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Systematic Review

Human Digital Twins for Smart and Sustainable Hospital Operations: Trends Analysis and a Value-Sensitive Framework

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Abstract

Human Digital Twins (HDTs) extend traditional Digital Twin (DT) concepts by modeling both humans and hospital processes to support smarter and more human-centered healthcare. By integrating Industry 4.0 (I4.0) technologies with the human-centric principles of Industry 5.0 (I5.0), HDTs offer new opportunities to improve hospital operations. This study presents a PRISMA-based systematic literature review to examine the role of HDTs in hospital operations. A total of 329 papers were identified through the initial search, and after the screening process, 22 studies were included for in-depth analysis. The review combines bibliometric analysis to examine publication trends, leading authors, contributing countries, and keyword co-occurrence with a content analysis to identify the main research themes. Three major themes emerged: (1) HDT architectures and data integration, (2) human-centric and governance aspects, including explainable artificial intelligence and privacy, and (3) operational and clinical outcomes, including patient flow, resource utilization, and staff support. Based on these findings, the study proposes a four-layer HDT framework for practical implementation in hospital operations. Although the reviewed studies indicate that HDTs have considerable potential to improve operational efficiency and strengthen human involvement, most existing research remains conceptual or simulation-based. Future research should therefore prioritize real-world implementation and validation while incorporating ethical, explainable, and sustainable design principles.

Keywords: human digital twins; I4.0; I5.0; smart healthcare; PRISMA review

1. Introduction

1.1. Industry 4.0 and 5.0: Evolution and Interaction

Industry 4.0 (I4.0) represents a major transformation in industrial systems through the integration of digital technologies that connect the physical and virtual worlds. Technologies such as Cyber–Physical Systems (CPSs), the Internet of Things (IoT), artificial intelligence (AI), big data analytics, and cloud computing enable interconnected, data-driven environments in which physical assets can be monitored and optimized in real time [1,2]. These technologies support automation, predictive analytics, and enhanced operational efficiency across a wide range of sectors. One of the most significant innovations emerging from I4.0 is the digital twin (DT), which provides a virtual representation of a physical system that remains synchronized with its real-world counterpart. Through continuous data exchange, DTs enable simulation, predictive maintenance, and evidence-based decision-making [1,3].

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Industry 5.0 (I5.0) builds upon the technological foundation established by I4.0 while introducing a broader perspective that emphasizes human-centricity, sustainability, and resilience [1]. Rather than focusing solely on automation and efficiency, I5.0 promotes collaboration between humans and intelligent technologies to ensure that digital innovations contribute to human well-being and societal value [4,5]. Within this paradigm, technologies such as AI and robotics are intended to augment human capabilities rather than replace them [6]. The integration of human creativity, ethical considerations, and sustainable resource utilization distinguishes I5.0 from the predominantly technology-centered orientation of I4.0.

This transition reflects a shift from purely automated systems toward socio-technical environments in which advanced technologies operate alongside human expertise. Such collaboration is particularly relevant in healthcare, where technological efficiency must be balanced with patient safety, clinician well-being, and ethical decision-making. In this context, digital twin technologies provide an important foundation for integrating technological capabilities with human-centered healthcare practices.

1.2. Digital Twins and Human Digital Twins in Hospital Operations

Digital twins (DTs) have emerged as a key technology supporting digital transformation across multiple sectors, including healthcare. Recent evidence synthesis indicates that DTs are increasingly being applied in healthcare for personalized medicine, predictive maintenance of medical equipment, and healthcare system optimization, although their implementation remains constrained by challenges related to privacy, validation, and implementation costs [7]. A DT is a virtual representation of a physical object, system, or process that remains continuously connected to its real-world counterpart through data exchange, thereby enabling monitoring, simulation, and predictive analysis [8,9]. By integrating historical and real-time data, DTs enable organizations to evaluate alternative scenarios, assess system performance, and support data-driven decision-making.

A digital model is a static virtual representation of a physical asset or process that does not maintain automated or continuous data exchange with its real-world counterpart. In contrast, a DT is a dynamic digital representation that maintains continuous bidirectional synchronization with a physical asset through real-time data acquisition, thereby enabling monitoring, prediction, and optimization of system performance. This distinction clarifies that although all DTs are digital models, not all digital models qualify as DTs because they lack real-time interactivity and continuous feedback [10–12].

Although DTs were initially developed for manufacturing and industrial optimization, their application has expanded to domains including smart cities, energy systems, and healthcare [13]. Within hospital environments, DTs have been applied to model clinical workflows, hospital infrastructure, and operational processes. This broader operational role is further supported by recent review evidence, which indicates that DTs have been investigated for hospital resource allocation, pandemic management, and predictive maintenance of critical medical equipment [7]. These models enable healthcare organizations to analyze patient flow, resource utilization, and system performance while supporting planning and operational decision-making [14]. For example, DT-based hospital simulations can assist in identifying bottlenecks in patient flow and evaluating alternative resource allocation strategies [3,15].

While traditional DTs primarily represent machines, infrastructure, or isolated biological systems, the concept of Human Digital Twins (HDTs) extends this paradigm to human entities. HDTs represent patients, clinicians, or care teams through digital models that integrate physiological, behavioral, and environmental data [16,17]. These systems are intended to represent aspects of human conditions within a virtual environment, enabling the simulation and prediction of health states and operational outcomes.

Yujia Lin et al. [17] describe an HDT as a digital representation of a human entity that may range from modeling specific organs to representing the entire human body. In healthcare systems, HDTs can integrate data from electronic health records (EHRs), medical imaging, wearable sensors, and environmental monitoring to support personalized healthcare and operational planning [18,19]. This perspective is consistent with Afshar et al. [7], who describe HDTs as an extension of DTs that incorporate behavioral, cognitive, and physiological characteristics, while healthcare DTs more broadly integrate diverse datasets, including genetic and real-time physiological information, to support personalized interventions. Similar to conventional DTs, HDTs maintain a continuous connection with their physical counterpart while placing greater emphasis on the integration of human-related information.

Recent studies classify human digital representations into three levels according to the degree of data integration [19]. A Human Digital Model is a static representation created from historical data. A Human Digital Shadow is automatically updated through one-directional data flow from the physical system to the digital system (physical $\rightarrow$ digital). A HDT represents a fully synchronized system with bidirectional interaction between the digital and physical domains (digital $\leftrightarrow$ physical) [10,19]. These systems may also incorporate explainable artificial intelligence (XAI) and privacy-preserving mechanisms to improve transparency, trust, and secure data management.

Within hospital operations, DTs and HDTs are increasingly being investigated to support both operational and clinical decision-making. Existing DT applications include patient flow analysis, bed management, operating room (OR) scheduling, and predictive maintenance of hospital equipment [20,21]. However, many existing models primarily focus on infrastructure and operational processes while providing only limited representation of human factors, such as patient conditions, clinician workload, and cognitive stress.

HDTs have the potential to address this limitation by integrating physiological, cognitive, and behavioral information to represent individuals within hospital systems [22,23]. For example, a patient HDT may combine vital signs, medical history, and lifestyle information to support personalized care decisions, whereas a clinician HDT could assist in predicting workload or cognitive fatigue during periods of high demand [24]. By incorporating human factors into digital simulations, HDTs have the potential to provide hospitals with a more comprehensive understanding of the interactions among people, technologies, and operational processes.

Despite their potential, several challenges remain regarding the implementation of HDTs in real healthcare environments. Maintaining real-time synchronization between physical individuals and their digital representations requires robust data infrastructures and interoperability among heterogeneous hospital information systems. In addition, HDTs involve the processing of sensitive medical data, raising important concerns related to privacy, security, and ethical governance [3]. Addressing these challenges will be essential for the development of reliable and trustworthy HDT-based healthcare systems.

Overall, the transition from traditional DTs to HDTs represents an important step in the digital transformation of healthcare. By integrating human-related data into digital representations, HDTs have the potential to support more comprehensive modeling of healthcare systems that considers both technological efficiency and human well-being.

1.3. Integrating I4.0 and I5.0 Through HDTs in Hospital Operations

Hospitals are complex socio-technical systems in which clinical staff, patients, technologies, and operational processes continuously interact. I4.0 technologies, including the IoT, CPSs, AI-based analytics, and DT platforms, enable the collection and analysis of large volumes of operational and clinical data [8,25]. More broadly, recent review

evidence indicates that healthcare DTs rely on real-time data integration and predictive modeling to support both personalized care and operational management, including hospital resource allocation and infrastructure-related applications [7]. These technologies enable hospitals to monitor patient conditions, track equipment utilization, and analyze clinical and operational workflows in real time, thereby supporting more efficient and data-driven management.

Although I4.0 technologies improve automation and connectivity, they do not fully address the human dimensions of healthcare systems. Furthermore, recent review evidence indicates that the adoption of healthcare DTs continues to face important challenges related to privacy, system integration, implementation costs, and limited real-world validation, highlighting the need for a more human-centered and governance-oriented perspective [7]. Issues such as clinician workload, patient experience, and ethical decision-making require approaches that extend beyond technological optimization. I5.0 addresses these aspects by emphasizing sustainability, resilience, and collaboration between humans and intelligent technologies [26,27].

HDTs provide a conceptual and technological bridge between these two paradigms. By integrating human-related data into DT systems, HDTs enable the representation of both operational processes and human factors within hospital environments [16,17]. For example, HDTs can be used to simulate how changes in staffing levels may influence nurse workload or how patient-specific conditions may affect treatment outcomes and hospital resource utilization [22].

Through this integration, HDTs connect the technological capabilities of I4.0 with the human-centered objectives of I5.0. They have the potential to support hospitals in improving operational performance while simultaneously considering human well-being, thereby contributing to more balanced and sustainable healthcare systems. For example, HDT-based simulations may support the optimization of operating room scheduling while also accounting for surgeon workload and recovery time between procedures [24].

Consequently, HDTs represent an emerging approach to supporting human-centered digital transformation in healthcare. By combining advanced digital infrastructure with human-oriented decision support, HDTs have the potential to help hospitals leverage the technological capabilities of I4.0 while advancing the sustainability and human-centric principles emphasized in I5.0.

This study investigates the role of HDTs in supporting smart and sustainable hospital operations by bridging the technological foundations of Industry 4.0 with the human-centric principles of Industry 5.0. Specifically, the study examines how HDT technologies have been applied to support hospital operational efficiency while considering human well-being, ethical governance, and sustainability. To achieve this objective, a systematic literature review was conducted following the PRISMA guidelines. A comprehensive search of the Scopus and Web of Science databases identified 329 records, of which 22 studies met the inclusion criteria and were included in the final analysis. The review synthesizes current evidence on the role of HDTs in facilitating human-centered, data-driven transformation within healthcare operations.

