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Technologies, Clinical Applications, and Implementation Barriers of Digital Twins in Precision Cardiology: Systematic Review

Fatemeh Sarani Rad[1*], MSc; Ehsan Bitaraf[2*], MD; Maryam Jafarpour[3*], PhD; Juan Li[1*], PhD

[1]Computer Science Department, North Dakota State University, 1320 Albrecht Blvd, Fargo, ND, United States

[2]Center for Technology and Innovation in Cardiovascular Informatics, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

[3]Center for Medical Data Science, Medical University of Vienna, Vienna, Austria

[*]all authors contributed equally

Corresponding Author:
Juan Li, PhD
Computer Science Department, North Dakota State University, 1320 Albrecht Blvd, Fargo, ND, United States

Abstract

Background: Digital twin systems are emerging as promising tools in precision cardiology, enabling dynamic, patient-specific simulations to support diagnosis, risk assessment, and treatment planning. However, the current landscape of cardiovascular digital twin development, validation, and implementation remains fragmented, with substantial variability in modeling approaches, data use, and reporting practices.

Objective: This systematic review aims to synthesize the current state of cardiovascular digital twin research by addressing 11 research questions spanning modeling technologies, data infrastructure, clinical applications, clinical impact, implementation barriers, and ethical considerations.

Methods: We systematically searched 5 databases (PubMed, Scopus, Web of Science, IEEE Xplore, and Google Scholar) and screened 330 records. Forty-two original studies met the predefined eligibility criteria and were included. Data extraction was guided by 11 thematic research questions. Mechanistic and artificial intelligence (AI) or machine learning (ML) modeling strategies, data modalities, visualization formats, clinical use cases, reported impacts, limitations, and ethical or legal issues were coded and summarized. Risk of bias was evaluated using a custom checklist for modeling studies, the Prediction Model Risk of Bias Assessment Tool (PROBAST) for prediction models, and the Risk of Bias in Non-Randomized Studies - of Interventions (ROBINS-I) for observational studies.

Results: Most digital twins (29/42, 69%) relied on mechanistic models, while hybrid mechanistic–data-driven approaches and purely data-driven designs were less frequent (13/42, 31%). Only 18 studies explicitly described ML or AI, most often deep learning, Bayesian methods, or optimization algorithms. Personalization depended primarily on imaging (32/42, 76%) and electrocardiography or other electrical signals (18/42, 43%). Visualization was dominated (41/42, 98%) by static figures and anatomical snapshots. Clinically, digital twins were most commonly applied to therapy planning, risk prediction, and monitoring. Reported benefits focused on improved decision-making and therapy-related impacts, with occasional (8/42, 19%) reports of increased accuracy or faster diagnosis, but there was limited evidence for downstream improvements in patient outcomes. Key barriers included strong model assumptions and simplifications; high computational cost; data quality and availability constraints; limited external validation; and challenges in real-time performance, workflow integration, and usability. Explicit discussion of ethical, legal, or governance issues was rare (7/42, 17%).

Conclusions: Cardiovascular digital twins show substantial potential to advance precision cardiology by linking personalized physiological models with clinical decision support, particularly for therapy planning and risk prediction in arrhythmia and heart failure. However, real-world implementation is constrained by methodological heterogeneity, restricted data and validation practices, limited openness of code and models, and sparse engagement with ethical and governance questions. Future research should prioritize standardized evaluation frameworks, robust clinical validation, interoperable and user-centered system design, and ethically grounded, patient-centered development to realize the full clinical value of digital twin systems.

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KEYWORDS

digital twin; cardiology; personalized medicine; simulation; machine learning; clinical decision support; ethics

Introduction

In recent years, the integration of digital twin technology into health care has opened new avenues for precision medicine, particularly within the field of cardiology. A digital twin is a dynamic, virtual representation of a physical system that is continuously updated with real-time data, advanced computational models, and artificial intelligence (AI) analytics [1,2]. In the context of health care, digital twins serve as virtual replicas of patients, organs, or biological systems, encompassing multidimensional, patient-specific information to inform clinical decisions [3-5].

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, underscoring the need for innovative, patient-centric approaches to diagnosis, treatment, and management [6,7]. The application of digital twins in cardiology involves the creation of virtual replicas of the human heart by integrating anatomical, physiological, and molecular data. These models are capable of simulating electrical activity [8], mechanical function, hemodynamics, and drug responses [9,10]. By combining data from cardiac imaging (eg, magnetic resonance imaging [MRI] and computed tomography [CT]), electrocardiography (ECG), hemodynamic profiles, electrophysiology recordings, electronic health records, and omics assessments, digital twin systems provide a basis for precision simulation and virtual experimentation [11].

These capabilities make cardiac digital twins uniquely positioned to support personalized treatment plans, enabling applications such as risk stratification, therapy optimization, surgical simulation, and drug safety testing. The integration of AI, particularly machine learning (ML) and deep learning (DL), has further improved the scalability and performance of digital twins in real-world applications.

However, despite promising technical progress, substantial challenges remain. These include (1) high computational costs and complex personalization pipelines; (2) data heterogeneity and interoperability limitations; (3) lack of standardized validation protocols and clinical benchmarks; and (4) ongoing concerns regarding privacy, explainability, and regulatory oversight.

While multiple reviews have surveyed digital twins in general health care [12] or addressed cardiovascular simulation from a technical standpoint [11], a comprehensive, domain-specific synthesis integrating technical, clinical, and implementation perspectives in personalized cardiology remains lacking.

To address this gap, we conducted a systematic review following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines [13,14]. This review explicitly examines original research articles on cardiovascular digital twin systems, emphasizing personalization, clinical relevance, and implementation feasibility. Our study followed a two-stage methodology:

1. Screening phase: We screened 330 articles from 5 databases (PubMed, Scopus, IEEE, Web of Science, and Google Scholar). After removing duplicates, non-English entries, and publications lacking abstracts or relevant context, 42 articles were retained.
2. Review phase: Three independent reviewers assessed full-text articles based on structured research questions (RQs). Each article was evaluated for relevance to 11 themes covering technology, data integration, clinical application, validation, ethics, and data sources.

The following RQs guided our review:

- RQ1-RQ4: What are the technological foundations of cardiovascular digital twins, including modeling strategies, AI integration, and open-source availability?
- RQ5 and RQ6: How is patient-specific data structured and visualized?
- RQ7 and RQ8: What are the clinical applications and disease targets of digital twins?
- RQ9: What clinical impacts have been reported as a result of digital twin use?
- RQ10 and RQ11: What barriers, limitations, and ethical or legal considerations are acknowledged in current studies?

The aim of this study was to systematically review the existing literature on cardiovascular digital twins to identify current technologies, clinical uses, and challenges to implementation.

Methods

Overview

This systematic review was designed and conducted following the PRISMA 2020 statement (Checklist 1). The protocol was developed in advance and used a transparent, reproducible approach to article retrieval, screening, and extraction. It was structured around 11 domain-specific RQs targeting the technological, clinical, and implementation dimensions of digital twin systems in cardiology.

Data Sources and Search Strategy

A comprehensive literature search was performed across 5 major academic databases: PubMed, Scopus, Web of Science, IEEE Xplore, and Google Scholar. These platforms were selected to ensure broad interdisciplinary coverage across biomedical, engineering, and computational sciences. The databases were searched between January and early February 2025, restricting records to publications from 2010 onwards. Only the first 115 results sorted by relevance were screened for Google Scholar due to indexing limitations. The reference lists of relevant reviews were also scanned to ensure inclusion of key foundational articles.

Data collection and initial preprocessing were streamlined using Triple-A software [15], which served as the main tool for managing and organizing the retrieved records.

The search strategy used Boolean combinations of controlled vocabulary (eg, MeSH) and free-text terms as follows: (“digital twin” OR “virtual heart” OR “patient-specific model”) AND (“cardiology” OR “cardiac” OR “heart” OR “cardiovascular”) AND (“simulation” OR “personalized medicine” OR “precision medicine” OR “in silico”).

To increase transparency, we conceptually structured the search according to the Population, Intervention, Comparison, and Outcome (PICO) framework:

- Population (P): Patients with CVDs, including arrhythmia, heart failure, ischemic heart disease, cardiomyopathy, and related conditions.
- Intervention (I): Digital twin systems designed for diagnosis, simulation, personalization, monitoring, risk prediction, or therapy planning in cardiology.
- Comparison (C): Not applicable, as the review did not evaluate digital twins against alternative interventions or standard care.
- Outcome (O): Descriptive outcomes related to modeling strategies, data infrastructure, clinical applications, reported clinical impact, implementation barriers, and ethical or governance considerations.

These PICO elements informed the design of our search and eligibility criteria, while the detailed content of the review was organized around 11 thematic RQs (RQ1-RQ11).

All search results were exported to a centralized reference manager and screened using Microsoft Excel. The complete search strings for the databases are provided in Multimedia Appendix 1.

Eligibility Criteria

Articles were included if they (1) were original empirical research studies, including journal articles, conference papers, and preprints; (2) reported on the development, implementation, or evaluation of digital twin systems in health care; (3) focused on cardiovascular applications, including anatomical, physiological, or functional heart modeling; (4) were related to individualized or personalized medicine, clinical decision-making, or patient-specific therapies; and (5) were published in English and provided a structured abstract.

Articles were excluded if they (1) were review papers, commentaries, editorials, book chapters, or theoretical position pieces; (2) did not focus on cardiovascular systems (eg, neurological or orthopedic digital twins); (3) were not available in full text or lacked an identifiable abstract; (4) were duplicate entries across databases; and (5) were published in languages other than English, including those labeled as “unspecified” or “null.”

These criteria were iteratively refined during the pilot screening of 50 records.

We did not apply the exclusion criteria based on study design, as the aim of this review was to comprehensively synthesize diverse contributions to the digital twin field, including conceptual, technical, and applied studies, without limiting the scope to any particular methodological framework.

Screening and Article Selection

The initial search returned 330 records. A multistep screening protocol was applied:

- Phase 1 (title and abstract screening): Three reviewers independently screened articles for relevance. Discrepancies were resolved by group discussion and majority vote.
- Phase 2 (eligibility review): Of 44 records identified in phase 1, 2 records were excluded. A final set of 42 articles was included in the synthesis.

Reviewers used a shared Microsoft Excel spreadsheet with predefined drop-down fields for coding decisions. Interreviewer consistency was monitored, and a senior reviewer adjudicated disagreements. The filtering questions used during study selection are presented in Table 1. The complete list of all screened records, along with their inclusion or exclusion status, is provided in Multimedia Appendix 2.

Table . Filtering questions used during study selection for the systematic review of cardiovascular digital twin research.

Screening question[a]	Decision criteria
Filtering question 1: Does the study relate to digital twins in health care or medicine?	Include if the study discusses digital twins applied in health care contexts.
Filtering question 2: Does the study specifically address the use of digital twins in cardiology?	Include if the study focuses on cardiovascular applications of digital twins.
Filtering question 3: Does the study involve personalized or patient-specific applications in cardiology?	Include if the study discusses patient-specific or precision medicine approaches.

[a]Each question aligns with predefined inclusion and exclusion criteria applied across titles, abstracts, and full texts.

RQs and Data Extraction

Data extraction was organized around 11 RQs, which were structured into six thematic categories:

1. Technological foundations: modeling methods (RQ1), mechanistic model types (RQ2), ML algorithms (RQ3), and open-source availability (RQ4)
2. Data infrastructure and visualization: patient-specific data (RQ5) and visualization formats (RQ6)
3. Clinical applications and conditions: clinical use cases (RQ7) and cardiovascular conditions addressed in digital twin studies (RQ8)
4. Clinical impact: reported outcomes and benefits (RQ9)
5. Implementation challenges: technical and validation barriers (RQ10)
6. Ethical considerations: legal, privacy, and governance issues (RQ11)

Each reviewer used a structured extraction form, built in Excel, to code articles across multiple predefined categories (eg, “FEM,” “ECG,” and “Heart Failure”) using a controlled

vocabulary. Note fields allowed for contextual elaboration and inductive theme discovery.

Categories were not mutually exclusive, allowing multiple responses per article. The full data extraction form is provided in Multimedia Appendix 3.

Data Extraction Process

Data extraction followed a structured workflow as follows:

1. Full-text review: Each selected study was fully reviewed to extract methodological details and research contributions.
2. Thematic classification: Studies were assigned to predefined thematic categories based on their focus area and objectives.
3. Double-reviewer validation: Three independent reviewers extracted data; any conflicts were resolved via discussion.
4. Database compilation: Extracted data were compiled into a structured dataset for further analysis.

Risk of Bias

The risk of bias of the included studies was assessed using the instrument most appropriate for the underlying study design. Three distinct tools were used. First, simulation-based and modeling-oriented studies, such as those involving digital twins, mechanistic models, or computational pipelines, were evaluated using a custom modeling checklist, which was developed to capture methodological risks specific to computational modeling (eg, data representativeness, validation strategy, overfitting, and reproducibility). Second, prediction-modeling studies were appraised using the Prediction Model Risk of Bias Assessment Tool (PROBAST), which evaluates risk of bias across 4 domains: participants, predictors, outcome, and analysis. Finally, observational cohort studies were assessed using the Risk of Bias in Non-Randomized Studies - of Interventions (ROBINS-I), which provides structured domain-level judgments for 7 bias domains, including confounding, selection of participants, classification of interventions, missing data, and outcome measurement.

For all tools, domain-level judgments were assigned according to published guidance or tool-specific documentation. Risk-of-bias assessments were conducted independently by multiple assessors, and any discrepancies were resolved through discussion, with arbitration applied when consensus could not be reached. Domain-level ratings were then synthesized into an overall judgment (low, unclear, or high risk of bias) based on the decision rules recommended for each tool.

Visualization of risk-of-bias judgments was performed using robvis [16], an R package and web application that supports structured display of traffic-light plots and summary plots.

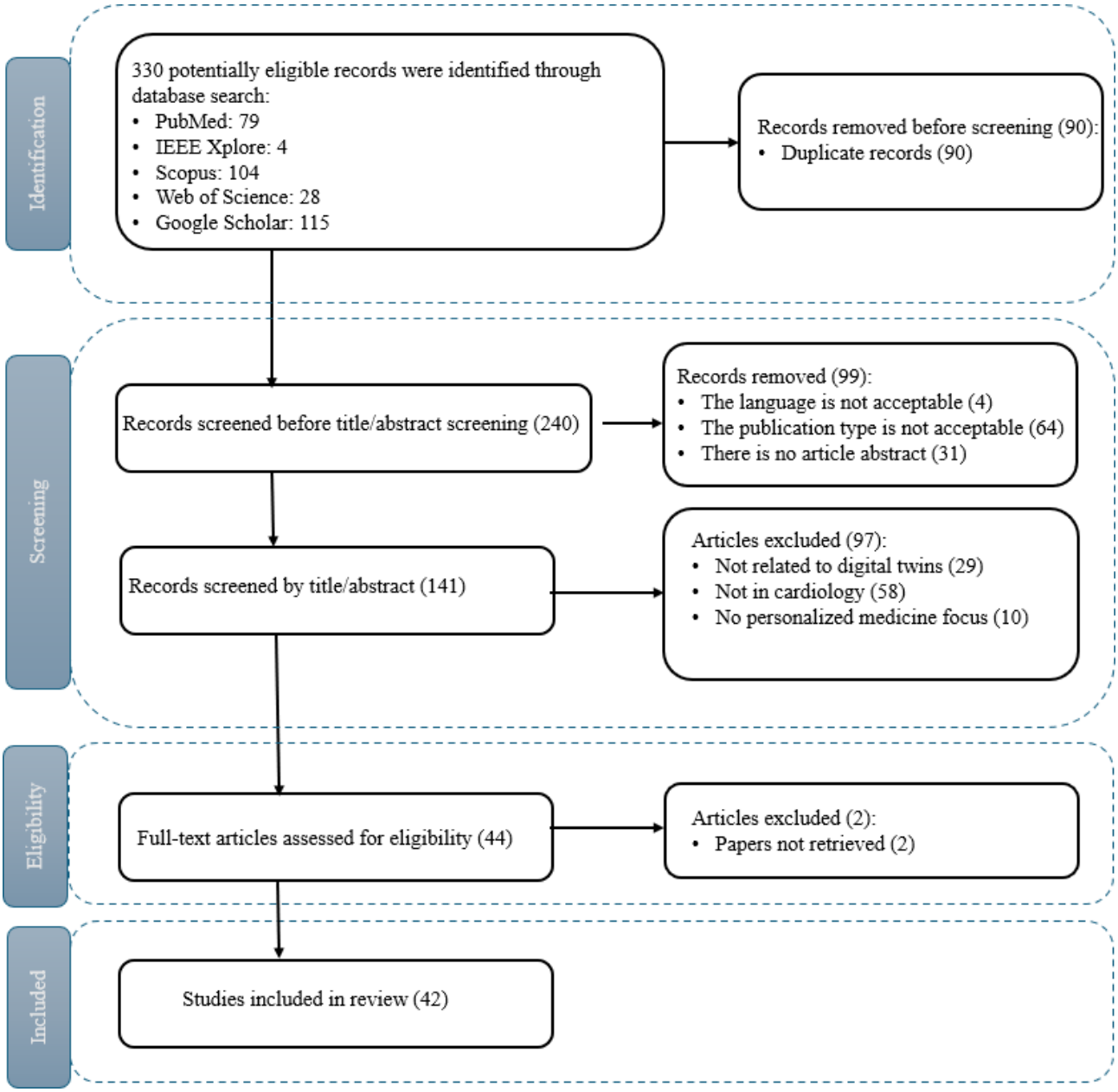
Results

Overview

We synthesized the findings from 42 original research articles on cardiovascular digital twins. The PRISMA flow diagram of the study selection process is presented in Figure 1. The results were structured around 11 predefined RQs, which were organized into 6 thematic domains: technological foundations, data infrastructure and visualization, clinical applications and conditions, clinical impact, implementation challenges, and ethical considerations. Each subsection follows a format: overview, key insights, and interpretation. For each RQ, we present summary patterns and cite representative studies in the main text. The complete mapping of all studies to the corresponding RQ categories is provided in Multimedia Appendix 4, and the mapping from raw extraction values to the harmonized categories used in the analyses is provided in Multimedia Appendix 5.

Funding sources were reported for a subset of studies and were most often public or academic, with a smaller number supported by mixed public-foundation or public-industry collaborations and relatively few funded solely by industry. Study-level funding details are summarized in Multimedia Appendix 4.

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 flow diagram illustrating the systematic selection process for cardiovascular digital twin studies. A total of 330 records were retrieved from 5 major databases and screened using predefined eligibility criteria. After removal of duplicates and exclusion of irrelevant or nonoriginal articles, 42 studies were included in the final synthesis for qualitative and quantitative analyses.



Technological Foundations (RQ1-RQ4)

We outline the core technical elements of cardiovascular digital twin systems, focusing on modeling strategies (RQ1), types of mechanistic models (RQ2), ML applications (RQ3), and open-source availability (RQ4). Together, these RQs characterized how digital twins were constructed, personalized, and shared, revealing trends in hybrid modeling, the integration of AI, and the challenges in reproducibility.

RQ1: What Primary Modeling Approach is Used to Develop Digital Twins?

Overview

All 42 studies were classified according to their dominant modeling approach: mechanistic, hybrid, or data-driven. These categories reflect the computational core of digital twins, ranging from physics-based simulation to statistical learning and their integration.

Key Insights

The key insights are as follows:

- Mechanistic models were the most common (29 studies [8,11,17-43]), and they relied on physics-based formulations (eg, finite element modeling [FEM], electrophysiological simulation, and hemodynamic flow analysis) to generate personalized physiological representations.
- Data-driven models were noted in 7 studies [44-50], and they were primarily based on statistical learning or machine-learning approaches without explicit biophysical constraints.

- Hybrid approaches were the least common (6 studies [51-56]), and they combined mechanistic frameworks with data-driven components, for example, using ML to estimate parameters, extract imaging features, or accelerate computational solvers.

Interpretation

The predominance of mechanistic approaches highlights the central importance of physiological interpretability in cardiovascular digital twin development. Studies involving these approaches focus on replicating biophysical behavior with high fidelity, supporting diagnostic and interventional simulation tasks.

Data-driven twins, while less common, demonstrate growing interest in leveraging large clinical datasets for prediction, classification, and risk estimation. Their scope is more limited in scenarios requiring detailed physiological realism.

Hybrid methods illustrate emerging strategies that balance accuracy and computational efficiency. In studies involving these approaches, ML is commonly used to tune physiological parameters, derive boundary conditions from imaging or ECG data, or build surrogate models that reduce the computational cost of mechanistic solvers. In a subset of hybrid digital twin studies [51-56], ML components were typically embedded within a mechanistic framework rather than used in isolation. Across these studies, we observed 3 main integration patterns. First, ML is used for parameter tuning and personalization of mechanistic models, for example, by estimating subject-specific parameters or boundary conditions that are then supplied to a physics-based simulator. Second, ML algorithms are applied for feature extraction from raw clinical data, such as imaging or ECG signals, and the extracted features are subsequently used to initialize or constrain the mechanistic model. Third, in a small number of cases, ML serves as a surrogate or complementary model that approximates the behavior of a more complex mechanistic solver or is combined with mechanistic equations in a joint statistical-mechanistic framework. Together, these hybrid strategies illustrate how data-driven methods can enhance mechanistic digital twins by improving personalization, leveraging high-dimensional data, and reducing computational cost.

RQ2: If the Model is Mechanistic, What Specific Model Type is Used?

Overview

Across the 42 included studies, we identified multiple types of mechanistic models used within cardiovascular digital twin frameworks. Because individual studies often combined more than one formulation, we classified mechanistic components into 9 categories based on their predominant mathematical and physiological characteristics.

Key Insights

The key insights are as follows:

- Electrophysiology models were the most common (19 studies [11,17,18,20,21,25,27,28,30,34,35,37,39,41,43,44,46,51,54]). These models typically used monodomain, bidomain, or related reaction-diffusion formulations to simulate cardiac electrical activation, sometimes coupled to downstream mechanical effects.
- FEM-based structural or biomechanical models were used in 10 studies [8,18,19,26,27,29-31,33,37] to represent myocardial or vascular deformation, geometry, and stress-strain behavior.
- Electromechanical models, which explicitly couple electrical activation with tissue mechanics, were identified in 8 studies [22,26,30,32,33,52,53,55]. They supported integrated simulation of excitation-contraction processes.
- Simplified or system-level models, which are most often lumped-parameter formulations, were noted in 7 studies [24,29-31,33,36,53]. They provided compact descriptions of global hemodynamics or chamber-level dynamics, particularly when large-scale or long-duration simulations were required.
- Multiscale models were reported in 7 studies [11,22,30,33,41,44,53], linking processes across spatial or temporal scales (eg, from cellular electrophysiology to organ-level function).
- Computational fluid dynamics (CFD) models were used in 3 studies [40,42,55] to simulate blood flow and pressure distributions in chambers or great vessels. An additional 4 studies [19,23,24,56] used other mechanistic formulations (eg, specialized anatomical or biophysical models), and 1 study [42] used a surrogate mechanistic model that approximated a more complex solver. In 1 study [38], mechanistic modeling was reported, but the specific model type was not clearly described.

