formulations such as that in Fig. 1(d), in each *i*-th layer, we measure half of the remaining qubits in that layer, forcing these measured qubits to be reduced to classical bits. Consequently, these channels  $\eta_{\theta_i}$  are defined on an increasingly smaller number of qubits as *i* increases, until only one qubit is left. The channels for each layer  $\eta_{\theta_i}$  are typically non-unitary, meaning that unlike quantum gates, these operations cannot be reversed or 'undone'. An example of a non-unitary channel is where the measurement outcomes of a pooling layer dictate how gates are applied to the remaining qubits in the next layer [58]. If we want to extract  $f(x,\theta) = \text{Tr}\left[\tilde{\eta}_{\theta}(\rho_x)\hat{O}\right]$ , then in general it appears that tunable parameters and data-dependent operations cannot be separated for QCNNs. However, if mid-circuit QCNN measurements do not affect future quantum operations and can all be safely pushed to the end of the QCNN circuit, then averaging over mid-circuit measurements can be implemented entirely in classical post-processing and the layers  $\eta_{\theta_i}$  can be unitary (i.e.  $\eta_{\theta_i}(\rho) := V(\theta_i)\rho V^{\dagger}(\theta_i)$ ). In this regime, we recover a linear quantum model for QCNNs,

$$f(x,\theta) = \operatorname{Tr}_{i \neq q} \left[ \rho_x \tilde{\eta}_{\theta}^{\dagger}(\hat{O}) \right],$$
 (11)

where the trace over i conveys that all pooling layers are marginalized at the end except for the last remaining qubit, q. There is some heuristic evidence that linear QCNN models of this form are unlikely to be useful for the analysis of classical data [10].

Quantum causal modeling is the use of quantum algorithms to solve causal inference problems. In medical settings, establishing causality between variables based on real-world medical data is an important classical learning task. If the direction of a certain causal relationship is known, then the causal effect, which represents the strength of the causal relationship, can be estimated via classical or quantum techniques. In this review, the quantum techniques used for causal inference were all linear quantum models of the form above.

Quantum deep reinforcement learning networks rely on the same underlying capabilities of a quantum neural network and the specific examples encountered in this review fit into the framework of linear quantum models. The only modification is the introduction of reinforcement learning, whereby a classical learning agent is trained to take optimal actions in a given environment to maximize a pre-determined reward function. Since the learning agent is classical, the underlying role of quantum technologies is the same as any other linear quantum model.

Quantum generative adversarial networks use the interaction between two artificial learning agents that have access to a quantum computer. The generator and discriminator are adversarial: the generator creates random, synthetic data samples with the goal of fooling the discriminator into believing it is real data, while the discriminator must assign a label of real or fake to each data sample. The end point of this game is a generator that has been trained to create high quality synthetic samples such that the discriminator is forced to guess randomly, i.e. discriminator guesses correctly with 50% probability. In the quantum versions of these algorithms, the data refers to quantum states of a quantum system, the generator has access to a quantum computer, and the discriminator can perform arbitrary quantum measurements. QGANs may demonstrate exponential quantum advantage for sufficiently high-dimensional quantum data [59]. For classical datasets, no provable quantum advantage exists. The quantum circuits formed by QGANs in this review were also linear quantum models.

# B PRISMA Checklist



### PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION	_		
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	S1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	S2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	S3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	S3 Appendix
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	S3 Appendix
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	S3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	S3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	S3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	NA
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	S3, S4.1
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	S4.1
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	S4.1
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	S4.1
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	S4.1
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	S4.1
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	S3, S4.1



# PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	S4.1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	S4.1
Study characteristics	17	Cite each included study and present its characteristics.	S4.1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	NA
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	S4.1, S4.2
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	S4.2
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	S4.2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	S4.2
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	\$4.2
DISCUSSION	*		
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	S5
	23b	Discuss any limitations of the evidence included in the review.	S5
	23c	Discuss any limitations of the review processes used.	S5
	23d	Discuss implications of the results for practice, policy, and future research.	S5
OTHER INFORMA	TION		
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	S3
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Declarations
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Declarations
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Declarations
Competing interests	26	Declare any competing interests of review authors.	Declarations
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Declarations

