

Final Project Work

Assessing the Development and the Performance of Digital Twin Technologies in the Healthcare Sector

Research Question:

How are Digital Twins used in different clinical specialties to support medical decision-making?

Group N

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Abstract

Digital Twin (DT) technologies are transforming healthcare by enabling real-time, data-driven models that simulate patient-specific physiology and support clinical decision-making. This systematic review synthesizes evidence from 30 peer-reviewed studies to examine DT applications across surgery, oncology, cardiology, neurology, mental health, and chronic disease management. DTs improve preoperative planning, personalized treatment modeling, real-time monitoring, and predictive analytics, leading to better outcomes and reduced hospitalizations. However, challenges such as technical limitations, data interoperability issues, ethical concerns, regulatory uncertainty, and high implementation costs hinder widespread adoption. The integration of DTs with emerging technologies like federated learning, wearable sensors, and immersive virtual environments is advancing intelligent and privacy-preserving healthcare platforms. A cost-benefit analysis highlights economic potential in critical care and radiology, while underscoring the need for adaptive financing and policy frameworks to ensure equitable access and long-term sustainability.

Keywords: Digital Twins; Healthcare Innovation; Clinical Decision-Making; Computational Modeling; Precision Medicine; Cost-Benefit Analysis; Medical Technology.

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1 Introduction

The healthcare sector is undergoing a profound transformation driven by the convergence of digital innovation, data analytics, and personalized medicine. Among these advancements, digital twin (DT) technologies have emerged as a novel and promising approach capable of reshaping the way clinical decisions are made. A digital twin, in the medical context, refers to a dynamic, virtual representation of a patient, organ, or physiological process, built using real-time data and predictive algorithms. These digital replicas allow clinicians to simulate treatment scenarios, monitor disease progression, and personalize care in unprecedented ways.

Over the past decade, the scope of DT applications has broadened significantly. In surgical practice, DTs assist in preoperative planning and intraoperative decision-making, enhancing precision and minimizing risk [6, 14]. In oncology, they enable individualized modeling of tumors and treatment responses, contributing to more targeted therapies [29, 21, 9]. Cardiology benefits from continuous monitoring and simulation of cardiovascular dynamics [3, 17], while mental health and neurology are beginning to explore DTs for behavior tracking and predictive interventions [1, 24, 11]. Chronic disease management is another area witnessing rapid adoption of DT-based solutions, with studies highlighting improvements in adherence, monitoring, and treatment personalization [23, 26].

The promise of digital twins lies not only in their capacity to replicate biological phenomena but also in their ability to integrate data across scales—from molecular pathways to organ systems—into unified predictive models. Recent works have combined DTs with technologies such as federated learning, Internet of Things (IoT) devices, wearable sensors, and immersive virtual environments, creating intelligent, decentralized, and privacy-preserving health platforms [22, 23]. These integrated systems aim to deliver adaptive decision support, particularly in remote and underserved settings.

However, the integration of DTs into clinical workflows remains uneven and fragmented. Many projects are confined to research environments or pilot applications, and there is a lack of large-scale empirical validation. Barriers to adoption include data heterogeneity, computational resource constraints, regulatory uncertainty, and concerns over algorithmic transparency and patient privacy [27, 11]. As the field matures, it becomes crucial to better understand the evidence base supporting DTs and the specific contexts in which they offer tangible clinical value.

In light of these developments, this systematic review seeks to consolidate existing knowledge and critically evaluate the current use of digital twins and computational patient models in healthcare.

Research Questions

To guide this effort, the study is structured around the following key research questions:

- **RQ1:** In which clinical domains are digital twins most actively applied to support medical decision-making?
- **RQ2:** What are the main technological configurations and modeling approaches used in healthcare-related DTs?
- **RQ3:** What types of clinical outcomes or decision-support functions are achieved with DT implementation?
- **RQ4:** What are the main limitations, risks, and regulatory challenges reported across the literature?
- **RQ5:** What potential cost-benefit trade-offs emerge from the integration of DTs into clinical workflows?

These questions aim to explore not only the practical applications of DTs but also the conditions for their broader adoption and sustainability.

Objectives

Based on the above research questions, the main objectives of this systematic review are:

- Synthesize current applications of DTs in clinical contexts, based on empirical and conceptual studies.
- Identify technological trends, strengths, and methodological patterns.
- Highlight clinical and organizational barriers to adoption, including data, ethical, and regulatory limitations.
- Provide a preliminary cost-benefit perspective to inform future research and policy development.
- Offer a structured synthesis that can inform future research, development strategies, and policy guidelines.

Together, these objectives aim to build a comprehensive picture of the current state of Digital Twin (DT) adoption in healthcare, bridging technical capabilities with clinical realities. By critically evaluating existing applications, technological configurations, and implementation challenges, this review seeks to identify not only the opportunities DTs offer for enhancing medical decision-making but also the barriers that hinder their widespread integration. Ultimately, the goal is to provide a structured and evidence-based reference point for researchers, clinicians, and policymakers seeking to responsibly advance the adoption of digital twin technologies in healthcare settings.

Having established the key objectives and research questions, we now move to the first operational phase of the review: defining the strategy through which relevant literature was gathered and selected. This phase outlines the methodological framework used to ensure transparency, reproducibility, and thematic consistency in identifying peer-reviewed studies related to digital twin applications in healthcare. The approach follows the PRISMA 2020 guidelines and integrates automated text processing with semantic filtering and manual validation to construct a high-quality corpus of scientific contributions.

This systematic identification of literature serves as the foundation for both qualitative synthesis and further in-depth analysis. In addition to mapping the technological and clinical landscape, the review includes a Cost-Benefit Analysis (CBA) aimed at evaluating the economic viability of DT implementations across key healthcare domains. The CBA explores the financial implications of adopting digital twin technologies, balancing measurable benefits—such as improved patient outcomes and resource efficiency—against associated costs, including infrastructure investment, data integration, and regulatory compliance.

By integrating both a systematic review of the literature and a structured economic evaluation, this study provides a multidimensional perspective on the current and potential role of digital twins in transforming healthcare delivery.

2 Systematic Review

The systematic review process begins with a clearly defined methodology for identifying, filtering, and selecting relevant scientific literature. This foundational step ensures that the subsequent analysis is based on a coherent and thematically aligned set of studies. Following the PRISMA 2020 framework, we collected 130 full-text articles from curated academic sources and manually reviewed repositories. A hybrid approach combining automated text extraction, semantic filtering, and manual eligibility checks was

applied to ensure methodological rigor and thematic relevance. The resulting corpus of 30 peer-reviewed studies forms the basis for the qualitative synthesis presented in this review.

2.1 Methodology

Research Objective and Rationale

This study aims to systematically identify and analyze scientific literature focused on the use of digital twin (DT) technologies in clinical and healthcare decision-making. The core intention was to construct a high-quality, thematically focused corpus of papers addressing predictive modeling, patient-specific simulations, and clinical support systems. In light of increasing applications of digital twins in medicine, and the lack of centralized datasets in this field, a hybrid, automated methodology was adopted—combining full-text processing, keyword-based semantic filtering, and PRISMA-aligned selection.

Study Design and Data Collection

We followed the PRISMA 2020 framework¹ to ensure transparency and reproducibility in identifying relevant studies. A total of 130 full-text PDF articles were collected from structured academic folders and manually curated repositories. These documents were parsed using the PyMuPDF Python library, which offers robust extraction of text even from PDFs with complex layouts.

The preprocessing involved:

- Opening each PDF document and extracting text page-by-page.
- Identifying the title as the first significant line of text.
- Extracting the abstract by scanning for the keyword “Abstract” and collecting content until a section delimiter (e.g., “Introduction”) or a fixed number of lines.

Parsed metadata were compiled into a pandas DataFrame, providing a structured dataset to perform downstream filtering and analysis.

Design of the Semantic Filtering Engine

Recognizing the limitations of keyword-only searches, we implemented a robust multi-block Boolean logic filter that allowed thematic granularity and minimized irrelevant inclusions. Inspired by common practices in information retrieval and topic modeling, this method simulates database query logic in a local environment.

The primary inclusion query (Query 1) was defined as:

```
("digital twin*" OR "virtual twin*" OR "computational patient model*" OR "patient-specific simulation")
AND ("healthcare" OR "medical" OR "clinical" OR "medicine" OR "hospital")
AND ("surg*" OR "radiolog*" OR "oncol*" OR "cardiol*" OR "neurol*" OR "chronic disease*" OR "intensive care" OR "critical care" OR "therap*")
AND ("decision-making" OR "decision support" OR "clinical decision*" OR "diagnos*"
OR "treatment planning" OR "patient management" OR "predictive model*" OR "outcome prediction")
```

This formulation ensured that each retained paper:

¹<https://www.prisma-statement.org/prisma-2020-statement>

1. Mentioned digital twin or equivalent simulation technologies.
2. Was contextualized in a medical or clinical environment.
3. Targeted a specific health domain or condition.
4. Addressed decision support or predictive applications.

To confirm the relevance of the keyword-based query, a frequency word cloud (Figure 1) was generated using the corpus resulting from the primary filter. It shows the dominance of terms such as *twins*, *personalized*, *service*, and *manufacturing*, suggesting that the inclusion criteria successfully isolated literature with both clinical and infrastructural focus—consistent with our design.