Interpretation

Taken together, the results show that electrophysiology-focused models form the backbone of mechanistic digital twin development in cardiology, with FEM-based structural models, lumped-parameter and multiscale formulations, and CFD models used in complementary roles. This diversity of model types illustrates how digital twin frameworks combine detailed biophysical fidelity with system-level abstractions to address specific clinical questions and RQs.

RQ3: If the Model Includes ML or AI, What Specific Algorithms are Applied?

Overview

Among the 42 reviewed studies, some explicitly reported using ML or AI techniques within the digital twin framework, while in others, the use or type of ML was absent or not clearly specified. Because several studies combined more than one method, we grouped algorithms into broad families, including DL, Bayesian methods, optimization algorithms, classical (statistical) ML, and other ML approaches.

Key Insights

The key insights are as follows:

- DL was the most frequently reported family of methods (9 studies [27,34,44-46,48,49,53,54]). These approaches included architectures, such as convolutional neural

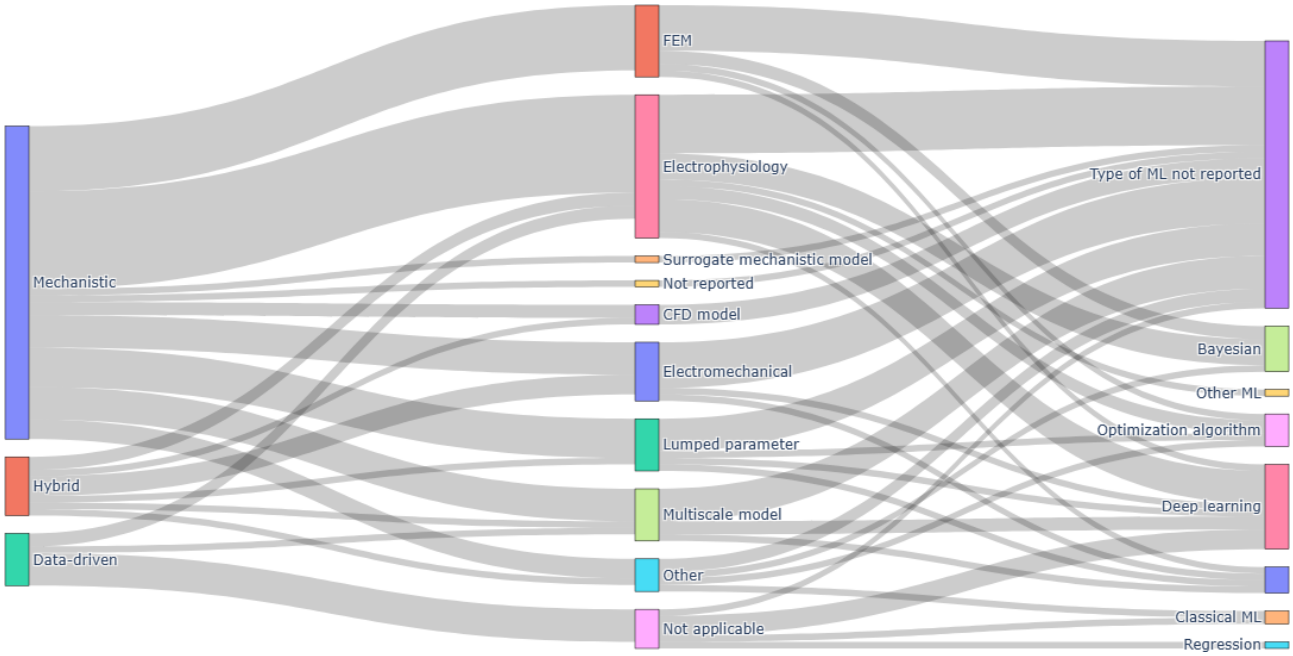
networks, neural operators, latent neural ordinary differential equation models, and related deep architectures, used for tasks like feature extraction, representation learning, or surrogate modeling.
- Bayesian methods were used in 5 studies [17,19,25,37,51], typically in the form of approximate Bayesian computation, Bayesian optimization, or Gaussian process–based models for probabilistic parameter estimation and uncertainty quantification.
- Optimization algorithms were noted in 4 studies [19,21,36,51]. These approaches included gradient-based schemes and metaheuristics that were used to tune model parameters, personalize simulations, or search over high-dimensional design spaces; in some cases, these optimizers were tightly integrated with Bayesian frameworks.
- Classical ML methods were identified in 2 studies [50,56]. These approaches included techniques, such as decision tree and logistic or linear regression, to model interpretable relationships between inputs and outcomes.
- Regression was explicitly highlighted as the primary approach in 1 of the studies [50]. One study used other ML strategies that did not fit neatly into the above categories but still relied on data-driven learning to support digital twin construction or personalization [46].

Interpretation

Overall, DL has emerged as the dominant explicitly reported ML family in cardiovascular digital twin research, supporting tasks such as feature extraction, surrogate modeling, and high-dimensional inference. Bayesian and optimization-based methods play a complementary role by enabling parameter estimation and uncertainty-aware personalization. Classical ML and regression, although less common, provide more interpretable models in selected use cases.

Figure 2 provides an integrated visualization of how primary modeling approaches, mechanistic model types, and ML or AI families co-occur across the included studies.

Figure 2. Relationships among modeling approaches, mechanistic model types, and machine learning (ML) or artificial intelligence (AI) methods in cardiovascular digital twin studies. Sankey diagram summarizing links among primary modeling approaches (research question [RQ] 1), mechanistic model types (RQ2), and ML or AI algorithm families (RQ3) across the 42 original research articles on cardiovascular digital twins included in this systematic review. The left column shows the dominant modeling approach for each study (mechanistic, hybrid, or data-driven). The middle column groups mechanistic model types into electrophysiology, finite element modeling (FEM), lumped parameter, electromechanical, computational fluid dynamics (CFD), other mechanistic models, and "not reported." The right column shows ML or AI families (deep learning, Bayesian methods, optimization algorithms, classical ML, regression, other ML, and "type of ML not reported"). The width of each flow is proportional to the number of studies combining the corresponding categories.



RQ4: Is the Framework or Model That is Created or Used Open-Source?

Overview

We evaluated the extent to which cardiovascular digital twin frameworks were shared as open-source resources. Code availability is a key indicator of scientific transparency and reproducibility, enabling independent validation and extension by other researchers and clinicians.

Key Insights

The key insights are as follows:

- Across the 42 included studies, 16 explicitly reported that their framework or model was available as open-source code [17-20,25,26,30,35,37,38,41,48,51,53,54,56].
- Two studies clearly stated that the code was not publicly released or that the implementation was proprietary [22,39].
- For the remaining 24 studies, code availability was either not mentioned or not described in sufficient detail to determine whether the implementation was accessible. Thus,

less than half of the studies (16/42, 38%) provided explicit evidence of open-source sharing, and in many cases, information on code availability was incomplete.

Interpretation

Despite increasing attention to reproducibility and open science, most studies in this review did not make their digital twin implementations publicly available. A lack of open-source code hinders transparency, reproducibility, and reusability. The few repositories that were shared provide valuable resources and serve as exemplars for future cardiovascular digital twin research.

Data Infrastructure and Visualization (RQ5 and RQ6)

The design and utility of cardiovascular digital twin systems depend heavily on how patient-specific data are structured, how outputs are visually communicated, and who the intended users are. This section addresses RQ5 and RQ6 by examining the types of data used to build or personalize digital twins, the formats used to present model outputs, and the target users of these visualizations. Together, these elements shaped the usability, interpretability, and clinical relevance of digital twin systems in practice.

RQ5: What Types of Patient-Specific Data are Used to Build or Personalize Digital Twins?

Overview

Patient-specific data underpin cardiovascular digital twin systems by enabling individual-level modeling. We explored the distinct categories of data used to personalize these models, ranging from electrical signals and anatomical imaging to omics and wearable-derived data. To facilitate interpretation, the data were grouped into consistent, semantically meaningful categories.

Key Insights

The key insights are as follows:

- Imaging data were the most commonly used (32 studies [8,11,17-19,21,22,24-27,29-31,33-40,42-44,46,48,49,51,53-55]). These data typically included modalities, such as MRI, CT, and other structural imaging, used to reconstruct patient-specific anatomy. Echocardiography was explicitly reported in 2 of these studies as a dedicated imaging source.
- Signal-based electrical data, primarily ECG, were used in 18 studies [8,17,21,25,27,33,36-39,43,46,48-51,53,54], reflecting its central role in modeling cardiac electrophysiology and conduction abnormalities.
- Vital signs were used in 12 studies [17,24,26,28,29,31,33,45,48,49,53,55], and demographics, such as age and sex, were reported in 9 studies [17,24,27,28,33,45-48], often to support model initialization, risk stratification, or cohort characterization.
- More detailed clinical information appeared in several categories: omics data were used in 4 studies [22,23,49,55], lab results were used in 4 studies [22,28,49,55], and general clinical data (such as clinical histories and visit summaries) were used in 3 studies [49,52,55]. Diagnosis [33,47,48] and treatment-related data [33,47,48] (eg, information on interventions or therapies) were each reported in 3 studies.
- Sensor-based and longitudinal monitoring information was less common: 3 studies used data from sensors [46,49,55], and 2 studies used activity tracker data [45,49], illustrating the early integration of wearable or home-based measurements into digital twin personalization. Synthetic patient data were explicitly used in 1 study [56].

Interpretation

Overall, there is a strong reliance on imaging and ECG data to define anatomy and electrophysiological behavior in cardiovascular digital twins, complemented by vital signs and demographic information for basic personalization. Omics, lab results, richer clinical records, and wearable or sensor-derived data are beginning to appear but remain less common, suggesting that truly multimodal, longitudinal personalization is still emerging. The presence of synthetic and other less conventional data sources indicates ongoing experimentation with alternative data strategies.

RQ6: What is the Primary Format Used to Visually Present Digital Twin Outputs?

Overview

We examined how digital twin outputs were visualized in cardiovascular studies, an essential aspect for interpretation, user interaction, and eventual clinical integration. Each study could use more than one visualization format, so outputs were classified into standard categories such as static figures, anatomical renderings, tables, dashboards, and interactive media.

Key Insights

The key insights are as follows:

- Static figures were the most common visualization format (41 studies [8,11,17-47,49-56]). These typically included plots, error curves, comparative graphics, and screenshots of simulations, and were primarily designed for inclusion in scientific publications.
- Two- or three-dimensional anatomical views were reported in 27 studies [8,11,17-19,21,22,24-27,29-31,33-35,37,39,40,42-44,46,51,54,55], where patient-specific geometries or simulated fields (eg, activation times, strain, and flow patterns) were mapped onto cardiac or vascular structures. These views served to visually link model predictions to underlying anatomy.
- Tabular formats were used in 7 studies [19,22,24,35,36,45,49] to report numerical outputs such as performance metrics, parameter values, and summary statistics.

Interpretation

Overall, visualization of cardiovascular digital twins remains dominated by static, publication-oriented formats such as figures and anatomical snapshots, with limited support for dynamic, interactive, or dashboard-based exploration. While anatomical views help contextualize outputs in patient-specific geometry, the scarcity of dashboards, animations, and interactive interfaces suggests that user-centric and real-time visualization capabilities are still underdeveloped. Enhancing interactive and clinically oriented visualization tools may be crucial for translating digital

twins from research prototypes into practical decision-support systems.

Clinical Applications (RQ7 and RQ8)

We explored how digital twins were applied in clinical cardiology (RQ7) and which cardiovascular conditions they targeted (RQ8). It highlighted current use cases, such as diagnosis, planning, and monitoring, and categorized the conditions based on thematic grouping identified during full-text analysis.

RQ7: What is the Main Clinical Application or Use Case of Digital Twin Systems?

Overview

We explored the primary clinical applications of cardiovascular digital twin systems, revealing the core motivations behind their development and deployment. Use cases ranged from therapy planning and risk prediction to monitoring, drug testing, and more exploratory clinical applications. Individual studies could contribute to multiple application categories.

Key Insights

The key insights are as follows:

- Therapy planning was the most common application (28 studies [8,11,17,19,20,22-25,29-34,36-39,41,45-47,49,51,54-56]). In these studies, digital twins were used to support the selection, personalization, or optimization of interventions, including device configuration, ablation strategies, or other patient-specific treatment plans.
- Risk prediction was noted in 11 studies [20,28,40,41,46-50,52,55], where digital twins were used to estimate the likelihood of adverse events, treatment responses, or disease trajectories, often to support patient stratification. Diagnosis-focused applications were identified in 7 studies [11,45,46,48-50,54], using digital twins to assist in identifying underlying pathophysiology or classifying clinical conditions.
- Surgical and device simulation was reported in 6 studies [36,38,42,46,51,55], in which digital twins provided virtual testbeds to explore procedural strategies or evaluate device performance in patient-specific anatomies. Another 6 studies used digital twins for drug testing [17,20,28,32,36,37].
- Monitoring applications were noted in 6 studies [45,48-50,52,55], where digital twins contributed to disease tracking or follow-up by integrating longitudinal data or repeated assessments. Disease progression modeling was explicitly highlighted in 3 studies [36,42,55], and a single study focused primarily on prognosis [55].

Interpretation

Overall, cardiovascular digital twins are most frequently positioned as tools for therapy planning and risk prediction, emphasizing their role in personalizing and optimizing clinical interventions. Diagnosis, surgical or device simulation, drug testing, and monitoring collectively demonstrate a broad range of applications along the care pathway, from early risk assessment to procedural planning and follow-up. As digital twin technologies mature, a clearer definition and reporting of clinical applications will be important for understanding their real-world impact.

RQ8: What Cardiovascular Conditions Are Studied Using Digital Twin Systems?

Overview

We examined the range of cardiovascular conditions addressed by digital twin systems, providing a disease-centered perspective on where digital twin technologies are currently being applied. Conditions were grouped into clinically meaningful categories, and the classification was reviewed by a physician on the research team to ensure clinical relevance and consistency.

Key Insights

The key insights are as follows:

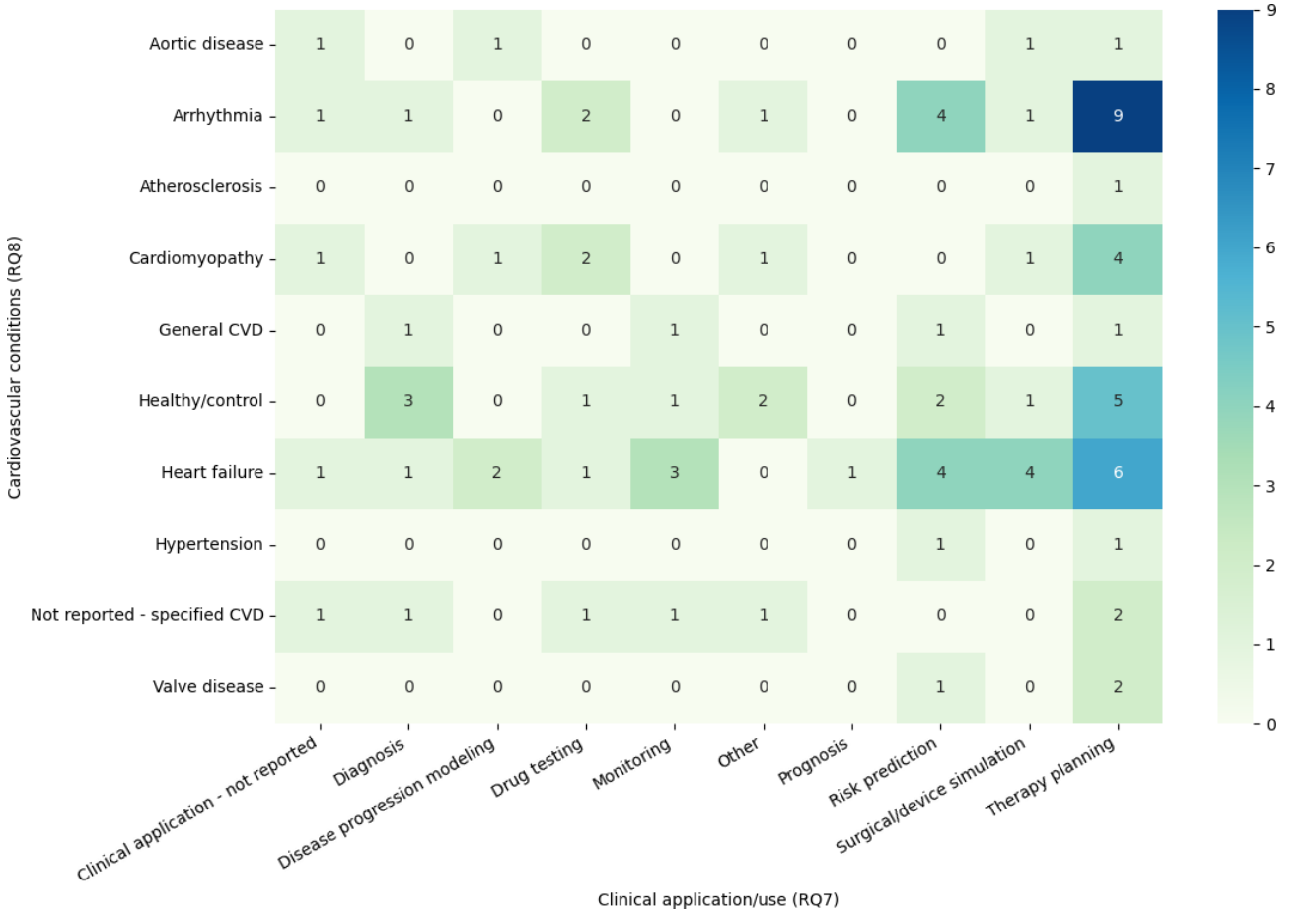
- Arrhythmia was the most frequently studied condition (13 studies [8,11,18,20,25,28,30,34,38-41,43]). The studies predominantly focused on atrial fibrillation and other rhythm disorders, reflecting the suitability of digital twins for simulating electrophysiological mechanisms and guiding rhythm-related interventions.
- Heart failure was investigated in 9 studies [33,36,38,41,48,51-53,55], often in the context of global cardiac function, ventricular remodeling, or device-based therapies. Cardiomyopathies, including hypertrophic cardiomyopathy and other structural myocardial diseases, were the primary focus in 5 studies [19,22,32,35,44], where digital twins were used to explore patient-specific mechanics and electrophysiology.
- Six studies centered on healthy or control populations [17,43,46,49,54,56], using digital twins to represent normal physiology, establish reference behaviors, or provide baselines for comparison with diseased states. Aortic disease was the focus in 3 studies [26,29,42], typically involving patient-specific modeling of the aorta for flow, wall stress, or device evaluation.

Interpretation

The distribution shows a strong emphasis on arrhythmia and heart failure, conditions in which digital twins can leverage detailed electrophysiological and hemodynamic modeling to support diagnosis, therapy planning, and risk assessment. Cardiomyopathies, aortic disease, and valvular disease are also emerging areas of application, particularly where structural and flow abnormalities can be represented in patient-specific models. By contrast, hypertension, atherosclerosis, and some other common cardiovascular conditions are only sporadically represented, and several studies do not clearly specify the underlying disease focus. These gaps suggest opportunities for expanding digital twin applications into a broader spectrum of cardiovascular conditions and for improving the clarity of disease reporting in future work.

Figure 3 summarizes how clinical applications are distributed across cardiovascular conditions. As shown in Figure 3, therapy planning and risk prediction are concentrated in arrhythmia and heart failure, whereas other conditions and applications are represented by only a small number of studies, underscoring the uneven distribution of digital twin work across CVDs.

Figure 3. Heatmap of cardiovascular conditions (research question [RQ] 8) versus clinical applications (RQ7) in cardiovascular digital twin studies. Rows show the primary cardiovascular condition modeled (eg, arrhythmia, heart failure, cardiomyopathy, aortic and valve disease, hypertension, atherosclerosis, general cardiovascular disease [CVD], healthy/control, and not reported). Columns show the main clinical applications (eg, diagnosis, disease progression modeling, drug testing, monitoring, prognosis, risk prediction, surgical or device simulation, and therapy planning). Cell color and numbers indicate how many of the 42 included studies reported each condition-application combination (darker cells indicate a higher number of studies).



Impact on Clinical Practice (RQ9)

We identified the reported clinical benefits of cardiovascular digital twin systems, including improved accuracy, personalization, therapy planning, and patient outcomes. The findings were organized into key impact categories to highlight where digital twins showed practical value in care delivery.

RQ9: What Clinical Impacts are Reported as a Result of Using Digital Twins?

Overview

We examined the concrete clinical or clinically relevant impacts attributed to cardiovascular digital twin systems. Rather than focusing on intended use alone, we captured reported effects where the use of a digital twin was described as influencing decision-making, therapy, diagnostic performance, or other aspects of care. Reported impacts were grouped into categories such as improved decision-making, therapy-related benefits, increased accuracy, and other specific outcomes.