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE	#		(Tes/No)
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND	1		
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	NA
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS	1		
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION	•		
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER	•		
Funding	11	Specify the primary source of funding for the review.	NA
Registration	12	Provide the register name and registration number.	NA

# C Nomenclature

Abbrev.	Definition
EHR	Electronic health records
EMR	Electronic medical records
GAN	Generative adversarial network
LDA	Linear discriminant analysis
PCA	Principal component analysis
PRISMA	Preferred reporting items for systematic reviews and meta-Analyses
PROSPERO	International prospective register of systematic reviews
PTRI	Phase space terrain ruggedness index, a proposed global metric for linking performance scores
PIKI	with a configuration space [12]
PQC	Parameterized quantum circuit
QC	Quantum computation
QCNN	Quantum convolutional neural network algorithms
QEC	Quantum error correction
QEM	Quantum error mitigation
QGAN	Quantum generative adversarial methods
QKM	Quantum kernel methods
QPIE	Quantum probability image encoding [60]
QML	Quantum machine learning algorithms
QNN	Quantum neural network algorithms
ODAC	Quantum random access coding of bitstring length $m$ into $n$ qubits so that any 1 out of $m$ bits
QRAC	can be recovered with probability $p>1/2$
QRAM	Quantum random access memory
QUBO	Quadratic unconstrained binary optimization
SVM	Support vector machine
VQC	Variational quantum circuit

# D Search strategies

Our database selection captures publishing practices in healthcare and medicine but also in quantum computing. While PubMed and Embase are popularly used in health, we additionally include IEEE and Scopus which typically index computer science, physics and engineering journals. Physics-centric publications such as APS journals and Quantum are indexed in Scopus. Meanwhile we independently

search quantum physics preprint server arXiv (quant-ph) to capture recent and unindexed computing and quantum machine learning literature.	quantum