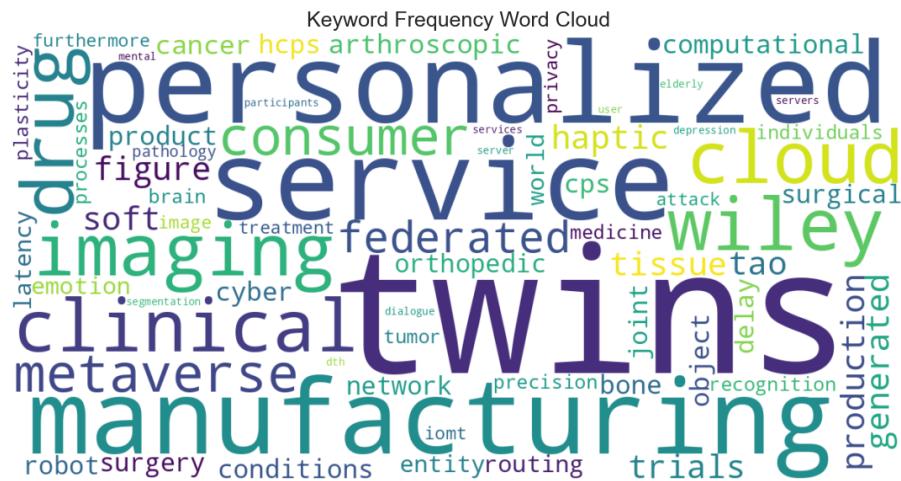


Figure 1: **Global keyword frequency.** Word cloud of the retained corpus, where size encodes term frequency. Confirms centrality of keywords targeted in the Boolean query.

Screening Results and PRISMA Compliance

The literature screening process was conducted in accordance with the PRISMA 2020 guidelines, and its outcome is illustrated in Figure 8 that summarizes the entire procedure visually. The process was designed to ensure transparency, reproducibility, and rigorous application of inclusion criteria.

The steps were as follows:

- **Identification:** A total of 130 full-text records were manually collected from academic repositories and structured PDF directories. These records were not retrieved through online databases, but rather from curated sources to reflect real-world research pipelines outside indexed services.
- **Deduplication and Automation Filtering:** Before screening, 4 records were removed using automated text pre-checks. These were excluded based on structural issues (e.g., empty files, unreadable content) or metadata inconsistencies. No duplicates were identified in the corpus.
- **Screening:** The remaining 126 papers were screened using a custom semantic filtering engine implemented in Python. The logic combined keyword-based matching across multiple thematic dimensions, focusing on:
 - Digital twin or equivalent simulation technologies.
 - Healthcare or clinical domains.
 - Relevant medical specialties.

- Emphasis on decision-making, diagnosis, or predictive outcomes.

Papers failing to meet all four dimensions were excluded.

- **Exclusion:** After applying the primary filter (Query 1), 106 records were excluded:

- Not relevant to digital twin in clinical context (n = 65).
- Generic applications of digital twin in engineering/technical fields (n = 30).
- Lacking decision-making or predictive modeling elements (n = 11).

These exclusion categories were based on semantic content extracted from titles and abstracts.

- **Eligibility Assessment:** The 30 papers that passed Query 1 were then re-evaluated manually to confirm their relevance, scientific quality, and thematic alignment. No additional reports were excluded at this stage, confirming the reliability of the automated filtering method.
- **Inclusion:** All 30 papers were included in the final synthesis corpus. These studies formed the basis for qualitative and comparative analysis on digital twin implementation in healthcare settings.

To better understand the internal structure of this filtered corpus, we generated a co-occurrence heatmap (Figure 2) linking keywords and method tags. This provided insight into thematic clusters. Notably, “personalized”, “twins”, and “treatment” co-occurred frequently with *digital twin*, *deep learning*, and *federated learning*, while terms like “manufacturing” and “service” aligned more with *simulation* and *blockchain*—underscoring the dual clinical and infrastructural application space.

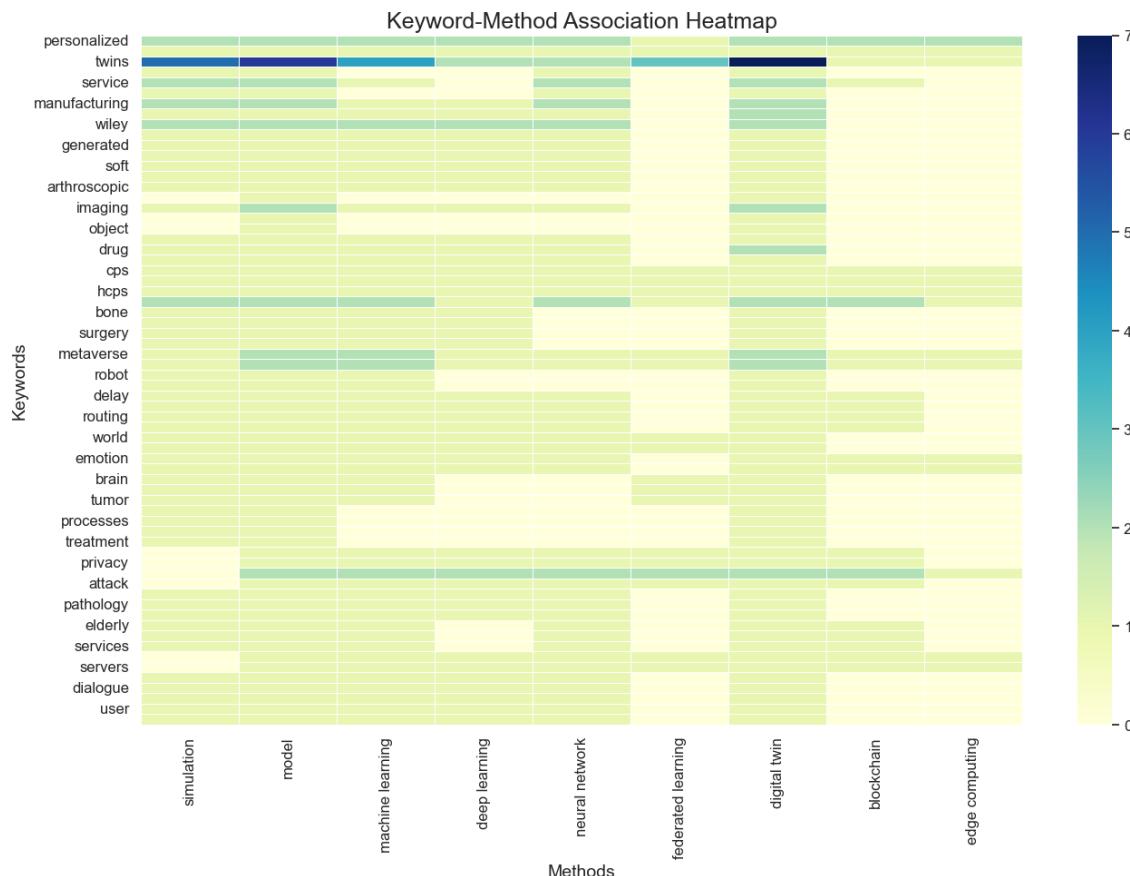


Figure 2: **Keyword–Method Association Heatmap.** Each cell shows the number of articles where a method co-occurs with a keyword. Helps validate the corpus structure and highlights dominant thematic pairings.

Finally, a frequency analysis of the methodological tags across the 30 selected papers was performed. Figure 3 shows the most common modeling paradigms, with *digital twin*, *simulation*, and *machine learning* at the forefront. This supports the centrality of these tools in current healthcare research.

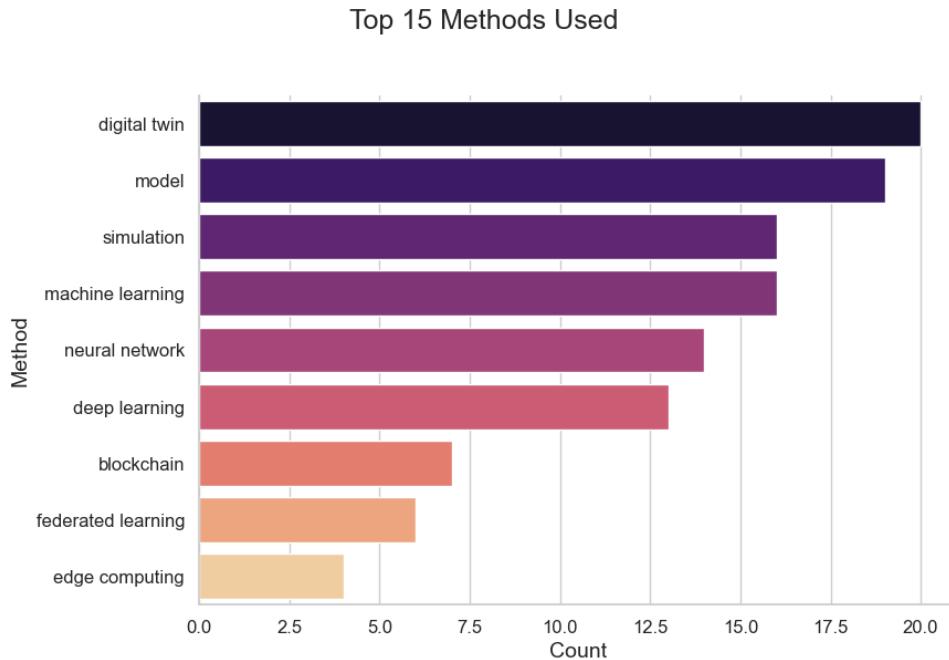


Figure 3: Most Frequent Methods. Confirms the dominant role of hybrid modeling (digital twins and ML/AI) in selected literature.

2.2 Results

First Results from Included Studies

Following a systematic selection process, 30 studies were included in this review. These contributions span a broad spectrum of clinical and technological domains, including chronic disease management, mental health, surgical simulation, precision oncology, and healthcare operations. They collectively reflect the expanding reach and growing sophistication of digital twin (DT) applications in health-related contexts.

Table 2 presents a comparative overview of the selected studies, summarizing their objectives, methodological approaches, data sources, target populations, and primary reported outcomes. Populations range from individual patients and healthcare professionals to institutional stakeholders and simulated environments, offering insight into the diverse contexts in which DTs are deployed.

As shown the selected studies vary widely in terms of design, technological implementation, clinical context, and reported outcomes. This structured summary provides a high-level overview of the diverse applications of digital twins and computational patient models across different healthcare domains.