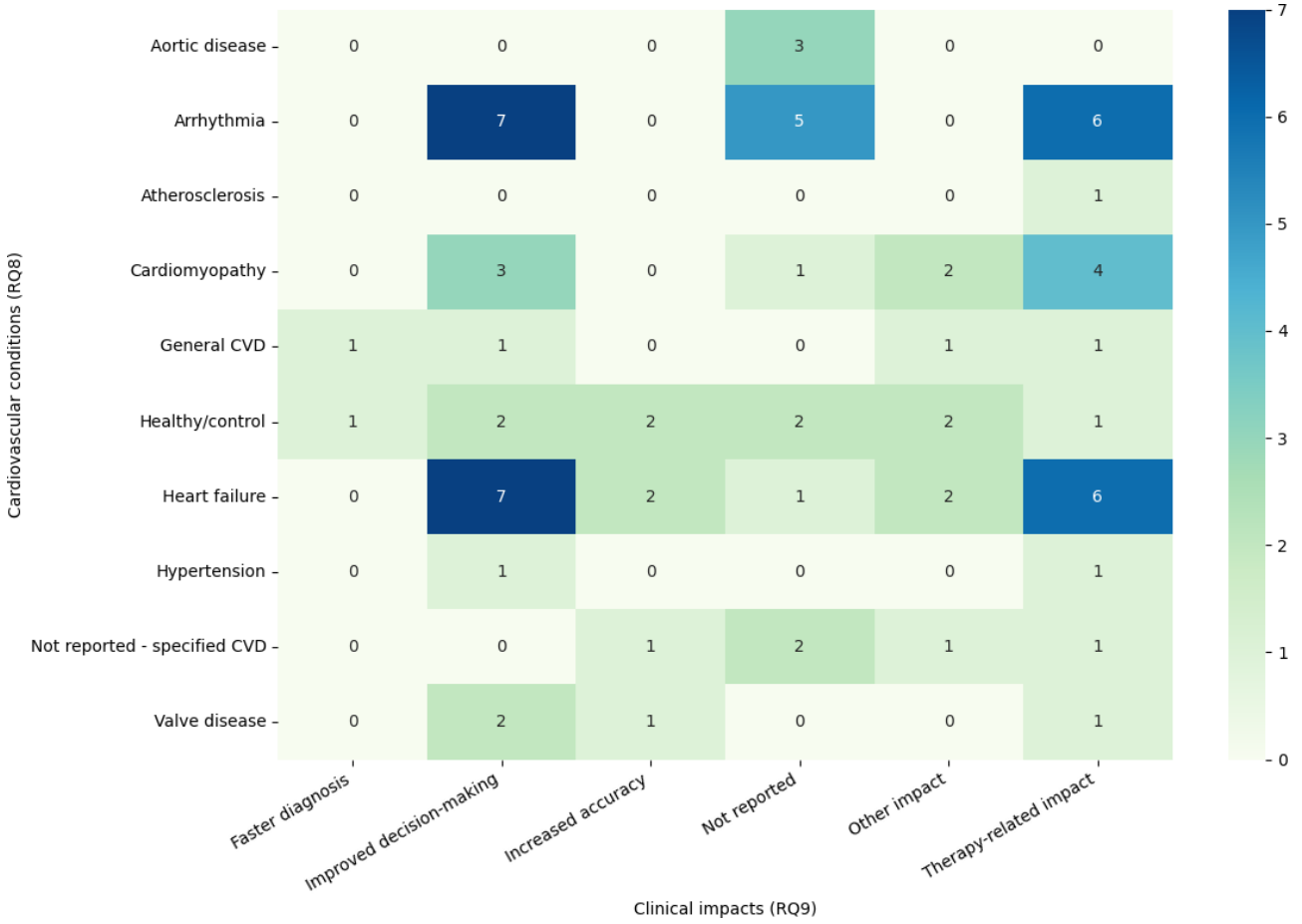
Key Insights

The key insights are as follows:

- Improved decision-making was the most frequently reported impact (19 studies [22,24,28,30-34,36,38-41,47-49,51,55,56]). In these cases, digital twins were described as helping clinicians compare alternative strategies, understand patient-specific mechanisms, or select interventions with greater confidence.
- Therapy-related impacts were reported in 18 studies [19,22-25,32,34,36,38-41,45,47-49,51,55], including optimization of device settings, refinement of ablation targets, adjustment of pharmacologic regimens, and more tailored procedural planning based on virtual simulations.
- Increased accuracy was explicitly identified in 6 studies [31,45,48,49,54,55], referring to improvements in predictive performance, better correspondence between simulations and measured clinical data, or more faithful reproduction of patient-specific physiology. Two studies [49,50] reported a faster diagnostic process, where digital twin–supported workflows were associated with quicker identification or clarification of clinical conditions.

Figure 4 illustrates how reported clinical impacts are distributed across cardiovascular conditions. Improved decision-making and therapy-related impacts were concentrated in arrhythmia and heart failure, whereas many other condition-impact combinations were represented by only one or two studies, highlighting the uneven evidence base across disease areas.

Figure 4. Heatmap of cardiovascular conditions (research question [RQ] 8) versus reported clinical impacts (RQ9) in cardiovascular digital twin studies. Rows represent the primary cardiovascular condition modeled by the digital twin (eg, arrhythmia, heart failure, cardiomyopathy, aortic and valve disease, hypertension, atherosclerosis, general cardiovascular disease [CVD], healthy/control, and not reported). Columns represent impact categories reported by study authors (faster diagnosis, improved decision-making, increased accuracy, impact not reported, other impact, and therapy-related impact). Cell color and numbers indicate how many of the 42 included studies reported each condition-impact combination (darker cells indicate a higher number of studies).

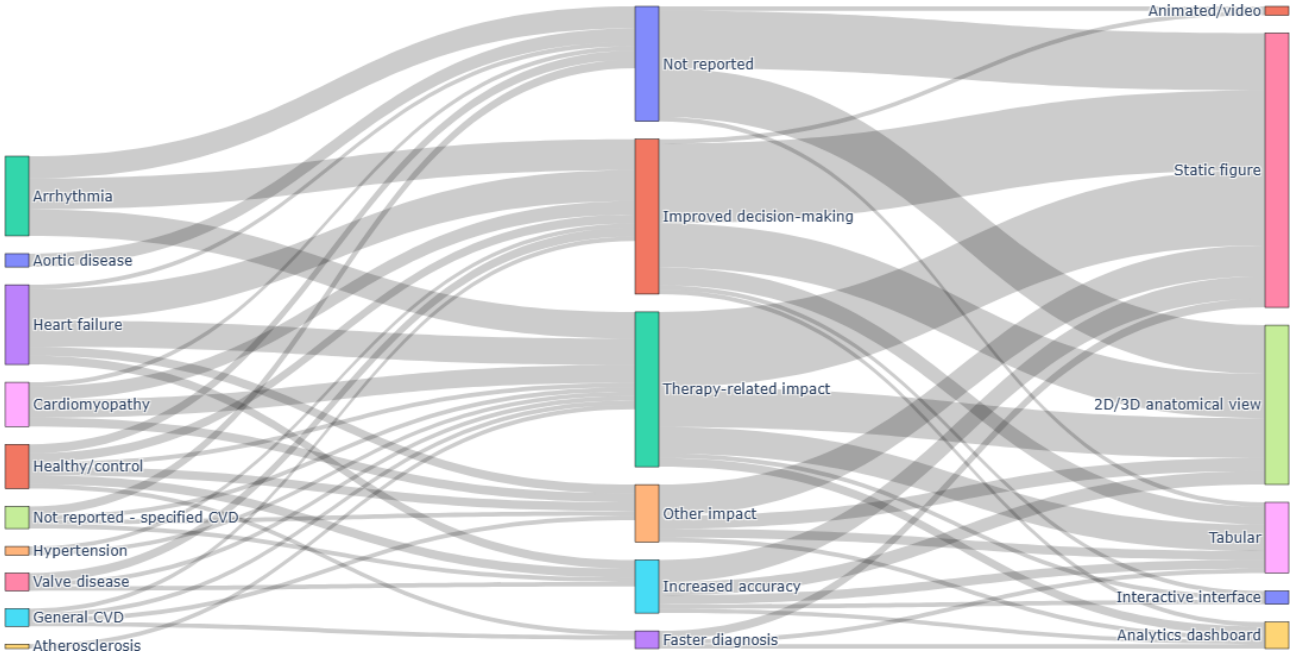


Interpretation

The most commonly reported benefits of cardiovascular digital twins relate to improved clinical decision-making and therapy-related impacts, suggesting that these systems are beginning to influence how clinicians choose and personalize interventions. Explicit gains in accuracy and diagnostic speed are less frequently reported but point toward the quantitative advantages of model-based approaches when they are carefully evaluated. At the same time, the substantial number of studies with no clearly articulated clinical impact indicates that much of the current literature remains focused on technical feasibility and validation rather than demonstrated downstream effects on care processes or patient outcomes. Strengthening the evidence base around measurable clinical benefits, such as improved decision quality, optimized therapy, and better outcomes, will be essential for wider clinical adoption.

Figure 5 shows that improved decision-making is the dominant reported impact across most cardiovascular conditions, particularly heart failure and arrhythmia, and that these impacts are almost always communicated through static figures and 2D or 3D anatomical views rather than dashboards, animations, or interactive interfaces. Therapy-related impacts and gains in accuracy are more sparsely reported and similarly rely on conventional publication-style visualizations, underscoring the limited development of user-facing, real-time visual tools, even in high-risk clinical scenarios.

Figure 5. Relationships among cardiovascular conditions, reported clinical impacts, and visualization formats in cardiovascular digital twin studies. Sankey diagram summarizing links among cardiovascular conditions (research question [RQ] 8), reported clinical impacts (RQ9), and primary visualization formats (RQ6) across the 42 original research articles on cardiovascular digital twins included in this systematic review. The left column shows the main conditions modeled by the digital twins (eg, heart failure, arrhythmia, valve disease, cardiomyopathy, hypertension, atherosclerosis, general cardiovascular disease [CVD], and healthy/control populations). The middle column displays impact categories reported by the authors (eg, improved decision-making, therapy-related impact, increased accuracy, faster diagnosis, and other impact). The right column shows the dominant visualization formats used to present model outputs (static figures, 2D/3D anatomical views, tabular displays, analytics dashboards, animated/video outputs, and interactive interfaces). The width of each flow is proportional to the number of studies combining the corresponding categories.



Barriers to Implementation and Ethical Considerations (RQ10 and RQ11)

We examined the key challenges limiting the adoption of cardiovascular digital twins, including technical barriers (RQ10) and ethical or legal concerns (RQ11). These issues highlighted the need for improved scalability, transparency, and responsible use in clinical settings.

RQ10: What Limitations or Practical and Technical Barriers are Described?

Overview

We identified the limitations and implementation barriers of cardiovascular digital twin systems as reported by the included studies. Rather than listing every individual issue, reported limitations were grouped into conceptually meaningful categories, such as model assumptions, computational constraints, data-related challenges, and integration or usability problems. This categorization helped highlight systemic obstacles that recur across the field.

Key Insights

The key insights are as follows:

- Model assumptions and structural simplifications were the most frequently cited limitations (26 studies [8,11,17,19-22,24,25,27-33,35,36,39,41,43,44,46,47,51,53]). These concerns included oversimplified anatomy or physiology, restrictive boundary conditions, and reduced model complexity that may limit generalizability or omit important mechanisms.
- Computational cost was highlighted in 21 studies [11,17,21,22,26,27,29-31,33,36,37,39,41,42,46,49,51,53,54,56], where authors noted long simulation times, high hardware requirements, or overall computational burden that can impede large-scale studies and real-time or near–real-time clinical use.
- Data-related challenges were prominent, with 16 studies [19,22,25,27-30,36,39,40,43,45,47,50,55,56] reporting issues with data quality or availability, such as incomplete or noisy clinical inputs, limited access to high-resolution or longitudinal data, and difficulties in acquiring truly personalized datasets. Limited validation was also mentioned in 16 studies [24,25,27-29,31,33-36,39,40,45,47,53,55], reflecting concerns about small sample sizes, restricted cohorts, synthetic data, or a lack of robust testing in real-world clinical environments.
- More specific barriers included a lack of real-time performance in 5 studies [33,42,50,54,55], indicating that even when models were accurate, their latency or compute demands were not compatible with time-sensitive clinical workflows. Workflow integration problems were identified in 4 studies [30,47,51,55], focusing on the challenges of embedding digital twins into existing clinical systems and processes. Clinician usability challenges were noted in 3 studies [45,49,55], where interfaces or outputs were considered difficult to interpret or not well aligned with clinical practice. High infrastructure cost was noted in 2 studies [49,53], and data security or privacy concerns were explicitly mentioned in 1 study [49].

Interpretation

The most common limitations—strong model assumptions, high computational cost, and data and validation constraints—reflect the technical and methodological complexity of deploying cardiovascular digital twins in practice. Simplifying assumptions and limited data can undermine generalizability, while computational burden and lack of real-time performance can restrict clinical usability. Integration issues, usability challenges, infrastructure demands, and security concerns, though mentioned less often, highlight important practical barriers that will become more pressing as digital twins move closer to clinical deployment. Addressing these limitations through improved model design, better data infrastructure, efficient algorithms, and user-centered integration will be essential for scalable, clinically viable digital twin systems.

RQ11: What Legal, Ethical, or Data Governance Issues are Raised Regarding Digital Twins?

Overview

We explored the ethical, legal, and data governance concerns raised in studies involving cardiovascular digital twin systems. Potential issues included privacy protection, regulatory compliance, informed consent, algorithmic transparency, and fairness. Reported concerns were grouped into categories to highlight common themes and gaps in current practice.

Key Insights

The key insights are as follows:

- Only a small subset of studies explicitly discussed legal, ethical, or governance issues. Privacy and data protection were the most frequently mentioned topics, identified in 4 studies [47,49,50,55], with references to compliance frameworks, such as General Data Protection Regulation (GDPR) and Health Insurance Portability and Accountability Act (HIPAA), and concerns about safeguarding sensitive patient data in the context of high-dimensional digital representations.
- Some studies raised other specific issues. Two studies discussed ethical or legal challenges in general terms [30,47], while another identified potential algorithmic bias, described problems or open questions around informed consent, and highlighted concerns about model transparency and the need for explainable or interpretable digital twin behavior [55].

Interpretation

Overall, explicit discussion of legal, ethical, and data governance aspects remains limited in the cardiovascular digital twin literature. While privacy and regulatory compliance are beginning to appear as concrete concerns, far fewer studies engage with broader questions around algorithmic bias, transparency, informed consent in the context of complex modeling, or downstream legal responsibilities. As digital twin systems move closer to clinical deployment and real-world decision support, more systematic attention to these dimensions, including fairness, accountability, liability, and data stewardship, will be critical to ensure trustworthy and responsible adoption.

Risk of Bias Assessment

The risk of bias was assessed for all included studies using the tool corresponding to the underlying study design. Among the 42 studies evaluated, 38 were computational or simulation-based studies assessed using the custom modeling checklist [8,11,17,18,19,20,21-27,28,29,30,31,32-34,35,36,37,38,40,41,42,43,44,45,46,48,51-53,54,55,56], 2 were prediction-modeling studies evaluated using the PROBAST [49,50], and 2 were observational cohort studies evaluated using the ROBINS-I [39,47].

Table 2 summarizes the distribution of overall risk-of-bias judgments across the 3 tools. For simulation and digital twin modeling studies, “unclear” was the most frequent overall rating (22/38, 58%), followed by “high risk” (16/38, 42%). The domains contributing most frequently to elevated risk included data representativeness, validation strategy, and sample size/overfitting. No modeling study received an overall low-risk judgment, reflecting commonly observed methodological limitations in data availability, external validation, and reproducibility practices across computational literature.

Table . Summary of overall risk-of-bias judgments across the included studies.

Tool	Total studies (N=42), n	Unclear risk, n (%)	High risk, n (%)
Custom modeling checklist	38	22 (58)	16 (42)
PROBAST[a]	2	0 (0)	2 (100)
ROBINS-I[b]	2	1 (50)	1 (50)

[a]PROBAST: Prediction Model Risk of Bias Assessment Tool.

[b]ROBINS-I: Risk of Bias in Non-Randomized Studies - of Interventions.

Both prediction-modeling studies assessed with the PROBAST were rated as having a high risk of bias, predominantly due to concerns in the analysis and outcome domains, including insufficient handling of model calibration, unclear predictor specification, and absence of prespecified analysis protocols.

Among the 2 observational cohort studies evaluated using the ROBINS-I, one was judged as having a high risk of bias, primarily due to serious confounding and selective reporting, while the other was rated as unclear.

Figures 6 and 7 present the traffic-light and summary plots, respectively, for all 38 modeling studies assessed using the custom modeling checklist. These visualizations highlight consistent methodological limitations across key domains, particularly external validation and representativeness of data inputs. Traffic-light and summary plots for the PROBAST and

ROBINS-I assessments are provided in Figures 8 and 9, respectively.

A structured visualization workflow was implemented using the robvis tool, which standardizes the graphical representation of domain-level and overall judgments and supports transparent reporting of risk-of-bias evaluations.

Figure 6. Risk of bias assessment (traffic-light plot) for modeling studies [8,11,17,18,19,20,21-27,28,29,30,31,32-34,35,36,37,38,40,41,42,43,44,45,46,48,51-53,54,55,56]. Traffic-light plot for the 38 simulation/digital twin modeling studies assessed using the custom modeling checklist. Domain-level judgments are categorized as low, unclear, or high. The plot has been generated using the robvis tool [16].

Figure 7. Risk of bias assessment (summary plot) for modeling studies [8,11,17,18,19,20,21-27,28,29,30,31,32-34,35,36,37,38,40,41,42,43,44,45,46,48,51-53,54,55,56]. Summary plot for the 38 simulation/digital twin modeling studies assessed using the custom modeling checklist. Domain-level judgments are categorized as low, unclear, or high. The plot has been generated using the robvis tool [16].

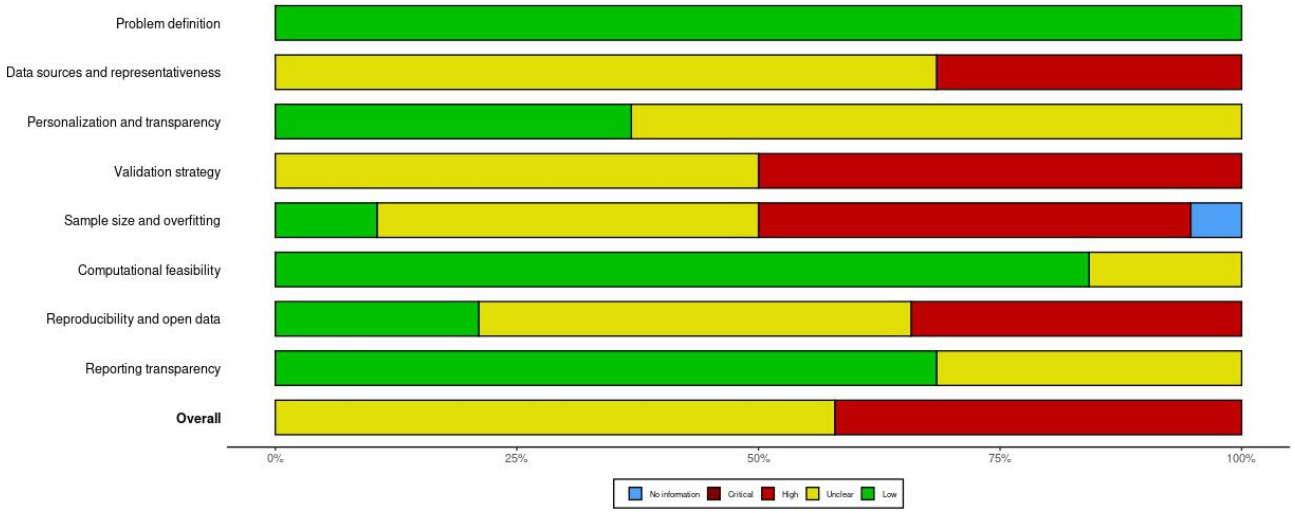
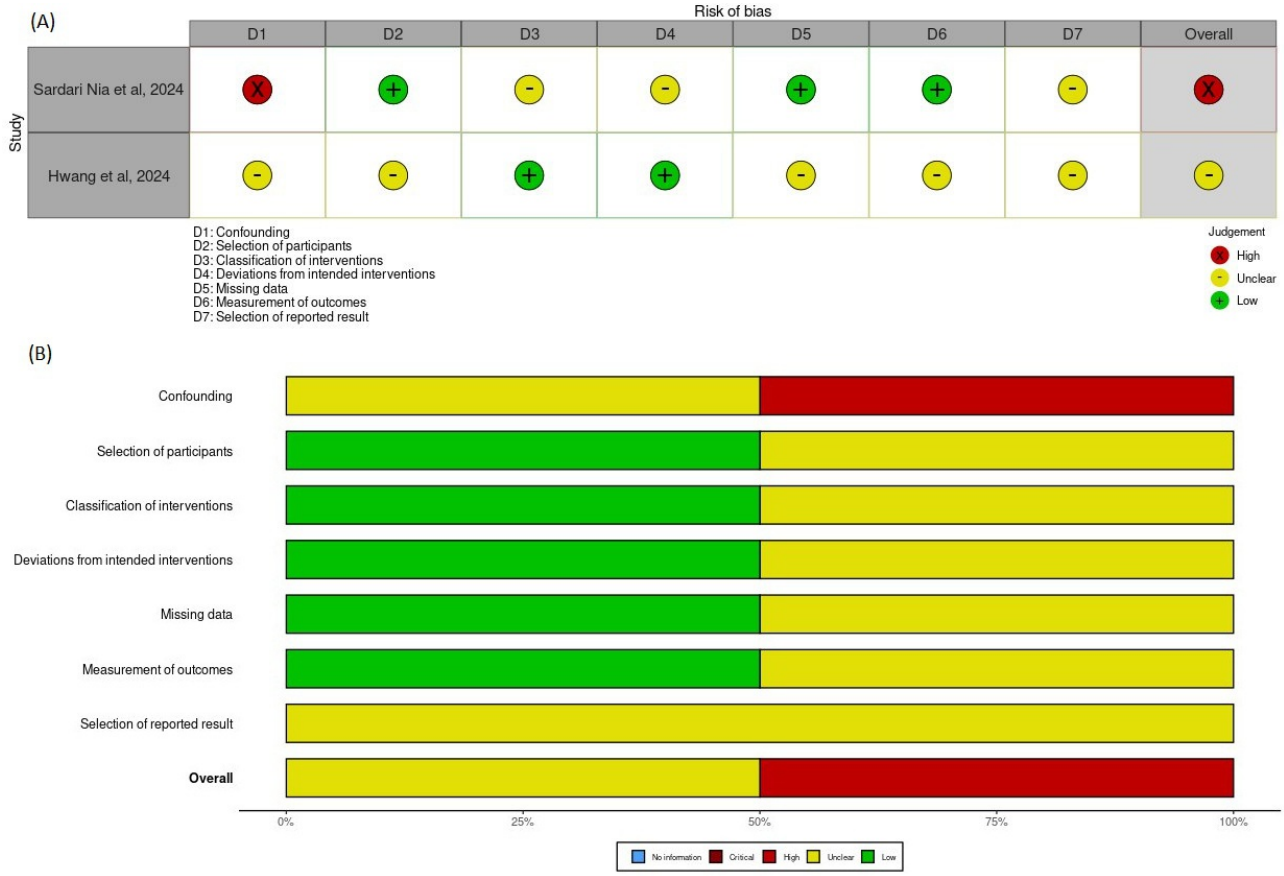


Figure 8. Risk of bias assessment for prediction-modeling studies (Prediction Model Risk of Bias Assessment Tool [PROBAST]) [49,50]. Traffic-light plot (A) and summary plot (B) for the 2 prediction-modeling studies evaluated using the PROBAST instrument. Judgments are shown across the 4 PROBAST domains (participants, predictors, outcome, and analysis) and the overall study-level rating. Visualizations are created using the robvis tool [16].