Database	Setting/Perspective	Intervention	Comparator	Eval / Study
arXiv	health OR clinical OR "medical data" OR "medical imaging" OR "medical imaging" OR "medical image" OR hospital OR "patient data" OR "radiography" OR "ECG" OR "EEG" OR "MRI" OR "electrocardiography" OR "uss" OR "ct" OR ultrasound* OR "s-ray" OR "x-ray" OR "x-ray" OR "x-ray" OR "sedography" OR "laboratory data" OR "laboratory data" OR "laboratory test" OR biostatistics OR radiology OR epiproteom* OR epigenom* OR gene OR transcriptom* OR gene OR transcriptom* OR gene OR transcriptom oR "leetroords" [MeSH Terms] OR "leetroonic health records" [MeSH Terms] OR "leetronic health records" [All Fields] OR "health record" [All Fields] OR "medical record" [All Fields] OR "medical record" [All Fields] OR "clinical record" [All Fields]	"quantum machine learning"[All Fields] OR "quantum comput*"[All Fields] OR "quantum inform*"[All Fields]	"machine learning" OR algorithm* OR Bayes* OR kernel* OR classif* OR "neural net" OR "reinforcement learning" OR "k-means" OR "support vector" OR "random forest" OR "adversarial net" OR "random walk" OR "regression" OR "monte carlo" OR "Markov"  All Fields  (machine learning" OR algorithm[MeSH Terms] OR "algorithm[MeSH Terms] OR "Bayes*"[All Fields] OR "Bayes*"[All Fields] OR "kernel*"[All Fields]	("2015"[Date - Publication]: "3000"[Date - Publication])
	OR "clinical record" [All Fields] OR ("hospital" [All Fields] AND "data*" [All Fields]) OR ("clinical" [All Fields] AND "data*" [All Fields]) OR ("medical" [All Fields] AND "data*" [All Fields]) OR ("health" [All Fields] AND "data*" [All Fields]) OR ("patient*" [All Fields] AND "data*" [All Fields]) OR ("patient*" [All Fields] AND "data*" [All Fields]) OR "medical history" OR "Routinely Collected Health Data" [Mesh] OR "Routinely Collected Health Data" [All Fields] OR "Administrative Data" [All Fields] OR "Administrative Health Data" [All Fields] OR "health information systems" [MeSH Terms] OR "health services administration" [MeSH Terms] OR "medical inform* [All Fields] OR "radiography" [MeSH Terms] OR "radiography" [All Fields] OR ("medical" [All Fields] AND "imaging" [All Fields]) OR "diagnostic imaging" [All Fields] OR "diagnostic imaging" [MeSH Terms] OR "cdiagnostic imaging" [All Fields] OR "diagnostic imaging" [MeSH Terms] OR "electrocardiography" [MeSH Terms] OR "electrocardiography" [MeSH Terms] OR "ecg" [All Fields] OR "radiography" [MeSH Terms] OR "electrocardiography" [MeSH Terms] OR "ekg" [All Fields] OR "radiograph*" OR "magnetic resonance imaging" [MeSH Terms] OR "magnetic resonance imaging" [All Fields] OR "nuclear magnetic resonance imaging" [All Fields] OR "nuclear magnetic resonance imaging" [All Fields]	Pields] OR quantum[Title/Abstract]	OR "classif*"[All Fields] OR "classif*"[All Fields] OR "neural networks, computer"[MeSH Terms] OR "deep learning"[MeSH Terms] OR (cnn) OR (svm) OR (svd) OR "pca"[Title/Abstract] OR "principal component analysis"[All Fields] OR "reinforcement learning"[All Fields] OR "k-means"[All Fields] OR "wavelet"[All Fields] OR "neural net*"[All Fields] OR "support vector*"[All Fields] OR "support vector*"[All Fields] OR "adversarial net*"[All Fields] OR "adversarial net*"[All Fields] OR "nonlinear regression"[All Fields] OR "nonlinear regression"[All Fields] OR "monte carlo method"[MeSH Terms] OR "Markov chain"[All Fields] OR "gaussian process regression"[All Fields] OR "gaussian process regression"[All Fields] OR "attificial intelligence"[All Fields] OR "attificial intelligence"[All Fields] OR "data pre-processing"[All Fields] OR "data post-processing"[All Fields] OR "feature selection"[All Fields] OR "feature selection"[All Fields] OR "feature extraction"[All Fields] OR "feature extraction"[All Fields] OR "feature extraction"[All Fields] OR "predictive model*"[All Fields]	NOT ("systematic review"[pt] OR "meta-analysis"[pt] OR "clinical trial protocol"[pt] OR "clinical conference"[pt] OR "case reports"[pt])

