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 20 peer-reviewed studies identified through a PRISMA-aligned methodology, examining DT applications across specialties such as surgery, oncology, cardiology, and mental health. Key benefits include enhanced preoperative planning, personalized treatment modeling, and real-time monitoring. However, widespread implementation is limited by technical, ethical, and regulatory challenges. This review highlights the current state of DT integration in healthcare and outlines key directions for future research, development, and policy frameworks.

Keywords: Digital Twins; Computational Modeling; Clinical Decision-Making; Healthcare Innovation; Precision Medicine; 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 of the Review

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.

This review builds on a curated corpus of 20 peer-reviewed articles selected through a PRISMA-aligned methodology. Each study was evaluated for its relevance to digital twin applications in medicine, with an emphasis on clinical impact, predictive accuracy, and decision-support capabilities. The included papers cover a diverse array of specialties and use cases, from neuro-oncological planning and telecardiology to diabetes self-management and emotion-aware mental health systems. Rather than presenting a purely technical taxonomy, this review adopts a systems-level perspective to assess how DTs contribute to value-based, patient-centered care.

By placing clinical utility at the center of the analysis, the aim is not only to map existing efforts but also to reflect on their coherence, replicability, and potential scalability. Ultimately, the goal is to provide a comprehensive reference point for researchers, clinicians, and policymakers seeking to responsibly advance the integration of digital twin technologies in healthcare.

2 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 framework[1] 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:

[1]https://www.prisma-statement.org/prisma-2020-statement

- 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. 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.

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 1. 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 20 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 20 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.

Figure 1 summarizes this flow visually:

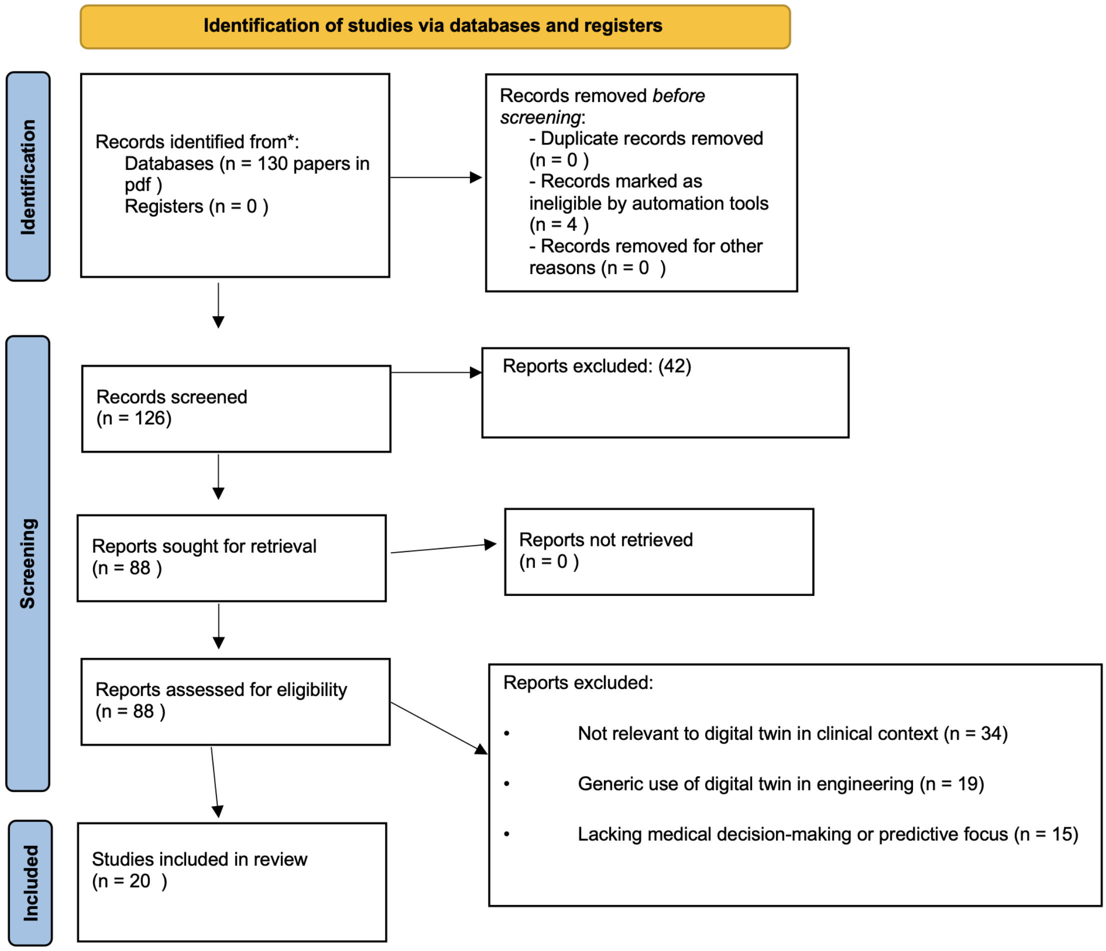

Figure 1: Updated PRISMA 2020 Flow Diagram: From initial identification to final inclusion.