The paper pursues two complementary objectives. First, a bibliometric analysis examines the research landscape by analyzing publication trends, leading authors, institutions, journals, and thematic clusters to understand the evolution of HDT research in healthcare. Second, a content analysis investigates the selected studies with particular attention to: (1) HDT architectures, data sources, and control mechanisms; (2) human-centric and governance aspects, including XAI, control loops, and privacy; and (3) operational, clinical, and sustainability outcomes, such as patient flow optimization, workload management, and energy efficiency. These objectives form the basis for the following research questions.

1.4. Research Questions

The paper addresses the following research questions:

1.4.1. Bibliometric Analysis

- RQ1: What are the publication trends, and who are the most active contributors to HDT research for hospital operations?
- RQ2: Which journals, authors, and countries have made the most significant contributions to this research field?
- RQ3: What are the major research themes and keyword clusters identified through bibliometric mapping?
- RQ4: How have the concepts of I4.0 and I5.0 emerged and evolved within this research domain?

1.4.2. Content Analysis

- RQ1: What architectural and data integration approaches are employed in HDTs for hospital operations?
- RQ2: Which human-centric and governance characteristics, such as XAI, privacy, and Human-in-the-Loop (HIL), are integrated into HDT systems?
- RQ3: What operational, clinical, and sustainability outcomes, including improvements in patient flow, staff workload, and resource efficiency, have been reported?
- RQ4: How do HDTs bridge the automation-oriented paradigm of I4.0 with the human-centric vision of Industry 5.0 in healthcare?

1.5. Research Gaps and Contributions

Although research on DTs and HDTs has expanded rapidly in recent years, existing review studies remain fragmented in scope and often focus on specific technological or conceptual aspects rather than the operational context of hospitals. During the literature search, ten relevant review papers were identified and analyzed to assess the current state of knowledge and identify the remaining research gaps. Although these studies provide valuable insights into DT and HDT technologies, their objectives, methodological scope, and application focus differ considerably, leaving several important issues unresolved in the context of hospital operations.

Several reviews primarily focus on conceptual definitions and theoretical modeling of DTs in healthcare. For instance, Pellegrino et al. [28] conducted a meta-review of 20 studies and synthesized 11 dimensions of healthcare DTs, proposing a super-conceptual model to clarify definitions and hierarchical structures. Although this work contributes to the conceptual standardization of healthcare DTs, it does not address empirical examples, benchmarking protocols, or the ethical and governance considerations required for practical implementation in healthcare environments.

Similarly, Tudor et al. [23] conducted a scoping review of HDTs in healthcare, evaluating existing models based on personalization, dynamism, and predictive capabilities. Their analysis revealed that only about 12% of the reviewed studies implemented fully developed HDTs, whereas most remained limited to statistical models or unidirectional digital shadows. Although the authors proposed directions for standardization and verification, the absence of a formal HDT ontology and objective evaluation metrics limits the comparability of existing systems.

Other studies concentrate on specific applications of DTs in healthcare monitoring and precision medicine. For example, Nadeem et al. [29] investigated DT applications for personalized health monitoring and developed two simulation prototypes based on patient vital signs using AnyLogic. Although their work illustrates the potential of DTs

for precision healthcare, it relies primarily on synthetic datasets and lacks validation using real clinical data. Likewise, Lin et al. [17] presented a comprehensive overview of HDT technologies and proposed a general architecture applicable across multiple domains, including healthcare, industry, and smart environments. However, the broad scope of their review does not permit a detailed analysis of hospital-specific operational processes and socio-technical constraints.

Several systematic and scoping reviews have also investigated DT applications in healthcare systems. Xames and Topcu [30] conducted a PRISMA-based systematic review that categorized DT studies according to the type of twin object (product or process) and the application context (patient body, procedures, hospitals, or public health). Their findings identified important gaps in human-in-the-loop integration and highlighted the limited implementation of DTs in real-world healthcare settings. Similarly, Katsoulakis et al. [3] provided a broad overview of DT initiatives in healthcare, emphasizing international collaboration and emerging technological opportunities. However, their analysis remains high-level and does not examine operational hospital processes in detail.

Other studies focus on design principles, ethical frameworks, and emerging technological challenges. Davila-Gonzalez et al. [22] examined 44 HDT design studies and proposed the ETHICA framework, which emphasizes iterative, human-centered development aligned with the principles of Industry 5.0. Although this framework provides valuable guidance from an ethical design perspective, it does not evaluate concrete technical implementations or operational applications within hospital environments. Shrivastava et al. [31] reviewed the key characteristics of DT technologies in healthcare, including real-time monitoring and AI-based predictive modeling; however, their analysis is based on a relatively limited body of literature. Pascual et al. [16] summarized academic and industrial developments related to HDTs and discussed cybersecurity and privacy challenges. Nevertheless, their review primarily provides an overview of current trends rather than proposing new methodological approaches.

Finally, Riahi et al. [21] synthesized 86 publications on DTs for clinical decision support systems. Although they proposed an architectural model and discussed future research directions, their review indicates that practical implementations remain limited, with only about 19% of the reviewed studies reporting concrete validation.

Overall, these reviews indicate that the literature has made considerable progress in conceptualizing DTs and identifying their potential applications in healthcare. Nevertheless, several important research gaps remain. First, most studies examine DTs within general healthcare contexts rather than focusing specifically on hospital operations, such as patient flow management, resource allocation, and staff workload. Second, although some studies discuss HDTs from a conceptual perspective, relatively few integrate the human-centered principles of Industry 5.0 with the technological foundations of Industry 4.0 within a unified analytical framework. Third, the majority of the reported studies remain conceptual or simulation-based, with limited validation in real-world hospital environments. Finally, sustainability and long-term operational performance are seldom considered as explicit evaluation dimensions in existing review studies.

To better illustrate these differences, Table 1 compares the scope and contributions of previous review studies with those of the present study across several key dimensions. The table reports the number of primary papers reviewed (#PR), the time horizon covered by each study (TH), and whether the review explicitly focuses on hospital operations (HOF). It also summarizes the inclusion of human-centered Industry 5.0 features (HC-I5), Industry 4.0 enabling technologies (I4-Enab), AI or decision-support approaches (AI-DS), and evidence of validation or real-world implementation (Valid). In addition, the table indicates whether sustainability aspects are considered (Sust), whether data in-

tegration and interoperability are discussed (DI-Int), and whether the study proposes a framework or architecture (FP). The final two columns distinguish between studies that explicitly focus on HDTs and DTs more broadly.

Table 1. Comparison of existing literature reviews and the contributions of the present study.

Ref	#PR	TH	HOF	HC-I5	I4-Enab	AI-DS	Valid	Sust	DI-Int	FP	HDT	DT
[32]	20	✗	✗	✗	✓	✓	✗	✗	✓	✓	✓	✓
[23]	149	2017–2024	✗	✗	✓	✓	✗	✗	✓	✓	✓	✓
[29]	✗	2019–2024	✗	✗	✓	✓	✗	✗	✓	✓	✗	✓
[17]	327	2018–2024	✗	✓	✓	✓	✗	✗	✓	✓	✓	✓
[30]	135	✗	✓	✓	✓	✓	✗	✗	✓	✗	✗	✓
[33]	44	2022–2023	✗	✓	✓	✓	✗	✗	✓	✓	✓	✓
[31]	16	2018–2022	✗	✗	✓	✓	✗	✗	✓	✗	✗	✓
[16]	15	✗	✓	✓	✓	✓	✗	✗	✓	✗	✓	✓
[3]	85	2016–2023	✓	✗	✓	✓	✓	✗	✓	✗	✓	✓
[21]	86	2017–2024	✓	✗	✓	✓	✓	✗	✓	✓	✓	✓
Our Study	22	2020–2025	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓

In Table 1, a 'Yes/✓" indicates that a study explicitly addresses a given dimension, whereas a 'No/✗" indicates that the dimension is not covered. To ensure consistency, each dimension was coded using predefined criteria. Specifically, HOF was marked as Yes only when the study explicitly focused on hospital operations. HC-I5 required the inclusion of human-centered Industry 5.0 aspects, such as ethics, human involvement, or worker well-being, whereas I4-Enab referred to the discussion of enabling technologies, including IoT, CPSs, cloud platforms, and AI analytics. AI-DS was coded as Yes when AI or decision-support methods were incorporated, while Valid referred to whether the study reported any form of validation or real-world implementation. Sust captured sustainability or continuous improvement considerations, DI-Int referred to data integration and interoperability issues, and FP indicated whether the study proposed its own framework or architecture. Finally, HDT and DT distinguish between studies explicitly focused on HDTs and those addressing DTs more broadly. These criteria provide a clear and consistent basis for comparing previous review studies with the present work.

The comparison presented in Table 1 indicates that, although previous review studies have addressed important aspects of DT and HDT research, none encompasses all of the dimensions considered in the present study. In particular, most existing reviews emphasize conceptual definitions, technical architectures, or general healthcare applications, while giving comparatively limited attention to hospital operations as a distinct application context. Furthermore, human-centered Industry 5.0 principles, including clinician involvement, ethics, well-being, and governance, are not consistently considered alongside Industry 4.0 technological enablers. Similarly, sustainability, data interoperability, and operational performance indicators are seldom examined within a single review. These observations indicate the need for a study that not only synthesizes DT and HDT research in healthcare but also examines hospital operations specifically while integrating technological, human-centered, and operational perspectives within a unified analytical framework.

Accordingly, the present review addresses these limitations by providing a systematic analysis of HDTs in the context of hospital operations. The study integrates Industry 4.0 technological capabilities with the human-centered principles of Industry 5.0 through complementary bibliometric and content analyses of the existing literature. In addition, it considers dimensions that have often been examined separately in previous reviews, including hospital workflows, human factors, sustainability, and data interoperability. Based on this synthesis, the study proposes a conceptual four-layer HDT framework tailored to hospital operational environments. By bringing together technological, human-centered, and operational perspectives, the review provides a comprehensive synthesis of

the current literature and offers insights into how HDTs may support the development of intelligent, human-centered, and sustainable hospital systems.

The remainder of this paper is organized as follows. Section 2 describes the research methodology, which adheres to the PRISMA guidelines. Section 3 presents the results of the bibliometric and content analyses, encompassing themes related to architectures and data integration, human-centric governance, and operational outcomes. Section 4 proposes a conceptual framework that demonstrates how HDTs can integrate the principles of I4.0 and I5.0 within hospital operations. Section 5 offers a comprehensive discussion of the findings, while Section 6 addresses the study's limitations and provides recommendations for future research. Finally, Section 7 concludes the paper.