Figure 9. Risk of bias assessment for observational cohort studies (Risk of Bias in Non-Randomized Studies - of Interventions [ROBINS-I]) [39,47]. Traffic-light plot (A) and summary plot (B) for the 2 observational cohort studies evaluated using the ROBINS-I tool. Judgments are shown across the 7 ROBINS-I bias domains and the overall risk-of-bias rating. Visualizations are created using the robvis tool [16].



Discussion

Principal Findings

This systematic review synthesized findings from 42 studies and showed that cardiovascular digital twin technology is progressing rapidly but remains largely preclinical and methodologically heterogeneous. Most systems relied on mechanistic models, with a smaller subset incorporating explicit ML or hybrid mechanistic–data-driven designs. Applications clustered around arrhythmia (13/42, 31%), heart failure (9/42, 21%), and therapy planning (28/42, 67%), yet relatively few studies reported real-world clinical deployment, rigorous validation (16/42, 38%), or patient-level outcomes, underscoring the gap between technical innovation and routine clinical use.

Across 11 RQs spanning modeling foundations, data infrastructure, clinical applications, clinical impact, and implementation challenges, the review identified steady technical progress alongside persistent limitations in data quality, external validation, usability, and ethical governance. Our structured risk-of-bias assessment further highlighted that most modeling and prediction studies were judged as having unclear or high risk of bias, particularly in relation to data representativeness, validation strategies, and analysis procedures. Together, these findings suggest that cardiovascular digital twins are scientifically promising but not yet ready for widespread clinical translation.

Technological Foundations and Modeling Strategies

Mechanistic models form the backbone of current cardiovascular digital twins. Electrophysiology, finite-element structural modeling, lumped-parameter formulations, multiscale frameworks, and CFD-based flow simulations were frequently combined to capture different physiological scales and processes. The predominance of mechanistic approaches reflects the central importance of physiological interpretability and explicit biophysical assumptions in cardiology, where understanding causal mechanisms is often as important as prediction performance.

Hybrid designs and explicit ML or AI integrations were present but less common than might be expected given the broader trends in digital health. Only a minority of studies (18/42, 43%) clearly described ML algorithms, with DL (9/42, 21%), Bayesian methods (5/42, 12%), and optimization algorithms (4/42, 10%) used for tasks such as parameter estimation, feature extraction, surrogate modeling, and uncertainty quantification. Many other papers referred to “ML” or “AI” without specifying algorithm families or training procedures, limiting reproducibility and comparability. Open-source dissemination was also limited; less than half of the studies (16/42, 38%) provided accessible code, constraining independent verification, reuse, and benchmarking.

Data Infrastructure and Visualization

Personalization of cardiovascular digital twins relied heavily on structural imaging (32/42, 76%) and electrical signals (18/42,

43%). Imaging data (most often MRI or CT, with occasional echocardiography) enabled patient-specific anatomical reconstruction, while ECG and related electrical measurements supported modeling of activation patterns and conduction abnormalities. Vital signs (12/42, 29%) and demographic variables (9/42, 21%) were commonly used as basic covariates, but richer data sources appeared in only a subset of studies (omics: 4/42, 10%; lab results: 4/42, 10%; detailed clinical records: 3/42, 7%; and wearable/sensor streams: 4/42, 10%). This pattern suggests that many digital twins remain anchored in traditional imaging and electrophysiology pipelines, with multimodal, longitudinal data integration still in an early stage.

Visualization practices were predominantly static and publication-oriented. Most studies communicated digital twin outputs through static figures (41/42, 98%), anatomical overlays (27/42, 64%), or tables summarizing simulation results (7/42, 17%). Only a few described dashboards, dynamic animations, or interactive interfaces that would support real-time exploration or clinical decision-making. As a result, the "front end" of many digital twin systems remains geared toward researchers rather than clinicians or patients, which may hinder adoption even when the underlying models are sophisticated.

Clinical Applications and Target Conditions

Clinically, cardiovascular digital twins were most frequently positioned as tools for therapy planning (28/42, 67%), risk prediction (11/42, 26%), and monitoring (6/42, 14%), with additional roles in diagnosis (7/42, 17%), surgical or device simulation (6/42, 14%), and drug testing (6/42, 14%). Conditions, such as atrial fibrillation and other arrhythmias (13/42, 31%), heart failure (9/42, 21%), cardiomyopathy (5/42, 12%), and aortic disease (3/42, 7%), were most commonly represented, reflecting both their high burden and the suitability of these conditions for simulation-based assessment. Several studies (6/42, 14%) used digital twins to model healthy or control populations, providing physiological baselines and enabling comparison with diseased states.

At the same time, important cardiovascular domains remain underrepresented. Hypertension, atherosclerosis, congenital heart disease, and some valvular pathologies appeared relatively rarely or were only indirectly addressed, despite their major contribution to global cardiovascular morbidity. Furthermore, in some studies (4/42, 10%), the underlying clinical condition was not clearly specified, blurring the line between generic modeling exercises and disease-focused digital twin applications. This uneven coverage limits our ability to generalize digital twin findings across the broader spectrum of CVD.

Impact on Clinical Practice

Reported clinical impacts aligned with the conceptual promise of digital twins but were often indirect or inferred. The most commonly cited benefits were improved decision-making (19/42, 45%) and therapy-related impacts (18/42, 43%), including better selection of interventions, refined device configurations, and more personalized procedural planning. Some studies (6/42, 14%) reported increased accuracy of predictions or simulations, and a small number of studies (2/42, 5%) documented faster diagnosis or workflow advantages.

However, very few studies (4/42, 10%) linked digital twin use to robust patient-level outcomes such as mortality, hospitalization, and long-term symptom burden. Most evidence came from retrospective analyses, in silico comparisons, or small proof-of-concept applications rather than prospective, real-world evaluations. Consequently, while digital twins appear to enhance mechanistic understanding and may plausibly improve decision quality, the causal pathway from digital twin use to improved patient outcomes remains largely hypothetical. This observation was reinforced by the risk-of-bias assessments, which highlighted frequent limitations in sample size, external validation, and outcome measurement.

Barriers to Implementation and Ethical Considerations

Several recurring barriers emerged across the included studies. Strong model assumptions and structural simplifications, while often necessary for tractability, raise questions about generalizability to broader populations or clinical settings. High computational cost and limited real-time performance constrain scalability and integration into time-sensitive workflows, particularly in acute care or interventional environments. Data-quality issues, including incomplete or noisy inputs and limited access to comprehensive, longitudinal datasets, further restrict personalization and increase uncertainty.

Workflow integration and clinician usability remain significant challenges. Only a minority of studies (4/42, 10%) described how digital twin systems might be embedded within electronic health records, imaging systems, or existing decision-support tools, and even fewer studies (3/42, 7%) reported formal usability testing with clinicians. Ethical, legal, and governance issues were discussed explicitly in only a small subset of articles (4/42, 10%), primarily in relation to privacy and data protection frameworks such as GDPR and HIPAA. Isolated studies mentioned algorithmic bias, informed consent, or transparency concerns (1/42, 2%), but systematic engagement with liability, accountability, data ownership, and equity was rare, despite their importance for future clinical deployment.

Sources and Implications of Heterogeneity

Across the included studies, we observed substantial heterogeneity in how cardiovascular digital twins were conceptualized, implemented, and evaluated. This variability spanned multiple dimensions, including the definition and scope of the "digital twin," the underlying modeling strategies (eg, electrophysiology, finite-element, lumped-parameter, multiscale, CFD, and hybrid ML-mechanistic designs), the types and combinations of data modalities used for personalization, the clinical applications and disease targets, and the choice of validation approaches and outcome metrics. As a result, the findings are difficult to compare directly across studies, and a quantitative synthesis or meta-analysis is not appropriate. This heterogeneity also limits the generalizability of individual results and makes it challenging to derive standardized performance expectations for cardiovascular digital twins. Future work will benefit from clearer definitions, minimum reporting standards, and shared benchmarks to enable a more systematic comparison and aggregation of evidence.

Implications and Future Directions

The findings of this review suggest that cardiovascular digital twins are technically promising but not yet consistently validated, standardized, or integrated into routine care. Heterogeneity in modeling approaches, data inputs, validation strategies, and reporting practices limits comparability and makes it difficult to draw firm conclusions about real-world effectiveness.

Future work should focus on strengthening clinical validation in real-world settings, ideally through prospective and multisite studies that link digital twin use to patient outcomes and workflow changes. In parallel, clearer definitions of what constitutes a digital twin; shared performance metrics; and minimum reporting standards for models, data, and validation would support meaningful comparisons and regulatory assessments. Methodological transparency and user-centered design are also essential. Explainable or interpretable modeling pipelines and clinician-oriented interfaces are likely to be critical for trust and adoption.

Finally, ethical and equity considerations need to be addressed proactively. Most existing studies draw on narrow populations and rarely examine algorithmic bias, informed consent for complex modeling, or long-term data governance. Future research should deliberately include diverse populations and care settings; evaluate generalizability across subgroups; and embed privacy protection, transparency, and fair data use into the design and deployment of digital twin systems. Closer collaboration with regulators and health care organizations will be important to ensure that these technical and ethical advances translate into safe, accountable, and clinically useful tools.

Limitations of This Review

While comprehensive, this review may have missed relevant studies, especially studies published in non-English sources or proprietary implementations outside academic literature. Reporting heterogeneity also limited the comparability of validation and outcome data. As the field evolves rapidly, some emerging developments may not have been captured in the included studies.

Although we conducted a structured risk-of-bias appraisal using a custom modeling checklist for simulation studies, the PROBAST for prediction models, and the ROBINS-I for observational cohort studies, these tools were not originally designed for all types of cardiovascular digital twin research and required judgment-based adaptation. In addition, the substantial heterogeneity in study designs, data sources, and evaluation strategies precludes quantitative synthesis and indicates that our risk-of-bias judgments should be interpreted as broad indicators of methodological robustness rather than definitive ratings for individual studies.

This review was based on searches of major bibliographic databases and Google Scholar but did not include dedicated, systematic searches of clinical trial registries (eg, ClinicalTrials.gov), conference proceedings, or specialized grey-literature repositories (eg, dissertation or technical report databases). Although Google Scholar can index some gray literature and conference outputs, our screening was not designed to comprehensively capture these sources. As a result, ongoing trials, conference-only presentations, and nontraditionally published or proprietary digital twin implementations may be underrepresented in this synthesis.

Finally, the review protocol was not registered on a public platform, such as the Open Science Framework (OSF), which may limit reproducibility and transparency. Future work would benefit from prospective protocol registration to reduce the risk of selective reporting and enhance methodological rigor.

Conclusion

This systematic review mapped the technological, clinical, and implementation landscape of cardiovascular digital twin systems across 42 original studies. We found that most digital twins are grounded in mechanistic modeling, with limited but growing use of hybrid and AI-driven approaches. Personalization relies predominantly on imaging and electrical signals, and applications are concentrated in therapy planning, risk prediction, and monitoring for arrhythmia and heart failure. Although the reported impacts on decision-making and therapy optimization are promising, evidence for downstream patient-level benefits remains sparse.

At the same time, substantial heterogeneity in model architectures, data modalities, clinical use cases, and validation strategies—combined with incomplete reporting of algorithms, data, and code—limits comparability across studies and precludes quantitative synthesis. Key barriers to clinical translation include strong modeling assumptions; high computational cost; constrained data quality and availability; and limited real-time performance, workflow integration, and usability. Ethical, legal, and governance issues are only rarely addressed explicitly, with most attention focused on privacy and data protection.

Taken together, these findings suggest that cardiovascular digital twins are technically mature enough to support sophisticated, patient-specific simulations but are not yet ready for routine care. Realizing their potential for precision cardiology will require coordinated progress in standardized evaluation and reporting, rigorous clinical and external validation, user-centered and explainable design, robust data governance, and engagement with regulators and health systems. With the strengthening of these elements, digital twins may evolve from exploratory research tools into trusted, clinically integrated assets for individualized cardiovascular diagnosis, risk assessment, and treatment planning.

Funding

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Data Availability

All data analyzed in this systematic review were extracted from publicly available publications. The complete list of screened records and their inclusion/exclusion status are provided in Multimedia Appendix 2. The full data extraction matrix for all included studies is provided in Multimedia Appendix 3, and detailed study characteristics (including research question categories, risk-of-bias judgments, and funding information) are summarized in Multimedia Appendix 4.

Authors' Contributions

Conceptualization: FSR, EB, MJ
Data curation: FSR, MJ
Formal analysis: FSR, EB
Methodology: FSR, EB
Supervision: JL
Writing – original draft: FSR, MJ
Writing – review & editing: JL
All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy.
[DOC File, 29 KB - cardio_v10i1e78499_app1.doc]

Multimedia Appendix 2
Screened records.
[DOCX File, 70 KB - cardio_v10i1e78499_app2.docx]

Multimedia Appendix 3
Data extraction form.
[DOCX File, 19 KB - cardio_v10i1e78499_app3.docx]

Multimedia Appendix 4
Research question categories.
[XLSX File, 37 KB - cardio_v10i1e78499_app4.xlsx]

Multimedia Appendix 5
Mapping of raw extraction values to harmonized research question categories.
[XLSX File, 23 KB - cardio_v10i1e78499_app5.xlsx]

Checklist 1
PRISMA checklist.
[PDF File, 213 KB - cardio_v10i1e78499_app6.pdf]

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Abbreviations

AI: artificial intelligence
CFD: computational fluid dynamics
CT: computed tomography
CVD: cardiovascular disease
DL: deep learning
ECG: electrocardiography
FEM: finite element modeling
GDPR: General Data Protection Regulation
HIPAA: Health Insurance Portability and Accountability Act
ML: machine learning
MRI: magnetic resonance imaging
PICO: Population, Intervention, Comparison, and Outcome
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROBAST: Prediction Model Risk of Bias Assessment Tool
ROBINS-I: Risk of Bias in Non-Randomized Studies - of Interventions
RQ: research question

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Mindfulness-Based Self-Management Program Using a Mobile App for Patients With Pulmonary Hypertension: Single-Arm Feasibility Study

Yuka Takita[1], PhD; Junko Morishita[2], PhD; Sunre Park[3], MA; Ayumi Goda[4], MD, PhD; Takumi Inami[4], MD, PhD; Hanako Kikuchi[4], MD; Takashi Kohno[4], MD, PhD; Masaharu Kataoka[5], MD, PhD; Daisuke Fujisawa[6], MD, PhD

[1]Department of Nursing, Faculty of Medical Technology, Teikyo University, 2-11-1, Kaga, Itabashi-ku, Tokyo, Japan

[2]Department of Nursing, National College of Nursing, Japan Institute for Health Security, Tokyo, Japan

[3]Department of Nursing, Faculty of Nursing and Medical Care, Keio University, Tokyo, Japan

[4]Department of Cardiovascular Medicine, Faculty of Medicine, Kyorin University, Tokyo, Japan

[5]The Second Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

[6]Division of Quality Assurance Programs, National Cancer Center Institute for Cancer Control, Tokyo, Japan

Corresponding Author:
Yuka Takita, PhD
Department of Nursing, Faculty of Medical Technology, Teikyo University, 2-11-1, Kaga, Itabashi-ku, Tokyo, Japan

Abstract

Background: Mindfulness-based interventions have been applied across various chronic illnesses, but no tailored program exists for individuals with pulmonary hypertension (PH).

Objective: This study aimed to develop and evaluate the feasibility of a mindfulness-based self-management program for patients with PH, delivered online to accommodate their limited mobility.

Methods: A single-arm pre-post study was conducted using an 8-session, weekly videoconference program incorporating PH self-management education and elements of mindfulness-based cognitive therapy. A mobile app linked to an Apple Watch was used to support symptom monitoring and mindfulness awareness. Outcomes included PH-related symptoms, quality of life (emPHasis-10), depression (Patient Health Questionnaire-9 [PHQ-9]), anxiety (Generalized Anxiety Disorder 7-item scale [GAD-7]), resilience (Connor-Davidson Resilience Scale [CD-RISC]), and loneliness (UCLA Loneliness Scale–short version). Assessments occurred at baseline, week 4, and program completion. Exit interviews explored perceived changes and experiences.

Results: Twelve participants (mean age 41.8, SD 10.5 years; range 26 - 56 years) were enrolled, and 9 completed the program (75% retention). Participants valued the online format and Apple Watch integration, while noting a need for optional on-demand sessions. Qualitative analysis identified themes such as increased self-awareness, use of meditation for pain management, and enhanced self-compassion. Quantitative analysis showed significant changes across 3 time points (baseline, week 4, and week 8) for emPHasis-10 (χ^2_2 =9.74; *P*=.008) and CD-RISC (χ^2_2 =7.27; *P*=.03). Trends toward change were observed for PHQ-9 (χ^2_2 =4.75; *P*=.09) and GAD-7 (χ^2_2 =5.07; *P*=.08), but week 12 data were limited (n=5). No significant changes in loneliness were observed.

Conclusions: The program appeared to support patients with PH in managing symptoms and emotions and suggested potential improvements in quality of life. These preliminary findings warrant evaluation in a future randomized controlled trial.

Trial Registration: UMIN Clinical Trials Registry UMIN000044075; https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000050319

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KEYWORDS

mindfulness; mindfulness-based intervention; pulmonary hypertension; self-management; digital health

Introduction

Pulmonary hypertension (PH) is a progressive disease characterized by shortness of breath as the primary symptom. Although recent advances in treatment have dramatically improved the prognosis of the disease [1], patients with PH may face various physical symptoms and may experience limitations in their activities and social roles. Self-management at home has become increasingly complex owing to the use of medications with various mechanisms of action and with various routes of administration [2]. Furthermore, side effects of

pulmonary vasodilative medications, such as headache, jaw pain, plantar pain, diarrhea, and nausea, may occur. These symptoms are more pronounced in continuous intravenous and subcutaneous infusion therapies. There is a certain level of risk for sudden death in severe PH cases with right heart failure; thus, patients with PH are forced to live with uncertainty.

Therefore, it is not surprising that patients with PH tend to experience high anxiety and depression. Past studies demonstrated that 21.9% - 56% of PH patients are comorbid with depressive symptoms [3-14], 10.7% - 62% with anxiety symptoms [3-6,8,12,13], and 27.6% - 40% with stress-related symptoms [4,11]. These findings suggest the need for psychological care for patients with PH.

Mindfulness has been described as "paying attention in a particular way—on purpose, in the present moment, and nonjudgmentally" [15]. Mindfulness-based interventions have gained increasing attention as a method of psychological care for patients with physical illnesses. The two major programs are mindfulness-based stress reduction (MBSR) [16] and mindfulness-based cognitive therapy (MBCT) [17]; however, flexible modifications of the program to fit with target populations, such as providing information on nutrition [18], grief care [19], and advance care planning [20,21], have been implemented.

Conventional mindfulness-based programs have been delivered on a face-to-face basis; however, in recent years, web-based programs have been developed and implemented quite widely [22,23]. In the field of cardiovascular disease, mindfulness interventions are being developed for patients with coronary artery disease and heart failure [24-26].

However, to the best of the authors' knowledge, there has been no mindfulness-based program that has been developed specifically for PH. Modification of the program may be needed for patients with PH to avoid physical overload that may worsen right ventricular function. For example, yoga, a standard component of MBSR and MBCT, could lead to cardiopulmonary overload. Furthermore, since patients with PH often have limited mobility, web-based programs, instead of on-site programs, are likely to be preferred.

Therefore, in this study, we developed and tested the feasibility of an online mindfulness-based self-management program for patients with PH using a smartphone app on Apple Watch. The intervention aimed to improve the quality of life (QOL) and resilience and to reduce depression, anxiety, and pain (a side effect of the treatment) of patients with PH.

Methods

Study Design

This study used a mixed methods, single-group, pre-post design.

Participants

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria are shown in Textbox 1.

Textbox 1. Inclusion and exclusion criteria.

The inclusion criteria for this study were as follows:

- A confirmed diagnosis of pulmonary hypertension (PH) [27].
- Age 20 - 75 years.
- The ability to attend at least six of the eight 60-minute online sessions.
- The ability to operate the self-administered mobile app on an iPhone or iPad and an Apple Watch.

The exclusion criteria were as follows:

- Severe physical symptoms, including but not limited to decompensated right-sided heart failure, as assessed by the attending physician.
- Patients with an active psychiatric disorder who were currently under psychiatric care or receiving psychotropic treatment. These individuals were excluded for safety reasons, as the program was delivered entirely online, and timely in-person support could not be ensured if psychological distress or other adverse emotional reactions were to occur during the intervention.
- Cognitive impairment or other conditions that, in the attending physician's judgment, would make it difficult for the patient to understand or participate in the program, based on routine clinical assessments and information in medical records.
- Individuals deemed by their attending physicians to be clinically unstable or otherwise inappropriate for participation.
- Individuals who had previously participated in structured mindfulness-based programs such as mindfulness-based cognitive therapy (MBCT) or mindfulness-based stress reduction (MBSR).