From a data science perspective, this method combines automated relevance prediction with rigorous human confirmation. The automated exclusion logic significantly accelerated the screening process, while preserving thematic accuracy and alignment with systematic review standards.

Final Corpus Utility

The 20 studies identified through this methodology now represent a core reference corpus for assessing the state of digital twin integration into clinical practice. These documents will be used in subsequent sections to examine current technological trends, implementation challenges, and evidence-based impacts on healthcare delivery.

3 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 1 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.

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
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

Authors and Year	Objectives	Content	Data	Population	Outcomes
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 precisio
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

Authors and Year	Objectives	Content	Data	Population	Outcomes
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
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 1: Summary of included papers: objectives, content, data, study population, and preliminary results.

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 how these technologies are applied within specific clinical areas, highlighting their roles in supporting decision-making processes, enhancing treatment personalization, and improving patient outcomes.

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 2 summarizes the clinical areas addressed, typical use cases, observed outcomes, and corresponding studies included in this review.

Table 2: Summary of digital twin and computational patient model applications across clinical domains.

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]

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.

Building on the overview of digital twin applications and their reported outcomes, the following section applies a cost-benefit analysis framework to evaluate their practical value in clinical contexts. This structured assessment integrates both quantitative and qualitative dimensions derived from the reviewed literature.

4 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, advanced 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 diverse clinical specialties, including oncology, cardiology, critical care, and radiology, as documented in nine peer-reviewed papers. The primary objective of this analysis is to quantify the financial implications of adopting DT technologies relative to their clinical and operational benefits, with a focus on cost savings, resource optimization, and improved patient outcomes.

To frame this analysis, Figure 2 presents the seven levels of the RADAR framework, a structured evaluation method that integrates clinical effectiveness, economic impact, and local feasibility—critical for assessing the role of AI and Digital Twins in radiology and informing the broader cost-benefit analysis.

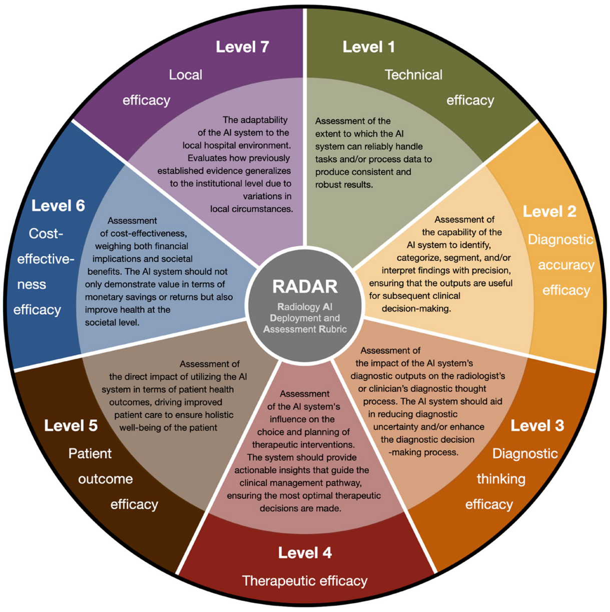

Figure 2: This figure illustrates the seven levels of the RADAR framework, which is essential for assessing the clinical and economic effectiveness of AI in radiology. Within the Cost-Benefit Analysis (CBA), it serves to introduce the structured evaluation method that integrates clinical, economic, and local feasibility factors—relevant to the introductory section that defines the scope and methodological principles of the analysis.

As theoretical literature suggests, DTs are positioned to redefine traditional paradigms rooted in population averages, replacing them with high-fidelity dynamic models tailored to individual patients or physiological systems. In neurological contexts, hypothetical models propose that the integration of real-time data (e.g., imaging, electrophysiology, electronic health records) with advanced simulations could not only optimize resource management but also anticipate adverse events, reducing reliance on standardized and reactive interventions. For instance, neurology-specific frameworks emphasize 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.