OR "coherence tomography" OR "optical coherence tomography" OR "computer assisted tomography" OR "uss"[All Fields] OR "ct"[All Fields] OR "computed tomography"[All Fields] OR "ultrasound\*" OR "echography" OR "x rays"[MeSH Terms]
OR "x rays"[All Fields] OR "xray"[All Fields] OR "mammogra\*" OR "holography" OR "electroencephalography"[MeSH Terms] OR "electroencephalography"[All Fields] OR "eeg"[All Fields] OR "radiology"[Title/Abstract] OR "laboratory data" OR "laboratory test\*"
OR "biostatistics"[Title/Abstract] OR epigenomics[Mesh] OR metabolomics[Mesh] OR biomarker[Mesh] OR transcriptomics[Mesh] OR proteomics[Mesh] OR genomics[Mesh] OR "epiproteom\*" OR "epiomic\*" OR "vaccin\*" OR "epigenom\*" OR "metabolom\*" OR "gene" OR "transcriptom\*" OR "proteom\* OR "genom\*" 'medical record'/exp NOT ('conference Embase 'quantum machine ('machine learning'/exp) OR 'electronic health record\*' (Elservier) learning' OR 'machine learning' abstract'/it OR OR 'health record\*' OR 'quantum comput\*' OR algorithm/exp 'review'/it) AND [2015-OR algorithm\* OR 'medical record\*' OR 'quantum inform\*' 2024]/py OR 'clinical record\* OR quantum:ti,ab OR Baves\* OR (hospital AND data\*)
OR (clinical AND data\*) OR kernel\* OR classif\* OR (medical AND data\*) OR (cnn) OR (health AND data\*) OR (svm) OR (patient\* AND data\*) OR (svd) OR 'medical history'
OR 'Routinely Collected Health Data'/exp OR (pca):ti,ab OR 'principal component analysis' OR 'Routinely Collected Health Data' OR 'reinforcement learning' OR 'Administrative Data' OR k-means OR 'Administrative Health Data' OR wavelet OR 'genetic algorithm\*'
OR 'neural net\*' OR 'medical information system'/exp OR 'medical information'/exp OR 'support vector\*' OR 'medical inform\*' OR radiography
OR (medical AND imaging) OR 'random forest\* OR 'Boltzmann mach\*' OR 'medical imaging'
OR 'diagnostic imaging'/exp OR 'adversarial net\* OR 'random walk\*' OR (diagnostic AND imaging) OR 'linear regression' OR 'diagnostic imaging' OR 'nonlinear regression' OR radiography/exp OR 'monte carlo' OR electrocardiography/exp OR 'Markov chain' OR 'qaussian process regression' OR ecg OR ChatGPT OR electrocardiography/exp OR ekg OR 'large language models' OR radiograph\* OR 'artificial intelligence' OR 'nuclear magnetic resonance imaging'/exp OR (magnetic AND resonance) OR 'big data' OR 'data pre-processing' OR 'magnetic resonance imaging' OR 'data post-processing' OR mri OR 'feature selection' OR 'nuclear magnetic resonance imaging' OR 'feature extraction' OR 'coherence tomography' OR 'predictive model\*' OR 'optical coherence tomography' OR 'computer assisted tomography' OR uss OR ct OR 'computed tomography' OR ultrasound\* OR echography OR 'X ray flim'/exp OR 'x rays' OR xray OR mammogra\* OR holography OR electroencephalography/exp OR electroencephalography OR eeg OR radiology:ti,ab OR 'laboratory data'