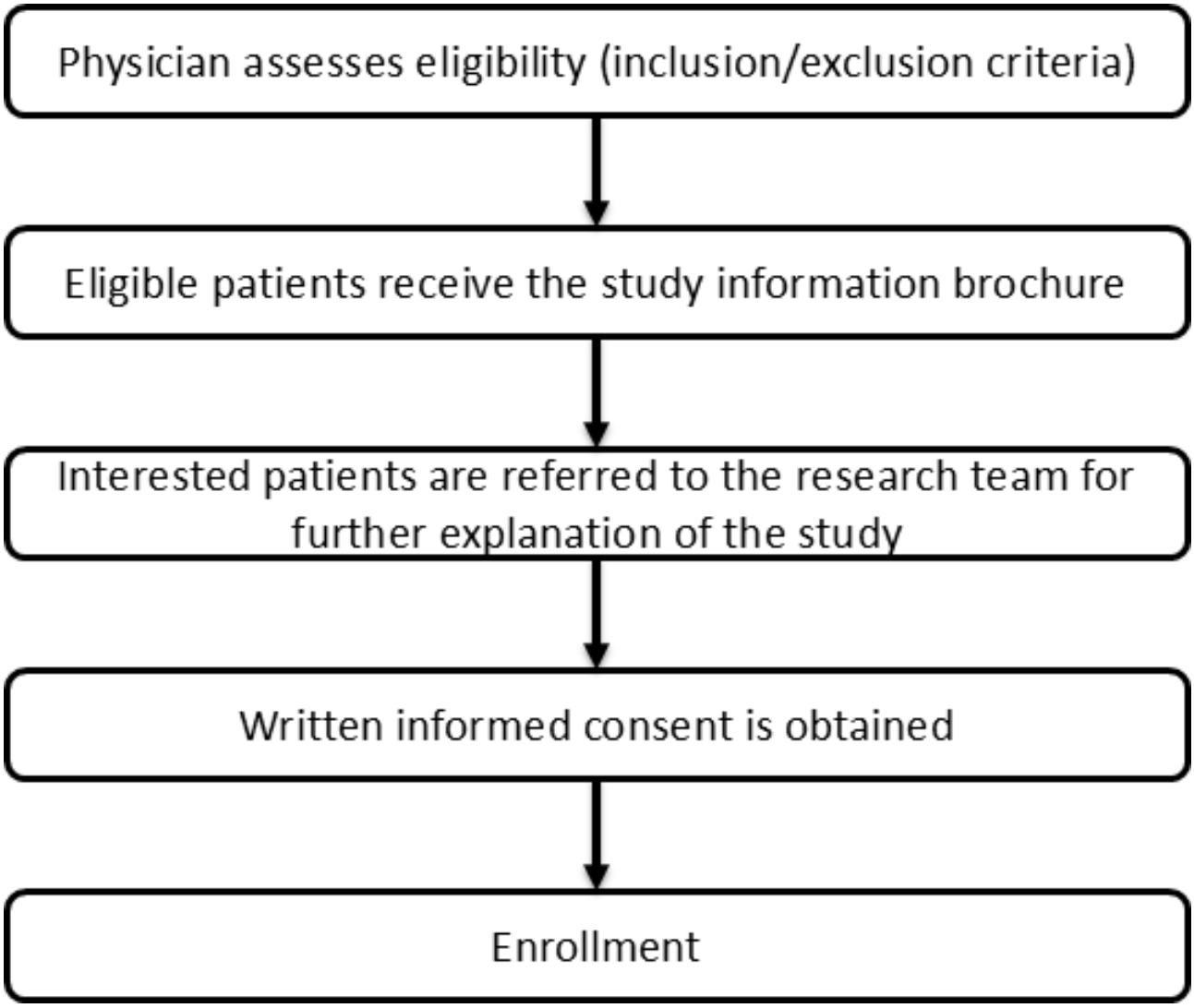
Individuals aged 18 - 19 years were not included, because at the time this study was initiated (December 2020), persons ages 20 years and younger were not considered adults for the purpose of providing independent informed consent under Japanese ethical guidelines, and thus, were unable to consent without guardian approval [28].

Recruitment and Screening Procedures

Participants were recruited through a structured, stepwise process. First, physicians screened patients during routine clinical visits to ensure they met the inclusion criteria and did not meet any exclusion criteria. Eligible patients were then provided with an informational brochure describing the study. Patients who expressed interest were referred to the research team, who provided a detailed explanation of the study

procedures. Written informed consent was obtained from all patients before enrollment. The overall recruitment and screening process is shown in Figure 1.

Figure 1. Flowchart illustrating the recruitment and screening.



Sample Size Justification

As this was a feasibility study, the primary aim was to evaluate acceptability, adherence, and operational feasibility rather than to test statistical efficacy; therefore, a formal power calculation was not required. We chose a target sample size of approximately 12 participants, which is comparable to previous feasibility studies of meditation or mindfulness-based interventions in cardiovascular populations that enrolled about 10 - 15 participants [29,30].

Intervention

Program Contents

The conceptual framework and content of the program are presented in Figure 2 and Table 1. We developed this program based on the findings of our previous research, which showed that the key elements of distress for patients with PH were the loss of the past and the threat of disease progression, including rumination about the past and concern about the future [14]. The fundamentals of the intervention were based on MBCT, which addresses rumination and has been proven effective for both physical and psychological symptoms in patients with critical illnesses [17]. Furthermore, we added psychoeducation and self-management skill-building as essential components, as the distress of patients with PH derives from PH-specific symptoms (eg, breathlessness) and the adverse effects (eg, pain or nausea) and difficulties associated with the treatment (eg, home oxygen therapy).

Figure 2. Conceptual framework of the mindfulness-based intervention program for patients with pulmonary hypertension.

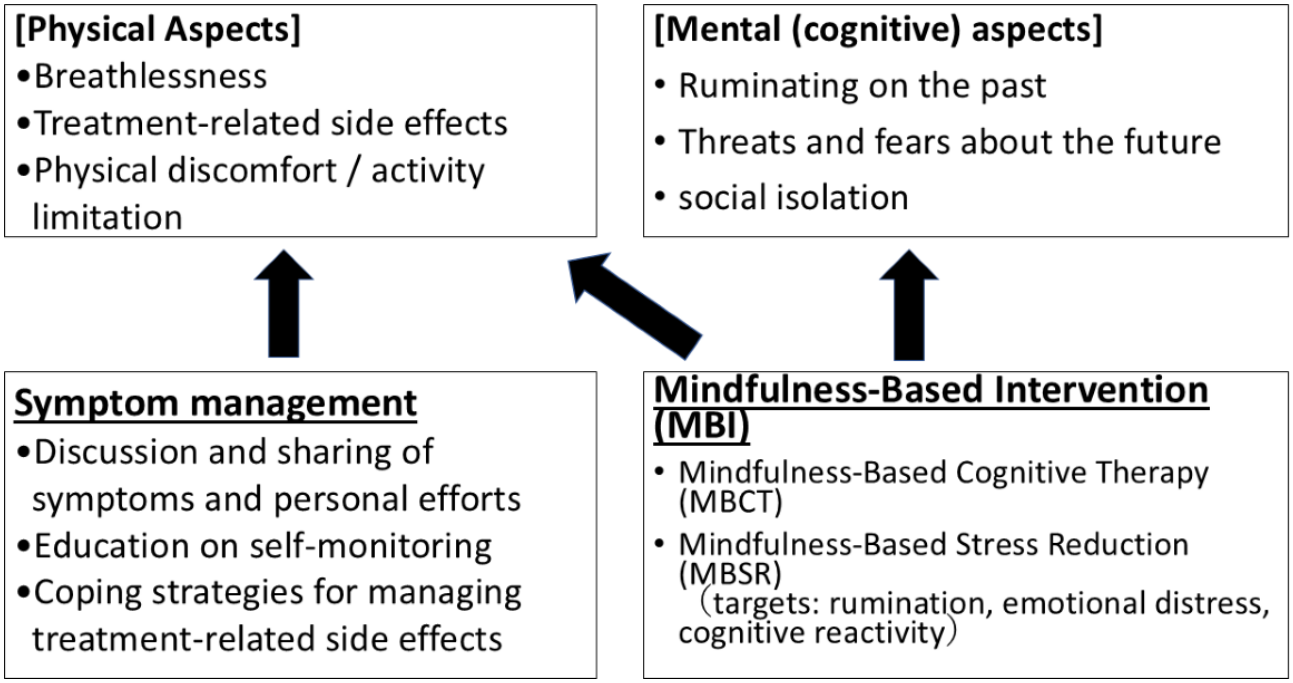


Table . Program content structured based on the results of previous research.

Elements of distress	Program content and expected effects
“Isolation from my surroundings”	Prevent isolation and reduce loneliness by regularly connecting with others and sharing thoughts and feelings through weekly online meetings.
“Loss of myself” and “Fear of illness progression or deterioration”	By reflecting on their physical and mental conditions through mindfulness practice and homework, participants become aware of their thought patterns and feelings, such as loss of abilities, regret regarding the past, and anxiety about the future; promoting meta-cognition stops rumination, thereby alleviating mood swings and anxiety.
“Hassle associated with oxygen therapy,” “Suffering from side effects,” and “Rumination on illness due to breathlessness”	Learning and sharing the basic knowledge and practical tips required for self-management and enhancing the ability to self-manage activities, shortness of breath, side effects, and other issues.

Program Structure

Table 2 presents the outline of the program. The basic structure of the program was similar to that of MBCT. To lessen the potential physical and psychological burden of the patients, we adapted an online format. We shortened the length of each session to 1 hour. We eliminated yoga, which has been supposed to be an integral component in conventional MBCT, for safety reasons, since patients with PH are at risk of circulatory collapse owing to direct right ventricular stress caused by increased pulmonary artery pressure, which could be exacerbated by physical exercise.

Table . Schedule and homework for the self-management mindfulness program for patients with pulmonary hypertension.

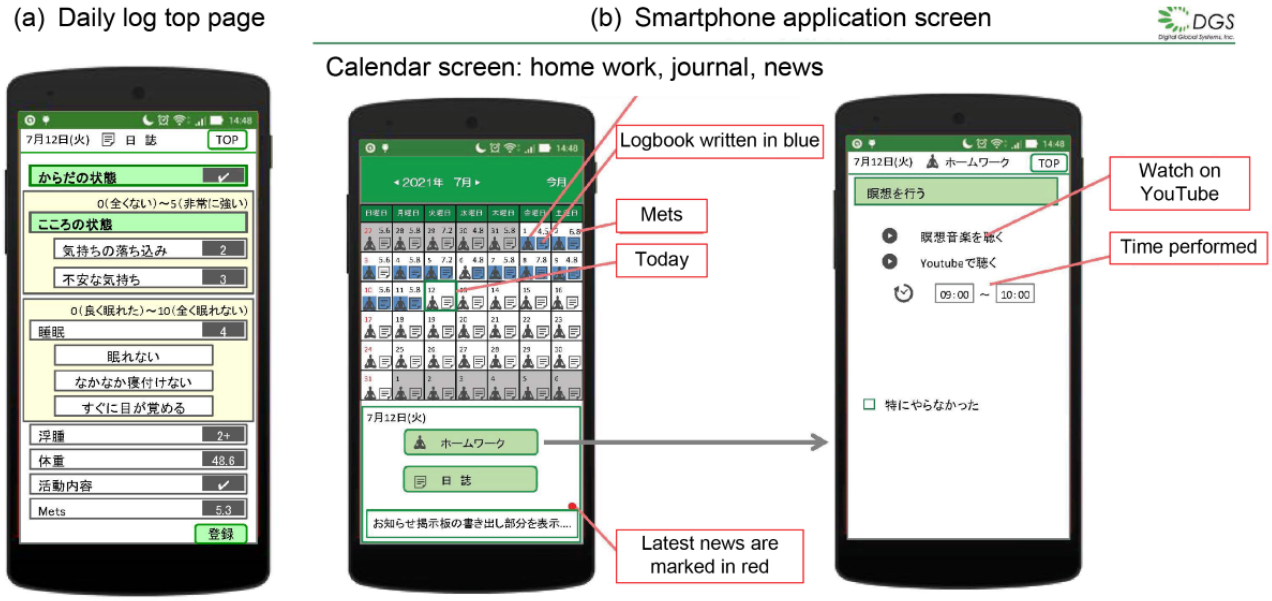
Session	Theme	Contents	Homework
1	Start the program	• What is mindfulness? • How to use the self-management app? • Short breathing meditation	• Using self-management app
2	Become aware of automatic reactions	• Short breathing meditation • Symptom management of pulmonary hypertension	• Mindful daily living
3	Focus on your body	• Body scan (meditation) • Cognitive strategies for managing treatment-related side effects	• Body scan
4	Focus on breathing	• Mindfulness meditation of breathing and body • Pleasant and unpleasant mode	• Pleasant and unpleasant life diary
5	Focus on your body and adjust it	• Short meditation • Adjustment of pulmonary hypertension activities	• Meditation • Focus on your pulse during activity
6	Thoughts are not facts	• Mindfulness meditation with sound and thought • Cognitive strategies for managing thoughts and emotions (guided imagery practice) • 3-step breathing space method	• Using 3-step breathing space method when feeling uncomfortable
7	Caring for yourself	• Compassion meditation • Positive habits	• Meditation • Appreciation list
8	Use skills for your future	• Meditation • Reflection on the past • Looking toward the future	• —[a]

[a]Not applicable.

The program was delivered in a group format once a week over a period of 8 weeks via video conference. The program was facilitated by the lead author, a nurse with 6 years of experience in practice and the teaching of mindfulness interventions. Each session lasted 60 minutes, which included 10- to 30-minute meditation practice, which was facilitated with the facilitator. At the beginning of each session, a reflection on homework was conducted, and an inquiry session was held after each meditation practice. Homework included daily mindfulness practice (eg, breathing meditation and body-scan meditation) and reflection journaling on emotional and physical experiences. Video lectures on the meaning of mindfulness, the pleasant and unpleasant mode, and mindfulness meditation were provided by a clinical psychologist and a nurse who had been a mindfulness provider for over 10 years. Pleasant mode and unpleasant mode involve mindfully reflecting on pleasant and unpleasant experiences in daily life, noting the physical sensations, emotions, and thoughts that arose at the time, thereby cultivating awareness.

To facilitate self-management skills, we developed a mobile app, which enabled users to record their daily physical conditions and to monitor their activity status using an Apple Watch (Figure 3). The mobile app (Self-management App, developed in collaboration with DGS Co Ltd) stored data on secure encrypted servers; all identifying information was anonymized and replaced by unique participant codes. For participants who did not own an Apple Watch, a device was lent to them free of charge for use during the study period. Participants were advised to use this mobile app throughout the program.

Figure 3. Screenshots of the self-management smartphone app used in the study.



Outcome Measures

Demographic Data

Demographic and clinical information, including age, sex, diagnosis, disease classification (World Health Organization functional class), duration of illness, and treatment status, were collected at baseline through participants' self-report and review of medical records. Demographic information was obtained to characterize the study sample and was used only for descriptive analyses.

Feasibility and Acceptability

The feasibility of the intervention was evaluated with participation and completion rates for the program. Acceptability was assessed by collecting and evaluating feedback from the program through interviews. The interviews included questions about changes in symptoms, self-management skills, and mental health conditions before and after the program. Furthermore, the participants were asked to describe the perceived benefits of the program, what should be changed, what they liked and disliked, and obstacles and facilitators for implementation of the program.

Secondary Outcomes

Secondary outcome measures comprised emPHasis-10, a disease-specific patient-reported outcome measure for evaluating the QOL of patients with PH [31]; the Patient Health Questionnaire (PHQ-9) for depression [32]; the Generalized Anxiety Disorder 7-item (GAD-7) scale [33]; the Connor-Davidson Resilience Scale (CD-RISC), a measure of one's ability to recover from various difficulties such as illness, emotional pressure, and pain [34]; and the UCLA Loneliness Scale-short version [35]. In addition, interviews were conducted regarding changes in awareness and behaviors related to self-management. These measures were obtained at baseline, 4 weeks after the program, and at the end of the program. The questionnaire was administered at four time points (baseline, week 4, week 8, and week 12). All questionnaires were provided in paper format, completed by participants at each time point, and returned by mail.

Analytical Methods

Content analysis was used to analyze the qualitative data from the interviews [36]. The characteristics and results of the participants were summarized using descriptive statistics, with median (range) for continuous variables and frequency (percentage) for categorical variables. The score changes between time points for each participant were plotted as line graphs for each scale. The Friedman test was conducted to evaluate the differences in scores across time points. This nonparametric test was chosen owing to its suitability for comparing repeated measures or related samples without assuming normality. Significance was set at $P<.05$. IBM SPSS (version 28) for Windows was used for all statistical analyses. MAXQDA (VERBI Software GmbH) was used for qualitative data analysis.

Ethical Considerations

This study was approved by the ethics review committees of Tokyo Kasei University and Kyorin University School of Medicine (SKE2020-11, number 1631) and was conducted in accordance with the ethical standards of the Declaration of Helsinki and relevant national guidelines.

All participants received a written explanation of the study's purpose, procedures, potential risks, and their right to withdraw at any time without disadvantage. Written informed consent was obtained from all participants prior to study participation.

To ensure privacy and confidentiality, all data were anonymized and assigned participant identification codes at the time of collection. No personally identifiable information was included in the datasets used for analysis. Data were securely stored on a password-protected hard disk drive.

Participants did not receive monetary compensation but were provided with the mindfulness program free of charge as part of the study.

No identifiable images or personal information of participants are included in this paper or the supplementary files.

The study was registered in the UMIN Clinical Trials Registry (UMIN000044075).

Results

Participant Characteristics

Participants' baseline characteristics are shown in Table 3.

Table . Participant characteristics at baseline (n=12).

Characteristics	Results
Age (years), mean (SD)	41.8 (10.5)
Age (years), range	26 - 56
Sex, n (%)	
Male	3 (25)
Female	9 (75)
Program completed, n (%)	9 (75)
PH[a] type, n (%)	
PAH[b]	11 (92)
CTEPH[c]	1 (8)
MeanPAP[d] (mmHg), median (range)	32.5 (20-47)
Treatment (pharmacological therapy), n (%)	
Epoprostenol (IV[e])	5 (42)
Treprostinil (IV)	2 (2)
Treprostinil (SC[f])	1 (8)
Only oral medicine[g]	4 (33)
Interventional history, n (%)	
Post BPA[h]	1 (8)
Therapeutic support, n (%)	
Oxygen therapy	3 (25)
Symptoms, n (%)	
Dyspnea on exertion	10 (83)
Fatigue	10 (83)
Palpitations	3 (25)
Pain	8 (67)
Nausea	3 (25)
Diarrhea	5 (42)
QOL[i] (emPHasis-10[j]), mean (SD), range	33.6 (10.1), 16 - 46
Depression (PHQ-9[k]), mean (SD), range	14.1 (6.6), 2 - 24
Anxiety (GAD-7[l]), mean (SD), range	11.1 (5.5), 1 - 18
Resilience (CD-RISC[m]), mean (SD), range	17.8 (8.0), 3 - 29
Loneliness (UCLA Loneliness Scale), mean (SD), range	26.6 (5.9), 13 - 34

[a]PH: pulmonary hypertension.
[b]PAH: pulmonary arterial hypertension.
[c]CTEPH: chronic thromboembolic pulmonary hypertension.
[d]MeanPAP: mean pulmonary arterial pressure.
[e]iv: intravenous injection therapy.
[f]sc: subcutaneous injection therapy.
[g]Including the 1 participant with post-BPA status.
[h]BPA: balloon pulmonary angioplasty (only applies to patients with CTEPH).
[i]QOL: quality of life.
[j]emPHasis-10: disease-specific patient-reported outcome (PRO) measures for evaluating quality of life in patients with pulmonary hypertension.
[k]PHQ-9: Patient Health Questionnaire-9.

[l]GAD-7: Generalized Anxiety Disorder 7-item scale.

[m]CD-RISC: Connor-Davidson Resilience Scale.

Feasibility

Of the 12 participants who agreed to participate in this study, 9 completed the program (75% retention rate). The 3 individuals dropped out due to hospitalization for exacerbation of hemoptysis, hospitalization for treatment of comorbidities, and catheter infection.

Acceptability of Program Structure

The responses by the 9 participants who completed the program are shown in Table 4. Furthermore, the following comments were received regarding the program's structure:

> *The weekly online real-time program made me feel as though I were back at work again, and it refreshed me and made me feel lively and excited.*
>
> *The Apple Watch helped me understand my physical condition better through objective numbers and data, and it gave me the opportunity to face my illness properly. Just experiencing symptoms can be vague, and they are easily forgotten, but being able to check the numbers and monitor my condition is really helpful.*
>
> *I didn't know anything about mindfulness at first, so I felt hesitant. I think it would be much easier to engage if I could learn why mindfulness is applied to this illness.*
>
> *I take diuretics every day, so it would be helpful if there were an on-demand option that allows me to participate calmly without worrying about needing to urinate.*

Table . Feedback on the number of sessions, duration per session, and session intervals (n=9).

Variable	Sample, n (%)
Number of programs (8 in total)	
Too many	2 (22)
Appropriate	6 (67)
Too few	1 (11)
Time per session (60 minutes per session)	
Too long	0 (0)
Appropriate	9 (100)
Too short	0 (0)
Program interval (once per week)	
Too long	0 (0)
Appropriate	7 (78)
Too short	2 (22)

Changes and Awareness After the Program

The qualitative content analysis identified 10 categories (Table 5).

Table . Qualitative analysis results: categories reflecting changes and awareness after the program.

Category	Frequency, n
Being able to objectively consider one's thoughts and feelings and not be bothered by them	14
Peace of mind from facing one's mind and body	13
Reduced pain and handling side effects	12
Being compassionate toward oneself	10
Focusing on one's body and conducting activities	10
Awareness of the importance of breathing	6
Increased happiness and positive feelings	4
Realization that actions during illness until the present were not erroneous	4
Reduced fatigue	3
Acquiring methods of thinking and coping when feeling anxious or restless	2

Being Able to Objectively Consider One's Thoughts and Feelings and Not Be Bothered by Them

Participants were able to understand that their mental instability was due to their poor physical condition.

> *I used to struggle to accept it, but now I can think, 'My physical condition is bad today, so it's natural [for my feelings to also decline]. It can't be helped.' […] And I can tell myself, 'It's the illness that makes me feel this way, so it can't be helped.'* [ID7]

Reduced Pain and Handling Side Effects

They experienced how meditation can help relieve pain and heartburn.

> *I had been having a headache for a long time, but while I was doing the body scan meditation, the pain disappeared… It's really strange, but the pain seems to move around. I always wonder why.* [ID5]

Being Compassionate Toward Oneself

Even when thoughts and feelings came to mind, they were able to observe them objectively and respond more adaptively. Consequently, they felt that this positive change reduced self-blame and harsh self-criticism.