2. Research Methodology

This study follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) methodology [30,34], as illustrated in Figure 1. The review considered publications published between 2020 and 2025, corresponding to the emergence and rapid development of HDT research in healthcare operations. A comprehensive literature search was conducted in November 2025 using the Scopus and Web of Science databases. The following Boolean search string was employed to identify relevant studies: ("Digital Twin" OR "Human Digital Twin" OR "Human-digital twin") AND ("Hospitals" OR "Hospital Operations" OR "Healthcare" OR "Health Care") AND ("I4.0" OR "Industrial Fourth Revolution" OR "I5.0" OR "Industrial Fifth Revolution"). A total of 329 records were identified from two major scientific databases: Scopus (n = 176) and Web of Science (n = 153). Before screening, records that did not meet the initial inclusion criteria, including non-English publications, books, book chapters, and non-open-access items, were removed (n = 42). Additionally, duplicate records were identified and removed (n = 58), resulting in 229 records entering the screening phase. During the screening stage, titles were evaluated, and 151 records were excluded for being unrelated to the study scope. Subsequently, the titles, keywords, abstracts, and conclusions of the remaining records were assessed, resulting in an additional 54 exclusions. This process yielded 24 records for full-text eligibility assessment. Among these, 10 review papers were excluded from the primary analysis but incorporated into the research gap and contribution (Section 1.5). Ultimately, 14 primary studies met the eligibility criteria and were included in the main systematic review. In addition, eight relevant studies were identified through Google Scholar and included based on their strong relevance to the research context.

In total, 22 studies formed the final body of literature analyzed in this review. The distinction between the 229-record screening corpus and the final 22-study corpus reflects their different analytical purposes: the former was retained for broad bibliometric characterization, whereas the latter was selected through the predefined eligibility process to provide the focused evidence base for the content analysis. This structured and transparent PRISMA approach ensured methodological rigor, comprehensive coverage, and thematic relevance in evaluating DT applications in the healthcare environment within the I4.0 and I5.0 frameworks.

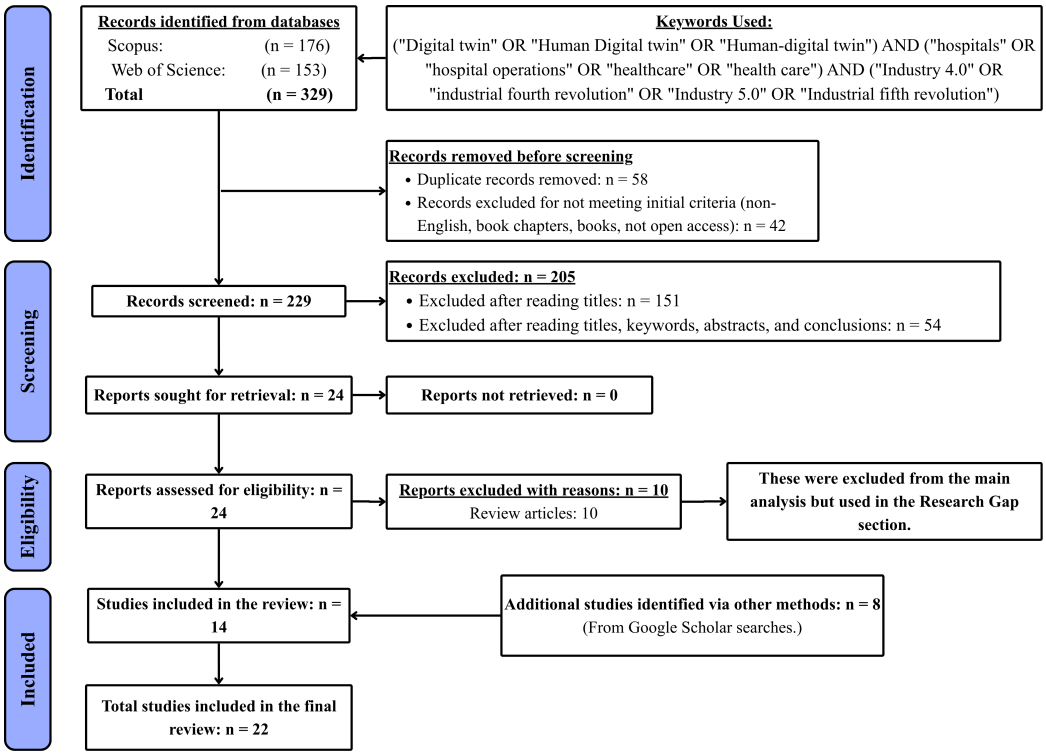

Figure 1. PRISMA flow diagram for systematic review.

3. Analysis and Findings

This section presents the analysis of the reviewed literature. As outlined earlier, the study is organized around a set of research questions corresponding to its two analytical phases: bibliometric analysis and document-based analysis. Each phase is addressed through its respective research questions to provide a systematic and comprehensive examination of the findings.

3.1. Bibliometric Analysis

This section presents the bibliometric analysis of the 229 records that entered the PRISMA screening stage. The bibliometric and content analyses were intentionally conducted on different analytical corpora because they address complementary objectives. The bibliometric analysis uses the broader 229-record screening corpus to characterize the overall publication landscape, research trends, geographical contributions, and thematic evolution of DT and HDT research related to healthcare before the application of the final eligibility criteria. In contrast, the subsequent document-based content analysis focuses on the final 22 studies that satisfied the predefined inclusion and exclusion criteria and specifically addressed HDTs in healthcare operations.

Accordingly, the two corpora are not intended to be directly equivalent or statistically representative of one another. The 229-record corpus provides a broad landscape-level view, whereas the final 22 studies constitute the focused evidence base for addressing the content-analysis research questions. Differences in the distribution of study characteristics between these corpora therefore reflect, in part, the deliberate application of the eligibility criteria rather than an assumption that the final evidence corpus reproduces the full bibliometric landscape.

The bibliometric analysis was conducted using Microsoft Excel (Version Office 16) to examine publication trends, journal impact based on publication and citation counts, the most highly cited papers, the leading institutions by publication output and citations, the most prolific authors, and the most active countries. In addition, VOSviewer (version

1.6.20) was used to visualize and map co-authorship networks, keyword co-occurrence patterns, and thematic clusters, providing a comprehensive overview of the evolution of DT- and HDT-related healthcare research.

3.1.1. Journal Statistics

This subsection addresses RQ1 and RQ2 of the bibliometric analysis. Figure 2 illustrates the annual distribution of publications between 2020 and 2025. The results indicate an overall increase in research output, rising from 15 publications in 2020 to 55 publications in 2025. Although a slight decline is observed in 2024, the overall trend suggests sustained growth in research activity throughout the study period, reflecting increasing academic interest in this research area.

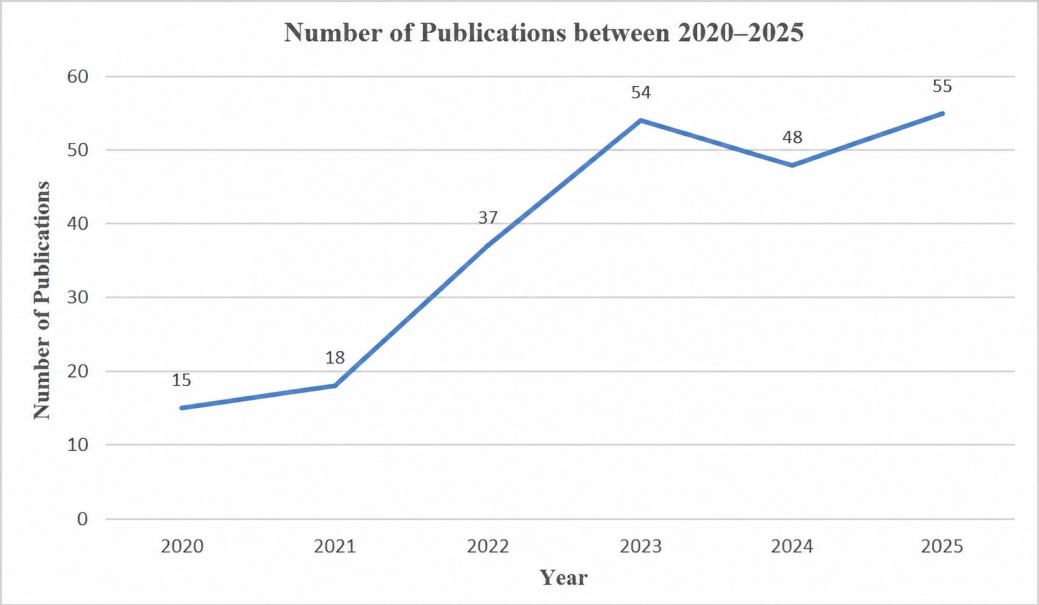

Figure 2. The trend of publications between 2020–2025.

Figures 3 and 4 present the top ten journals ranked by total citations and number of publications, respectively. In terms of publication output, *IEEE Access* ranked first with 12 publications, followed by *Sensors* with 10 publications. *International Journal of Integrated Manufacturing* and *Applied Sciences* each published five papers, while *IFAC-PapersOnline*, *IEEE Communications Surveys and Tutorials*, and *Lecture Notes in Networks and Systems* each contributed four publications.

When ranked by total citations, *IEEE Access* also ranked first, with 1974 citations, followed by the *Journal of Industrial Information Integration* (1506 citations) and *Robotics and Computer-Integrated Manufacturing* (1229 citations). These findings indicate that publication volume and citation impact do not necessarily correspond across journals. For example, *IEEE Communications Surveys and Tutorials* has a comparatively smaller number of publications but a relatively high citation count. Overall, the results identify *IEEE Access* as the leading publication venue in terms of both research output and citation impact within this dataset.

The ten most-cited papers in the reviewed dataset are presented in Table 2, ranked according to their total citation counts and the average number of citations per year to provide an indication of their scholarly influence over time. The article by Fuller et al. [35], entitled "Digital Twin: Enabling Technologies, Challenges and Open Research," ranks first with 1771 citations and an average of 295.17 citations per year, indicating its strong influence on Digital Twin research. Similarly, the article by Maddikunta et al. [36], entitled "I5.0: A Survey on Enabling Technologies and Potential Applications," has received

1496 citations, corresponding to an average of 374 citations per year, reflecting its substantial influence on research related to Industry 5.0 and enabling technologies.

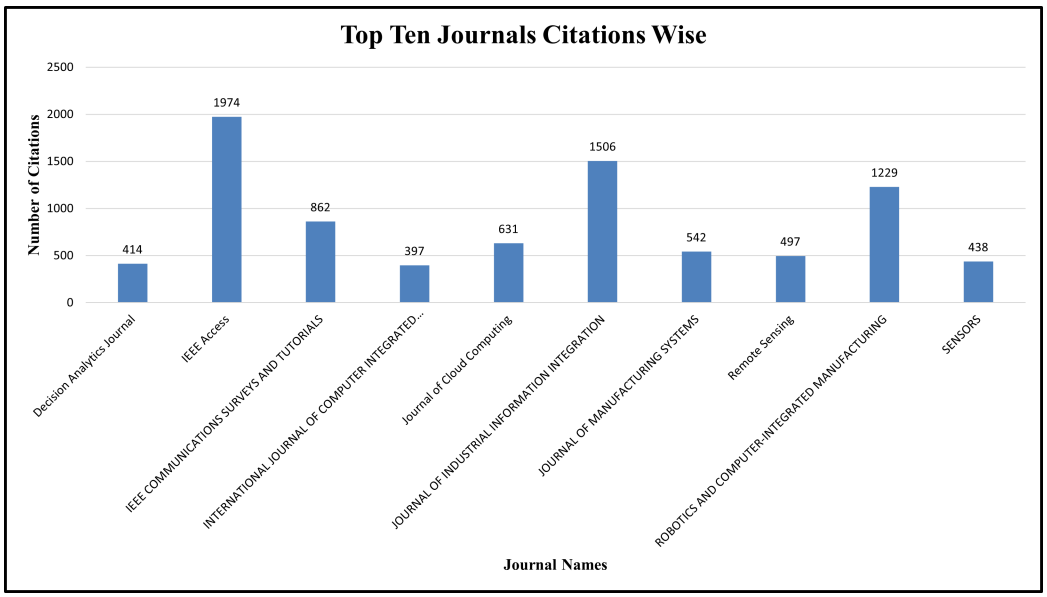

Figure 3. Top ten journals citation-wise.