OR 'laboratory test\* OR biostatistics:ti,ab OR epigenomics/exp OR metabolomics/exp OR biomarker/exp OR transcriptomics/exp OR proteomics/exp OR genomics/exp OR epiproteom\* OR epiomic\* OR vaccin\* OR epigenom\* OR metabolom\* OR gene OR transcriptom\* OR proteom\* OR genom\* INDEXTERMS("medical records") INDEXTERMS("machine learning") Scopus ALL("quantum machine 2015 > OR INDEXTERMS("electronic health learning") OR "machine learning" OR INDEXTERMS(algorithm) OR ALL("quantum Exclude: Reviews, records") OR ALL("electronic health record\*") comput\*") OR ALL(algorithm\*) Conference Reviews, OR ALL("health record\*")
OR ALL("medical record\*") OR ALL("quantum OR ALL(Bayes\*) Books, Book Chapters OR ALL(kernel\*) inform\*") OR ALL("clinical record\*") OR TITLE-OR ALL(classif\*) OR (ALL(hospital) AND ALL(data\*)) OR INDEXTERMS("neural networks, ABS(quantum) OR (ALL(clinical) AND ALL(data\*)) computer") OR INDEXTERMS("deep learning") OR (ALL(medical) AND ALL(data\*)) OR (ALL(health) AND ALL(data\*)) OR (cnn) OR (ALL(patient\*) AND ALL(data\*)) OR (svm) OR "medical history"
OR INDEXTERMS("Routinely Collected OR (svd) OR TITLE-ABS(pca) Health Data") OR ALL("principal component OR ALL("Routinely Collected Health Data") analysis") OR ALL("Administrative Data")
OR ALL("Administrative Health Data") OR ALL("reinforcement learning") OR ALL(k-means) OR INDEXTERMS("health information OR ALL(wavelet) systems") OR ALL("genetic algorithm\*") OR INDEXTERMS("health services OR ALL("neural net\*") OR ALL("support vector\*")
OR ALL("random forest\*") administration") OR INDEXTERMS("medical informatics OR ALL("Boltzmann mach\*")
OR ALL("adversarial net\*") computing") OR ALL("medical inform\*") OR INDEXTERMS(radiography) OR ALL("random walk\*") OR ALL("linear regression")
OR ALL("linear regression")
OR ALL("Markov carlo")
OR ALL("Markov chain") OR ALL(radiography) OR (ALL(medical) AND ALL(imaging))
OR ALL("medical imaging")
OR INDEXTERMS("diagnostic imaging") OR ALL("gaussian process OR (ALL(diagnostic) AND ALL(imaging)) OR ALL("diagnostic imaging") regression") OR INDEXTERMS(radiography) OŘ ChatGPT OR ALL("large language models")
OR ALL("artificial intelligence") OR INDEXTERMS (electrocardiography) OR ALL(ecg) OR INDEXTERMS(electrocardiography) OR ALL("big data") OR ALL(ekg) OR ALL("data pre-processing") OR radiograph\* OR ALL("data post-processing") OR ALL("feature selection")
OR ALL("feature extraction") OR INDEXTERMS("magnetic resonance imaging") OR (ALL(magnetic) AND ALL(resonance)) OR ALL("predictive model\*") OR ALL("magnetic resonance imaging") OR ALL(mri) OR "nuclear magnetic resonance imaging" OR "coherence tomography" OR "optical coherence tomography" OR "computer assisted tomography" OR ALL(uss) OR ALL(ct) OR ALL("computed tomography") OR "ultrasound\*" OR "echography" OR INDEXTERMS("x rays") OR ALL("x rays")
OR ALL("xray") OR "mammogra\*" OR "holography" OR INDEXTERMS(electroencephalography) OR ALL(electroencephalography) OR ALL(eeg) OR TITLE-ABS(radiology) OR "laboratory data" OR "laboratory test\*' OR TITLE-ABS(biostatistics) OR INDEXTERMS(epigenomics) OR INDEXTERMS (metabolomics) OR INDEXTERMS (biomarker) OR INDEXTERMS (transcriptomics) OR INDEXTERMS(proteomics) OR INDEXTERMS (genomics) OR "epiproteom\*"

OR "epiomic\*" OR "vaccin\*" OR "epigenom\*" OR "metabolom\*" OR "gene" OR "transcriptom\*" OR "proteom\*" IEEE "Mesh\_Terms":"medical record" ("machine learning") "quantum machine Manual OR "electronic health record?" learning" OR "Mesh\_Terms": "machine OR (("hospital" OR "clinical" OR "medical" OR OR "quantum comput\*" learning" OR "Mesh\_Terms":"algorithm" "health" OR "patient") AND "record?") OR "quantum inform\*" OR (("hospital" OR "clinical" OR "medical" OR "health" OR "patient") AND "data\*") OR "Document OR "algorithm?" Title":"quantum" OR ("Bayes" OR "Bayesian") OR "Abstract":"quantum" OR "medical history"
OR "Mesh\_Terms":"Routinely Collected OR "kernel?" OR ("classifier" OR "classification") Health Data" OR ("cnn") OR "Routinely Collected Health Data"
OR "Administrative Data" OR ("svm") OR ("svd") OR "Administrative Health Data" OR "Document Title": "pca" OR "Abstract":"pca"
OR "principal component analysis" OR "Mesh\_Terms": "medical information system" OR "Mesh Terms": "medical information" OR "reinforcement learning" OR "k-means" OR "medical inform\*" OR "radiography"
OR ("medical" AND "imaging") OR "wavelet"
OR "genetic" ORNEAR/2 OR "medical imaging" ("algorithm?") OR "neural" ORNEAR/2 ("network?" OR "net?") OR "Mesh\_Terms":"diagnostic imaging"
OR ("diagnostic" AND "imaging") OR "diagnostic imaging"
OR "Mesh\_Terms":"radiography"
OR "Mesh\_Terms":"electrocardiography" OR "support vector?" OR "random forest?" OR "Boltzmann" ONEAR/3 "machine" OR "adversarial" ONEAR/3 ("network?" OR "net?") OR "ecg" OR "Mesh\_Terms":"electrocardiography" OR "random walk?" OR "ekg" OR "radiograph\*" OR "linear regression" OR "Mesh\_Terms": "nuclear magnetic OR "nonlinear regression" resonance imaging"
OR ("magnetic" AND "resonance") OR "monte carlo" OR "Markov chain" OR "gaussian process regression" OR "ChatGPT" OR "magnetic resonance imaging" OR mri OR "nuclear magnetic resonance imaging" OR "large language models" OR "coherence tomography" OR "artificial intelligence" OR "optical coherence tomography" OR "big data" OR "data pre-processing" OR "data post-processing" OR "computer assisted tomography" OR uss OR ct OR "feature selection" OR "computed tomography" OR "feature extraction" OR "ultrasound?" OR "predictive" ORNEAR/2 OR "echography"
OR "Mesh\_Terms":"X ray flim" ("model?" OR "modelling") OR "x rays" OR "xray" OR "mammogra\*" OR "holography"
OR "Mesh\_Terms":"electroencephalography" OR "electroencephalography" OR "eeg" OR "Document Title": "radiology" OR "Abstract":"radiology"
OR "laboratory data" OR "laboratory test\*" OR "Document Title": "biostatistics" OR "Abstract": "biostatistics" OR "Mesh\_Terms":"epigenomics"
OR "Mesh\_Terms":"metabolomics" OR "Mesh\_Terms":"biomarker" OR "Mesh\_Terms":"transcriptomics"
OR "Mesh\_Terms":"proteomics" OR "Mesh\_Terms":"genomics"
OR "epiproteom\*" OR "epiomic\*"
OR "vaccin\*" OR "epigenom\*" OR "metabolom\*" OR "gene" OR "transcriptom\*" OR "proteom\*