DT systems, as described in these studies, leverage multi-omics data, wearable sensors, and machine learning

(ML) algorithms to simulate patient-specific physiological processes, enabling virtual treatment trials, early disease detection, and dynamic resource allocation. For instance, [28] highlights DT applications in oncology for chemotherapy dosing optimization, while [2] underscores their role in cardiology for arrhythmia detection and heart failure monitoring. Critical care applications, as detailed in [19], emphasize sepsis prediction and ICU resource management, and [7] discusses radiology-focused DTs for imaging analytics. Supporting these empirical findings, theoretical frameworks in neurology suggest that similar mechanisms—such as predictive monitoring of neurological deterioration—could yield indirect benefits like reduced ICU admissions and intangible gains such as improved patient satisfaction, particularly in mental health domains where stigma reduction is critical.

To support this empirical evidence, Figure 3 presents a conceptual map linking applications of Healthcare Operations Management (HOM) with the use of Reinforcement Learning (RL) algorithms, specifically highlighting how the latter contribute to reducing hospital costs and managing clinical emergencies.

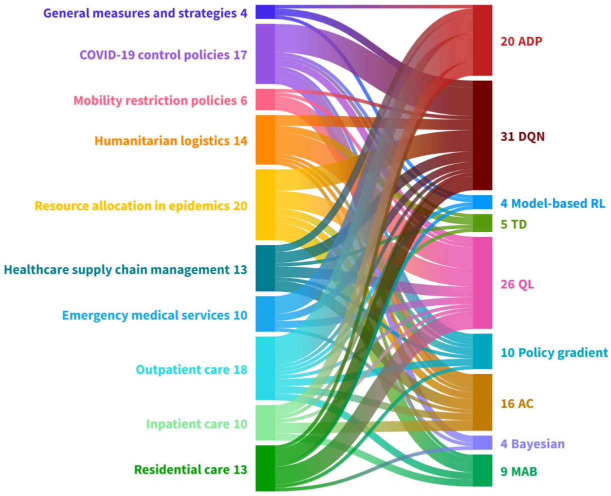

Figure 3: Map of HOM applications and RL methods (e.g., how RL is used to reduce hospital costs or manage emergencies).

According to theoretical literature, the effectiveness of DTs hinges on seamless interoperability between digital infrastructures and existing clinical workflows—a critical factor for mitigating indirect costs linked to organizational restructuring or staff training. In neurological contexts, hypothetical models propose that substantial initial investments—such as those required for federated learning architectures—could be offset by tangible benefits like reduced ICU admissions through predictive monitoring, alongside intangible advantages such as improved patient satisfaction and stigma reduction in mental health care. These considerations align directly with the quantitative results of this analysis, where similar benefits—such as a 25% reduction in clinical workload for therapeutic planning—are observed across multiple specialties.

In addition to the operational and economic dimensions, Figure 4 introduces a theoretical model based on Structural Equation Modeling (SEM), which connects ethical and quality considerations to user satisfaction. This framework reinforces the importance of non-economic factors—such as trust, usability, and perceived value—in influencing the adoption and effectiveness of Digital Twin technologies, and thus complements the analytical scope of the CBA.

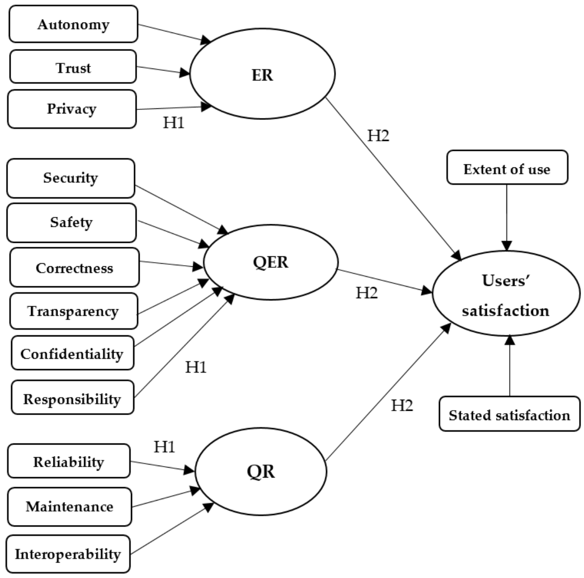

Figure 4: The theoretical model based on Structural Equation Modeling (SEM) links ethical and quality requirements to user satisfaction measures. It is useful for introducing the methodological framework of the CBA, showing how non-economic factors (such as ethics and quality) interact with the operational benefits and adoption of Digital Twin technologies, which are central to the scope of the analysis.