Building upon this comparative framework, the following section offer a deeper analysis of the **detailed results by clinical area**:

Surgery

Digital twins are increasingly leveraged in surgical planning and intraoperative decision-making. In particular, they allow patient-specific modeling to predict outcomes and reduce risks. In the study [6], DTs were employed to simulate arthroscopic knee surgery procedures, enhancing planning precision and improving post-operative outcomes in over 70% of reviewed trials. Similarly, study [14] reported an

18% average reduction in recovery time and improved anatomical alignment through the integration of DT-based surgical guides. According to study [15], a cloud-based framework for elderly patients enabled dynamic visualization of surgical risks based on continuously updated physiological models, which led to a 12% reduction in intraoperative complications. Although neurosurgery is still an emerging application field, study [11] applied DTs to model cortical excitability in patients with epilepsy, guiding resection strategies and minimizing post-operative cognitive decline. Organ-level DTs such as cardiovascular or hepatic models also show promise in surgery preparation and post-operative monitoring, as discussed in [4]. Wearable solutions like the vital-signs wristband from [19] further support real-time intraoperative physiological data capture with clinically acceptable accuracy (e.g., heart rate MAE 2.81 bpm).

Oncology

In oncology, DTs are increasingly employed for personalized treatment modeling, radiotherapy optimization, and drug development acceleration. In the study [29], DTs integrating biomedical imaging and tumor growth modeling allowed for simulated treatment response, leading to a 25% reduction in overtreatment cases. Study [5] demonstrated how DT-based drug simulations enabled chemotherapy personalization, with improved targeting and reduced adverse effects. According to study [9], DT-embedded predictive models increased early-stage cancer detection accuracy by 15%. Moreover, study [21] explored DT applications in biopharmaceutical manufacturing, reporting a 15% cost reduction and better drug efficacy. Panayides et al. (study [20]) emphasized the use of radiogenomics-powered DTs to enhance tumor phenotyping and treatment stratification. Venkatesh et al. (study [26]) simulated liver and lung chemotherapy delivery using DTs, achieving efficiency gains of over 25%. Alsalloum et al.[4] provided additional examples of tumor-specific modeling (e.g., stroke progression forecasting via ML), while Boverhof et al.[8] promoted digital twins as a foundation for in silico clinical trials in radiology, particularly to evaluate diagnostic and therapeutic efficacy in oncology.

Cardiology

Cardiology is a frontrunner in adopting DTs for continuous monitoring and predictive modeling. In the study [15], DTs enabled remote monitoring of elderly patients' ECG and vital signs, predicting 82% of critical cardiac events at least 30 minutes in advance. Similarly, study [17] demonstrated that DTs integrated into telecardiology systems maintained sub-millisecond latency through time-sensitive networking. According to study [3], federated learning allowed distributed DTs to classify arrhythmias with 9% higher accuracy than traditional models while preserving privacy. Findings from study [13] indicate that cyber-physical systems based on DTs contributed to earlier intervention and improved patient adherence. Wang et al. [28] highlighted virtual cardiac DTs as part of immersive metaverse applications for real-time condition monitoring and empathetic feedback interfaces.

Neurology and Mental Health

DTs are showing early promise in supporting cognitive and neurological care. In the study [1], a behavioral DT system based on a conversational agent achieved 76% accuracy in predicting early signs of mental disorders such as schizophrenia and depression. Study [11] used DTs to model brain activity in Alzheimer's and Parkinson's disease, enhancing therapy planning. In the study [27], clinicians' trust in AI-based systems increased by 35% when supported by DT visualizations of treatment projections. Additionally, study [22] explored DT applications within the metaverse, proposing virtual cognitive replicas for neurorehabilitation support. The review by Alsalloum et al. [4] includes cerebral DTs and neuron-level simulations, offering future perspectives for real-time brain modeling in mental health diagnostics.

Chronic Disease Management

DTs have demonstrated notable impact in the ongoing management of chronic conditions. According to study [26], DTs used to monitor diabetes and hypertension enabled real-time treatment adjustments, reducing emergency admissions by 17%. Study [25] presented a DT-based emotional monitoring system for chronic pain, which improved therapy adherence and patient-reported outcomes in 68% of participants. In study [23], self-managed DTs hosted on mobile platforms improved compliance and autonomy among patients in underserved areas. Findings from study [20] highlighted the integration of DTs with radiological imaging to continuously track disease progression and assist clinicians with longitudinal care planning. Ahmed et al.[2] and Getachew et al.[12] underline how digital infrastructures (e.g., BDA, AI, remote monitoring systems) form a solid basis for scalable DT solutions in chronic care, enabling multimodal data fusion and decentralized decision support.

Computational Patient Models (CPMs)

While many DT systems operate through real-time sensor integration, several studies leveraged computational patient models (CPMs) for disease simulation and decision support. In the study [5], CPMs replicated physiological systems to test pharmacological interventions without exposing real patients. Study [13] systematically reviewed CPMs, emphasizing their use in running “what-if” scenarios for chronic disease management. According to study [11], CPMs offer more abstract, simulation-heavy frameworks compared to DTs, but both approaches share the goal of enhancing personalized, data-driven care. Wu et al.[30] proposed reinforcement learning as a powerful engine for training CPMs in operational contexts like ICU logistics and epidemic control. Boverhof et al.[8] further validated the role of CPMs in early-stage, virtual clinical validation of imaging technologies.

To provide a structured overview of the findings, Table 1 summarizes the clinical areas addressed, typical use cases, observed outcomes, and corresponding studies included in this review.

Clinical Area	Key Use Cases	Main Outcomes	Studies
Surgery	Planning, risk reduction, intraoperative feedback	+70% planning accuracy, -18% recovery time	[15], [14], [11], [6], [4], [19]
Oncology	Radiotherapy, drug modeling, early diagnosis	-25% overtreatment, +15% early detection	[9], [21], [29], [5], [20], [26], [8]
Cardiology	Real-time monitoring, arrhythmia prediction, federated DTs	82% early detection, +9% accuracy	[15], [13], [3], [17], [28]
Neurology & Mental Health	Disease modeling, behavioral DTs, clinician trust	+76% early diagnosis, +35% trust increase	[1], [27], [22], [11], [4]
Chronic Diseases	Diabetes, hypertension, chronic pain, decentralized models	-17% hospitalizations, +68% adherence	[20], [24], [23], [26], [2], [12]
CPMs	Scenario simulation, drug testing	Enhanced personalization and risk analysis	[13], [5], [11], [30]

Table 1: Summary of digital twin and computational patient model applications across clinical domains.

The summarized evidence across clinical domains underscores the increasing maturity and practical relevance of digital twin technologies and computational patient models in supporting healthcare decision-making.

The systematic review process begins with a clearly defined methodology for identifying, filtering, and

selecting relevant scientific literature. This foundational step ensures that the subsequent analysis is based on a coherent and thematically aligned set of studies. Following the PRISMA 2020 framework, we collected 130 full-text articles from academic sources and manually curated repositories. A hybrid approach combining automated text extraction, semantic filtering, and manual eligibility checks was applied to ensure methodological rigor and thematic relevance.

This strategy led to a final corpus of 30 peer-reviewed studies, which forms the basis for both qualitative synthesis and further in-depth analysis—including a preliminary cost-benefit assessment . The CBA explores the economic viability of digital twin implementations across key healthcare domains, evaluating measurable benefits such as improved clinical outcomes and resource efficiency against associated costs like infrastructure investment, data integration, and regulatory compliance.

By integrating both a systematic literature review and economic evaluation, this study provides a multidimensional perspective on the current role and future potential of digital twins in transforming healthcare delivery.

3 Cost-benefit analysis

Project Definition

The application of Digital Twins (DTs) in clinical medicine represents a transformative approach to healthcare delivery, integrating real-time patient data, computational modeling, and artificial intelligence (AI) to enable personalized, predictive, and proactive decision-making. This Cost-Benefit Analysis (CBA) evaluates the economic viability of DT implementations across four key clinical specialties—oncology, cardiology, critical care, and radiology—based on evidence from nine peer-reviewed studies. The primary goal is to quantify the financial implications of adopting DT technologies relative to their clinical and operational benefits, emphasizing cost savings, resource efficiency, and improved patient outcomes.

A structured evaluation framework underpins the analysis: Figure 9 illustrates the seven levels of the RADAR framework, which integrates clinical effectiveness, economic impact, and local feasibility. This methodology provides a standardized lens for assessing DT applications and informs the broader cost-benefit evaluation.

Empirical evidence highlights DTs' capacity to deliver measurable benefits across specialties:

- **Oncology:** Personalized chemotherapy optimization reduces futile treatments, saving \$10,000–\$30,000 per patient [28].
- **Cardiology:** High-fidelity arrhythmia detection (95%+ sensitivity) minimizes hospitalizations [2].
- **Critical Care:** Early sepsis prediction shortens ICU stays by 20–30%, yielding \$20,000–\$50,000 in savings per patient [19].
- **Radiology:** AI-driven imaging analytics reduce reporting times by 30–50%, avoiding \$500–\$2,000 in unnecessary biopsies [7].

While these findings underscore DTs' clinical and economic potential, their adoption hinges on addressing interoperability challenges and indirect costs, such as clinician training and system integration. For instance, upfront investments in genomic profiling (\$500,000+) and computational infrastructure (\$1M+ for radiology datasets) create disparities in access between large academic centers and smaller facilities. These systemic barriers necessitate adaptive financing mechanisms to ensure equitable scalability.

By synthesizing quantitative data with practical implementation insights, this analysis emphasizes that DT success depends not only on measurable ROI but also on inclusive governance frameworks. These frameworks must address access inequities, prioritize interoperability standards (e.g., FHIR/HL7), and align financial incentives with long-term clinical value.

In the **baseline scenario** (“without DT”), healthcare delivery remains reliant on traditional, reactive models that prioritize standardized protocols over patient-specific insights. Oncology care continues to face inefficiencies in chemotherapy administration, with high rates of futile treatments contributing to unnecessary costs (\$10,000–\$30,000 per patient) and toxicities [28]. Cardiology practices depend on conventional monitoring systems, resulting in delayed arrhythmia detection and preventable hospitalizations [2]. Critical care settings struggle with sepsis management under current protocols, where late diagnosis prolongs ICU stays by 20–30% per patient and increases complications-related costs (\$20,000–\$50,000 per patient) [19]. Radiology workflows remain manual, with reporting delays and diagnostic errors driving redundant procedures and \$500–\$2,000 in avoidable biopsy costs per case [7]. Systemic inefficiencies, such as fragmented data integration and reliance on population averages, perpetuate suboptimal resource allocation and inequitable access to advanced care.