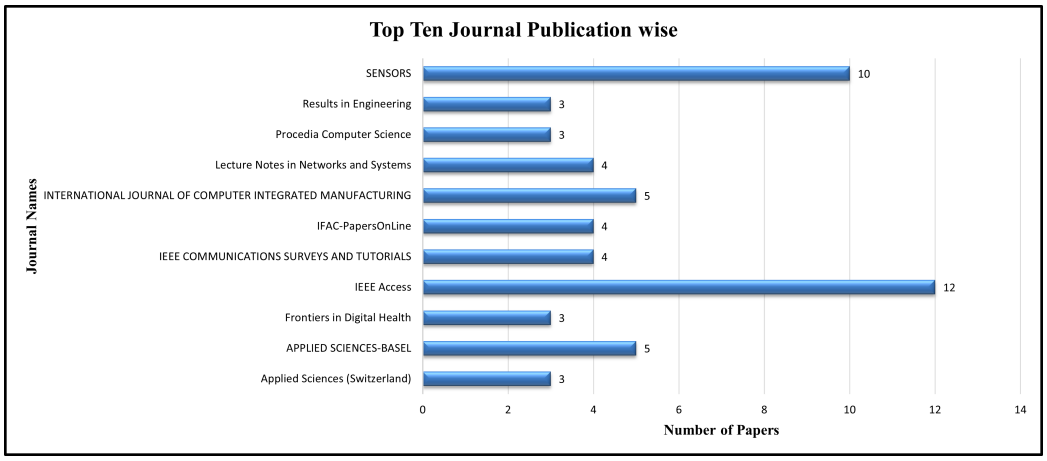

Figure 4. Top ten journals publication-wise.

Table 2. Top ten most-cited papers in the reviewed dataset.

Authors	Title	Citations	Citations/Year
[36]	I5.0: A Survey on Enabling Technologies and Potential Applications	1496	374.0
[35]	Digital Twin: Enabling Technologies, Challenges and Open Research	1771	295.17
[37]	Digital Twins: A Survey on Enabling Technologies, Challenges, Trends and Future Prospects	698	174.50
[38]	Digital Twin-Driven Smart Manufacturing: Connotation, Reference Model, Applications and Research Issues	1009	168.17
[25]	Future of Industry 5.0 in Society: Human-Centric Solutions, Challenges and Prospective Research Areas	631	157.75
[39]	Digital Twin: Benefits, Use Cases, Challenges, and Opportunities	414	138.00
[40]	Digital Twin Technology Challenges and Applications: A Comprehensive Review	477	119.25
[3]	Digital Twins for Health: A Scoping Review	220	110.00
[15]	Human Digital Twin in the Context of Industry 5.0	220	110.00
[41]	Digital Twins-Based Smart Manufacturing System Design in Industry 4.0: A Review	473	94.60

Other highly cited studies, including those by Lu et al. [38] and Mihai et al. [37], address topics related to DT-enabled smart manufacturing, human-centered industrial systems, and emerging research challenges. Collectively, these highly cited publications

illustrate the conceptual and technological developments that have contributed to the evolution of Industry 4.0 and Industry 5.0, particularly in the areas of smart manufacturing, digital healthcare, and human digital integration.

Some of the studies included in Table 2 focus on general DT technologies or Industry 4.0/5.0 architectures rather than healthcare-specific applications. These studies were included because they provide foundational technological concepts and frameworks that have informed the development of HDT systems in healthcare.

Figures 5 and 6 present the leading institutions in the field, ranked by publication output and citation impact, respectively. As shown in Figure 5, Harvard University recorded the highest number of publications, followed by the Vellore Institute of Technology, Guangdong University of Technology, and the State University System of Florida, all of which made substantial contributions to the reviewed literature. Other notable contributors include Beihang University, Virginia Polytechnic Institute and State University, Harvard University Medical Affiliates, Massachusetts General Hospital, Dalian Medical University, and The Hong Kong Polytechnic University. In terms of citation impact (Figure 6), the University of Auckland ranked first with 2018 citations, followed by Keele University (1771 citations) and the Vellore Institute of Technology (1527 citations). These findings indicate that institutions with the highest publication output are not necessarily those with the greatest citation impact, reflecting a diverse distribution of research productivity and scholarly influence across the field.



Figure 5. Top ten institutes by published papers.

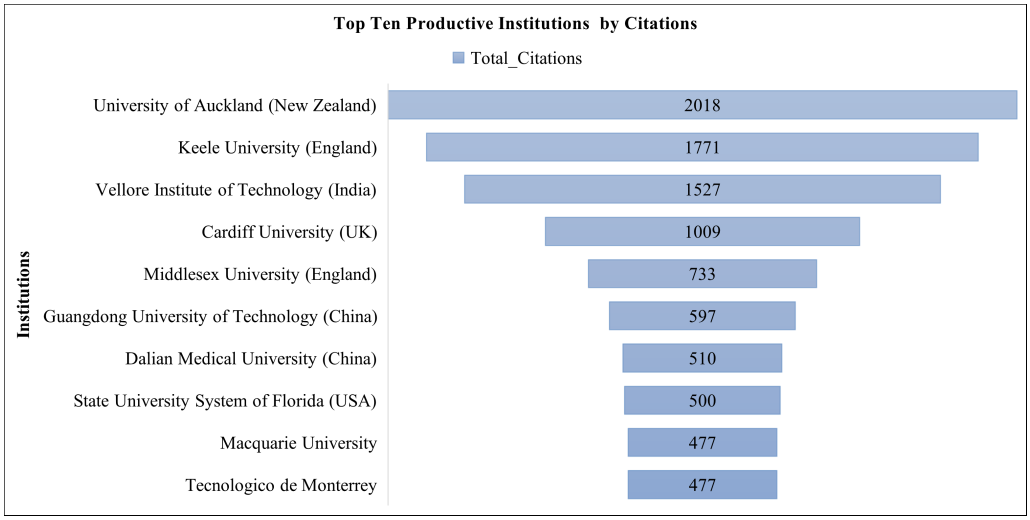

Figure 6. Top ten productive institutes by citations.

Table 3 presents the top 15 authors in the reviewed dataset, together with their publication counts, total citations, and average citations per paper. Praveen Kumar Reddy

Maddikunta and Thippa Reddy Gadekallu each contributed three publications and accumulated 1581 citations, corresponding to an average of 527 citations per paper. Other authors, including Abid Haleem, Mohd Javaid, Ravi Pratap Singh, and Rajiv Suman, also contributed three publications each, with an average of approximately 68 citations per paper. In contrast, Prabadevi Boopathy, Deepa N., Madhusanka Liyanage, and Pham Quoc Viet each authored two publications but achieved an average of more than 750 citations per paper, indicating a high citation impact. Similarly, Mohsin Raza and William Davis each recorded an average of 366.5 citations per publication. Overall, these results suggest that scholarly influence within this research area is associated not only with publication volume but also with the citation impact of individual studies.

Table 3. Top 15 authors by publication count and citations in the reviewed dataset.

Authors	Publications	Total Citations	Avg. Citations/Paper
Gadekallu, Thippa Reddy	3	1581	527.0
Maddikunta, Praveen Kumar Reddy	3	1581	527.0
Haleem, Abid	3	205	68.33
Javaid, Mohd	3	205	68.33
Singh, Ravi Pratap	3	205	68.33
Suman, Rajiv	3	205	68.33
Khan, Sagheer	3	120	40.0
Bhatia, Munish	3	36	12.0
Boopathy, Prabadevi	2	1501	750.5
Deepa, N	2	1501	750.5
Liyanage, Madhusanka	2	1501	750.5
Pham, Quoc Viet	2	1501	750.5
Liu, Chao	2	1025	512.5
Davis, William	2	733	366.5
Raza, Mohsin	2	733	366.5

Table 4 presents the distribution of publications and citations across countries, highlighting differences in both research output and citation impact. India recorded the highest number of publications (21), whereas the United Kingdom accumulated the largest number of citations (2035) despite contributing only eight publications. The United States ranked third, with seven publications and 745 citations, reflecting a consistent research contribution. Ireland contributed three publications but accumulated 1502 citations, indicating a comparatively high citation impact. Italy, France, and Brazil also contributed multiple publications, although with lower citation counts. In addition, Singapore, South Korea, and Switzerland exhibited relatively high citation-to-publication ratios, while Egypt, Nigeria, Germany, and Canada made comparatively smaller contributions within the reviewed dataset. Overall, the results indicate differences between research productivity and citation impact across countries, with India leading in publication output and the United Kingdom and Ireland demonstrating comparatively higher citation performance.

3.1.2. Theme-Based Assessment

In this section, RQ3 of the bibliometric analysis is addressed. Bibliometric mapping using VOSviewer was employed to identify thematic and keyword clusters, as this approach provides a systematic means of examining the conceptual structure and dominant research themes within the field. The bibliometric mapping was performed on the 229 records that entered the PRISMA screening stage. Therefore, the resulting clusters represent the broader thematic landscape of DT and HDT research related to healthcare prior to the final eligibility assessment.

VOSviewer (full counting method; minimum occurrence threshold = 5) was used to analyze the author keywords from the combined Scopus and Web of Science datasets, resulting in the identification of 111 distinct keywords organized into five thematic clusters. In VOSviewer, Total Link Strength (TLS) represents the cumulative strength of all

co-occurrence relationships associated with a given keyword, indicating the extent to which it is connected to other keywords within the dataset. Higher TLS values indicate greater thematic centrality and stronger integration within the intellectual structure of the research domain.

Table 4. Top 15 Country-wise Distribution of Publications and Citations.