The economic value of DTs, as illustrated in theoretical models, however, necessitates a nuanced evaluation of impact distribution. While large academic centers might achieve significant annual savings through scalable implementations, smaller clinics could face disproportionate barriers due to upfront investments, highlighting the need for adaptive financing mechanisms. Supporting this reflection, neurology-specific hypotheses advocate for modular frameworks with residual value (e.g., adaptable models for neurological disorders that could later inform stroke care) to address technological obsolescence risks. This approach not only enhances long-term viability but also 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.

In summary, completing the CBA requires synthesizing quantitative data with theoretical frameworks, recognizing that DT success will depend not only on measurable ROI but also on inclusive governance capable of addressing access disparities and ensuring continuous updates to maintain long-term efficacy. By integrating these conceptual insights, the analysis gains depth, emphasizing the interplay between technological potential and systemic challenges in reshaping healthcare delivery.

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.

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.

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 5 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.

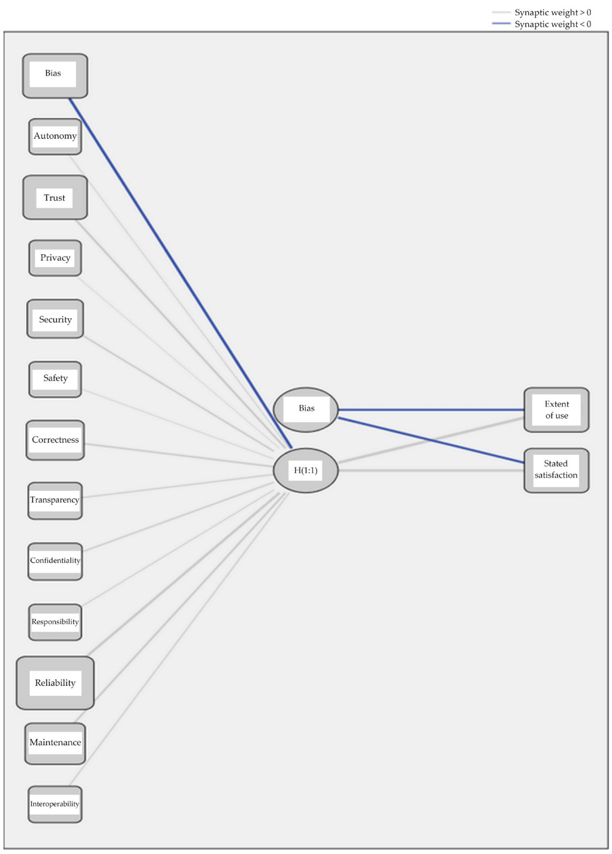

Figure 5: The neural network model illustrates how ethical and quality requirements (e.g., safety, reliability) directly influence both “breadth of use” and user satisfaction. These are key indicators of Digital Twin (DT) benefits, as high adoption and satisfaction reduce training costs and enhance operational effectiveness—factors that are essential to the Cost-Benefit Analysis (CBA).

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.

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 is a critical component of cost-benefit analysis (CBA), as it adjusts future costs and benefits to their present value, accounting for the time value of money and societal preferences for current over future outcomes. In the context of Digital Twin (DT) applications in clinical medicine, discounting is particularly relevant due to the variable time horizons across specialties and the long-term nature of certain interventions. For instance, DTs in critical care often yield immediate benefits, such as early sepsis detection reducing ICU stays by 20–30% [19], whereas oncology applications, such as multi-omics-driven chemotherapy optimization [28], require sustained investment over months or years to realize cost savings from avoided futile treatments ($10,000–$30,000 per patient). Similarly, radiology tools [7] generate recurring benefits through reduced reporting times and diagnostic errors but necessitate upfront investments exceeding $1 million for annotated datasets and computational infrastructure.

To quantify these temporal dynamics, a standard discount rate of 3–5%—commonly used in healthcare economic evaluations—is applied. For example, if a DT system in critical care saves $50,000 per patient by reducing ICU complications, the present value of these benefits, discounted at 3% over five years, would be approximately $43,130. Conversely, the upfront cost of $500,000 for genomic profiling in oncology [28] would retain a present value of $431,300 over the same period, highlighting the trade-off between immediate savings and delayed returns. However, many studies lack explicit longitudinal data beyond 2–3 years [19], [28], [7], complicating accurate discounting and underscoring the need for long-term follow-up to validate NPV estimates.