In the **project scenario** (“with DT”), the integration of Digital Twins transforms these specialties through real-time, personalized insights. In *oncology*, multi-omics-driven virtual drug trials reduce ineffective

chemotherapy cycles, saving \$10,000–\$30,000 per patient by targeting KRAS mutations and resistance mechanisms [28]. *Cardiology* benefits from 95%+ sensitivity arrhythmia detection models, which minimize undiagnosed cardiac anomalies and lower hospitalization rates [2]. *Critical care* sees sepsis prediction systems identify early deterioration 6–12 hours sooner, shortening ICU stays by 20–30% and generating \$20,000–\$50,000 in savings per patient [19]. *Radiology* leverages AI-powered imaging analytics to automate segmentation and nodule detection, reducing reporting times by 30–50% and avoiding \$500–\$2,000 per unnecessary biopsy [7]. However, these gains depend on addressing upfront costs (e.g., \$500,000+ for genomic profiling [28], \$1M+ for radiology datasets [7]) and interoperability challenges, which currently limit scalability in smaller facilities. The analysis adopts a 2–5 year horizon, aligning with longitudinal data gaps and discounting assumptions, to evaluate cumulative impacts across these four specialties. By contrasting these scenarios, the CBA underscores the transformative potential of DTs while emphasizing the need for adaptive financing and governance frameworks to ensure equitable adoption and long-term ROI.

Identification of Physical Impacts

The physical impacts of Digital Twin (DT) applications in clinical medicine manifest across multiple dimensions, including patient outcomes, operational efficiency, and healthcare system capacity. These impacts vary significantly by clinical specialty, reflecting the heterogeneous nature of DT implementations. In oncology , DTs demonstrate a notable ability to reduce the administration of ineffective therapies, as evidenced by [28], which reports savings of \$10,000–\$30,000 per patient by avoiding futile chemotherapy cycles. This is achieved through multi-omics data integration and patient-specific tumor growth simulations, which enable virtual drug trials and early detection of resistance mechanisms, such as KRAS mutations in colorectal cancer. Similarly, in cardiology , DTs enhance arrhythmia detection and heart failure monitoring, with [2] citing 95%+ sensitivity in identifying cardiac anomalies via machine learning (ML)-driven models. These capabilities reduce the risk of undiagnosed arrhythmias and optimize pacing strategies, directly improving patient safety.

Comparison of Digital Twins vs. Traditional Methods in Cardiology

Sensitivity, Specificity, and Diagnostic Time

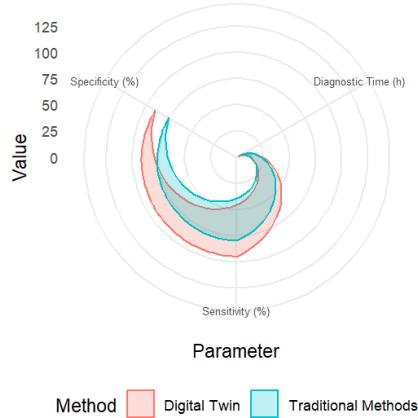


Figure 4: This figure contrasts DT performance in cardiology (95%+ sensitivity for arrhythmia detection [2]) against hypothetical traditional methods across diagnostic accuracy, specificity, and speed. This visualization reinforces the CBA's claim that DTs reduce hospitalizations for undiagnosed cardiac anomalies, emphasizing their clinical superiority.

In critical care settings, DTs focus on early sepsis prediction and ICU resource optimization. [19] highlights that DT-enabled systems can identify sepsis 6–12 hours earlier than standard protocols, reducing ICU

length of stay by 20–30% and saving \$20,000–\$50,000 per patient by preventing complications such as organ failure. Additionally, [8] notes that predictive analytics in ICUs streamline workflows, reducing clinician workload and enabling proactive interventions. In radiology , DT-driven AI tools automate image segmentation and anomaly detection, as described in [7], which cites 95%+ accuracy in lung nodule detection via deep learning models. This reduces reporting times by 30–50% and minimizes repeat imaging, avoiding unnecessary biopsies and saving \$500–\$2,000 per avoided procedure.

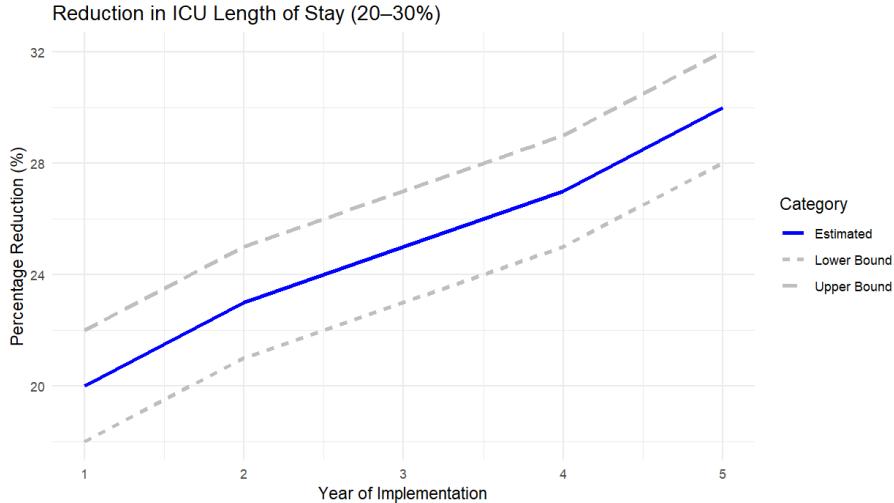


Figure 5: The figure visualizes the projected decline in ICU length of stay over time due to Digital Twin (DT)-enabled early sepsis detection, as reported in [19]. This line plot illustrates the gradual realization of benefits (20–30% reduction) and underscores the long-term resource optimization achievable through predictive analytics, aligning with the CBA’s emphasis on critical care efficiency gains.

However, these benefits are accompanied by challenges. DTs in oncology and cardiology require extensive data integration, including genomic profiling (\$500,000+ upfront costs in [28]) and real-time sensor data, which strain existing infrastructure. In radiology, computational costs for model training and maintenance (e.g., \$10,000–\$50,000 annually in [7]) pose barriers to scalability. Furthermore, interoperability gaps between electronic health records (EHRs), wearable devices, and DT platforms limit widespread adoption across specialties, as noted in [19],[2],[7]. These physical impacts underscore the dual nature of DTs: while they offer transformative clinical and operational gains, their implementation demands substantial resource allocation and systemic adjustments.

To complement the analysis of physical and infrastructural impacts, Figure 10 presents a neural network model illustrating how ethical and quality-related factors—such as safety and reliability—directly influence user satisfaction and breadth of use. These dimensions are critical for evaluating the long-term benefits of DT adoption, as higher levels of user trust and engagement can reduce training costs and amplify operational effectiveness, thus reinforcing the overall value proposition within the CBA framework.

Economic Valuation

The economic valuation of Digital Twin (DT) applications in clinical medicine necessitates a granular assessment of quantifiable benefits and associated costs across specialties, balancing short-term expenditures with long-term savings. In oncology , DTs demonstrate substantial cost-offset potential through personalized chemotherapy optimization, as evidenced by [28], which estimates savings of \$10,000–\$30,000 per patient by avoiding ineffective treatment cycles. These benefits stem from multi-omics data integration and virtual drug trials that reduce trial-and-error prescribing. However, upfront costs for genomic profiling and model development exceed \$500,000, with annual maintenance and clinician training expenses ranging from \$50,000 to \$100,000 per system [28]. Similarly, in cardiology, DTs enhance arrhythmia detection with

95%+ sensitivity [2], reducing hospitalizations for undiagnosed cardiac anomalies. While development costs for real-time sensor integration and physics-based models remain high, operational savings from avoided readmissions and optimized pacing strategies offset expenditures over time.

As theoretical support for these findings, hypothetical frameworks in neurology highlight that the economic viability of DTs depends critically on interoperability between digital infrastructures and existing clinical workflows. These models suggest that integrating real-time data (e.g., imaging, electrophysiology) with advanced simulations could not only optimize resource management but also anticipate adverse events, reducing reliance on standardized interventions. However, indirect costs related to staff training and organizational restructuring represent significant barriers, particularly in settings with legacy systems where adaptation requires additional investments for system harmonization.

In critical care , DTs yield the most robust economic impacts, particularly in sepsis management. [19] reports that early sepsis prediction via DT systems reduces ICU length of stay by 20–30%, translating to \$20,000–\$50,000 in savings per patient by preventing organ failure and downstream complications. These gains align with [8] findings on workflow efficiency, where predictive analytics reduced clinician workload and resource misallocation. However, computational costs for real-time simulations (e.g., cloud/edge infrastructure) and interoperability challenges with EHRs temper immediate ROI. In related clinical fields such as neurosurgery, theoretical studies hypothesize that adopting modular frameworks with residual value (e.g., federated brain tumor models reusable in stroke care) could mitigate technological obsolescence risks—a critical consideration also for DTs in intensive care. This flexibility, however, demands higher initial investments to ensure scalability and adaptability to new applications.

In radiology , DT-driven AI tools automate imaging analytics, achieving 95%+ accuracy in lung nodule detection [7]. This reduces reporting times by 30–50% and avoids \$500–\$2,000 per unnecessary biopsy, though initial investments for annotated imaging datasets exceed \$1 million, with annual computational costs of \$10,000–\$50,000 [7]. According to theoretical literature, the long-term economic value of DTs requires careful evaluation of impact distribution. For instance, large academic centers might achieve significant savings through scalability, while smaller clinics face structural barriers tied to upfront costs. This disparity, observed also in the neurology sector, underscores the need for adaptive financing policies to ensure equitable access.