> *I really felt that the number of times I thought, 'Oh no, this is terrible,' had decreased...I really felt that the number of times I thought.* [ID2]

Focusing on One's Body and Conducting Activities

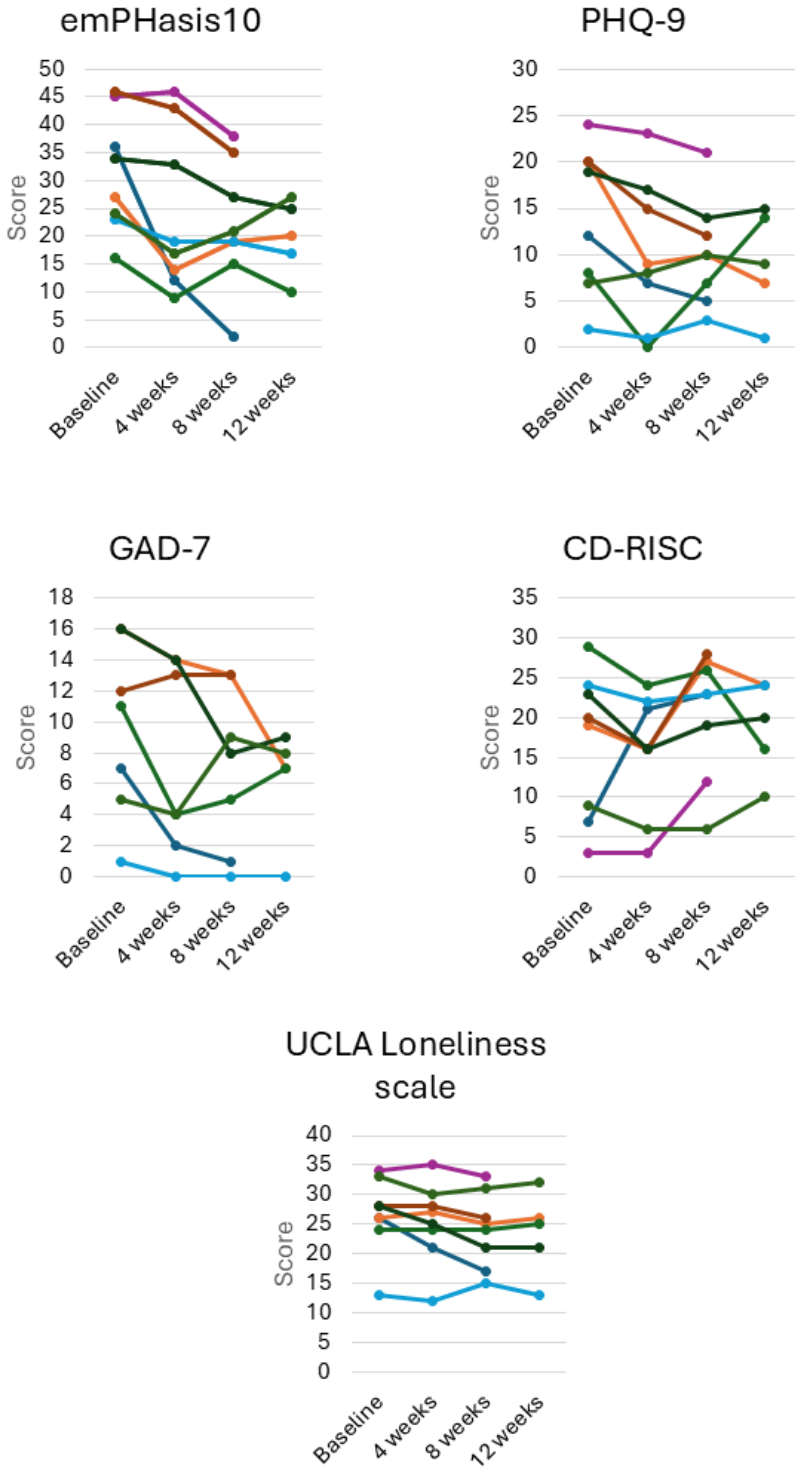
By focusing on bodily sensations and intentionally attending to their internal states during daily activities, participants reported reduced pain.

> *At night, after eating dinner and taking my medication, my heart used to start pounding faster. But now, after I finish eating, I take a moment and tell myself, 'Let's breathe slowly and take a little rest,' and the breathlessness goes away.* [ID4]

Secondary Outcomes

Although 9 participants completed the program (75% completion rate), the week 8 quantitative analysis—the primary endpoint—included data from 8 participants (67% data retention rate) because one completer did not return the postprogram questionnaire. Figure 4 shows score trends from baseline, week 4, week 8, and week 12. At week 12 (one month after the end of the program), responses were obtained from 5 participants (56% response rate).

Figure 4. Individual trajectories of patient-reported outcome measures across the four assessment time points (baseline, 4 weeks, 8 weeks, and 12 weeks). The figure displays individual-level changes in 5 psychosocial and clinical measures used in this study: the emPHasis-10 (disease-specific quality of life), PHQ-9 (depressive symptoms), GAD-7 (anxiety symptoms), CD-RISC (resilience), and the UCLA Loneliness Scale (loneliness). Each colored line represents a single participant's score over time. These descriptive data illustrate variability in symptom patterns and potential trends in psychological well-being during and after the mindfulness-based intervention. CD-RISC: Connor-Davidson Resilience Scale; GAD-7: Generalized Anxiety Disorder 7-item scale; PHQ-9: Patient Health Questionnaire-9.



The emPHasis-10 (χ^2_2=9.74; *P*=.008) and CD-RISC (χ^2_2=7.27; *P*=.03) scores showed significant differences at baseline (preprogram), 4 weeks (during the program), and 8 weeks (postprogram; n=8). The significant differences were not maintained at 12 weeks (follow-up). In addition, although no significant difference was found, a trend toward improvement in the PHQ-9 (χ^2_2=4.75; *P*=.09) and GAD-7 (χ^2_2=5.07; *P*=.08) was observed. Moreover, a few participants showed sudden deterioration in QOL and experienced depressive and anxiety symptoms a month after the program; however, they reported

that this coincided with the timing of replacing the subcutaneous Treprostinil injection needle. No significant changes were observed in feelings of loneliness. Individual score trajectories are shown in Figure 4.

Discussion

Principal Findings

This study evaluated the feasibility, accessibility, and preliminary psychological changes associated with an online mindfulness-based program designed for patients with PH. The program achieved good retention, with a completion rate of 75% (9/12), and was generally well accepted by participants. Quantitative analyses revealed positive changes in QOL, depression, anxiety, and resilience scores, while qualitative findings indicated that participants experienced greater bodily awareness, emotional regulation, and self-compassion through mindfulness practice. Together, these results suggest that an online mindfulness-based intervention is both feasible and acceptable for patients with PH and may have the potential to improve their psychological well-being and symptom management.

Feasibility and Accessibility

With a completion rate of 75% (9/12), the program demonstrated a relatively high level of retention. However, the primary reason for participant dropout was hospitalization due to physical deterioration associated with underlying or comorbid conditions. As PH progresses, patients may develop worsening right heart failure or experience hemoptysis, necessitating hospitalization. Therefore, future implementations of the program should target individuals with stable PH and take into account the potential for physical decline during participation.

The 60-minute session length appeared appropriate; however, participants indicated that the total number of sessions (n=8) was excessive and that the weekly interval was too short. Additionally, some participants expressed a desire for on-demand sessions, citing difficulties caused by frequent urination due to diuretic use. These findings suggest the need to reconsider the program's frequency and delivery format.

The program consisted of eight 60-minute real-time sessions conducted weekly via an online conferencing system. For PH patients who experience challenges leaving their homes, this online delivery format effectively reduced their physical burden. Nevertheless, the requirement to connect online at a fixed time each week imposed an additional burden that may have negatively affected retention. Conversely, participants who had stopped working due to illness reported a sense of fulfillment and accomplishment from attending regularly scheduled sessions.

As discussed above, offering the entire program on an on-demand basis could further reduce participant burden and improve retention. However, inquiry—a central element of mindfulness—requires real-time interaction between instructors and participants. Inquiry, also referred to as mindful dialog, provides participants with opportunities for self-reflection through guided conversation. To preserve this essential component, at least part of the program should be conducted synchronously rather than fully on-demand. Although traditional MBSR and MBCT programs comprise 8 sessions, recent studies have developed and validated shorter mindfulness-based interventions [37-40]. Based on these findings, we propose a hybrid format that reduces the total number of sessions and delivers approximately half of them on demand. This approach may lessen participant burden while maintaining the feasibility and therapeutic integrity of the intervention. Nevertheless, some patients may require individualized support to manage specific physical symptoms, treatment-related side effects, or emotional distress. Therefore, it may be necessary to consider implementing individual consultations before the program or during the intervention period to provide tailored support for such patients.

Furthermore, this intervention was implemented as an individual program. Expanding individual programs to a larger population poses logistical challenges and limits generalizability. Future studies should therefore examine the effectiveness of group-based formats. In addition, since mindfulness interventions require trained facilitators, the current shortage of qualified personnel represents a barrier to broader dissemination. To promote scalability, two approaches may be considered: (1) developing on-demand mindfulness modules that can be facilitated by health care professionals without formal mindfulness training, or (2) establishing training programs to cultivate health care providers capable of delivering mindfulness interventions.

Although the response rates for pre- and midprogram questionnaires were high, those at program completion and 4 weeks postcompletion were notably low. In this study, paper-based questionnaires were distributed and returned by mail. For PH patients who find it burdensome to leave home, this method likely contributed to the low response rate. Therefore, future studies should employ web-based questionnaires that allow participants to respond online, thereby reducing the response burden and improving data collection rates.

Qualitative Findings: Psychological and Physical Experiences During the Program

Qualitative analysis identified themes such as "finding peace of mind through connecting with the body and mind" and "recognizing the importance of breathing." Interoception refers to perceiving, accessing, and evaluating internal bodily signals [38]. In mindfulness meditation, participants focus nonjudgmentally on present-moment bodily sensations. Rumination arises when attention drifts toward the past or future; mindfulness meditation helps disengage from rumination by redirecting awareness to the present body and activating interoceptive processing [41]. In this program, body-scan and breath-focused meditations enhanced participants' interoceptive awareness, helping them notice their breathing patterns, bodily reactions during activities, and the thoughts and emotions arising in their minds. Through nonjudgmental observation, participants experienced decentering, which enabled them to view their situations from a distance, thereby reducing rumination and perceived pain.

In addition, lectures and cognitive-behavioral activities addressing emotions and physical symptoms related to treatment side effects provided opportunities to learn coping strategies and methods for engaging with these symptoms. By increasing bodily awareness and practicing mindful engagement during activities, participants reported decreased fatigue and pain. These observations suggest that, in addition to mindfulness practice itself, learning management strategies tailored to PH-related side effects and adaptive coping methods may contribute to reducing treatment-related discomfort and improving activity tolerance.

Breathing was a key element of mindfulness meditation. Before the study, there was concern that focusing on breathing might exacerbate dyspnea in PH patients. Contrary to expectations, meditation focusing on breathing appeared to lessen perceived breathlessness. For individuals experiencing daily dyspnea, increasing awareness of breathing helped them recognize shallow breathing patterns and intentionally breathe more deeply and slowly, which may have contributed to reduced shortness of breath during exertion.

Furthermore, improvements in self-compassion, well-being, and positive emotions were observed after program participation. Many PH patients tend to blame themselves, thinking, “If only I had sought treatment earlier,” or “I became sick because I was weak.” Mindfulness may have helped reduce self-critical thinking by fostering objective awareness of mental states and thought patterns, encouraging nonjudgmental observation, and supporting more positive self-recognition. Overall, these findings suggest that the program may have a favorable influence on mental health and emotional well-being, though further investigation in larger, controlled studies is needed.

Comparison With Previous Work

Changes observed in QOL, depression, anxiety, and resilience scores suggest that the intervention may have the potential to support improvements in psychological well-being. However, immediate effects on rapidly worsening physical symptoms should not be expected. In this study, standardized self-administered questionnaires were conducted at four time points (baseline, week 4, week 8, and week 12). Because this was a feasibility study with a small sample size and a low response rate at week 12, statistical analyses across all time points were limited. Analyses of the first three time points (baseline, week 4, and week 8) indicated preliminary improvements in QOL, with several participants demonstrating downward trends in depression and anxiety scores. While these findings are not sufficient to determine efficacy, they suggest possible patterns of change that merit further investigation in future controlled trials.

Previous studies of mindfulness-based interventions in cardiovascular populations provide context for interpreting these findings. A randomized controlled trial (The Stress Reduction, Meditation, and Mindfulness Program) targeting patients with chronic heart failure reported reductions in perceived stress and improvements in clinical outcomes [26]. Similarly, a meta-analysis of randomized controlled trials in patients with coronary artery disease demonstrated significant reductions in depression, anxiety, and stress following mindfulness-based interventions [25]. Although the present study focused on patients with PH, the observed trends—increased emotional regulation, decreased rumination, and enhanced self-compassion—are consistent with mechanisms reported in these previous studies.

The mean CD-RISC score in this sample was lower than that reported in patients with cancer (29.3) [42] or multiple sclerosis (26.8) [43], suggesting relatively low baseline resilience in participants. While the small sample size limits interpretation, the observed changes in resilience scores suggest that mindfulness-based programs may hold potential for supporting resilience in PH populations. These preliminary findings align with previous literature indicating that mindfulness practice may contribute to improvements in adaptive coping and emotional well-being across diverse chronic illness populations.

Limitations

This study has several limitations that should be acknowledged.

First, as a single-arm feasibility study, it did not include a control group. Without a comparison to usual care or another intervention, it is difficult to determine whether the observed improvements in quality of life or psychological measures were attributable to the program itself or to other factors, such as natural adaptation or social interaction with facilitators. To mitigate this, standardized self-report measures were used at multiple time points to examine within-participant changes. Future studies should include a randomized controlled design to allow more robust evaluation of efficacy.

Second, the sample size was small, which limits the statistical power and generalizability of the findings. Because of the limited number of participants, subgroup analyses could not be performed, and some trends may have gone undetected. Nevertheless, the study provided valuable preliminary data on feasibility and participant experiences, which will help inform sample size estimation and stratification criteria for future trials.

Third, the study duration was relatively short, and no long-term follow-up was conducted. Consequently, it remains unclear whether the improvements observed immediately after the intervention can be sustained over time. Future studies should incorporate follow-up assessments to examine the persistence of psychological and physical benefits and to identify factors that influence continued engagement with mindfulness practice.

Fourth, response rates for the postprogram and 4-week follow-up questionnaires were low, possibly because of the paper-based mailing method, which may have introduced response bias. Participants who continued responding may have been those more motivated or satisfied with the program. To improve response rates and minimize bias, future research should use web-based data collection methods to facilitate participation and reduce the burden on patients with PH.

Future Directions

Based on these findings, several future directions for research and program development can be proposed. First, future studies should conduct randomized controlled trials with larger and more diverse samples to verify the program’s efficacy and assess its long-term impact. Longitudinal follow-up is necessary to

evaluate whether the psychological and physical benefits observed in this feasibility study can be sustained over time. Multisite or decentralized clinical trial designs may also facilitate participation among patients with PH who face difficulties traveling to research facilities.

Second, refinement of the program content is warranted. Adjustments to session frequency and duration, as well as partial incorporation of on-demand components, may help reduce participant burden and improve accessibility. Developing a group-based version of the program could further enhance social connectedness and scalability.

Third, to promote broader dissemination and generalization of mindfulness-based interventions, it will be important to develop and implement educational programs that train cardiovascular health care professionals to practice and facilitate mindfulness. Increasing the number of qualified practitioners is expected to contribute to the sustainable delivery and expansion of such programs in clinical and community settings. In addition, future efforts should focus on expanding the availability of mobile apps across different digital platforms and, ultimately, adapting and implementing the program in international settings. Such developments may facilitate broader accessibility and cross-cultural validation of mindfulness-based interventions for patients with chronic cardiopulmonary diseases.

Conclusions

This feasibility study suggests that an online mindfulness-based self-management program may help patients with pulmonary hypertension engage more effectively with symptoms, treatment-related side effects, and emotional distress. Participants reported preliminary improvements in perceived pain and aspects of quality of life, indicating potential psychological benefits. Further refinement of the program and evaluation in larger randomized controlled trials are needed to determine its efficacy and long-term impact.

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Data Availability

The raw data analyzed qualitatively will not be disclosed to maintain the confidentiality of the responses, but the quantitatively analyzed datasets may be provided by the corresponding author upon reasonable request.

Authors' Contributions

Conceptualization: YT (lead), DF (equal), SP (equal)
Data curation: YT
Formal analysis: YT (lead), JM (equal)
Funding acquisition: YT
Investigation: YT (lead), JM (equal), AG (supporting), TI (supporting), HK (supporting)
Methodology: YT (lead), SP (equal), JM (supporting), DF (supporting)
Project administration: YT
Resources: YT (lead), SP (equal), AG (equal), JM (supporting), DF (supporting)
Supervision: DF (lead), SP (equal)
Validation: YT (lead), SP (equal), AG (equal), JM (supporting), DF (supporting)
Visualization: YT (lead), SP (supporting), JM (supporting), DF (supporting)
Writing – original draft: YT
Writing – review & editing: DF (lead), TK (supporting), MK (supporting)

Conflicts of Interest

TI receives lecture fees from MSD and Bayer outside the submitted work. YT receives lecture fees from MSD and Mochida Pharmaceutical and serves as an advisor for an international meeting organized by MSD, outside the submitted work. The other authors declare no conflicts.

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Abbreviations

CD-RISC: Connor-Davidson Resilience Scale
GAD-7: Generalized Anxiety Disorder 7-item scale
MBCT: mindfulness-based cognitive therapy
MBSR: mindfulness-based stress reduction
PAH: pulmonary arterial hypertension

PH: pulmonary hypertension
PHQ-9: Patient Health Questionnaire-9
QOL: quality of life

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Perceived Potential and Challenges of Supporting Coronary Artery Disease Treatment Decisions With AI: Qualitative Study

Khara Sauro[1,2,3], PhD; Bishnu Bajgain[3], MSc; Cody van Rassel[4,5], PhD; Bryan Har[5], MD, MPH; Robert Welsh[6], MD; Joon Lee[3,4,5], PhD

[1]Department of Surgery, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
[2]Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
[3]Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
[4]Data Intelligence for Health Lab, Cumming School of Medicine, University of Calgary, 3280 Hospital Dr NW, Calgary, AB, Canada
[5]Department of Cardiac Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
[6]Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada

Corresponding Author:
Joon Lee, PhD
Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Abstract

Background: Coronary revascularization decision-making for patients with coronary artery disease (CAD) can be complex and challenging. Artificial intelligence (AI) has the potential to improve this decision-making by bringing data-driven insights to the point of care.

Objective: We aimed to elicit, collect, and analyze various stakeholders' perceived potential and challenges related to developing, implementing, and adopting AI-based CAD treatment decision support systems.

Methods: A facilitated small-group discussion method, known as a World Café, was conducted with general cardiologists, interventional cardiologists, cardiac surgeons, patients, caregivers, health system administrators, and industry representatives. One-on-one interviews were conducted for participants who could not attend the World Café. Perceived potential and challenges of AI-based CAD treatment decision support systems were solicited by asking participants three broad questions: (1) What is most challenging about revascularization decision-making? (2) How could an AI tool be integrated into the existing clinical workflow? (3) What are the critical components that need to be considered when developing the AI tool? Thematic analysis was performed to identify themes from the data.

Results: Nine participants completed the World Café, and 3 participants completed the one-on-one interviews. Five main themes emerged: (1) evidence-based care, (2) workload and resources, (3) data requirements (subthemes: patient-centered approach, evidence-based AI, and data integration), (4) tool characteristics (subthemes: end user built; generation and presentation of decision support information; user-friendliness and accessibility; and system logic, reasoning, and data privacy), and (5) incorporation into clinical workflow (subthemes: AI as an opportunity to improve care and knowledge translation).

Conclusions: While health care providers aim to provide evidence-based care, CAD treatment decision-making can often be subjective due to the limited applicability of clinical practice guidelines and randomized controlled trial evidence to individual patients. AI-based clinical decision support systems may be an effective solution if the development and implementation focus on the issues identified by end users in this study (patient preference, data privacy, integration with clinical information systems, transparency, and usability).

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KEYWORDS

coronary artery disease; clinical decision support; artificial intelligence; technology adoption; implementation science; stakeholder engagement

Introduction

Coronary artery disease (CAD) is characterized by reduced blood flow to the heart muscles caused by plaques in the coronary arteries. The gold standard diagnostic procedure for CAD is coronary angiography performed in cardiac catheterization laboratories, using radiocontrast agents and x-rays to diagnose the disease. Typically, the treatment decision involves determining whether the problematic coronary arteries need to be revascularized via either percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery,

or whether the most appropriate treatment is medical therapy only.

While clinical practice guidelines based on randomized controlled trials exist [1], coronary revascularization decision-making can be complicated by complex CAD (eg, multivessel disease), challenging coronary anatomies, comorbidities, unique patient characteristics, and patient preferences. Although multidisciplinary Heart Team approaches, where diverse specialists, including general cardiologists, interventional cardiologists, and cardiac surgeons, discuss the patient case and formulate the best treatment as a group, are recommended for revascularization decision-making for complex CAD [2,3], they are neither standardized nor evidence-based, making it difficult to operationalize complex treatment decision-making systematically.

Artificial intelligence (AI) has the potential to support coronary revascularization decision-making via data-driven insights. By leveraging patterns and relationships learned from a large amount of patient data, AI models can generate and present personalized decision support insights at the point of care. However, even if AI models with good performance are available for deployment, their technical and operational implementation in real-world clinical environments remains challenging and requires adoption from a variety of stakeholders, including patients, clinicians, health system administrators, health care payors, researchers, and developers [4]. Understanding the barriers and enablers to adopting AI-based clinical decision support systems (CDSS) is critical to developing and implementing such systems in clinical practice.

This study aimed to understand the perceptions of how an AI-based CDSS can facilitate CAD treatment decision-making.

Methods

Study Design and Setting

A World Café [5] was used to elicit and collect stakeholder perceptions about the use of an AI-based CDSS for CAD treatment decision-making. A World Café is a formal, semistructured method that engages diverse stakeholders through multiple rounds of small group discussions, each guided by a targeted question. It is designed to create an open, café-style atmosphere that encourages equitable participation and the flow of ideas across groups. This method enables intimate discussions among participants with varied perspectives, supporting the identification of themes relevant to a topic.

This study intended to complete a single World Café; however, some of our key end users (clinician participants) were unable to attend the World Café due to unexpected urgent patient cases. To ensure that these participant perspectives were captured in the dataset, 3 additional one-on-one interviews were conducted at a later date using the same semistructured protocol and targeted questions used in the World Café.

The World Café and interviews took place in Alberta, Canada, from May 2, 2022, to July 18, 2022, using the videoconferencing and online meeting platform, Zoom (Zoom Communications). Only participants and researchers were present during the meetings and interviews.

Participants and Recruitment

Study participants were recruited in Alberta and included: (1) clinicians involved in the care of patients with CAD including general cardiologists, interventional cardiologists, and cardiac surgeons; (2) health system administrators; (3) private-sector representatives from the cardiovascular information system industry; and (4) patients and caregivers (individuals aged 18 y and older with CAD, or caregivers supporting individuals with CAD).