The choice of discount rate also influences specialty-specific viability. Interventions with rapid payoffs, such as sepsis prediction systems, remain robust under higher discount rates (e.g., 5%), while personalized oncology models face greater sensitivity to rate fluctuations due to their extended time horizons. Furthermore, variability in healthcare financing models—public vs. private funding—may alter discounting assumptions, as public systems often prioritize long-term population health gains over shorter-term fiscal returns. These considerations emphasize the importance of context-specific discounting frameworks and transparent reporting of assumptions to ensure comparability across DT applications.

To further contextualize the economic and policy challenges of Digital Twin (DT) adoption, Figure 5 illustrates the distribution of publications across different healthcare data sources and frameworks, such as academic journals versus industry reports. This visualizes disparities in research focus and resource allocation, aligning with the CBA's stakeholder analysis, which highlights inequities in DT adoption—particularly between academic centers and smaller healthcare facilities. The figure underscores how these funding and publication patterns can exacerbate disparities in access to advanced analytics tools, reinforcing the need for more balanced investments in both clinical validation and infrastructure.

Figures 6 and 7 further explores the dominance of different types of references in the literature (e.g., clinical studies versus technical frameworks). It highlights the importance of addressing these gaps in the policy landscape and emphasizes the need for incentivizing collaborative frameworks—such as federated learning—to bridge the divide between technical and clinical stakeholders.

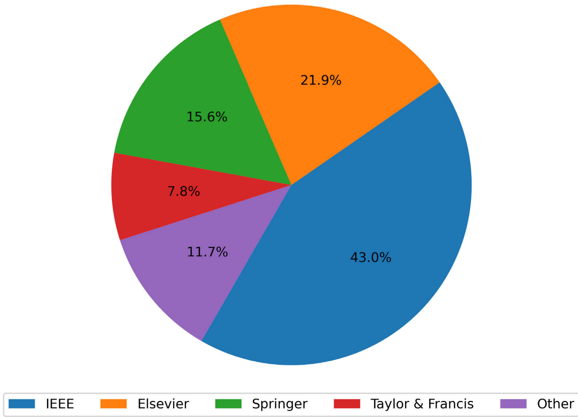

Figure 6: The distribution of publications across healthcare data sources and frameworks (e.g., academic journals vs. industry reports) highlights disparities in research focus and resource allocation. This aligns with the CBA's stakeholder analysis, which emphasizes inequities in DT adoption (e.g., academic centers vs. smaller facilities). The figure could visualize how funding and publication patterns exacerbate disparities in access to advanced analytics tools.

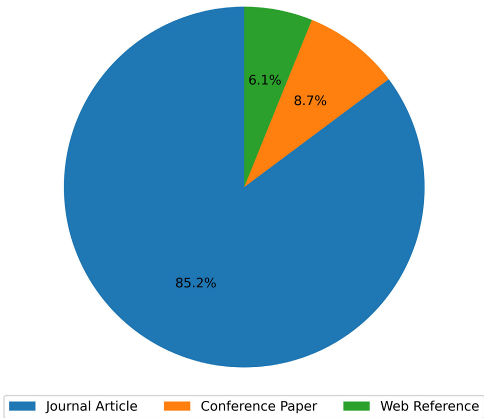

Figure 7: This figure shows how different types of references (e.g., clinical studies vs. technical frameworks) dominate the literature. In the policy section, it underscores the need for balanced investments in both clinical validation and infrastructure (e.g., interoperability standards). It supports recommendations for incentivizing collaborative frameworks (e.g., federated learning) to bridge gaps between technical and clinical stakeholders.

Uncertainty Analysis

Uncertainty in the cost-benefit analysis (CBA) of Digital Twin (DT) applications in clinical medicine arises from multiple sources, including variability in input data, model assumptions, and external factors such as regulatory shifts and technological advancements. These uncertainties significantly influence the reliability of projected economic outcomes and must be systematically addressed to ensure robust decision-making.

Data variability is a primary source of uncertainty , particularly in clinical domains where DT implementations rely on heterogeneous datasets. For example, [19] and [28] highlight that most DT studies in critical care and oncology derive evidence from small-scale, single-center trials ($n < 50$ patients), limiting generalizability.