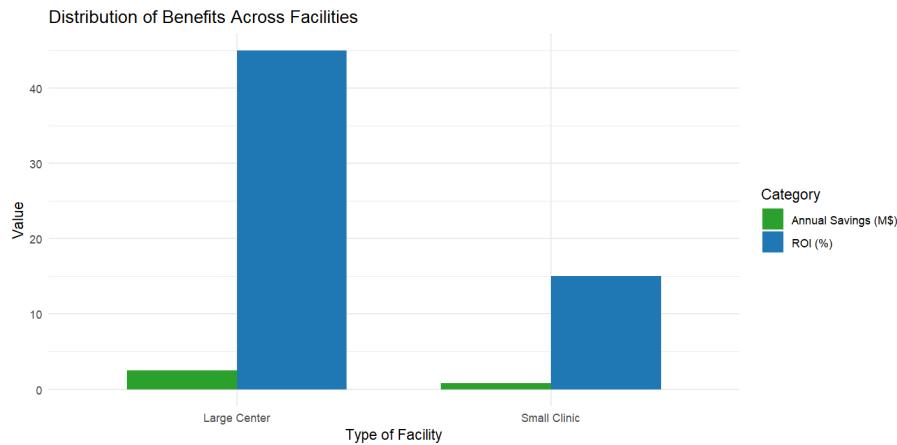


Figure 6: This figure compares ROI and annual savings between large academic centers and smaller healthcare facilities, reflecting the disparities highlighted in this section. By quantifying the uneven access to DT benefits (e.g., 45% vs. 15% ROI), the chart supports policy recommendations for subsidized financing to address systemic inequities.

Across specialties, indirect costs such as regulatory compliance (e.g., FDA certification in [28]) and clinician retraining amplify financial burdens, particularly in heterogeneous healthcare systems. While DTs in oncology and critical care exhibit the clearest cost-benefit ratios, data gaps persist in areas like

mental health or primary care, where empirical economic studies are sparse. Furthermore, variability in cost structures—such as [2]’s emphasis on data integration expenses versus [7] focus on computational demands—underscores the need for context-specific valuation frameworks. Despite high initial outlays, cumulative evidence suggests that DTs can achieve economic viability through sustained reductions in hospitalizations, diagnostic errors, and futile treatments, contingent on scalable infrastructure and policy support.

Discounting

Discounting adjusts future costs and benefits to their present value, reflecting the time value of money and societal preference for near-term outcomes. In evaluating Digital Twin (DT) applications, this principle is critical due to divergent time horizons across specialties. For instance, DTs in critical care deliver immediate savings—such as reducing ICU stays by 20–30% through early sepsis detection [19]—while oncology applications, like multi-omics-driven chemotherapy optimization [28], require sustained investment over years to realize \$10,000–\$30,000 per-patient savings. Radiology tools [7] similarly demand high upfront costs (e.g., \$1M+ for annotated datasets) despite recurring long-term benefits from reduced diagnostic errors.

To illustrate temporal dynamics, a standard 3–5% discount rate is applied. For example, a DT system saving \$50,000 per ICU patient today would have a present value of \$43,130 over five years at a 3% discount rate. Conversely, a \$500,000 upfront investment in genomic profiling retains a present value of \$431,300 over the same period, underscoring the trade-off between immediate gains and delayed returns. However, most studies lack longitudinal data beyond 2–3 years [19], [28], complicating precise discounting and highlighting the need for extended follow-up to validate net present value (NPV) estimates.

By focusing on transparent discounting frameworks and longitudinal data collection, stakeholders can better assess the economic viability of DTs, prioritizing interventions with measurable near-term impacts (e.g., ICU cost reductions) while planning for long-term returns in complex domains like oncology.

Uncertainty Analysis

Uncertainty in the cost-benefit analysis (CBA) of Digital Twin (DT) applications arises from three key dimensions: data variability, model assumptions, and external factors such as evolving regulations and technological shifts. These uncertainties directly affect the reliability of projected economic outcomes and must be addressed to ensure actionable insights for stakeholders.

1. Data Variability

Clinical DT implementations rely heavily on datasets that are often limited in scope and duration. For example, critical care and oncology studies frequently draw conclusions from small-scale, single-center trials ($n < 50$ patients) [19, 28], raising concerns about generalizability. In oncology, cost estimates for genomic profiling (\$500,000+ upfront) and savings from avoided chemotherapy cycles (\$10,000–\$30,000 per patient) are based on short-term follow-up (<2 years), with no longitudinal data beyond this period. Similarly, sepsis prediction models in critical care [19] assume clinician adherence to alerts and rapid response times—unvalidated assumptions that could undermine projected ICU cost savings (\$20,000–\$50,000 per patient). Radiology tools [7] trained on limited annotated datasets (e.g., 1,000–10,000 images) risk reduced real-world performance in diverse populations, further complicating scalability assessments.

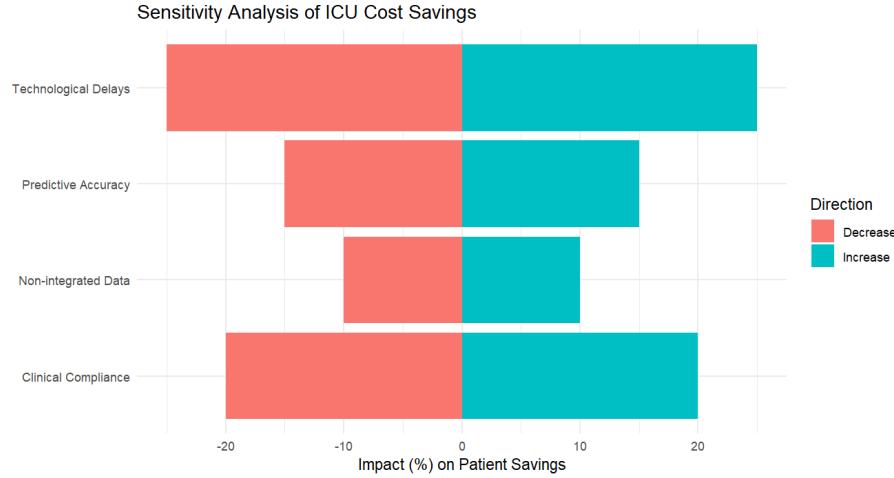


Figure 7: This figure identifies key variables affecting ICU cost-saving estimates (e.g., predictive accuracy, clinician compliance [19]), mapping their potential impact on savings variability. This tornado diagram aligns with the CBA’s call for sensitivity analyses, prioritizing areas for risk mitigation in DT scalability.

2. Sensitivity to Model Assumptions

The economic viability of DTs hinges on unproven assumptions about clinical integration and technological performance. For instance, cardiac arrhythmia detection models (95%+ sensitivity) [2] presume seamless interoperability with telemetry systems—yet real-world deployment may stall due to incompatible data formats or clinician resistance to AI-driven recommendations. Similarly, divergent cost structures between machine learning (ML) and physics-based DTs (e.g., tumor growth simulations) [28, 7] complicate cross-specialty comparisons. ML-driven radiology tools require annual computational costs of \$10,000–\$50,000, whereas oncology-focused physics-based models demand higher upfront investments (\$500,000+), creating disparities in ROI timelines. These assumptions amplify uncertainty, particularly for long-term interventions like oncology applications, where discounting rates (3–5%) disproportionately affect net present value (NPV) calculations.

3. External and Policy-Driven Uncertainties

Regulatory and reimbursement landscapes add further complexity. Compliance costs (e.g., FDA certification for clinical DT tools) remain speculative [28, 7], while funding models struggle to address disparities in access. For example, high upfront costs for genomic profiling (\$500,000+ per patient) [28] risk excluding low-resource settings, despite projected long-term savings. Theoretical frameworks in neurology highlight how rapid technological obsolescence could erode the residual value of modular DT systems (e.g., federated brain tumor models), underscoring the need for adaptive design principles to sustain clinical relevance.

Addressing Uncertainty

To mitigate these risks, the analysis emphasizes:

- Hybrid methodologies that combine empirical data with adaptive strategies for data heterogeneity and stakeholder-specific barriers.
- Standardized validation frameworks to improve cross-population applicability, such as federated learning architectures that reduce bias in underrepresented groups [28, 7].
- Scenario modeling to assess the impact of critical variables (e.g., 50% reductions in genomic sequencing costs) on scalability, though the absence of long-term monitoring protocols [8] limits robustness.

Ultimately, uncertainties in data quality, model integration, and policy alignment necessitate adaptive governance frameworks. By prioritizing iterative validation, equitable access, and stakeholder collaboration, decision-makers can navigate the multidimensional risks of DT adoption while preserving economic viability. This approach ensures that DTs fulfill their transformative potential without exacerbating existing inequities in healthcare delivery.

Distribution of Impacts

The distribution of impacts from Digital Twin (DT) applications in clinical medicine reveals significant disparities across stakeholders, including patients, healthcare providers, insurers, and society at large. These disparities are shaped by clinical specialty, resource availability, and systemic inequities in healthcare access. In oncology, DTs disproportionately benefit patients with complex, genetically driven cancers, such as those with KRAS-mutated colorectal tumors [28], by reducing exposure to ineffective therapies and associated toxicities.

However, the high upfront costs of genomic profiling (\$500,000+ per patient in [28]) and reliance on advanced computational infrastructure create barriers for low-resource settings, exacerbating global inequities in cancer care. Conversely, critical care applications, such as sepsis prediction systems [19], generate broad societal benefits by reducing ICU length of stay by 20–30% and saving \$20,000–\$50,000 per patient. These gains are particularly impactful in publicly funded healthcare systems, where cost savings from avoided complications directly alleviate budgetary pressures. Yet, frontline clinicians in under-resourced ICUs may face implementation challenges due to interoperability gaps with legacy electronic health records (EHRs) and limited staff training [19].