All clinician participants were practicing physicians within Alberta Health Services (AHS), which is one of the largest fully integrated provincial health systems in North America. AHS oversees centralized delivery of acute care, emergency medical services, diagnostics, and many community-based programs for over 4.4 million Albertans. Although Alberta operates within Canada's universal, publicly funded health care system, its structure differs from many jurisdictions in Canada and abroad by unifying services under a single provincial authority rather than regionally or privately administered systems [6].

Participants were identified using purposive sampling to maximize variation in backgrounds and sex differences. Potential participants (World Café participants [WCPs] and one-on-one interview participants [OIPs]) were recruited using our research network and invited to participate via email. Once potential participants indicated an interest, the consent script was sent to them via email. They were provided with multiple opportunities to ask questions before completing the oral consent process. The consenting process occurred before the World Café and one-on-one interviews.

Data Collection

Consistent with the World Café methodology [7], data were collected through facilitated discussion on broad questions. Three questions were posed to both the WCPs and OIPs sequentially: (1) What is most challenging about revascularization decision-making? (2) How could an AI tool be integrated into the existing clinical workflow? (3) What are the critical components of the AI tool that need to be considered when developing the tool?

A facilitator guided the discussion and used prompts to generate discussion for each question. A note-taker collected field notes to document the context of the discussion (eg, the physical environment and individuals' nonverbal communication) and captured a summary of the discussion, which was shared with the participants at the end of the session (member checking). The World Café session and interviews were digitally recorded and transcribed verbatim, and the field notes were incorporated into the transcripts for analysis.

Reflexivity

The World Café and interviews were conducted by trained, experienced male and female facilitators who had formal graduate-level and experiential training in qualitative methodology and interview facilitation. Several members of the research team, including the facilitators and principal

investigators, had pre-existing professional and nonprofessional relationships with some participants, which may have influenced rapport and data interpretation. One principal investigator was a family member of a patient with CAD who had recently been diagnosed and had an urgent CABG. During the analysis phase, these pre-existing relationships and researchers' personal backgrounds were explicitly discussed during team meetings to reflect on how personal experiences, disciplinary backgrounds, and expectations may shape data interpretation and the construction of final themes.

Data Analysis

Transcripts from both the World Café and one-on-one interviews were uploaded, managed, and analyzed using NVivo (version 12.0, Lumivero). The Clarke and Braun [8] approach to thematic analysis was used to analyze the data. An inductive approach was used to identify codes and themes from the data. A first analyst familiarized themselves with the data and identified and established codes in a coding book as a reference. A second independent analyst then familiarized themselves with the data and reviewed the preliminary codes identified by the first analyst, revising and adding new codes while interpreting the data as a circular process that moved back and forth between smaller parts of the transcript and the whole text. This iterative coding process was applied as new themes emerged, and the transcripts were reread to verify that the codes and themes were not missed. These coding "nodes" were discussed among the research team and then consolidated into themes [8]. Coding discrepancies between analysts were addressed through discussion and joint review of the relevant transcript segments. Consensus was achieved through iterative comparison of interpretations, and any disagreements were resolved collaboratively to ensure consistent application of codes across the dataset.

In contrast to the group dynamic characteristic of the World Café, individual interviews may elicit more detailed and individualized reflections. To reconcile these methodological differences and enable direct comparison between formats, all transcripts were coded using the same unified coding framework. Codes and themes were examined for convergence and divergence, and only themes supported by patterns across both data sources were used in the final analysis. Although the one-on-one interviews were conducted following the World Café, the interview guide was not refined or modified based on World Café findings, and the same semistructured protocol was used across formats.

Trustworthiness

Various strategies were used to ensure the trustworthiness of the findings [9]. The transcripts were reviewed by the World Café and interview facilitators for accuracy before analysis. We used member checking at the end of the World Café and each interview by summarizing the discussion and asking participants if we accurately captured the discussion. Regular peer debriefing and discussion took place between members of the research team about the representation of this study's population, recruitment, data collection strategies, and data analysis, from the data coding process to the emerging themes, to enhance the accuracy of the results. The results were reviewed and refined by all authors, some of whom were participants.

Ethical Considerations

The University of Calgary Conjoint Health Research Ethics Board approved this study (REB20-1879). Before participation, explicit oral informed consent was sought and obtained from all study participants. The privacy and confidentiality of participants' data and identity were maintained by following the approved research data security and privacy protocol. Participants were not compensated. Additionally, this paper follows the COREQ (Consolidated Criteria for Reporting Qualitative Research) guideline (Checklist 1) [10].

Results

Overview

The World Café was conducted on May 2, 2022, and the interviews were conducted between June 15 and July 18, 2022. The World Café lasted about 120 minutes, and each interview ranged from 45 to 60 minutes. The participants (9 male; 3 female) were cardiologists (n=4), interventional cardiologists (n=2), cardiac surgeons (n=2), health system administrators (n=1), patients and caregivers (n=2), and an industry representative (n=1). Clinician participants (n=8) included early-career (n=3), middle-career (n=4), and senior professionals (n=1).

Five overarching themes emerged from the data: (1) evidence-based care, (2) workload and resources, (3) data requirements (subthemes: patient-centered approach, evidence-based AI, and data integration), (4) tool characteristics (subthemes: end user built; generation and presentation of decision support information; user-friendliness and accessibility; and system logic, reasoning, and data privacy), and (5) AI incorporation into clinical workflow (subthemes: AI as an opportunity to improve care and knowledge translation). Each theme is described in detail in the ensuing sections, with example quotes tabulated in Tables 1-5 for each theme. Quotations are identified by stakeholder group and by data collection source (ie, WCPs or OIPs).

Table . Example quotes related to evidence-based care (theme 1).

Description	Example quotes
The importance of evidence-based clinical practice.	• "We need more evidence when the areas we do have evidence still aren't standardized… Could more evidence help standardize things? And I do want to say that there are areas, certainly, that we need more evidence, but just like the counterbalance, there is, there are areas where we have evidence, and it still hasn't standardized practice." [OIP #1, surgeon] • "It certainly does. And I think it would for everybody. Everybody should be thinking of the guidelines, but it's kind of a starting point because it's often the nuances, or there's the other clinical variables that aren't in the classic guidelines that are important considerations." [OIP #3, interventionalist] • "It can be challenging identifying which patients you're going to want to proceed with revascularization versus proceeding with medical therapy… it does become somewhat knee-jerk that a person has in anginal symptoms or they have a non-invasive test that's suggestive of ischemia, and automatically they get sent to the cath lab with the thought that they're going to be revascularized. Now, the existing literature and the existing guidelines don't actually support that… it can be challenging…" [OIP #2, interventionalist]
Uniform and standardized decision-making between clinicians: different priorities based on their values & success rates (PCI[a] vs CABG[b]).	• "I think most decisions for revascularization are made ad hoc, on the spot, and I think that's reasonable for most of the time, but it really is the setup for a practitioner dependent practice… I think all of us see variation in practice, and I think all of us see that there's areas that aren't standardized… It would be nice if things were standardized, it simplifies things and allows everyone to ensure that we're aligned or at least the expectations are clear." [OIP #1, surgeon] • "I think there is variation in practice. But, say, between different surgeons, there's definitely variability. But, ultimately, say, if it's in the middle of the night, then it's basically what my preference or opinion is, I guess, at that point. What my colleagues might do might be different, but it doesn't really affect my decision process at that point." [OIP #3, interventionalist]

[a]PCI: percutaneous coronary intervention.

[b]CABG: coronary artery bypass grafting.

Table . Example quotes related to workload and resources (theme 2).

Description	Example quotes
The impact of decision-making process due to workload and physician burnout. Lack of time to explore and discuss patient information due to high volume of work.	• "When I have been burnt out, of course that impacts my practice, of course that impacts my decision making. I imagine that each of these... I think there's a very high resiliency rate within each of these groups, and I think, a lot of self-awareness to monitor burnout. It's impossible for me to quantify the impact, I'd just be speculative, but I think that all of us have to be mindful of that impact in decision making." [OIP #1, surgeon] • "When we're burnt out and we're overloaded sometimes, there's a tendency towards the path that's going to give us a more definitive answer more quickly." [OIP #2, interventionalist] • "The other considerations are the timing of revascularization. Is there active ischemia at the time? Is it an emergency that needs to be done right away? Or is it something that can wait until something else is optimized, either antiplatelet strategies or anticoagulation or other patient variables? Clinical status? Timing on like ... Is it emergency or not? Or is it urgent? Or is it elective?" [OIP #3, interventionalist] • "I was thinking about time as being one of the biggest issues for me and also acuity. So, I find that you have more time to weigh those risks and benefits and do your own cost-benefit analysis in the more stable scenario. But, in the acute phase, that time to do that goes at the side of trying to get the intervention going and the case started… It should be standardized for all patients, regardless of the presentation. But in my own individual experience, I find that time is really an issue, and it depends on the urgency of the scenario." [WCP #6, cardiologist] • "One is synthesizing all of the data that comes in. So, whether it's the anatomy, the patient comorbidities presentation, and what everyone's perspective on feasibility of getting a good result, whether it's by angioplasty or bypass surgery. So, I think it's putting everything together… you're trying to get through all of these patients, being comfortable that you've gathered all the relevant data to make the right decision is quite difficult…" [WCP #5, interventionalist] • "We might get a mailing list the day before…, you might spend a little bit of time in the evening reviewing the angiogram films. And the next day they might only spend five minutes on a patient… So, you're trying to get through all of these patients, being comfortable that you've gathered all the relevant data to make the right decision is quite difficult, given the fact that a lot of times you have never met the patient… So, certainly that you can get time pressure and not discuss patients thoroughly enough." [WCP #5, interventionalist]

Description	Example quotes
Considering cost of care (PCI[a] vs CABG[b]) vs value of care.	• "Back to our patient's perspective, I think we do look at risks of the non-discussed pieces of it when we make our decisions with patients. So, obviously as clinicians, we talk about death or MI stroke, but there are a lot of other things that go into the decision-making like time in hospital, recovery status… we would want to discuss with the patient to make sure they understand. So, at 10 years you may have a slightly better risk of death, but in the meantime, you've got a recovery period that would be hard to manage. So, cost may be less so than the patient discussions, but as the healthcare system tightens, cost will become more and more important in the future." [WCP #4, interventionalist] • "We do talk about value, defining value as outcome over cost. So, it's not that the cost doesn't matter. And I think the system is willing to pay the cost as long as the outcome achieved from that cost makes sense. So, I think in our system, we would talk more about value" [WCP #3, administrator] • "When you're pressed for beds if the results are close enough between bypass and PCI, does your resource limitation push you more towards one or the other?... And so, certainly we did have those discussion... you just deal with one or the other either with surgery or angioplasty, then the fact that five years down the road they might be back for a second procedure. But you just try to keep the resources freed up in the system, whether it's time or money or beds." [WCP #5, interventionalist] • "Everything that we're talking about is incredibly expensive… I would think, in the scheme of budget for this, this would be relatively small, and anything that makes things more efficient probably will save money more than whatever it costs." [OIP #3, interventionalist]
Considering resources (e.g., cost, investment), and willingness to invest and implement the AI[c] tool.	• "If we want these tools to be adopted, they have to be purchased… a lot of the times we are making those arguments as a return on investment, essentially saying that if they pay this much for this software, it will save them time, it will lead to improvements in quality for value-based reimbursement or these sorts of things… So, I do think there's the clinical perspective in terms of, directly with the patient and beds and everything. And then there's also the administrative perspective around time and resources and whether they are willing to put in the effort to implement this in practice in order to actually see the results. I think it's an important consideration, even this early on in the process." [WCP #9, industry partner]

[a]PCI: percutaneous coronary intervention.

[b]CABG: coronary artery bypass grafting.

[c]AI: artificial intelligence.

Table . Example quotes related to data requirements (theme 3).

Subtheme and description	Example quotes
Patient-centered approach	
Complex patients with multimorbidity	• "I think one of the bigger challenges that's happening more and more now is our patients are older. They're more complex. They have more comorbidities. The risks of everything are higher. Their disease is getting more complex. There are sometimes not reasonable PCI options… And so, you are not infrequently trying to treat a patient who has complex multi-vessel disease, who is a poor candidate for surgical revascularization, or a very high-risk candidate for surgical revascularization, who is equally a high-risk candidate for percutaneous revascularization." [OIP #2, interventionalist] • "There are the anatomic things like the coronary anatomy. There are the other comorbidities are a big role... I guess the factors that relate to their potential benefits. Are they potentially receiving a symptom or a survival benefit? And then what are their risk factors?... Because it's always a balance of benefit versus risk." [OIP #3, interventionalist]
Understanding patient expectations and preferences	• "If you give the patients a choice, they'll all pick PCI. And PCI is great for a lot of them, but it's not right for everybody. And that's where that education has to come in, and then they can make their decision." [OIP #3, interventionalist] • "I chose a course of treatment that had the lowest chance of incontinence over the others. So, it's weird, I'm not sure patients really think exactly like clinicians in this situation. I was opting for quality of life over other factors, and it served me well… But those would be important to me." [WCP #2, patient] • "Nobody wants to have surgery, but people are interested in their long-term outcomes. They don't want repeated heart attacks… the second one is also understanding what the patient's preference is and how much of that weighs on the decision. So, if it's 60% in favor of bypass and 40% in favor of angioplasty from a clinician standpoint, but what if the patient feels very strongly that they want to have angioplasty and you would need to tell them various substantial risk… or substantial benefit of bypass surgery. So, understanding what the patient preference is based upon what would happen if they were presented with the data." [OIP #3, interventionalist]
Evidence-based AI[a]	
Representation of diverse patients in the data used to develop the model	• "I think that making sure that you want the largest pool of data possible, but making sure that data represents a wide cross-section of demographics, and that you're not trying to ultimately end up generalizing it to populations that haven't been involved in generating the model. That's really important." [OIP #2, interventionalist]

Subtheme and description	Example quotes
Complementing and improving upon the existing clinical practice and evidence	• "I would love to see both strengths of AI put to work… there are a lot of things we know, and honestly, I think we're maybe not that bad at this, but it would be great to see if AI comes up with information or predictors that we didn't know, which would be the real beauty of this model." [WCP #4, interventionalist] • "You're going to do the standard stuff that we all think about, age, diabetes, hypertension, dyslipidemia, frailty, down the list, but the black box approach where you basically ask the computer to tell us what's in the model, I think would be very interesting and potentially the validation moving forward would be very exciting." [WCP #4, interventionalist] • "AI-based technologies is to be able to give us information that some standard studies don't give us… It may be possible that by applying more complex machine learning, you might actually be able to find an answer that we haven't been able to find so far in our existing evidence. So, I think that you have to be aware of what the existing evidence is, but if you find a different answer using new technology, well, I don't think you adopt it wholeheartedly and ignore what we have figured out already, but I think you need to integrate that in." [IP #2, interventionalist] • "The evidence is coming typically from trials that have a lot of nuances to them. Applying guidelines or a specific trial to a specific patient can be real challenge because they don't always directly apply. That's where the clinical judgment and oversight and gestalt, I think, play a role and is trying to say, well, the evidence that we have ... How well does it apply to this patient? And that's where they don't always directly apply." [IP #3, interventionalist]
Data integration	

Subtheme and description	Example quotes
Ethics, privacy, and confidentiality	• "I think that from a patient privacy perspective, that's going to be a really important thing to have a really good grasp on the ethics before that happens, because machine learning can be used to generate all sorts of models for all sorts of risks. And whether those things in the future are going to... Say, my EMR is plugged into machine learning, and it's able to automatically generate a detailed risk for, for cardiac death over the next 10 years, is that going to affect my patient's ability to get insurance? So, there needs to be a consent aspect in there for sure." [OIP #2, interventionalist] • "Obviously, confidentiality and privacy are massive when it comes to medical information. It certainly would have to be secure." [OIP #3, interventionalist]
Integration with the EMR[b].	• "Something that can be incorporated directly into the EMR, so you can just say, 'Oh, well, I want to calculate the whatever score for this patient,' so you can click on it and it can pull in whatever data that it needs. I think that the simpler you make it, the more likely you're going to see uptake." [OIP #2, interventionalist] • "When we talk about how this could be integrated in the existing workflow, I think we have to consider Connect Care as part of this…, Healthcare institutions have put significant investment into the implementation of electronic medical record systems… which opens up an opportunity for us, if we can integrate with those systems and make it fairly seamless experience." [WCP #9, industry partner]
Integration of comprehensive data elements	• "The critical components one is, as everyone's mentioned, is the APPROACH CARAT diagram and all the different components of it, whether it's the anatomy or the jeopardy score, lesion characteristics, previous stents, the comorbidities that are the classic comorbidities, whether it's renal failure or diabetes, left ventricular dysfunction, patient age, BMI, whether it's super high or super low. The ones that are harder to capture, I think, beforehand… other one is frailty… it's something that's really hard to capture, but I think the frailty piece is really important." [WCP #5, interventionalist]

[a]AI: artificial intelligence.

[b]EMR: electronic medical record.

Table . Example quotes related to tool characteristics (theme 4).

Subtheme and description	Example quotes
End user built	
Engaging end users throughout the development and implementation processes	• "When developing something that is intended to be used as a tool for someone, that person is the stakeholder and they should be engaged and heavily involved in all aspects of the development, training, implementation, and subsequent follow up and iterations. It's hard for me to imagine a step a clinician shouldn't be involved…" [OIP #1, surgeon] • "Physicians and patients would be the end-users for those models that are generated. So, matter of asking what more information the end-users actually need." [OIP #2, interventionalist] • "I think something like this could be complicated enough that, without a physician or surgeon or an interventionist… clinical feedback would be important in order to tailor it to what the clinicians need to see." [OIP #3, interventionalist] • "What data are available, what data are easy to get, which ones would require the physician to do extra steps? And maybe prioritizing ones that are accessible or prevalent versus ones that might require extra work and therefore prevent adoption. So, I think that's, figuring out what we can do with Connect Care or very similar systems is important here." [WCP #9, industry partner]
Engaging patients throughout and capturing patients' voices	• "If the AI tool was developed with the patient-centered focus with patient researchers actually involved in developing the tool. And it might provide a communication roadmap for some of your colleagues… and coach them in both the language and what the patient is actually looking from their clinician to provide in the way of information, so that the discussion is actually much more robust." [WCP #4, interventionalist] • "Asking the patients how they're doing, their mobility, quality of life, frailty, we know from other research that's been done that PROMs are quite predictive of outcomes, and they come out, when you run the AI with all the different features, PROMs often come out as contributing to that final prediction." [WCP #9, industry partner]
Family physicians as potential end users	• "Is that possible that it could be starting with a family physician instead of specialist cardiologist? I don't know where else it potentially could start. That way, it's an easier conversation for the family physician to have with the patient." [WCP #1, patient] • "I would fully agree with that (integrating AI in PHC)… The only thing is that some family physicians are overwhelmed by the breadth of knowledge they need to know about your diabetes, your heart's arteries, your medical therapy, and they really look to the cardiologists and the surgeons, where appropriate… the intricacies of decision-making." [WCP #4, interventionalist]
Generation and presentation of decision support information	

Subtheme and description	Example quotes
Need for scores as a way to summarize granular information for easy interpretability and communication	• "Making decisions about revascularization would be the development of more complex risk-prediction models… through machine learning, there would be the ability to generate a more sophisticated model for helping to estimate risk. And again, you're not going to ultimately have an AI making the decision about whether or not you're going to proceed with revascularization, but to be able to go into an interaction with a patient and be able to give them more granular information about what their risks are, that could be helpful." [OIP #2, interventionalist] • "I think it'll be determining what all risk factors need to go into this tool (AI) and what weight are you going to give to each risk factor and does presentation…, How do you give mobility a number, and comorbidities… but some of these risk factors are going to be a little bit difficult to try to quantify." [WCP #7, cardiologist] • "My first thought was on the APPROACH diagram, there's a jeopardy score and the jeopardy score is used, to a degree, to guide our revascularization decisions. It would almost make sense that this prediction tool puts some sort of either score or recommendation was my first thought." [WCP #4, interventionalist] • "Overlay how AI has actually helped populate the data in the various columns of chart data. That, to me, I think would be perhaps a good marriage of data… on the various success factors that you're striving towards by each treatment option. And then that would provide a good discussion basis for the physician and the patient and their family… if you stack them all together, you would have what would logically be the optimal treatment plan, just because the higher score and whatever it would add up, it would be ably demonstrated… it's easy to explain at the bedside, I think would be a big benefit rather than talking in clinical jargon." [WCP #2, patient]
Importance of data quantity and quality	• "I think that's how you would harness the true power of AI and machine learning. As much data as you could get in, I think that's how you could really…harness the power of this method." [OIP #1, surgeon] • "In order to get high quality information out of any machine learning system, it's entirely based on the volume of data you're able to provide it… I think the broader the data you're able to plug into a machine learning system, the better, because one of the big issues that I'm aware of with machine learning is just the impact of the bias of the information that you put in." [OIP #2, interventionalist] • "As a surgical resident who's doing a lot of research with clinical data, being able to extract that data efficiently would be key... I think we've struggled a little bit with the comprehensiveness of data and the efficiency of it." [WCP #8, surgeon]
User-friendliness and accessibility	

Subtheme and description	Example quotes
Importance of an easy-to-use, intuitive user interface and automation.	• "User interface are really important… I'm not still clear how to evaluate an algorithm… I don't have a good sense as to how to actually perform due diligence on a product or algorithm. And in the absence of the ability to do that, it's very difficult to know how much weight you would put on the response from an algorithm. So, I think that a bit of knowledge translation, or trying to validate an AI model in a manner that's understandable to clinicians is critical." [OIP #1, surgeon] • "I think a lot of what it comes down to is really just convenience, and speed, and ease of use… certainly, automated measurements, automated tracing of the left ventricle and calculation of, for example, a 3D left ventricular ejection fraction. These are areas that accuracy is improved… so I think usability becomes really, really important, particularly at a time when technology has in certain areas of medicine, led to a lot of added complexity with an unclear value proposition. And so I think that really providing an easy to use interface and easily digestible material is our answers, is really helpful." [OIP #1, surgeon] • "When I think about kind of AI tools, they're going to be things that physicians reach for when they want them… you're going to be reaching for every patient… for something as simple as like MDCalc to put in someone's Framingham risk score. So, you would want something that is easily accessible, something that is smartphone-based, or even something that can be incorporated directly into the EMR, so you can just say, 'Oh, well, I want to calculate the whatever score for this patient,' so you can click on it and it can pull in whatever data that it needs. I think that the simpler you make it, the more likely you're going to see uptake" [OIP #2, interventionalist] • "In general, surgeons aren't very technically or at least computer savvy. The simpler, the better, for sure. Because not too many surgeons will commit to a lot of learning for something like that, computer work, or have a lot of time to commit to it. Actually, it is quite important that it's something that's intuitive or easy to work with. Being user friendly, for sure, is important. Being accessible. Something that we can use remotely is important because that's when, I think, it'd be pretty useful. And then just current, I guess. Data or information that's real time." [OIP #3, interventionalist]
System logic, reasoning, and data privacy	

Subtheme and description	Example quotes
Transparency and accountability	• "I think that there does need to be some sort of transparency in how the tool is working… For decisions, an overall gestalt is used a lot... is this person a candidate for this? Is this person ... Would it be ... Would they do well with this? And so, the gestalt is an important part. With artificial intelligence, I don't know if gestalt is a part of it. That would be a challenge, I would think. Having some transparency, though, in how the algorithms or whatever it is that are making recommendations or decisions or things like that ... A transparency so that people can see how this tool comes to these conclusions." [OIP #3, interventionalist] • "I think the only thing that we have to be fully aware of and cognizant of… from a medical legal point of view, having a statement that X is the desired outcome without all of the qualifying pieces, if the Y procedure is done and the patient has a bad outcome, which may or may not be predictable, usually not predictable, it may lead to a medical legal nightmare… So, we just have to be cognizant of that and decide where this decision tool lands in terms of its availability and to who." [WCP #4, interventionalist]
Living documents and real-time feedback	• "From a workflow perspective, AI really needs to be almost synchronous with the test itself and providing real time feedback or near time feedback to be really clinically useful." [OIP #1, surgeon] • "I think it needs to be part of the living document and available at the time we do the angiogram to be most valuable. I would say that 90% of the time the revascularized option, which is anatomically best for the patient and comorbidly best for the patient, taking their patient profile is obvious 90% of the time. It's either a straightforward stent, we deal with it, move on. It's either ongoing medical therapy, we optimize that and move on, or it's a clear-cut patient that should be moved forward for bypass..." [WCP #4, interventionalist] • "Being user friendly, for sure, is important. Being accessible. Something that we can use remotely is important because that's when, I think, it'd be pretty useful. And then just current, I guess. Data or information that's real time." [OIP #3, interventionalist]
Data privacy and confidentiality	• "I think that from a patient privacy perspective, that's going to be a really important thing to have a really good grasp on the ethics before that happens, because machine learning can be used to generate all sorts of models for all sorts of risks. And whether those things in the future are going to... Say, my EMR is plugged into machine learning, and it's able to automatically generate a detailed risk for, for cardiac death over the next 10 years, is that going to affect my patient's ability to get insurance? So, there needs to be a consent aspect in there for sure." [OIP #2, interventionalist] • "Obviously, confidentiality and privacy are massive when it comes to medical information. It certainly would have to be secure." [OIP #3, interventionalist]

Table . Example quotes related to AI[a] incorporation into clinical workflow (theme 5).