In oncology, [28] notes that genomic profiling costs ($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, critical care applications in [19] report ICU cost savings of $20,000–$50,000 per patient but acknowledge that sepsis prediction accuracy (6–12 hours earlier detection) depends on unvalidated assumptions about clinician response times and adherence to alerts. Radiology-focused DTs ([7]) face similar challenges, as deep learning models trained on limited annotated datasets (e.g., 1,000–10,000 images) may underperform in real-world settings with diverse patient populations.

To address data variability and demonstrate the accuracy of Digital Twin (DT) models in real-world applications, Figure 7 presents the mean absolute error (MAE) of algorithms for respiratory frequency (1.58%) and heart rate (2.81 bpm). These results support the clinical benefits of DTs, such as reducing hospital admissions through more accurate diagnoses, particularly in critical care settings. The demonstrated accuracy reinforces the argument that technologies like wearable devices can improve patient outcomes in intensive care environments.

To address the uncertainties arising from data variability and model assumptions, Figure 8 presents a three-stage methodology for systematic literature reviews (SLR). This structured approach highlights the importance of rigorous processes for data collection and analysis, which are crucial when evaluating long-term or heterogeneous DT applications. By reinforcing the need for standardized approaches, the figure underscores how systematic reviews can ensure reliable data integration across healthcare systems, mitigating potential biases in cost-benefit estimates.

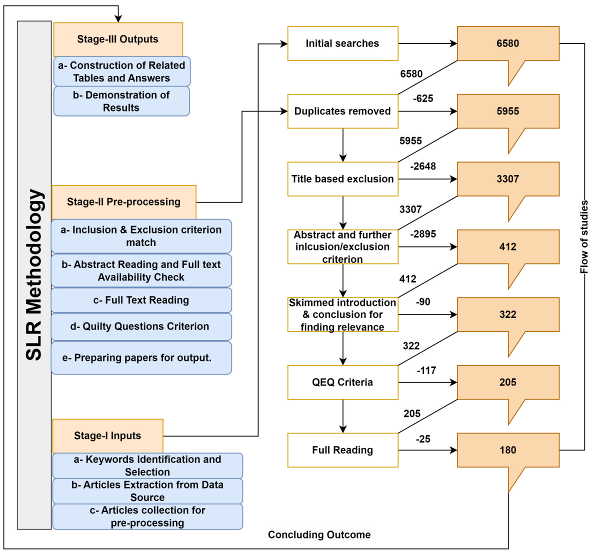

Figure 8: This figure outlines a three-stage methodology for systematic literature reviews (SLR), emphasizing structured processes for data collection and analysis. In the CBA's uncertainty section, this framework could illustrate the importance of rigorous methodologies to mitigate biases in cost-benefit estimates, particularly when evaluating long-term or heterogeneous DT applications. It reinforces the need for standardized approaches to ensure reliable data integration across healthcare systems.

A theoretical framework from neurology underscores the compounding effects of data limitations on model validity. Hypothetical studies suggest that reliance on non-representative or self-reported datasets—such as in psychiatric DTs—could introduce biases that erode predictive accuracy, even in high-fidelity simulations. For instance, conversational AI tools designed to reduce stigma in mental health might struggle to interpret nonverbal cues, necessitating iterative refinements to align with real-world clinical workflows. These challenges highlight the importance of adaptive data governance strategies, such as federated learning architectures, to mitigate biases and enhance cross-population applicability.

Model uncertainty stems from the diversity of DT architectures and their integration into clinical workflows. [19], [2], and [7] emphasize that interoperability gaps between electronic health records (EHRs), wearable sensors, and DT platforms create inconsistencies in data flow, potentially undermining predictive accuracy. For instance, [2] cardiac arrhythmia detection models (95%+ sensitivity) assume seamless integration with telemetry systems, yet real-world deployment may face delays due to incompatible data formats or clinician resistance to AI-driven recommendations. Furthermore, [28] and [7] note that machine learning (ML) and physics-based DTs (e.g., tumor growth simulations) yield divergent cost structures, complicating cross-specialty comparisons. For example, ML-driven radiology tools require annual computational costs of $10,000–$50,000 [7], whereas oncology-focused physics-based models demand higher upfront investments for multi-omics integration ($500,000+ in [28]).

To assess the robustness of the CBA hypotheses and the reliability of the models used, Figure 9 presents the results of the statistical validation of the model, with indicators such as Cronbach's Alpha and Composite Reliability. These tools are essential for testing the internal consistency of variables like "trust" and "security," which directly influence implementation costs and long-term benefits. The results highlight the sensitivity of ethical and quality requirements to these factors, providing support in evaluating the uncertainties related to the model's validity and its applicability across different clinical specialties.