Country Name	Papers	Total Citations
India	21	901
United Kingdom	8	2035
United States	7	745
Italy	7	126
France	6	87
Brazil	5	3
China	4	35
Ireland	3	1502
Singapore	2	201
South Korea	2	199
Switzerland	2	186
Egypt	2	149
Nigeria	2	22
Germany	2	7
Canada	2	2

According to Figure 7, the keyword co-occurrence analysis identified five major thematic clusters representing the principal research directions related to DT and HDT research in healthcare. Because the co-occurrence network is derived from the author keywords of the 229 records that entered the PRISMA screening stage, the resulting clusters reflect the broader thematic landscape of DT and HDT research related to healthcare. Consequently, some clusters are centered on DTs, IoT, CPSs, AI, and I4.0/5.0 terminology. This is expected because the bibliometric analysis was designed to capture the evolution of the broader research landscape prior to applying the final eligibility criteria, whereas the subsequent document-based thematic analysis is based exclusively on the final 22 studies focused on HDTs for healthcare operations. Accordingly, the presence of broader DT- and I4.0-related themes reflects the interdisciplinary foundations from which HDT research has evolved in healthcare.

The blue cluster focuses on DTs, I4.0, and AI, emphasizing predictive and data-driven approaches to healthcare management. The red cluster centers on IoT infrastructure and data architectures, highlighting interoperability and system integration for smart hospital environments. The green cluster encompasses CPSs, edge computing, and machine learning (ML), reflecting research on distributed intelligence and real-time decision-making [6]. The yellow cluster emphasizes human-centric concepts associated with Industry 5.0, including clinician collaboration, ethical considerations, and sustainability. Finally, the purple cluster links these enabling technologies to healthcare applications such as personalized healthcare and clinical decision-support systems. Collectively, these clusters illustrate the broad research landscape underpinning HDTs and demonstrate how HDT research draws upon both the technological foundations of I4.0 and the human-centered principles associated with Industry 5.0.

The thematic framework derived from the keyword co-occurrence analysis is presented in Table 5, which summarizes the five clusters identified using VOSviewer. Each cluster represents a distinct yet interconnected research theme within the broader field of DT and HDT applications in healthcare. The table presents the dominant research focus of each cluster, the keywords with the highest TLS, and their relevance within healthcare and hospital contexts. This classification provides an overview of the technological foundations associated with I4.0, the principal application domains of HDTs, and the emerging human-centered perspectives associated with Industry 5.0. Together, these clusters illustrate how

technological, analytical, and human-centered concepts are interconnected within the existing body of literature. Although several clusters focus on broader DT and I4.0/5.0 technologies, these themes represent the technological and conceptual foundations that support the development and implementation of HDT systems in healthcare. Therefore, the presence of broader DT-related clusters should not be interpreted as a limitation of the review sample; rather, it reflects the broader ecosystem of enabling digital, analytical, and human-centered technologies within which HDT research for hospital operations has developed.

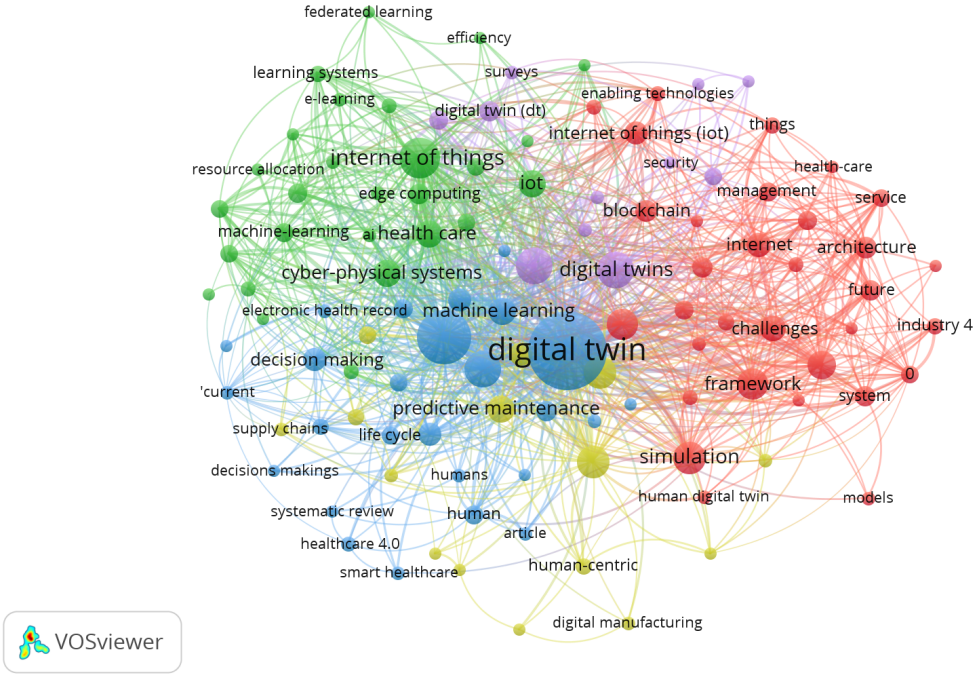

Figure 7. Keyword co-occurrence network generated using VOSviewer based on 111 author keywords (minimum occurrence = 5). Node size indicates keyword frequency, and link thickness represents Total Link Strength. Five major clusters were identified, highlighting the dominant research themes around DTs, IoT integration, AI-driven analytics, human-centric systems, and blockchain-enabled security.

Table 6 presents the co-authorship analysis of the top 15 influential authors based on publication volume, citation impact, and the strength of collaborative links. Gadekallu, Thippa Reddy, and Maddikunta, Praveen Kumar Reddy exhibit the largest number of citations (1581) and TLS (25) as a mark of both a powerful scholarly base and a large research team. Haleem, Abid, Javaid, Mohd, Singh, Ravi Pratap, and Suman, among others, are also researchers with strong research activity and active co-authorship. Meanwhile, Boopathy, Prabadevi, Deepa, N., Liyanage, Madhusanka, and Pham, Quoc Viet have significant collateral connections (TLS = 16) and citation influence (1501), highlighting their contribution to the new fields of DTs, IoT, and AI-driven smart systems. Even though these clusters demonstrate tight inter-group cooperation, the interconnections outside these networks are narrow, which indicates that additional cross-institutional and interdisciplinary research alliances in the DT and smart manufacturing environment are possible. Co-authorship analysis was conducted to identify leading researchers and collaboration networks shaping the development of DT technologies and their emerging applications in healthcare and HDT systems.

Table 5. Thematic clusters identified from the keyword co-occurrence analysis using VOSviewer.

Cluster (Color)	Theme/Research Focus	Representative Keywords (Top TLS)	Interpretation (HDT in Hospital Operations Context)
Cluster 1 (Red)	IoT and Data Architecture for Smart Hospitals	Internet of Things, big data, framework, architecture, system design, cybersecurity	Concentrates on the technological infrastructure supporting real-time hospital data exchange through IoT-based patient monitoring, interoperability, and secure integration of physical and digital assets [24,42].
Cluster 2 (Green)	Edge Analytics and Distributed Intelligence in Care Systems	Edge computing, ML, IoT, data processing, cyber–physical systems	Highlights real-time hospital intelligence using distributed edge systems that provide computational capabilities close to medical devices and patients, enabling rapid monitoring and diagnosis [43].
Cluster 3 (Blue)	DT and AI Core in Hospital Decision Support	Digital twin, Industry 4.0, artificial intelligence, machine learning, predictive analytics, Healthcare 4.0	Represents the central research area of DTs and AI-driven analytics for hospital decision support, including predictive maintenance, resource allocation, and patient-flow optimization as the technological foundation of smart hospitals [3,42].
Cluster 4 (Yellow)	Human-Centric and Industry 5.0 Approaches in Hospital Operations	Smart manufacturing, Industry 5.0, virtual reality (VR), augmented reality (AR), real-time monitoring, human–robot collaboration	Extends the Industry 5.0 paradigm to hospital operations through human-in-the-loop collaboration, immersive AR/VR technologies, and ergonomic system design to improve clinician safety and operational efficiency [24].
Cluster 5 (Purple)	AI-Powered HDT Applications in Healthcare Delivery	Digital twins, artificial intelligence, healthcare, simulation, modeling	Focuses on clinical and operational applications of HDTs, including virtual simulation, intensive care management, and personalized treatment planning by integrating Industry 4.0 automation with Industry 5.0 human-centered healthcare principles [3].

Table 6. Co-authorship analysis of authors.

Author	Documents	Citations	TLS
Gadekallu, Thippa Reddy	3	1581	25
Maddikunta, Praveen Kumar Reddy	3	1581	25
Haleem, Abid	3	205	9
Javaid, Mohd	3	205	9
Singh, Ravi Pratap	3	205	9
Suman, Rajiv	3	205	9
Khan, Sagheer	3	120	8
Bhatia, Munish	3	36	4
Boopathy, Prabadevi	2	1501	16
Deepa, N.	2	1501	16
Liyanage, Madhusanka	2	1501	16
Pham, Quoc Viet	2	1501	16
Liu, Chao	2	1025	7
Davis, William	2	733	17
Raza, Mohsin	2	733	17

3.1.3. I4.0 vs. 5.0 Lens: Emergence and Development

This section addresses RQ4 of the bibliometric analysis. The analysis provides a thematic interpretation of the research landscape based on keyword co-occurrence clusters generated using VOSviewer. Rather than representing a chronological progression,

the identified clusters reflect dominant technological and conceptual themes associated with Industry 4.0 and Industry 5.0 within the broader HDT research landscape. These thematic relationships illustrate how the literature links technological foundations, including DTs, the IoT, and AI, with emerging human-centered and governance-related perspectives in healthcare systems.

The keyword co-occurrence analysis suggests three broad thematic stages in the evolution of this research domain.

First, the Industry 4.0-oriented themes emphasize the technological foundations of HDTs, including DTs, IoT connectivity, big data infrastructures, AI and ML, edge computing, and CPSs. These themes, primarily represented by the Blue, Red, and Green clusters, focus on data integration, interoperability, predictive analytics, and the automation of hospital processes through digital technologies.

Second, the Purple cluster represents a transitional theme in which Industry 4.0 technologies are increasingly associated with clinical and operational applications, including intensive care unit (ICU) and OR simulations, patient-specific modeling, and clinical decision-support systems. This thematic cluster reflects growing attention to applying digital infrastructures in healthcare settings while supporting interactions between technological systems and healthcare professionals.

Finally, the Yellow cluster reflects themes commonly associated with the Industry 5.0 perspective, including human-centered design, HIL approaches, AR and VR, transparency, privacy, explainability, safety, and governance. These themes indicate an increasing research interest in complementing technological capabilities with ethical, human-centered, and resilient healthcare practices.

Overall, the thematic mapping suggests that the literature has progressively expanded from technology-oriented Industry 4.0 concepts toward the inclusion of Industry 5.0 principles. While the Blue, Red, and Green clusters primarily emphasize enabling technologies and digital infrastructures, the Purple cluster highlights their application in healthcare contexts, and the Yellow cluster reflects growing attention to human-centered, ethical, and governance-related considerations. Collectively, these themes indicate that HDT research increasingly combines technological capabilities with human-centered perspectives to support digital transformation in healthcare.