OR "genom\*"

# E Data extraction template

	Field name	Туре	Details
1	Title	Free text	Title of the article
2	Year	Free text	Publication year
3	Country	Country	Country of first author affiliation
4	Input health dataset(s)	Multi- select; Free text "Other"	Medical images: MRIs Medical images: CT Medical images: XRays Medical images: XRays Medical images: Warn Medical images: ultrasound Time varying signals: EEG Time varying signals: EEG Time varying signals: EEG Time varying signals: heart rate Medical data: patient demographics Medical data: laboratory tests Medical data: other (specify) Textual or handwritten medical data Other
5	Input data is sourced from	Multi- select; Free text "Other"	Open sourced or public datasets Privately sourced datasets EHR / EM or hospital records Data collected during study Other
6	QML intervention(s):	Multi- select; Free text "Other"	Quantum kernels Quantum neural networks (QNN) Quantum convolutional neural net (QCNN) Quantum gong short time memory (QLSTM) Quantum long short time memory (QLSTM) Quantum FOA Quantum FOA Quantum FOA Quantum FOA Quantum Forer transform Grover search HHL algorithm Quantum transfer learning Variational/parameterized quantum circuits Quantum genetic / evolutionary Quantum adversarial network Q K-means / clustering Other
7	Classical comparator(s)	Multi- select; Free text "Other"	Support vector machines Principal component analysis Classical kernels Regression Tensor networks Bayesian analysis Neural networks (NN) Convolutional neural networks (CNN) Genetic or evolutionary algorithms Gaussian process regression Nonlinear or particle filters