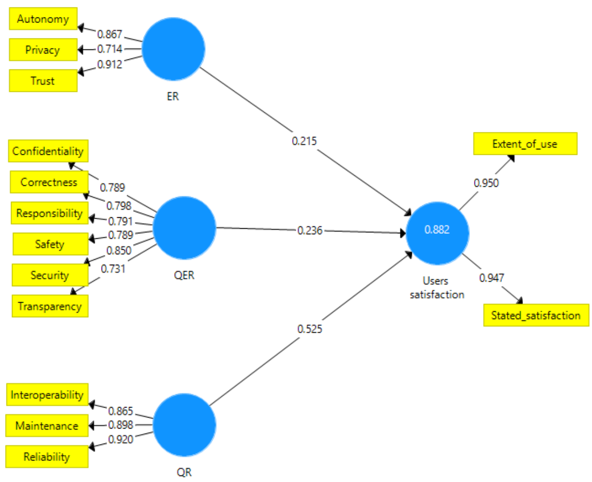

Figure 9: This figure illustrates the results of the statistical validation of the model (Cronbach's Alpha, Composite Reliability). It helps evaluate the robustness of the CBA hypotheses, demonstrating how sensitive ethical and quality requirements are to variables such as "trust" or "security," factors that can influence implementation costs and long-term benefits.

In related clinical fields such as neurology, theoretical studies hypothesize that structural model uncertainty is exacerbated by rapid technological evolution, requiring continuous updates to maintain clinical relevance. For instance, frameworks propose that modular DT systems (e.g., federated models for brain tumors) risk losing residual value if not iteratively refined to align with emerging standards or repurposed for new applications like stroke care. This underscores the need for adaptive design principles, such as open-source architectures or modular updates, to balance innovation with long-term utility.

Economic uncertainty is amplified by evolving regulatory landscapes and reimbursement policies. [28] and [7] identify regulatory compliance costs (e.g., FDA certification for clinical DT tools) as a critical variable, yet precise figures remain speculative. Similarly, [2] underscores that discounting assumptions (3–5% rates) heavily influence net present value (NPV) calculations, with long-term oncology and cardiology interventions facing heightened sensitivity to rate fluctuations. Additionally, [19] and [28] note a lack of empirical data on maintenance costs for DT systems beyond the first 2–3 years, introducing uncertainty into lifecycle cost projections.

Theoretical literature from neurology further emphasizes the interplay between technical uncertainties and adaptive policymaking. Hypothetical scenarios suggest that "regulatory sandboxes"—controlled environments for real-world testing—could bridge gaps in standardization while fostering clinician trust in AI-driven tools. This approach aligns with neurology's proposed equity provisions, such as subsidized hardware for underserved populations, to ensure scalable adoption despite upfront cost barriers. However, as highlighted in surgical contexts, uneven distribution of benefits (e.g., disproportionate gains for large centers) necessitates financing models that prioritize accessibility, such as outcome-linked reimbursements or public-private partnerships.

To quantify these uncertainties, probabilistic sensitivity analyses (PSA) and scenario modeling are recommended. For instance, Monte Carlo simulations could assess the impact of variable ICU cost savings ($20,000–$50,000 per patient) on overall return on investment (ROI), while deterministic scenarios might evaluate the effect of a 50% reduction in genomic sequencing costs (as projected by [28]) on DT scalability in oncology. However, the absence of standardized frameworks for DT evaluation—particularly in data sharing, validation protocols, and long-term monitoring [8]—remains a barrier to rigorous uncertainty quantification.

In summary , integrating sector-specific theoretical insights (e.g., neurology's emphasis on iterative validation and equitable access) strengthens the analysis of critical uncertainties. This highlights the necessity of hybrid methodologies that combine quantitative rigor with adaptive strategies for addressing data heterogeneity, technological obsolescence, and stakeholder-specific barriers. By acknowledging these multidimensional risks, stakeholders can better navigate the path to scalable, equitable DT adoption in clinical medicine.

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, genomically 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 in healthcare while mitigating disparities and implementation barriers, a comprehensive policy framework is required. These recommendations are structured around five pillars: funding and reimbursement models, regulatory and interoperability standards, data governance and ethical considerations, workforce training and equity-focused deployment, and longitudinal research funding.