3.2. Content (Documents) Analysis

This section presents a synthesis of the 22 studies included in the final review on HDTs in hospital operations. The analysis is organized into three themes: (i) architectural patterns and data integration, (ii) human-centric and governance characteristics, and (iii) operational outcomes. Finally, a bridge matrix is presented to relate Industry 4.0 technological enablers with Industry 5.0 principles based on the thematic findings, providing an integrated system-level perspective.

3.2.1. Thematic Synthesis of HDT Architecture in Healthcare

Theme 1: Architecture and Data

This theme addresses RQ1 of the content analysis by examining the architectural characteristics of HDTs in healthcare. The objective is to understand how these systems are designed and implemented across different clinical settings, with particular attention to the relationship between physical healthcare environments and their digital counterparts. The analysis focuses on data types, integration mechanisms, synchronization approaches, and system architectures.

The reviewed studies indicate that HDT architectures commonly integrate multiple data sources, including EHRs, medical imaging, wearable devices, and sensor networks,

to support patient-specific monitoring and clinical decision-making [19,44,45]. For example, ref. [44] presents a modular and extensible HDT architecture designed for personalized healthcare, whereas [45] demonstrates the integration of heterogeneous data streams to identify locomotion modes, illustrating an approach for combining multiple data sources within a unified framework. Together, these studies illustrate different architectural approaches for implementing DT systems in healthcare environments while supporting both operational functions and human-centered healthcare objectives.

Among the 22 reviewed studies, 12 were selected for detailed architectural analysis because they explicitly describe key architectural characteristics (Table 7).

The comparison considers hospital setting, twin type, data modalities, update cadence, integration mechanism, data-flow directionality, and computing architecture. These dimensions were selected because they provide a consistent basis for comparing how HDTs manage data acquisition, synchronization, interoperability, and computational deployment across different healthcare applications. Studies that did not provide sufficient architectural detail were not included in this comparative analysis. As summarized in Table 7, the selected studies cover diverse healthcare environments, including ICUs, ORs, Emergency Departments (EDs), hospital-wide monitoring systems, and laboratory or robotic healthcare settings.

The reviewed studies also demonstrate considerable variation in HDT architectures across hospital settings, reflecting differences in application requirements [46]. For example, HDTs designed for ICUs and patient-monitoring applications are generally patient-specific and operate in real time by integrating multiple data sources, such as bedside monitoring systems, EHRs, and wearable devices, often using healthcare interoperability standards such as HL7/FHIR. One ICU-based HDT, for instance, streams patient vital signs through an HL7/FHIR interface to a cloud-based platform [19]. In contrast, a rehabilitation monitoring HDT continuously acquires wearable sensor data through an IoT gateway to support real-time patient monitoring and feedback [47].

Twins developed for OR and ED settings commonly employ batch or event-driven updates, with an emphasis on operational decision support rather than continuous closed-loop feedback. For example, studies on ED patient flow [48], OR scheduling [49], and emergency call center queuing models [50] describe one-way digital shadows (open-loop simulations) designed for planning and resource management without direct actuation of the physical environment [51]. Similarly, ward-level and hospital-wide operational twins primarily focus on workflow optimization using historical or simulated data. For instance, a ward bed-management twin employs an ontology-driven, agent-based simulation using historical patient and room data to evaluate bed allocation strategies [52]. Likewise, a hospital operations twin for discharge and bed turnover uses process logs together with Monte Carlo and agent-based simulations to identify bottlenecks and assess strategies for improving turnaround times [53]. These systems generally operate as digital shadows, supporting retrospective analysis and process optimization rather than real-time intervention, in contrast to many patient-centered twins that are designed to support real-time monitoring and decision-making.

Studies involving high-frequency, data-intensive applications more frequently report two-way (closed-loop) DTs that support adaptive feedback and control, particularly in critical care, rehabilitation monitoring, and human–robot interaction domains [46]. For example, an ICU patient twin is designed to support real-time adjustment of therapy or alarm settings based on continuously streamed vital-sign data [19], while a rehabilitation DT provides immediate biofeedback through wearable sensors and actuators [47]. Similarly, in a robotics application, a digital twin linking a bionic hand with its virtual counterpart enables real-time bidirectional control and actuation [54]. These closed-loop

implementations commonly adopt cloud–edge or hybrid computing architectures to facilitate low-latency synchronization of data and control signals. For example, the ICU and rehabilitation twins utilize cloud or edge resources for timely data processing and decision support [19,47], whereas the robotic-hand twin operates entirely on local hardware to achieve millisecond-level responsiveness [54].

In contrast, most process-oriented twins operate as one-way digital shadows without automated actuation. This architecture is commonly reported in ED and OR applications. For example, an ED triage DT applies discrete-event simulation for scenario analysis [48], whereas an OR scheduling twin employs what-if simulations to support surgical planning [49]. In both cases, the generated outputs inform clinical or operational decision-making but do not automatically modify physical processes. Even where real-time events are incorporated into the digital model, such as an outpatient pathway DT that receives live RFID-based patient location updates [55], the system functions primarily as a monitoring and prediction tool rather than an interactive control system. These one-way twins therefore serve as analytical or simulation platforms that support situational awareness and operational planning without directly controlling clinical workflows.

The reviewed studies also demonstrate considerable variation in data integration mechanisms. Only a limited number of advanced prototypes explicitly adopt healthcare interoperability standards. For example, one ICU twin incorporates HL7/FHIR interfaces to retrieve electronic health record data in real time [19]. Most studies instead rely on custom application programming interfaces (APIs), IoT communication protocols, or simulation-specific software platforms. For instance, a bionic-hand DT uses an MQTT broker to exchange sensor and actuator data [54], while several OR and ED twins are implemented entirely within discrete-event simulation environments such as Arena®and FlexSim®, without direct integration with EHRs [48,49]. In other cases, IoT cloud platforms are used instead of healthcare interoperability standards. For example, an ICU workflow twin employs Microsoft Azure IoT Hub together with the Digital Twin Definition Language (DTDL) to integrate streaming telemetry from the clinical environment rather than using HL7-based communication [42]. Overall, these findings indicate substantial variation in integration approaches across current healthcare DT implementations.

The selected studies also illustrate that the choice of computing architecture depends on application requirements, particularly regarding latency, privacy, and scalability. Edge or on-premises deployments are more frequently reported in latency-sensitive and privacy-critical applications. For example, the prosthetic-hand DT operates entirely on a local computer to minimize network delays and achieve rapid system response [54], while an OR patient-tracking twin processes data within a private hospital local area network to support security requirements and integration with existing hospital systems [28]. In contrast, cloud-based or hybrid architectures are adopted when large-scale data integration and computational scalability are required. For example, a conceptual hospital-wide digital twin framework proposes combining edge devices with cloud analytics to integrate clinical, wearable, and genomic data for precision health monitoring [56]. Similarly, a critical-care unit twin employs a hybrid Azure IoT cloud architecture together with local edge devices to monitor staff workflows and patient care processes in near real time [42].

Taken together, the reviewed studies indicate increasing interest in distributed cloud–edge architectures that support large-scale data integration and computationally intensive analytics. At the same time, these architectures introduce additional implementation complexity related to interoperability, system management, and data synchronization. Emerging frameworks that combine hybrid cloud–edge infrastructures with standardized data-exchange mechanisms [56] illustrate one possible direction for supporting more interoperable and data-driven healthcare digital twin systems aligned with Industry 5.0 principles.

The reviewed literature also highlights several engineering trade-offs in the design of HDT systems, particularly regarding latency, privacy, scalability, and computational performance. One important trade-off concerns the use of edge versus cloud computing. Edge computing processes patient data close to the data source, thereby reducing latency and supporting real-time monitoring in applications such as intensive care. However, edge-based systems generally provide more limited computational resources and require additional infrastructure management [44,57]. In contrast, cloud computing offers greater scalability and computational capacity for large-scale data integration and advanced analytics but introduces additional privacy and regulatory challenges because sensitive medical data must be transmitted to and stored on remote infrastructure [57,58].

Another important trade-off concerns scalability and security. Cloud-based HDT systems facilitate the integration of large datasets and support system-level optimization but may also increase exposure to cybersecurity risks. Consequently, secure system design requires measures such as data encryption, multi-factor authentication, and appropriate governance mechanisms to protect sensitive patient information [58]. In addition, AI-based analytics enhance prediction and decision support within HDTs but often require substantial computational resources. Balancing these computational demands with the real-time performance requirements of healthcare applications remains an important implementation challenge [57].

Because of these trade-offs, the design of HDT systems requires balancing reliability, privacy, scalability, and implementation feasibility. The reviewed literature suggests that hybrid architectures offer a practical approach by combining low-latency local processing for time-critical tasks with cloud resources for scalable analytics and broader system integration [44,57]. In addition, centralized architectures simplify system integration and management but may increase cybersecurity risks by concentrating data and services within a single infrastructure. Conversely, distributed architectures enhance resilience and data locality but typically introduce greater system complexity and coordination requirements [57].

Overall, the reviewed studies highlight distinct advantages and trade-offs associated with different architectural choices. Edge computing provides low-latency processing suitable for real-time applications but is constrained by limited computational resources and increased infrastructure requirements. Cloud computing offers greater scalability and computational capacity but introduces additional privacy and data security challenges. Centralized architectures facilitate system management and integration but may increase cybersecurity risks, whereas distributed architectures improve resilience and data locality while increasing implementation complexity [44,57,58]. Table 8 summarizes the principal architectural alternatives together with their associated advantages and trade-offs in HDT-enabled hospital systems.

Theme 2: Human-Centric and Governance Characteristics

This theme addresses RQ2 of the content analysis by examining the human-centric and governance characteristics of HDTs. The analysis focuses on three interrelated pillars: HIL, XAI, and privacy and governance mechanisms. Collectively, these dimensions contribute to the trustworthiness, transparency, and ethical oversight of HDTs in hospital environments. In this analysis, HIL (Y = implemented, P = conceptual/partial, N = absent) represents the level of human involvement in the system; XAI reflects the extent to which AI-based decisions are interpretable; and Privacy/Governance indicates the mechanisms adopted to protect data and support regulatory compliance. Together, these dimensions provide a basis for assessing the development of secure, transparent, and human-centered HDTs within the context of Industry 5.0.

Table 7. Architecture and Data Summary of Selected Studies (Theme 1).