	=:	_	2.43
	Field name	Туре	Details Other
			=
8	Simulators for quantum algorithms	Multi- select; Free text "Other"	Pennylane Cirq Qiskit IBM Lab / IBM Composer MATLAB Mathematica Other
9	Experimental data collection on hardware	Multi- select; Free text "Other	None used / not applicable IBM Falcon IBM Heron IBM Heron IBM Eaple Older IBM device Quantinuum H1 Quantinuum H2 Google Sycamore Google Bristicone Rigetti Xanadu Psi-Quantum Other
10	Approx circuit depth	Free text	NR: Not reported; NA: Not applicable
11	Approx circuit size (e.g. qubit number)	Free text	NR: Not reported; NA: Not applicable
12	Code and data is accessible	Boolean	Yes/ No Not sufficient to provide link to public datasets. Must provide access to codebase via Github or other public link
13	Q1: Explains quantum algorithm selection by referencing learning problem class or dataset structure:	Single choice	No theory or empirical rationale for quantum algorithm selection discussed or cited     Ouantum algorithm selection is empirical or mostly cites empirical literature     Cuantum algorithm selection is linked to underlying class of learning problem or data structure     Ouantum algorithm has provable advantage with respect to class of learning problem or data structure
14	Q2: Identifies/ discusses impact of data encoding on quantum algorithm performance:	Single choice	O: Encoding methodology omitted or incomplete O: Impact of different encoding strategies on overall performance is not analyzed T: Performance impact is discussed with incomplete analysis (e.g. compares at least 2 methods) 2: Performance impact is well characterized empirically or theoretically
15	Q3: Identifies/	Single	0 : Data pre-processing methodology is omitted
	discusses impact of	choice	or incomplete

	Field name	Туре	Details
	classical input data processing on quantum algorithm performance:		Compact of different data pre-processing strategies on overall performance is not analyzed     Performance impact is discussed with incomplete analysis (e.g. compares at least 2 methods)     Performance impact is well characterized empirically or theoretically     Not applicable (no classical input data processing)
16	Q4: (EMPIRICAL ONLY) Dimensionality of data input for quantum algorithm	Single choice	0 : Not reported or discussed; or unclear 0 : Negligible i.e. O(10) 1 : Small i.e. O(10) 2 : Intermediate i.e. O(10^2) 3 : Large i.e. O(10^3) or greater Not applicable (theory study)
17	Judgement	Single choice	Do not proceed if at least two scores from Q1, Q2, Q3, or Q4 is zero.  EXCLUDE STUDY  CONTINUE EXTRACTION
18	Any judgement comments?	Free text	
19	Sample size	Single choice	This refers to the sample size of data processed by a quantum algorithm e.g. 256 images.  0: Applicable but not reported  0: Negligible O(1)  1: Small i.e. O(10^1)  2: Medium i.e. O(10^2)  3: Large i.e. O(10^3)  4: XLarge i.e. O(10^4) or greater Not applicable (theory study)
20	QML and classical algorithms received input data of same dimensionality	Single choice,	True False Not described / unknown
21	QML and classical algorithms received training data of same sample size	Single choice	True False Not described / unknown
22	Loss function	Single choice; free text "Other"	Not applicable Not described / unknown Lp norm Other
23	Regularization	Single choice, free text "Other"	Not applicable Not described / unknown Explicitly regularized Other
24	Hyperparameter tuning	free text "Other"	Not applicable Not described / unknown / not tuned Known apriori initialization conditions

	Field name	Туре	Details
			Manually tuned / ad hoc Grid-search Optimization via meta-protocol Other
25	Discussion of realistic operating conditions:	Multi- select	Shot noise Noise: depolarizing, bit flip or amplitude Noise: : Pauli channels Noise: : Pauli channels Noise: Hardware noise sources Data noise: Missing data Data noise: Missing data Data noise: Incorrect training data Model generalization error Model optimization: hyper parameter tuning Model optimization: hyper parameter tuning Model optimization: number of qubits Hardware execution: layout / connectivity Hardware execution: gates, msmls, control Clinical efficacy / implementation Other
26	Discussion of realistic operating conditions:	Single choice	O: None of the above operating conditions discussed     1: Between 1 to 3 operating conditions discussed (without analysis)     2: Between 1 to 3 operating conditions discussed with at least one with quantitative analysis     3: More than 3 operating conditions discussed with at least one with quantitative analysis
27	Simulators (ML)	Multi- select	None reported Python Library: TensorFlow Python library: scikitlearn Python library: other NVIDIA CPU/GPU simulator Julia library MATLAB Mathematica C++ libraries Google Colab Other
28	Risk of bias assessment	Boolean	Not applicable Applicable
29	For synthesis?	Boolean	Applicable Must be INCLUDED for full extraction Must use hardware or discuss / simulate the affect of noise

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