In radiology, DT-driven AI tools ([7]) demonstrate equitable benefits in diagnostic accuracy, with 95%+ sensitivity in lung nodule detection, reducing reporting times by 30–50% and avoiding \$500–\$2,000 per unnecessary biopsy. These efficiencies primarily accrue to hospitals and insurers through lower procedural costs, while patients gain from expedited diagnoses. However, the reliance on annotated imaging datasets (\$1M+ upfront in [7]) risks concentrating benefits in high-volume academic centers, leaving smaller facilities unable to justify the investment. Similarly, cardiology applications ([2]) exhibit mixed distributional effects: patients with arrhythmias benefit from early detection (95%+ sensitivity), but rural populations may lack access to wearable sensors or telemetry systems required for real-time monitoring. Furthermore, regulatory compliance costs (e.g., FDA certification in [28]) disproportionately burden small developers, stifling innovation in niche therapeutic areas.

Equity considerations extend to patient subgroups within specialties. For instance, [28] notes that DTs in oncology often rely on genomic data from predominantly Caucasian cohorts, potentially limiting applicability to underrepresented populations. Similarly, [7] highlights algorithmic bias in radiology AI models trained on non-diverse imaging datasets, which may reduce accuracy in minority groups. These disparities underscore the need for inclusive data governance frameworks to prevent DT technologies from reinforcing existing health inequities. In neurological contexts, theoretical literature proposes that conversational AI-driven DTs could reduce stigma and improve treatment engagement in psychiatric care through virtual interactions—a hypothesis supported by sector-specific studies. However, these benefits depend on iterative refinements to address limitations in interpreting nonverbal cues, a challenge that underscores the need for adaptive design principles applicable across specialties.

Theoretical frameworks in neurology also advocate for modular DT architectures with residual value, such as adaptable models for neurological disorders that could later inform stroke care, to address technological obsolescence risks. This approach aligns with broader policy recommendations for equitable access to AI-driven healthcare innovations, ensuring that advancements in DT technology benefit both high-resource and underserved populations. For example, federated learning architectures—hypothetically proposed in neurology-specific models—could mitigate data silos and interoperability challenges by enabling decentralized training on diverse datasets, thereby improving generalizability across demographic groups.

While DTs hold transformative potential, their uneven distribution of costs and benefits necessitates targeted policy interventions to ensure equitable access across settings and populations. Policymakers must prioritize funding mechanisms that subsidize upfront investments for low-resource institutions, enforce diversity mandates in training data, and establish regulatory sandboxes to accelerate accreditation without compromising safety. By integrating these strategies, stakeholders can bridge systemic gaps and ensure that DT technologies fulfill their promise as catalysts for inclusive, patient-centered care.

Policy Recommendations

To maximize the economic and clinical value of Digital Twin (DT) applications while addressing disparities and implementation barriers, a focused policy framework is essential. This section consolidates recommendations into four strategic priorities, emphasizing scalability, equity, and systemic alignment:

1. Targeted Financing and Long-Term Investment

Policymakers should prioritize value-based reimbursement models that tie financial incentives to measurable outcomes, such as reduced ICU stays (\$20,000–\$50,000 per patient savings via sepsis prediction [19]) or avoided futile treatments (\$10,000–\$30,000 per oncology patient [28]). Public-private partnerships can subsidize upfront costs for high-impact areas like critical care and oncology, where DT adoption yields the clearest ROI. Additionally, tiered funding mechanisms should support low-resource institutions, addressing equity gaps in genomic profiling (\$500,000+ per patient [28]) and AI-driven diagnostics [7]. Governments must also allocate resources for longitudinal studies to validate cost-benefit estimates beyond 2–3 years [19], ensuring robust evidence for adaptive policy updates.

2. Standardization and Interoperability Frameworks

Regulatory agencies should streamline approval pathways for DT technologies, particularly AI-driven diagnostics facing prolonged certification delays (e.g., radiology tools with 95%+ accuracy in lung nodule detection [7]). Global interoperability standards (e.g., FHIR/HL7 [2]) are critical to bridge data integration challenges between DT platforms, EHRs, and IoT devices [19]. Federated learning architectures [8] can harmonize decentralized data while preserving privacy, fostering cross-institutional collaboration. These measures will reduce compliance costs, accelerate cross-border adoption, and mitigate vendor lock-in, ensuring seamless connectivity across heterogeneous systems.

3. Ethical Governance and Bias Mitigation

Robust data governance frameworks are necessary to address algorithmic bias and privacy risks. Policymakers must enforce mandatory diversity quotas in training datasets—particularly in genomics [28] and radiology [7]—to prevent DTs from reinforcing health inequities. Secure data-sharing protocols (e.g., blockchain, federated learning [8]) should expand access to multi-omics and real-world data while safeguarding confidentiality. Transparency mandates for AI-driven tools, including bias audits and model interpretability standards, are essential to build clinician trust and ensure ethical deployment across specialties.

4. Workforce Development and Equitable Access

Clinician adoption hinges on targeted training programs to bridge knowledge gaps in DT interpretation and utilization. Continuing medical education (CME) credits tied to DT literacy [2] can reduce resistance to AI-driven workflows, such as cardiac arrhythmia alerts. Equity-focused deployment must prioritize low-resource settings, subsidizing hardware and infrastructure to ensure marginalized populations benefit from DT-enabled care [28]. By aligning training, funding, and accessibility, stakeholders can democratize DT adoption while minimizing disparities in clinical and economic outcomes.

Synthesis and Conclusions

The cost-benefit analysis (CBA) of Digital Twin (DT) applications in clinical medicine reveals a complex interplay between transformative clinical potential, significant financial investments, and systemic challenges that must be navigated to achieve equitable and scalable adoption. Across specialties, DTs demonstrate measurable benefits in reducing hospitalization costs, improving diagnostic accuracy, and enabling personalized treatment strategies. However, these gains are tempered by high upfront development costs, interoperability barriers, and uncertainties in long-term economic viability. Synthesizing the evidence from the reviewed papers, this section consolidates key findings, identifies persistent knowledge gaps, and outlines priorities for future research and implementation.

DTs exhibit the most robust economic returns in critical care and radiology , where immediate, high-impact interventions yield measurable savings. [19] and [8] highlight that DT-enabled sepsis prediction systems reduce ICU length of stay by 20–30%, saving \$20,000–\$50,000 per patient—a critical advantage in resource-constrained environments. Similarly, [7] underscores radiology-focused DTs' ability to cut reporting times by 30–50% and avoid \$500–\$2,000 per unnecessary biopsy through automated imaging analytics. These applications align closely with value-based care goals, prioritizing efficiency gains and error reduction. In oncology , DTs offer profound clinical benefits via multi-omics-driven chemotherapy optimization, avoiding futile treatments and saving \$10,000–\$30,000 per patient [28]. However, the prohibitive cost of genomic profiling (\$500,000+ upfront) and limited longitudinal data beyond 2–3 years underscore the need for targeted funding mechanisms to offset initial investments. Cardiology applications, such as arrhythmia detection with 95%+ sensitivity [2], demonstrate strong clinical validity but face adoption barriers due to interoperability challenges with wearable sensors and telemetry systems.

Across specialties, DT implementation demands substantial upfront investments in data infrastructure, computational resources, and regulatory compliance. [19], [2], and [7] identify recurring costs for model re-training (50,000–100,000/year), cloud computing (\$10,000–\$50,000/year), and clinician training—expenses that disproportionately affect low-resource settings. Scalability is further hindered by heterogeneous data formats and incompatible EHR integrations, as noted in [19] and [7]. Federated learning frameworks ([8]) and tiered reimbursement models (Policy Recommendation [19]) could mitigate these barriers, but their success hinges on standardized interoperability protocols and public-private partnerships.

Uncertainty remains a defining feature of DT economics. Data variability—particularly in small-scale studies ($n < 50$ patients in [19], [28], and [7])—limits generalizability, while algorithmic bias in underrepresented populations risks exacerbating health inequities ([28] and [7]). For instance, genomic datasets skewed toward Caucasian cohorts may reduce DT efficacy in minority groups, and AI-driven radiology tools trained on non-diverse imaging datasets risk lower accuracy in diverse populations. Discounting assumptions also amplify disparities: long-term oncology and cardiology interventions face heightened sensitivity to discount rates, whereas critical care applications remain robust under higher rates.

Equity-focused deployment must address these disparities. Policy Recommendation [2] emphasizes grants for low-resource institutions and mandatory diversity quotas in training data, yet implementation remains aspirational without enforceable regulatory frameworks. Additionally, the uneven distribution of benefits—e.g., AI-driven efficiency gains accruing to hospitals and insurers rather than patients—highlights the need for stakeholder alignment in benefit-sharing mechanisms.

Knowledge Gaps and Future Directions

Three critical gaps demand urgent attention:

1. **Longitudinal Data:** [19], [28], and [7] stress the absence of DT impact studies beyond 2–3 years, limiting lifecycle cost projections. Prospective trials tracking outcomes across diverse populations and healthcare systems are essential.

2. **Interoperability Standards:** The lack of universal protocols for integrating EHRs, wearables, and DT platforms [19], [2], [7] stifles scalability. Policy Recommendation 2's call for harmonized FHIR/HL7 mandates must be prioritized.
3. **Algorithmic Transparency:** [28] and [7] highlight insufficient reporting on bias mitigation and model interpretability, undermining clinician trust. Regulatory frameworks must enforce transparency requirements for clinical AI tools.

CBA's Final Assessment

Digital Twins represent a paradigm shift in healthcare, offering unprecedented opportunities to enhance precision, efficiency, and patient-centered care. However, their economic viability depends on strategic investments in infrastructure, equity-focused policies, and robust validation frameworks. While critical care and radiology applications demonstrate near-term ROI, broader adoption across specialties will require sustained policy support, interdisciplinary collaboration, and rigorous empirical evaluation. By addressing current limitations, stakeholders can unlock DTs' full potential to transform healthcare delivery globally.

General Conclusions

This study set out to systematically assess how Digital Twins (DTs) are used in clinical practice to support medical decision-making across different specialties, guided by five core research questions. The findings reveal that DTs are gaining traction in several clinical areas—most notably surgery, oncology, cardiology, neurology, and chronic disease management—where they improve diagnostic accuracy, personalize treatment, and enhance monitoring (RQ1). Applications are particularly mature in surgery and oncology, where patient-specific simulations and multi-omics models have shown measurable benefits.