Study	Hospital Setting	Twin Type	Data Modalities	Update Cadence	Integration Mechanism	Directionality	Compute Architecture
[19]	ICU/Inpatient Care	Patient-specific DT (for clinical monitoring and decision support)	EHR, bedside monitors, wearable sensors	Streaming (real-time updates)	FHIR/HL7 + HIS (hospital information system)	Two-way (closed-loop actuation and feedback)	Cloud-based architecture
[47]	Rehabilitation/Hospital-wide Monitoring	Patient Activity and Environment DT (motion and physiological monitoring)	Wearables (smartwatch HR/GPS, accelerometers arm/leg), smartphone IMU, environmental sensors (light/temp/humidity)	Streaming + Event-driven (priority-based real-time updates)	IoT Gateway + Azure DTDL platform	Two-way (closed-loop actuation for feedback/control)	Hybrid (IoT Edge + Cloud via Azure DT platform)
[54]	Lab/Robotics (HRC)	Equipment/robotic-hand twin (DT3: human–physical–virtual)	Control glove potentiometers (24 joint angles), bionic-hand joint telemetry, MQTT messages (no EHR)	Streaming (real-time)	MQTT broker; Unity DT app; Arduino over USB; no HL7/FHIR	Two-way (monitoring + control/actuation)	Edge/Local PC (Unity) + microcontroller
[56]	Healthcare-wide (precision health/perioperative to chronic care)	Patient-specific HDT (monitoring, prediction, anomaly detection)	EHR/clinical, medical imaging, wearables/IoMT, PGHD/self-reports, genomics/omics, environment/exposome, digital behavior (smartphone/social)	Real-/near-real-time + continuous updates (conceptual)	Interoperability across heterogeneous sources via cloud/standardized APIs; privacy-preserving pipelines (no concrete HL7/FHIR build specified)	Two-way (closed-loop decision support envisioned, conceptual)	Cloud/Hybrid (conceptual; edge + cloud discussed at framework level)
[48]	Emergency Department	Process Flow/Hospital Operations DT	ED operational data: patient arrivals, triage levels (3–5), treatment times, bed occupancy, lab turnaround time (TAT), historical datasets from European hospitals	Batch (historical data; continuous synchronization discussed conceptually)	Arena® Discrete Event Simulation (DES); statistical validation using hospital data; no HL7/FHIR integration	One-way (decision-support/what-if analysis; no automatic actuation)	Local (on-premise simulation environment)
[49]	Operating Room (Surgical Suite)	Process Flow/Schedule Execution Digital Twin (DT-DSS)	OR master schedule, scheduled-case attributes, procedure durations (relational DB)	Batch (prospective & retrospective simulations; not real-time)	FlexSim Healthcare® DT-DSS; relational database; no HL7/FHIR integration	One-way (decision-support only, no automatic actuation)	Local (desktop simulation environment)
[28]	OR + Recovery Room (Operating Block)	Process/flow twin for OR–RR with indoor patient tracking and schedule monitoring	RTLS BLE bangles (patients), Raspberry Pi detectors, central server logs (JSON), anamnestic/EHR-linked patient data	Streaming (BLE adv 800 ms; real-time MQTT pub/sub)	Private LAN; MQTT-based publish/subscribe; integrated with hospital legacy system (no HL7/FHIR reported)	One-way (monitoring, dashboards, alerts; no automatic actuation)	Edge + On-prem server (private LAN)
[42]	Critical Care Unit (ICU/CCU)	Workflow/Process HDT with dual-layer twins (physical + conceptual)	Observation forms (tasks/events), barcode readers as IoT edge, web dashboard events; (framework ready for EMR/devices later)	Streaming/event-driven (near-real-time; Azure IoT Hub telemetry, ∼200 ms typical routing latency)	Azure IoT Hub → Event Grid → Function Apps → Azure Digital Twins (DTDL v2) → Azure SQL; no concrete HL7/FHIR build in this phase	One-way (monitoring/analytics & decision support now; two-way/actuation envisioned in roadmap)	Hybrid (edge devices + Azure cloud services)

Table 7. *Cont.*

Study	Hospital Setting	Twin Type	Data Modalities	Update Cadence	Integration Mechanism	Directionality	Compute Architecture
[52]	Ward (in-patient bed management)	Process/operations twin for ward bed-bay allocation	Patient stream: diagnosis, gender, contagiousness; ward/room ontology (monitoring categories); treatment task sequences; historical ward dataset from Rikshospitalet	Timed/event stream (online runs) + Monte Carlo simulations	DT stack: Orchestrator + Knowledge Base (ontology) + ABS patient-flow simulator + Z3 optimizer via SMOL; no HL7/FHIR/EHR interface	One-way (decision support; no automatic actuation to hospital systems)	On-prem/edge (Java/ABS + Z3; local DT components)
[53]	Hospital-wide operations (ICU/Med-Surg/Telemetry; ED/DA/OR inflow)	Process/operations twin for discharge→bed-ready (Bed Turnaround Time)	Per-shift discharges (day/eve/night); UA & EVS staffing per shift; four cleaning step durations (assign dirty, assign EVS, clean, recycle); multi-facility ops logs (2021-04-11→2022-03-30)	Batch (historical inputs; stochastic simulations 100 days)	AnyLogic agent-based DT; validated vs. historical + ML surrogate (SHAP for sensitivity); no HL7/FHIR/EHR interface	One-way (decision support; no automatic actuation to hospital systems)	On-prem/local simulation environment
[55]	Outpatient department/ hospital patient pathways (experimental platform, pre-deployment)	Process/pathway DT with DTM (monitoring) + DTP (predicting)	IoT geofencing sensors (RFID/RTLS tags & readers/beacons), event logs (start/end), real-time DB with Patient_ID, MAC, timestamp; historical log files for model build/validation	Streaming/near real-time (events on occurrence; RTLS example ∼1 s)	IoT sensors → real-time database → FlexSim DT models (replay/prospective → DTM/DTP); emulator used for testing; no HL7/FHIR	One-way (monitoring/ prediction & decision support; no automatic actuation back to hospital systems)	On-prem/hospital servers (DT models installed locally; synchronized to real time)
[50]	Emergency Medical Communication Centers (EMCCs)	Process/operations DT of EMCC front-office (call reception & queuing)	Telephony event logs + medical regulation software logs; per-slot inputs: incoming calls, ECO staffing, call-duration empirical distributions	Batch (replay of real production data; not real-time sync)	Witness™ DES DT; process-mining–informed model; no HL7/FHIR/ EHR linkage	One-way (decision support; organization scenarios tested, no auto actuation)	Local/desktop simulation (e.g., Intel Core i7; multi-replication runs)

Note: → indicates the direction of data or information flow between connected system components.

Table 8. Architectural Design Trade-offs in Digital Healthcare Systems.

Architectural Choice	Advantage	Trade-Off
Edge Computing [44,57]	Low latency, real-time monitoring	Limited computational resources
Cloud Computing [57,58]	High scalability and processing power	Privacy and data transmission concerns
Centralized Data Architecture [57]	Simplified integration and management	Higher cybersecurity risk
Distributed Architecture [44,57]	Improved resilience and data locality	Greater system complexity

As shown in Table 9, most of the selected studies incorporate at least one of these three pillars, whereas only a limited number address all three simultaneously. Human involvement is the most commonly represented dimension, with many systems incorporating users in supervisory or decision-support roles, although this involvement is often partial. For example, several studies implement explicit HIL mechanisms through clinical or managerial decision interfaces, including clinician review in [19], direct operator override in the bionic-hand application presented by [54], and interactive dashboards supporting managers and healthcare staff in operational digital twins for emergency departments, operating rooms, and hospital logistics [28,42,48–50,52,53,55]. In contrast, a substantial proportion of studies incorporate human participation only conceptually through decision-support functions or general interaction and educational features without a clearly defined control mechanism [18,20,56,57,59–65]. Only one study explicitly reports the absence of human involvement in the operational loop, focusing exclusively on device-level sensing and recognition [47]. Overall, these findings suggest that human participation is widely acknowledged in current HDT research; however, in most cases it is limited to advisory interfaces or simulation-based decision support rather than full human supervision and control of the HDT.

Similarly, privacy and ethical governance are addressed in many of the reviewed studies, although the extent of their implementation varies considerably. Some studies explicitly align their systems with established regulatory frameworks, such as GDPR, HIPAA, the EU AI Act, and ISO 27001, while also incorporating technical safeguards including encryption, access control, identity and access management (IAM), intrusion detection systems (IDSs), and federated or blockchain-based architectures [18,57,59,63,64]. Other studies discuss privacy, security, informed consent, and governance primarily at the conceptual or policy level, for example through on-premises deployment and pseudonymization [19], privacy-oriented discussions and certification frameworks [20,60,61,65], or broader references to ethics approval, regulatory requirements, and ethical considerations in operational hospital DTs [48,50,55,62]. Detailed technical security measures are reported in only a subset of studies, including private local-area networks, role-based access control (RBAC), anonymization techniques, and cloud-security solutions [28,42]. By contrast, some studies propose privacy-enhancing technologies, such as blockchain, without describing their implementation within a complete regulatory framework [47]. A small number of studies do not report specific privacy or security mechanisms despite involving sensitive healthcare data, leaving governance and data protection measures insufficiently described [49,52–54].

Compared with HIL and privacy mechanisms, XAI receives comparatively less attention across the reviewed literature. Only a limited number of studies implement explicit explainability techniques, including post-hoc SHAP analyses and rule-based interpretation methods within HDT pipelines [19,53], or interpretable and hybrid ML models, such as physics-informed neural networks (PINNs) and statistical approaches for clinical decision support [56]. Several other studies acknowledge the importance of explainability but address it only conceptually, either by identifying XAI as a desirable requirement without specifying implementation methods [57,60,61,63–65] or by explicitly recognizing existing AI models as black boxes that require future XAI integration [18,62]. In contrast, most implementations, including many opera-

tional DTs designed for hospital workflow management, do not report the use of any explainability technique despite relying on complex predictive or optimization models [20,28,42,47–50,52,54,55,59]. These findings suggest that current HDT research places greater emphasis on human oversight and governance than on transparent AI-based decision-making. Moreover, these limitations are interrelated. The absence of explainability may reduce users' ability to understand and trust HDT recommendations, while limited implementation of robust privacy mechanisms, such as encryption, access control, or federated architectures, may introduce security and governance challenges that could affect stakeholder confidence.

Table 9. Comparison of Human-in-the-Loop, Explainable AI, and Privacy and Governance Mechanisms in HDT implementations (Theme 2).