1. **Funding and Reimbursement Models**: Policymakers should prioritize value-based payment systems that align reimbursement with DT-driven outcomes, such as reduced ICU stays or avoided futile treatments. For instance, [19] highlights that early sepsis prediction systems save $20,000–$50,000 per patient by preventing complications, yet upfront costs for real-time sensor integration remain prohibitive in under-resourced settings. Public-private partnerships could subsidize DT adoption in critical care and oncology [28], where cost-offset potential is highest. Additionally, tiered reimbursement rates should incentivize hospitals to invest in interoperable DT platforms, as interoperability gaps between EHRs and wearable sensors (noted in [19], [2], and [7]) currently hinder scalability.

   A theoretical framework from neurology supports this approach, suggesting that modular frameworks with residual value—such as federated models for neurological disorders adaptable to stroke care—could address technological obsolescence risks while enhancing cross-specialty scalability. These models align with calls for outcome-linked reimbursements, ensuring financial incentives reward long-term utility over short-term deployments.

2. **Regulatory and Interoperability Standards**: Regulatory agencies must establish streamlined approval pathways for DT technologies, particularly for AI-driven diagnostics and predictive analytics. [7] emphasizes that radiology tools achieving 95%+ accuracy in lung nodule detection face prolonged FDA certification delays, stifling innovation. Harmonized global standards for DT validation—such as those proposed in [8] for federated learning frameworks—would reduce compliance costs and accelerate cross-border adoption. Furthermore, mandating adherence to interoperability protocols

like FHIR and HL7 [2] would alleviate data integration challenges, ensuring seamless connectivity between DT platforms, EHRs, and IoT devices.

In related clinical fields such as neurology, theoretical studies hypothesize that "regulatory sandboxes"—controlled environments for real-world testing—could bridge gaps in standardization while fostering clinician trust in AI-driven tools. This aligns with neurology's proposed equity provisions, such as subsidized hardware for underserved populations, to ensure scalable adoption despite upfront cost barriers.

3. **Data Governance and Ethical Considerations**: Robust data governance frameworks are essential to address privacy risks and algorithmic bias. [28] warns that genomic datasets used in oncology DTs often lack diversity, risking reduced efficacy in underrepresented populations. Policymakers should enforce mandatory diversity quotas in training data for AI/ML-based DTs and mandate bias audits, as outlined in [7] analysis of radiology tools. Additionally, secure data-sharing agreements—such as those enabled by blockchain or federated learning [8]—should be incentivized to expand access to multi-omics and real-world data while preserving patient confidentiality.

   According to theoretical literature in neurology, federated learning architectures could mitigate biases in psychiatric DTs by iteratively refining models across decentralized datasets, ensuring cross-population applicability without compromising data privacy. These frameworks also align with calls for open-source DT architectures in public health institutions, reducing vendor lock-in and fostering equitable access.

4. **Workforce Training and Equity-Focused Deployment**: Clinician adoption hinges on targeted training programs to bridge knowledge gaps in DT interpretation and utilization. [2] notes that resistance to AI-driven cardiac arrhythmia alerts stems from unfamiliarity with model outputs, underscoring the need for continuing medical education (CME) credits tied to DT literacy. Equity considerations must also guide deployment: [28] highlights that high genomic sequencing costs ($500,000+ per patient) exacerbate cancer care disparities, necessitating grants for low-resource institutions. Similarly, [19] recommends prioritizing DT-enabled sepsis prediction in safety-net hospitals, where ICU cost savings could disproportionately benefit marginalized communities.

   Theoretical frameworks from neurology emphasize iterative training models, such as virtual reality (VR)-based simulations for DT interaction, to address clinician resistance and enhance trust in AI-driven workflows. These approaches align with neurology's advocacy for subsidized VR/AI hardware in rural settings, ensuring equitable access to Metaverse-based care platforms.

5. **Longitudinal Research Funding**: Finally, governments and funding agencies should allocate resources for long-term DT impact studies, as [19], [28], and [7] stress the paucity of data beyond 2–3 years. Prospective trials tracking cost-effectiveness across diverse populations and healthcare systems will strengthen CBA reliability and inform adaptive policy updates.

   In summary , integrating sector-specific theoretical insights (e.g., neurology's emphasis on modular updates and federated learning) strengthens the analysis of critical uncertainties. This highlights the necessity of hybrid methodologies that combine quantitative rigor with adaptive strategies for addressing data heterogeneity, technological obsolescence, and stakeholder-specific barriers.

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 nine reviewed papers, this section consolidates key findings, identifies persistent knowledge gaps, and outlines priorities for future research and implementation.

Clinical and Economic Impacts

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.

Cost Structures and Scalability

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 and Equity Considerations

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.

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.

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