Subtheme and description	Example quotes
AI as an opportunity to improve care	
Considering AI as an opportunity in the existing clinical workflow.	• "For sure, there's many opportunities… I think risk stratifying the lesion or identifying high risk lesion characteristics… identifying a culprit lesion, the predicted success of revascularization or subsequent stent complications. In another way of saying that would be determining what method of revascularization. I think those are all-important real-time feedback that an operator could receive… It would be really nice to pair that with non-invasive cardiac diagnostics, which would include echo, MRIs… Those are all areas that I think will be very, very interesting." [OIP #1, surgeon] • "I think that having some artificial intelligence to make suggestions is helpful. And like I said, to provide supporting information like risk profiles and stuff like that, but I think that ultimately, the conversation between the physician and the patient is always going to be a pretty big driving force for what path we go down." [OIP #2, interventionalist]
Knowledge translation	
The importance of knowledge translation among end users.	• "One of the challenges for us in knowledge translation here, trying to translate something that's extremely technical. And in fact, we're front-runners in the industry into something that's useful for both patients and caregivers. So, I don't think it's a game stopper, it's just something we have to be aware of and be knowledgeable about." [WCP #2, patient] • "You guys do such important work, really the patient should be knowing this stuff, like what's going on with their body at a doctor's visit, at a family physician. So, I think if this information's being shared." [WCP #1, patient] • "I don't have a good sense as to how to actually perform due diligence on a product or algorithm. And in the absence of the ability to do that, it's very difficult to know how much weight you would put on the response from an algorithm. So, I think that a bit of knowledge translation, or trying to validate an AI model in a manner that's understandable to clinicians is critical." [OIP #1, surgeon]

[a]AI: artificial intelligence.

Theme 1: Evidence-Based Care

Overview

All participants emphasized the importance of evidence-based guidelines to minimize variation in care and unify the Heart Team that makes treatment decisions for patients with CAD. The clinician participants explained that their clinical practice was based on their clinical knowledge and experiences, as well as existing medical evidence (including clinical practice guidelines). They stated that although there are some clinical guidelines, many are of low quality and endorsed the need for better guidelines. They also noted that while evidence and experience are foundational, CAD treatment decisions tend to be biased by the opinion of a single clinician and that each clinician has different priorities and experiences.

The clinician and health system administrator participants noted that, in addition to the evidence informing treatment decisions, factors such as the urgency of the case, provider workload, patient preferences, and time of day also influence treatment decisions. This led to comments related to timely and complete patient data (medical history and comorbidities), which is discussed in greater detail under theme 3 (data requirements).

Contrasting Perspectives

While all participants endorsed the importance of evidence-based care, clinicians primarily framed the issue as a challenge of guideline clarity and individual bias. In contrast, it was suggested that administrators may instead focus on the broader system-level influences that contribute to variability in revascularization decisions (explored in further detail in theme 2).

Theme 2: Workload and Resources

Overview

Most clinician participants stressed that time is a significant issue for making treatment decisions around revascularization. They stated that due to the high volume of cases, there is minimal time available to comprehensively review patient information and discuss the patient. This challenge, combined with the urgency required to revascularize patients with CAD, makes it difficult to fully assess all the risks and benefits of each treatment approach and consider patient preferences. All participants endorsed the challenges related to the current strain on the health care system and clinicians.

There was also discussion about physician burnout due to persistently high workloads. Clinician participants expressed that when they are overloaded and burnt out, there is a chance they will make a treatment decision more quickly, without fully considering all factors.

Participants suggested that having access to all relevant information for making treatment decisions in one, easily accessible spot would facilitate decision-making, which might help to improve patient outcomes and resource use. This is further discussed in theme 5 (AI incorporation into clinical workflow). Further noted by the patient participants was the importance of also considering patient preferences, which is discussed under themes 3 - 5 below.

Furthermore, there was some discussion about the cost of care vs the value of care (outcomes). Most of the clinician participants emphasized that they valued results over cost when making decisions about revascularization. However, they did suggest that long-term resource consumption should be considered before making treatment decisions, provided the evidence for effectiveness is comparable (eg, CABG vs percutaneous coronary intervention). The health care system administrator also discussed the issue of the value of care, especially in the current context of a resource-strained health care system.

Considerations of the cost and resources of implementing a new AI system into clinical workflow were discussed. It was noted that adopting AI in the clinical workflow is expensive and needs investment (time and money). However, participants suggested that the investment in AI may be relatively small if it eventually saves time and improves the quality of care. The industry participant expressed the importance of engaging and understanding health system administrators' willingness to invest (time and resources) and implement the AI technology into practice from the early stages of the development process.

Contrasting Perspectives

Although all participants acknowledged the strain created by limited time and resources, clinicians emphasized how high workload, case urgency, and burnout directly affect their ability to thoroughly review patient information and weigh treatment options. Patients highlighted the importance of ensuring that their preferences are considered despite time constraints, whereas administrative concerns remained focused on the value of care despite resource limitations. From an industry perspective, attention was drawn to the investment required to implement AI tools and the willingness of administrators to support such adoption.

Theme 3: Data Requirements

Patient-Centered Approach

All participants agreed that patient characteristics were the most critical factor in making a revascularization decision. The clinician participants indicated that making decisions around revascularization is particularly difficult for complex patients with multimorbidity.

Understanding and considering patient preference was another key factor in making revascularization decisions. The clinician participants indicated that giving patients a choice or following their preferences can be challenging, because the patient's preference can sometimes be highly divergent from the evidence-based recommendation.

All participants agreed that respecting patient preference is important, and a conversation between the clinician and the patient, including hearing the patient's perspective while educating patients about the risks and benefits of each intervention, should guide the decision-making process. It was noted that an AI-based CDSS could facilitate this discussion.

Evidence-Based AI

Participants stated that AI-based tools are expected to be based on evidence. The clinician participants emphasized that integrating existing evidence is important. They were intrigued by data standardization that could help AI to address real and predictable risks efficiently and consistently.

In addition, the clinician participants wondered if AI-based recommendations would differ from the current evidence and how they would reconcile such discrepancies. Despite this concern, they also expressed their excitement toward practicing data-driven revascularization decision-making.

Data Integration

Participants voiced the importance of integrating patient data into AI-based CDSSs. Participants stated that AI tools integrated with the electronic medical record could facilitate the clinical use of large volumes of patient data more efficiently and precisely. All participant groups also stated that integrating all critical patient data, including a comprehensive list of risk factors (eg, patient history, comorbidities, anatomical presentation, and frailty), is essential for AI-based CDSSs. Given the size and comprehensiveness of the data involved, some participants raised concerns regarding ethics, privacy, and confidentiality.

Contrasting Perspectives

All participants emphasized both the importance and the challenges of incorporating patient perspectives into revascularization decision-making. Clinicians suggested that an integrated AI-based CDSS may facilitate clinician-patient discussions and enhance decision-making; however, they also raised concerns regarding patient confidentiality and the potential unintended consequences of risk profiling that may adversely affect patients.

Theme 4: Tool Characteristics

End User Built

All participants emphasized the importance of meaningfully involving all key end users when developing the tool. All participant groups stressed that end users should be involved not only in tool development but also in training, implementation, and evaluation. Furthermore, the patient and clinician participants noted that a patient-centered approach that captures patient voices and their perspectives about clinicians' use of AI-based tools would lead to effective communication between patients and care providers. Some participants identified family physicians as potential end users as well.

Generation and Presentation of Decision Support Information

Participants were interested in the possibility that AI-based CDSSs have the capacity to provide a comprehensive score or recommendation that takes into account patient characteristics to optimize treatment plans and have the ability to interact with patients and families. Summary risk scores were preferred for easy interpretability and communication. Conversely, participants expressed concerns about the validity of the CDSS and including a comprehensive list of potential risk factors. Comprehensive data that integrated patient medical history and comorbidities were perceived as core components for successful AI-based CDSSs.

User-Friendliness and Accessibility

A user-friendly interface and being accessible beyond a networked computer (eg, mobile access) would increase uptake. In addition, participants stated that the CDSS needs to be intuitive and integrated seamlessly within the existing clinical workflow. Technical support would improve the usability and implementation of a CDSS, which would also address the concern about resources and workload associated with the tool (discussed in theme 2). The clinician participants also stressed that revascularization decisions require a high-level summary of accurate information, which must be easy to navigate and access.

System Logic, Reasoning, and Data Privacy

Most of the clinician and patient participants focused on the importance of the transparency of the CDSS and knowing how the CDSS works and generates treatment recommendations, including its logic and limitations.

Some participants also expressed their concern about regulatory compliance, liability, and accountability of the CDSS before implementation can be considered. This concern was based on medical ethics and legal perspectives. However, some participants also felt that if data privacy standards could be met, there was excitement about leveraging the advantages of AI.

Similarly, another major concern expressed by many participants was data privacy, particularly whether the AI-based CDSS could maintain the required confidentiality and privacy of health information. They pointed out that CDSS developers should be aware of various regulatory requirements that protect health information privacy. The patient participants were worried that AI recommendations could have unintended consequences on other health-related issues.

Contrasting Perspectives

Although all stakeholder groups agreed that AI-based CDSSs should be user-friendly, accessible, and developed with meaningful end user involvement, clinicians emphasized medico-legal considerations and the desire for such tools to support real-time decision-making and seamlessly integrate into clinical workflow. In contrast, patients may be more likely to view such tools as a means to facilitate discussion with care providers rather than solely functioning as a real-time decision aid. Both clinicians and patients emphasized the importance of validity and transparency of an AI-based CDSS; however, similar to theme 3, concerns remain regarding patient data privacy.

Theme 5: AI Incorporation Into Clinical Workflow

AI as an Opportunity to Improve Care

Most participants perceived AI as an opportunity in the clinical workflow. They were quite positive and supportive about the development of AI-based CDSSs for revascularization decision-making. The clinician participants felt that AI would add support to their decision-making process, provided that recent scientific evidence is incorporated into the CDSS. Many participants mentioned that integration between the electronic medical record and AI, and end user engagement with both clinicians and patients, would be crucial to integration into the clinical workflow.

Knowledge Translation

Participants underlined knowledge translation as one of the core components required before integrating AI into the clinical workflow. For instance, the clinician participants were intrigued by how AI algorithms work, how comprehensive AI-based risk scores can be, as well as the system logic, reasoning, benefits, and limitations of the technology. However, many participants expressed that they still lacked knowledge about how AI works and suggested that continuous knowledge translation would be helpful.

Participants also noted that identifying end users is critical before integrating AI into the clinical workflow. For instance, a patient participant questioned whether AI-based CDSSs could be integrated into not only cardiac care but also primary care. The participant further expressed that integrating AI into primary care would facilitate conversations between patients and their primary care providers.

Contrasting Perspectives

While some clinicians emphasized the potential role of AI-based CDSSs as real-time supports within existing clinical workflows, others highlighted their value in supporting clinician-patient conversations across care settings. Differences in perspectives were most apparent in relation to knowledge translation, with clinicians emphasizing their desire for a deeper understanding of AI system functionality and validity, while other participants highlighted the importance of making AI-derived information simple and accessible to patients and primary care providers.

Discussion

Principal Results

This study provides an exploratory examination of AHS stakeholder perspectives on the use of an AI-based CDSS for CAD treatment strategy. Across stakeholder groups, participants emphasized that delivering evidence-based care when making coronary revascularization decisions for patients with CAD is often challenging due to conflicting or inadequate clinical practice guidelines. Although AI has the potential to improve the current state of CAD treatment decision-making, the need for timely access to comprehensive patient data through integration with hospital information systems, clinicians' heavy

workloads, data privacy concerns, and end users' desire for transparency regarding how the AI generated a particular recommendation may complicate the successful development, deployment, and adoption of AI-based CDSSs. The likelihood of successful adoption can be enhanced by incorporating scientific evidence and patient preference into decision support information, involving end users (both patients and clinicians) in the entirety of technology development, designing systems that are intuitive and easy to use, and presenting information in a succinct and easy-to-understand manner. In addition, this study's participants also raised the importance of systemic issues, including regulatory requirements, the need for resource commitments from health systems, and health care cost considerations.

Despite these challenges, the participants expressed excitement about AI's potential to improve CAD care. Many acknowledged that they had limited AI knowledge and wanted to be educated in an ongoing manner. They felt that although substantial investments may be required to develop, implement, and adopt AI-based CDSSs, the potential cost savings and improved patient outcomes will likely make it a worthwhile endeavor.

Contrasting Perspectives

Across themes, consistent patterns emerged in how different stakeholder groups framed the challenges and opportunities associated with AI-supported revascularization decision-making. Clinicians primarily focused on the practical realities of care delivery, emphasizing limitations in guideline clarity, time pressure, workload, and difficulties with synthesizing large amounts of data. Many described how an AI-based CDSS could help synthesize complex data, enhance clinical efficiency, and support real-time decision-making. Clinician concerns centered on liability and accountability of implementing AI-based tools, how to reconcile AI recommendations with clinical judgment, and emphasized the importance of patient data security and privacy. While clinicians often focus on mitigating long-term mortality and major adverse event risk, patients emphasized the importance of considering both short and long-term risks and benefits, valuing AI-based CDSS as a tool to help facilitate communication between clinicians and care providers. Industry perspectives highlighted the potential challenges surrounding an AI-based CDSS implementation, emphasizing the need for early alignment with administrative priorities, investment considerations, and demonstrable value to support adoption. Health system administrative perspectives, in contrast, tended to frame decision-making through a system-level lens, prioritizing standardization and value of care, viewing an AI-based CDSS as a short-term cost with potential long-term benefits and cost savings. Finally, differences were evident in expectations around knowledge translation, with clinicians seeking a deeper understanding of transparency, validation, and functionality of AI-based systems, while other participants emphasized the importance of making AI-derived information accessible to patients and primary care providers. Together, these contrasting perspectives highlight that the successful implementation of AI-based CDSSs requires not only technical accuracy but also careful alignment with the distinct priorities, responsibilities, and expectations of diverse stakeholder groups.

Comparison With Prior Work

The potential of AI in improving CAD or cardiovascular care at large has previously been discussed [11,12], and a number of machine learning models have been developed in this space for a variety of clinical use cases (eg, in other studies [13-17]). Although much of this research has focused on the technical aspects of development, rather than implementation and adoption [18], many of the themes that emerged from the World Café are echoed in the existing literature. Challenges introduced by the availability, quality, and standardization of data are consistently raised in discussions surrounding the use of AI in health care [19-21], and concerns about data privacy and security are also common [22,23]. Many studies investigating clinician uptake of AI-based CDSSs emphasize the importance of providing evidence-based decision support information [21,24-27], using development data that are reflective of the patient populations the AI is intended to support [28-30], and increasing the transparency of model reasoning as important facilitators to adoption [22-24,31]. These studies also underline the issues resulting from an absence of AI education in the current medical curricula and call for increased knowledge translation efforts to build trust and credibility with clinicians [24,32]. It is worth noting that several issues discussed by the participants, including time constraints and the need for intuitive and user-friendly applications, are pervasive issues in health care that are not necessarily unique to the adoption of AI-based tools [33,34]. Indeed, with a greater than 50% failure rate among many types of CDSS [35], the need for end user involvement in development has been highlighted as crucial to successful implementation [35,36].

While many of the issues identified in this study appear to be universal across health care, contextual idiosyncrasies remain. For example, the WCPs often stressed the importance of patient preference in CAD treatment decision-making and suggested that an AI-based CDSS may help facilitate patient discussions. In contrast, some prior studies have reported concerns about AI-based CDSSs negatively impacting the patient-clinician relationship, suggesting that using such systems could reduce the amount of time available for patient interaction or, in extreme cases, cut out contact altogether should clinical interactions be shifted to a digital format [22,25]. However, one of these studies interviewed only general practitioners [25], whose responsibilities are arguably more conducive to digitization than coronary revascularization decision-making. Similarly, other studies have discussed technical barriers beyond data requirements, including insufficient computing resources and inconsistent access to Wi-Fi, which are more pervasive in low-to-middle-income countries [28,37]. Thus, the importance of this work also lies in understanding the context within which the AI-based CDSS will be implemented, which is essential for successful adoption [38-41].

Finally, although AI-based clinical tools are increasingly being evaluated for their potential to enhance clinical decision-making and efficiency [42], their utility should be met with both optimism and caution. Recent evidence suggests that while AI-based systems can accurately perform specific clinical tasks and support information delivery, these capabilities may not necessarily translate into improved patient or system-level

outcomes [43,44]. Indeed, despite substantial investment and academic efforts, there remains limited prospective evidence demonstrating that AI-based tools have improved patient outcomes at scale [45]. Concerningly, among approved medical devices that use AI, clinical validation studies are inconsistently reported, and when reported, rarely include prospective and randomized evaluations [46,47]. Accordingly, while the technical performance of AI-based tools remains important, prospective randomized controlled trials are needed to demonstrate true clinical benefit. In parallel, future investigations should explicitly evaluate the fairness and equity of these tools and aim to determine whether such tools can alleviate clinician burden rather than add to cognitive or administrative loads [48].

We hope the diverse contextual factors described here can serve as a helpful foundation for the future development and implementation of CDSSs for CAD treatment decision-making.

Limitations

This study has several limitations. First, 3 clinician participants were unable to attend the World Café, and they were engaged in one-on-one interviews instead. Although efforts were made to engage these participants using comparable prompts and facilitation techniques, inherent differences between one-on-one and group-based World Café discussions may have influenced the data generated. As a result, some themes may reflect methodological differences despite efforts to reconcile findings across formats. Second, within our relatively small sample size, clinicians outnumbered the other stakeholder groups (8 vs 4), and their opinions may have dominated the discussions and results. For instance, some patient perspectives were articulated by clinicians rather than patients directly and may not necessarily represent the views or priorities of the patients themselves. Third, all participants were recruited in Alberta, limiting the generalizability of our findings to other jurisdictions. As the overall structure of AHS, including the clinical flow of patients and delivery of care, may not mirror that of other health care systems, some of the themes identified in the current investigation may be unique to this publicly funded and integrated health care system. Accordingly, while the themes and perspectives derived from this investigation provide valuable insight into the intricacies of implementing AI-based CDSS into practice, future work incorporating larger and more heterogeneous participant populations, balanced stakeholder representation, consistent data collection formats, and diverse health care system contexts may provide additional insights.

Conclusions

Various stakeholders, including patients and clinicians, believe that current coronary revascularization decision-making for patients with CAD is only partially evidence-based. AI-based CDSSs have the potential to improve this, leading to improved patient outcomes and health care cost savings. The successful development and implementation of such AI-based CDSSs hinges upon extensive end user involvement, data integration, data privacy protection, incorporation of patient preference, alignment with scientific evidence, and great usability. Integrating end user co-design and iterative usability testing may help support these priorities in future work.

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Authors' Contributions

KS designed and oversaw this study and wrote the manuscript. BB conducted this study, analyzed the data from the World Café and interviews, synthesized findings, and wrote the manuscript. CvR edited and revised the manuscript. BH and RW participated in the World Café and validated the main findings from this study. JL oversaw this study, provided resources, and prepared the manuscript. All authors proofread and approved the manuscript.

Conflicts of Interest

JL is a cofounder and major shareholder of Symbiotic AI, Inc. BH is a minor shareholder of Symbiotic AI, Inc. CvR is a paid independent contractor or consultant for Symbiotic AI, Inc. RW is an interventional cardiologist.

Checklist 1
COREQ checklist.
[PDF File, 432 KB - cardio_v10i1e81303_app1.pdf]

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Abbreviations

AHS: Alberta Health Services
AI: artificial intelligence
CABG: coronary artery bypass grafting

CAD: coronary artery disease
CDSS: clinical decision support system
COREQ: Consolidated Criteria for Reporting Qualitative Research
OIP: one-on-one interview participant
WCP: World Café participant

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Phone: (+1) 416-583-2040
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