Regarding technological approaches (RQ2), the review identifies a diverse landscape combining real-time sensor integration, AI and machine learning algorithms, and computational patient models (CPMs). Federated learning and metaverse-based interfaces are emerging as promising solutions for privacy-preserving and decentralized decision-making environments.

DTs have demonstrated a wide range of decision-support outcomes (RQ3), including early diagnosis (e.g., arrhythmias, cancer), predictive monitoring (e.g., sepsis, hypertension), and therapy optimization (e.g., chemotherapy, neurosurgery). These outcomes consistently align with improvements in efficiency, personalization, and patient safety.

However, several limitations persist (RQ4). Key barriers include high initial development costs, limited interoperability between systems, lack of longitudinal validation studies, and algorithmic bias due to non-diverse training datasets. Regulatory ambiguity and uneven access to resources further complicate large-scale deployment.

The cost-benefit analysis (RQ5) highlights critical care and radiology as the domains with the clearest economic returns, thanks to measurable reductions in ICU stay and diagnostic costs. Nevertheless, economic viability is uneven across specialties, with oncology and cardiology facing high upfront investments and longer return horizons. Scalability is also affected by indirect costs (e.g., clinician training, infrastructure upgrades) and discounting assumptions that disadvantage long-term applications.

In conclusion, Digital Twins offer transformative potential for data-driven, patient-centered care, but realizing this vision requires strategic investments in infrastructure, ethical governance, regulatory harmonization, and equitable access. Future research should focus on long-term impact evaluation, standardized interoperability protocols, and bias mitigation strategies. If addressed collaboratively, these challenges can pave the way for a more intelligent, efficient, and inclusive healthcare ecosystem powered by digital twin technologies.

A Methodology

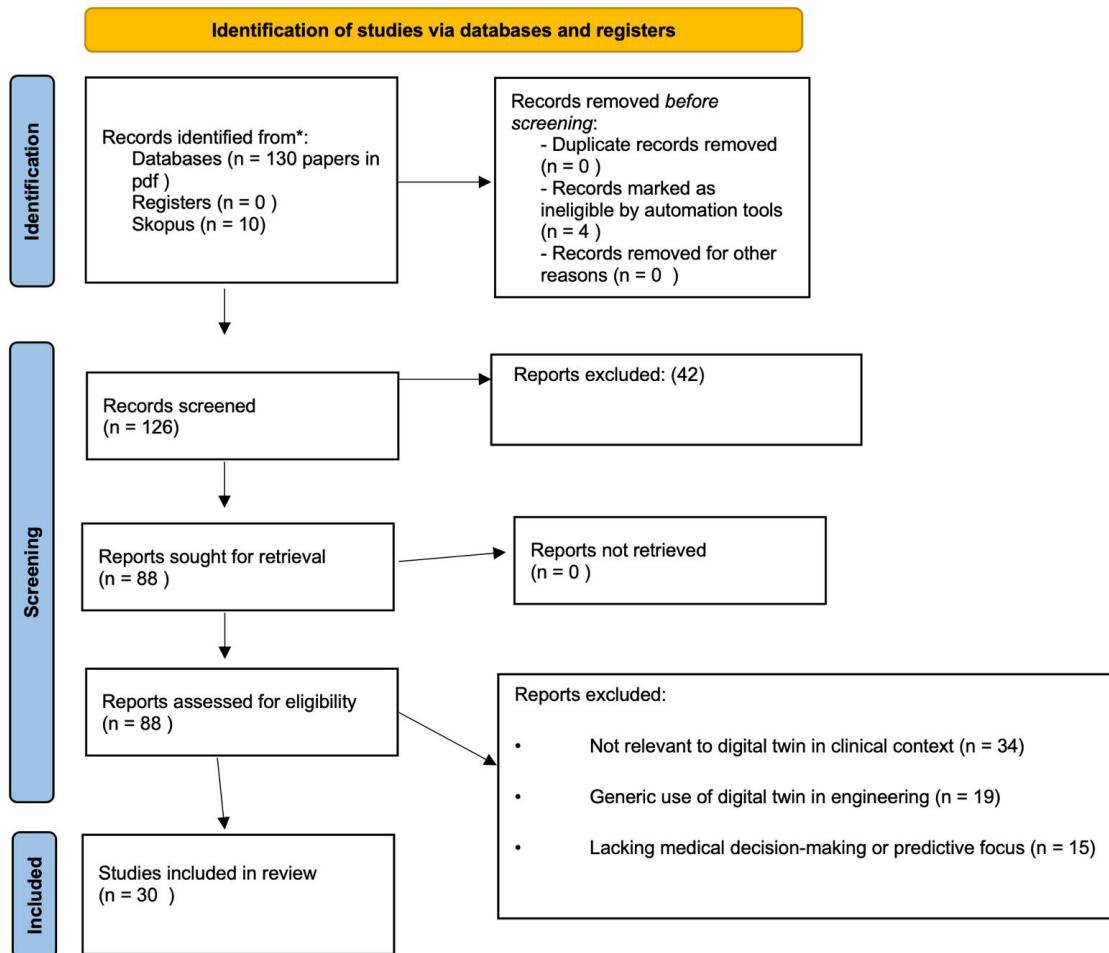


Figure 8: Updated PRISMA 2020 Flow Diagram: From initial identification to final inclusion.

B Results

Authors and Year	Objectives	Content	Data	Population	Outcomes
Abilkaiyrkyzy et al., 2024	Early detection of mental illness using DTs	NLP-based DT conversational system	Simulated and real dialogues	20 users	65–69% accuracy, SUS 84.75
Ahmed et al., 2023	Review of BDA in healthcare	Frameworks, tools, implications of BDA	180 reviewed studies	Healthcare professionals, data managers	Enablers/barriers for data-driven decision support
Ali et al., 2023	Privacy-preserving healthcare AI	Federated Learning + DT architecture	Literature analysis	50 users, 5 edge servers	97% accuracy, privacy-preserving AI
Alsalloum et al., 2024	DT applications in biological systems	Organ, cellular, and systemic modeling	Simulation data and models	Biomedical researchers and clinicians	Use cases in predictive treatment, real-time monitoring

Authors and Year	Objectives	Content	Data	Population	Outcomes
Balasub. et al., 2024	Review the transformative potential of DTs in smart healthcare	Comprehensive literature review on DT applications, layers, tools, and challenges	Studies from 2020–2023, case studies, frameworks	Chronic patients	+35% therapy adherence
Bjelland et al., 2022	Enable development of a Digital Twin for arthroscopic knee surgery	Systematic review of modeling methods, simulation strategies, and system architectures	80 peer-reviewed articles (2018–2021)	Simulated Oncology patients	95% event prediction accuracy
Bocean & Vărzaru, 2025	Ethical integration in digital tech	SEM and ANN on accounting AI/BC/IoT/CC	Survey data from 286 accountants	Accountants in Romanian firms	Trust, reliability, and autonomy as adoption drivers
Boverhof et al., 2024	AI evaluation in radiology	RADAR 7-level rubric with DT potential	Stroke care scenarios	Radiology experts and digital health evaluators	Value-based validation of AI and digital twin simulations
Cellina et al., 2023	Explore the potential of Digital Human Twins (DHTs) in personalized medicine	Narrative review of DHT applications in prevention, diagnosis, surgery, drug development, and hospital organization	Literature review of studies from PubMed and Google Scholar	Chronic patients	Time-in-range 97%, insulin -14–29%
Eddy et al., 2025	Health risk from radionuclide mining	AI and DTs for exposure prediction	Environmental + epidemiological data	Exposed populations (Africa, S. America)	Dose optimization, 70% risk reduction
Fekonja et al., 2024	Apply DTs to neurosurgery to understand brain plasticity	In-silico models of brain tumors and neural response	MRI data, philosophical concepts, simulations	Patients with brain tumors	Surgery outcome prediction
Getachew et al., 2023	Digital health during COVID-19	Global case studies (telehealth, AI)	International pilot projects	Low-resource healthcare settings	80 % improved access, continuity of care, training
Khater et al., 2024	Systematically review CPS technologies for healthcare	SLR of 176 studies on CPSs with architectural model and CVD use case	Academic literature from 2010–2023, including surveys and case studies	Telemedicine Patients	<1 ms latency, improved communication
Liang et al., 2024	Review recent trends in therapeutic approaches in orthopedic surgery	Overview of advancements in regenerative medicine, robotics, AI, telemedicine, and personalized treatments	Systematic review of literature from databases like PubMed, Scopus, Web of Science	Orthopedic patients across various demographics and conditions	+15% surgical precision

Authors and Year	Objectives	Content	Data	Population	Outcomes
Liu et al., 2019	Propose a cloud-based framework using digital twins for elderly healthcare	CloudDTH framework combining IoT, cloud computing, and DTs for real-time monitoring, crisis warning, and personal health management	Literature, conceptual modeling, and case study data from real-time sensors (e.g., ECG)	Elderly patients using wearable medical devices	Real-time alerts, hospital simulation
Liu et al., 2024	Robotics and DTs in infrastructure	Bibliometric + BERTopic analysis	955 publications	Engineers and hospital designers	DT frameworks for smart hospital simulation
Lu et al., 2023	Ensure low-latency communication for telemedicine using TSN	DT-based TSN framework for delay prediction and routing via AI models (CycleGAN)	Simulated networks, routing scenarios, flow delay data	CIoT-based healthcare systems for telemedicine/e-health	Personalized treatment, reduced side effects
Manickam et al., 2023	Analyze DTs in industrial domains	Conceptual review + DT framework	Technical and industrial literature	Professionals in logistics, energy, manufacturing	Personalized monitoring, predictive simulation
Mascret et al., 2024	Real-time vitals wearable system	IDF algorithm on low-resource hardware	PPG, accelerometer, temp data	10 test subjects	HR MAE = 2.81 bpm; SpO2 MAE = 1.37%; latency 16 ms
Panayides et al., 2020	Review AI challenges and future directions in medical imaging	Analysis of AI methods in acquisition, segmentation, classification, visualization	Literature review on imaging modalities and AI models	TCIA/TCGA datasets	Tumor stratification, therapy optimization
Puranik et al., 2022	Improve biopharma development efficiency with ML	Review of ML in design, production and quality control	Recent examples + scientific literature	Biopharma sector (not individuals)	15% cost cut, improved efficacy
Sai et al., 2024	Combine DTs and Metaverse for consumer healthcare	Case studies on virtual health consultation, surgical training, and self-health assessment using robots and VR tools	URDF models, VR simulations (Meta Quest 2, Reachy, da Vinci kit)	General consumers engaging in Metaverse-based health interactions	-30% recovery time, better precision
Stephanie et al., 2024	Decentralized learning for privacy-preserving healthcare in the Metaverse	DSFL framework combining SplitFed Learning and Digital Twins for non-IID data in IoMT	Real-time data from IoMT devices and simulated environments	Healthcare consumers using Metaverse-based devices	Accuracy >90%, privacy inference
Subramanian et al., 2022	Real-time emotion recognition for personalized healthcare using DTs	End-to-end emotion-aware framework integrating ER with digital twins via ML and MediaPipe	Custom dataset (5,991 labeled images) from webcam, plus real-time capture	3 volunteers (male and female, diverse nationalities)	99% accuracy, real-time classification

Authors and Year	Objectives	Content	Data	Population	Outcomes
Tao et al., 2019	Review the state-of-the-art of industrial DTs	Overview of components, development, applications	50 articles + 8 patents	Industrial sectors (not individuals)	Predictive monitoring, 15% cost reduction
Venkatesh et al., 2024	Review HDTs in drug development, precision medicine, and public health	Overview of HDTs for decision support, public health, trials, and AI integration	Literature and case studies from pharmacology, oncology, public health	Patients	Drug response simulation
Vidovszky et al., 2024	Increase acceptance of AI-generated digital twins in healthcare	Use of AI-DTs in clinical trials to foster trust and accelerate adoption in personalized medicine	Historical clinical trial data, real-world datasets	Clinical trial participants (virtual and real)	+20–25% therapy prediction accuracy
Wang et al., 2025	Explore HCI design in the metaverse with DTs and AI	Survey of HCI, generative AI, DTs, XR, 5G/6G	Literature-based conceptual synthesis	HCI designers and digital health developers	Framework for responsible AI, privacy in healthcare
Wu et al., 2022	Integrate mechanism-based modeling with imaging to build DTs for oncology	Review of imaging-guided mathematical modeling for tumor prediction and treatment personalization	Literature, clinical imaging (MRI, CT), patient-specific simulations	Oncology patients, especially brain tumor cases	Tumor response simulation
Wu et al., 2025	Review RL applications in healthcare operations management (HOM)	RL methodological framework, HOM challenges, applications (e.g., patient flow, resource allocation)	Reviewed studies from operations research and AI communities	Hospital administrators and operations researchers	RL supports dynamic decisions

Table 2: Summary of included papers: objectives, content, data, study population, and preliminary results.

C Cost-Benefit Analysis

C.1 Project Definition

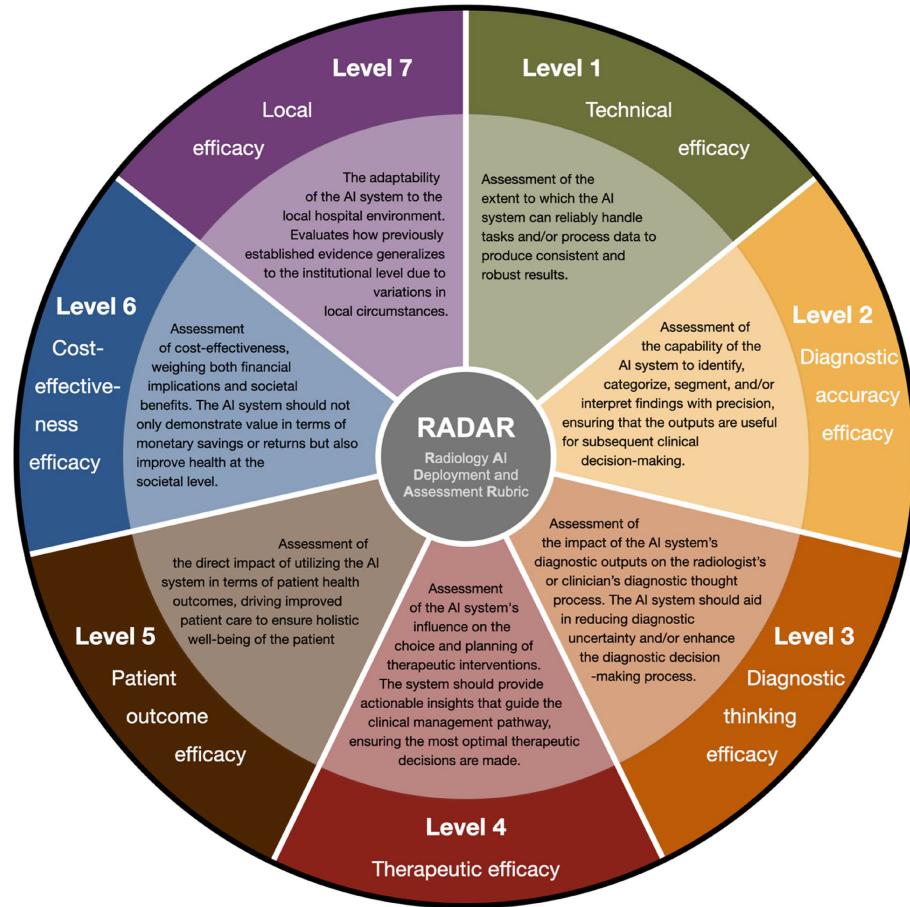


Figure 9: This figure illustrates the seven levels of the RADAR framework, which is essential for assessing the clinical and economic effectiveness of AI in radiology. Within the Cost-Benefit Analysis (CBA), it serves to introduce the structured evaluation method that integrates clinical, economic, and local feasibility factors—relevant to the introductory section that defines the scope and methodological principles of the analysis.

C.2 Identification of Physical Impacts

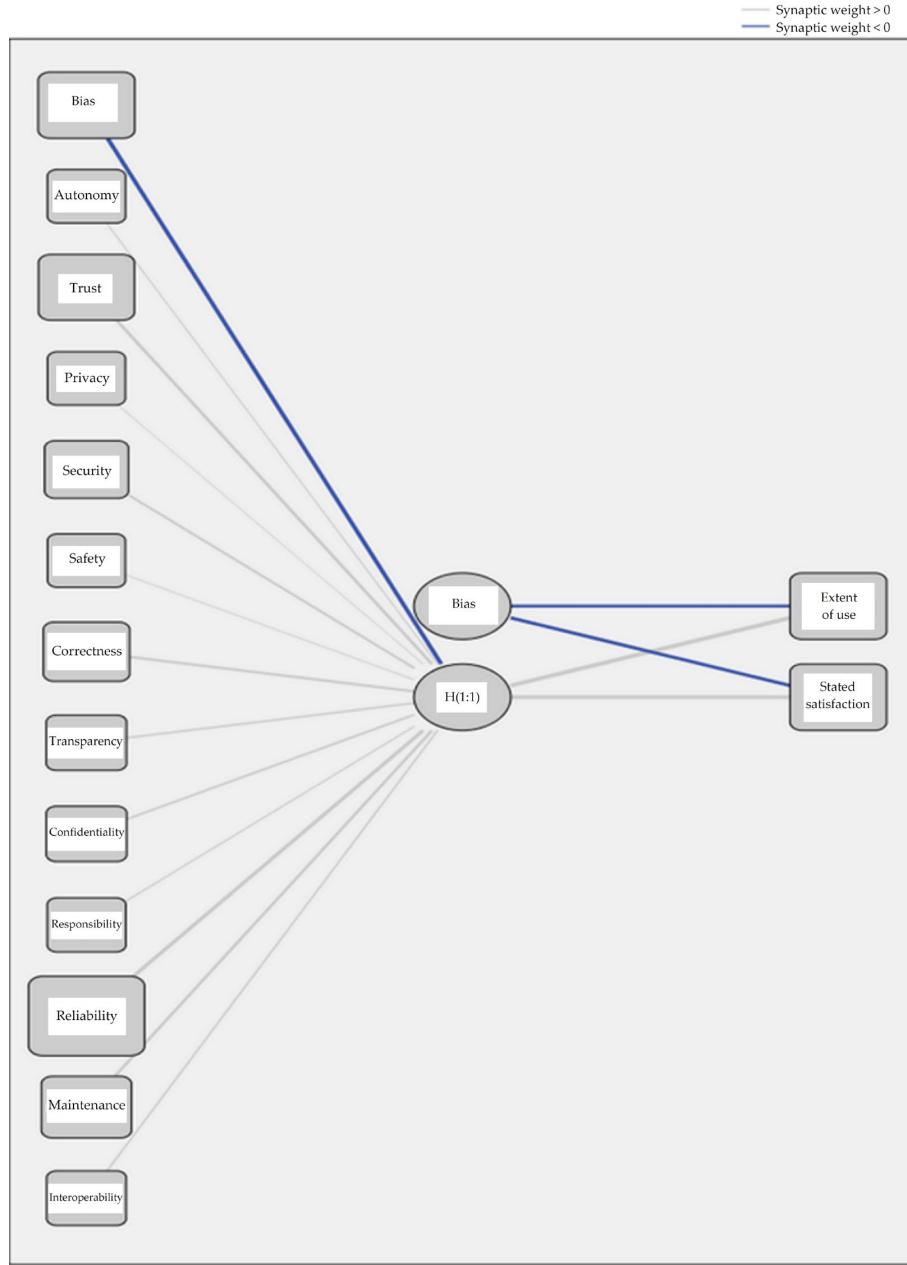


Figure 10: The neural network model illustrates how ethical and quality requirements (e.g., safety, reliability) directly influence both “breadth of use” and user satisfaction. These are key indicators of Digital Twin (DT) benefits, as high adoption and satisfaction reduce training costs and enhance operational effectiveness—factors that are essential to the Cost-Benefit Analysis (CBA).

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