Study	HIL (Y/P/N)	XAI (Method/Evaluation)	Privacy (Mechanism)
[19]	Y (clinician review)	SHAP/rules	On-prem + pseudonymized
[47]	N	None reported	Privacy discussion + blockchain proposal (no GDPR implementation)
[59]	P (UI/UX discussed; no mechanism)	None reported	HIPAA/GDPR + encryption + IAM + IDS
[54]	Y (direct override via UI/glove)	None reported	Not discussed
[60]	P (no explicit mechanism)	XAI-based diagnosis (no method)	Security/privacy emphasized + certification
[61]	P (conceptual decision support)	XAI/AI discussed broadly	Privacy/security + consent + governance
[62]	P (human–machine collaboration)	Opacity flagged (no methods)	GDPR + EU AI Act + consent/governance
[20]	P (shared decision-making + patient engagement)	None reported	Privacy/security + ethics
[18]	P (patient/clinician UI access + interaction)	Black-box concern; call for XAI	Encryption + access control + blockchain + consent
[56]	P (clinical decision support & alerts)	Interpretable/statistical + hybrid ML (PINNs)	Ethics + bias/fairness + auditability
[48]	Y (managers choose interventions)	None reported	Ethics approval + governance
[49]	Y (OR managers compare strategies)	None reported	Not reported
[28]	Y (clinical dashboard monitoring)	None reported	On-prem + private LAN + RBAC + authentication
[42]	Y (staff barcode/web dashboard)	None reported	Anonymization + Azure Defender + data minimization
[52]	Y (simulation interface for staff)	None reported	Not reported
[53]	Y (leadership resource decisions)	SHAP (post-hoc feature importance)	Not reported
[55]	Y (proactive manager decisions)	None reported	Privacy/security concerns + social/ethical limitations
[63]	P (patient–clinician interaction)	XAI requirement (no method)	Federated learning + edge + blockchain + auditability
[64]	P (decision support + clinician interaction)	XAI broadly discussed (no SHAP/rules)	GDPR/HIPAA + ISO 27001 [66] + bias/misuse risks
[50]	Y (managerial decisions; stakeholder input)	None reported	Regulatory + security constraints
[65]	P (decision support + education)	XAI broadly discussed (no SHAP/rules)	Privacy/security + ethics + regulatory gaps
[57]	P (decision support + interaction)	Interpretability imperative (no method)	Authentication + blockchain + storage/governance

None of the reviewed studies fully integrates Human-in-the-Loop, explainable AI, and comprehensive governance mechanisms within a single HDT framework, and only a limited number explicitly evaluate human-centric characteristics beyond technical performance metrics [19,56]. This limited attention to user-centered evaluation makes it difficult to assess the influence of human involvement and explainability on user trust and decision quality. As HDT research continues to evolve toward the human-centered vision of Industry 5.0, these aspects are likely to become increasingly important, with HDTs being positioned as human-centered enablers rather than purely technical artefacts [19,57,62,64]. From this perspective, future HDT systems would benefit from integrating meaningful human participation, interpretable AI, and robust governance mechanisms within a unified framework. Such integration has the potential to strengthen user trust while supporting the Industry 5.0 objective of ensuring that humans remain informed, engaged, and ultimately responsible for decisions supported by AI-enabled digital twin systems.

Theme 3: Operational Outcomes

This theme addresses RQ3 of the content analysis by examining the operational outcomes associated with the implementation of HDTs in hospital environments. Given that hospitals represent complex human–cyber–physical systems, understanding the operational implications of HDT adoption is essential for assessing their practical value. The analysis considers the effects of HDTs on clinical workflows, resource utilization, human factors, safety, and quality outcomes across EDs, ICUs, ORs, and hospital wards.

Within this theme, all operational key performance indicators (KPIs) reported in the included hospital-based HDT studies were identified and extracted. These KPIs were subsequently classified into five standardized categories: Flow, Capacity, Human Factors, Safety/Quality, and Sustainability, representing the principal operational domains influenced by HDT implementation. For detailed analysis, 12 of the 22 included studies were selected because they reported sufficiently detailed and quantifiable operational KPIs. Studies conducted outside hospital settings or lacking meaningful KPI information were excluded. However, two hospital-based studies [60,65] were retained despite providing limited quantitative KPI data because of their relevance to hospital operations.

Each column in Table 10 provides complementary analytical information. The KPI label identifies the measured outcome, whereas the Direction and Magnitude (with unit) column indicates both the direction of change (↑ = improvement, ↓ = reduction, ↔ = no observable change) and its reported quantitative value. The Evidence Type identifies whether the findings are derived from simulation, retrospective analysis, or prospective evaluation, while Comparator (Y/N) indicates whether a baseline or control condition was included.

To improve transparency in interpreting the reported findings, a Quality Flag is assigned to each study: ✓ denotes comparator-validated empirical evidence, ▲ indicates simulation-based evidence without real-world validation, and ✎ represents conceptual or qualitative contributions. In addition, the Evidence Strength classification (High, Moderate, or Low) summarizes the overall robustness of the reported findings. Together, these indicators provide a structured evidence matrix that links reported operational outcomes with their methodological rigor and the strength of supporting evidence.

Across the studies summarized in Table 10, HDT implementations most consistently improve flow-related KPIs, although the magnitude of improvement varies across hospital settings and is sometimes accompanied by trade-offs in capacity utilization and human factors. In operating-room applications, ref. [19] reports a 0.8-day reduction in hospital length of stay together with a 5% relative increase in operating-room utilization based on simulation combined with retrospective calibration. In contrast, the prototype decision-support system presented by [49] qualitatively reduces patient waiting time but reports a 9% reduction in operating-room utilization (77.3% compared with an 85% target) and a 92% increase in staff overtime, illustrating that improvements in patient flow may be accompanied by increased workload or reduced resource utilization.

Emergency-care applications report larger and more consistently quantified improvements in patient flow. Using discrete-event simulation, refs. [48,51] report a 64% reduction in treatment waiting times for Emergency Severity Index (ESI) triage levels 3–5, decreasing from 4.68 to 1.66 h. Similarly, the emergency call-center digital twin proposed by [50] increases the proportion of calls answered within 30 s (QoS_{30}) by 22% during a one-week evaluation period.

Table 10. Canonicalized and normalized KPI results across studies.

Study	Setting	KPI Bucket	KPI Label	Direction & Magnitude	Evidence Type	Comparator	Notes	Quality Flag	Evidence Strength
[19]	OR	Flow	LOS	↓ 0.8 days (sim + retro)	sim + retro	Y	TRL 6–7; absolute ↓, baseline not given	✓	Moderate
		Capacity	OR utilization	↑ 5% (sim + retro)	sim + retro	Y	Relative increase; TRL 6–7	✓	Moderate
		Human factors	Workload	↓ (qualitative improvement)	sim + retro	Y	Qualitative only	✓	Moderate
[47]	Ward	Safety/ Quality	Accuracy	↑ 4% (sim)	sim	N	Classifier gain (97% vs. 93%)	▲	Low
		Flow	Queuing delay	↓ (sim)	sim	N	Reduced with edge computing	▲	Low
[54]	ICU	Flow	Control latency	↓ 180 ms (prospective)	Prospective prototype	N	Triple verification; low TRL	▲	Low
		Flow	Monitoring latency	↓ ≈33% (prospective)	Prospective prototype	N	≈33% vs. control; FPS 40–55	▲	Low
[60]	ED	Other	None	↔ (no effect)	Survey/SEM	N	No KPI quantified	✎	Low
[48]	ED	Flow	Treatment waiting time (Triage 3–5)	↓ 64% (4.68 h → 1.66 h, sim)	sim (Arena DES)	Y	Validated vs. historical (p = 0.8); VVUQ steps	✓	Moderate
[49]	OR	Capacity	OR utilization	↓ 9% (77.3% vs. 85%)	sim (prototype)	Y	TRL 4–5; target benchmark	✓	Moderate
		Human factors	Staff overtime	↑ 92% (9.6% vs. ≤5%)	sim (prototype)	Y	Exceeded target; workload strain	✓	Moderate
		Flow	Waiting time	↓ (sim prototype)	sim (prototype)	Y	Not quantified; direction only	✓	Moderate
[28]	Ward	Safety/ Quality	Tracking errors	↓ (prospective pilot)	Prospective prototype	Y	Fewer errors vs. manual logs	✓	High
[42]	CCU	Safety/ Quality	Tracking coverage	↑ 72% (prospective)	Prospective prototype	Y	Comparator vs. SOPs	✓	High
		Flow	Platform latency	↓ (prospective)	Prospective prototype	Y	Improved real-time sync	✓	High
[52]	Ward	Sustainability	Feasibility rate	↓ (unsatisfiable steps)	sim (Monte Carlo)	Y	Lower infeasibility → improvement	✓	Moderate
		Capacity	Bed-bay changes/ satisfiable step	↔ (no change)	sim (Monte Carlo)	Y	Neutral effect	✓	Moderate
[55]	Ward	Safety/ Quality	Prediction accuracy (DTP vs. emulator)	↑ (±5% threshold gain)	sim (emulator + DT validation)	Y	HospiT'Win pipeline; TRL 3–4	✓	Moderate
[50]	ED	Flow	QoS_{30} (≤30 s answer rate)	↑ 22% (sim + retro)	sim + retro	Y	Validated vs. real data; 10 replications	✓	Moderate
[65]	ICU	Other	None	↔ (no effect)	Narrative review	N	Validation gaps only	✎	Low

At the technical level, ICU and coronary care unit (CCU) implementations primarily demonstrate improvements in system responsiveness. The HDT proposed by [54] reports a reduction of approximately 180 ms in control latency and approximately 33% in monitoring latency, whereas [42] reports reduced platform latency together with improved real-time synchronization. In contrast, the ward-level Monte Carlo planning approach presented by [52] reduces infeasible bed-allocation steps without affecting the number of bed–bay changes per satisfiable allocation step. Non-interventional studies, including the emergency department survey and structural equation model presented by [60] and the ICU narrative review by [65], provide conceptual insights into workflow improvement but do not report measurable operational KPIs. Overall, these findings suggest that simulation-based and prototype HDT implementations consistently demonstrate improvements in timeliness, whereas outcomes related to resource utilization and staff workload remain dependent on the specific operational context.

Safety, quality, and sustainability outcomes are generally reported as positive, although the supporting evidence varies in methodological strength. At the ward level,

ref. [47] reports a 4% improvement in human activity recognition accuracy together with reduced queuing delays using a simulation-based implementation. Similarly, ref. [28] provides prospective evidence that digital twin-enabled patient tracking reduces documentation errors compared with conventional manual recording procedures.

Likewise, ref. [42] reports improved tracking coverage within a coronary care unit, increasing by 72% over seven days, together with lower platform latency. In addition, ref. [55] demonstrates that the HospiT'Win digital twin predicts discharge-to-placement outcomes within a ±5% accuracy threshold when validated against an emulator. Sustainability is explicitly evaluated in only one study [52], where Monte Carlo-supported HDT planning reduces infeasible allocation steps without increasing capacity utilization, suggesting improved operational robustness rather than higher throughput.

Overall, the evidence ranges from low-strength simulation studies and narrative reviews [47,60,65] to moderate evidence derived from simulation combined with retrospective analysis [19,48–50,52,55], and prospective prototype evaluations providing comparatively stronger empirical evidence [28,42]. Collectively, these findings suggest that HDTs most consistently improve patient flow and tracking-related safety outcomes, whereas their effects on capacity utilization, staff workload, and sustainability remain more variable and dependent on implementation context.

Table 11 summarizes these findings using a vote-counting approach, a descriptive synthesis method that records the number of KPIs reported as improved, unchanged, or worsened across the included studies. Rather than combining numerical effect sizes, vote counting summarizes the overall direction of reported outcomes, allowing consistent comparison among studies that employ different metrics and reporting approaches.

Table 11. Vote-Counting Summary by Clinical Setting and KPI Category.

Setting	KPI Bucket	N_Improved (+1)	N_No_Effect (0)	N_Worse (−1)	Total n	Share Improved (%)
ED	Flow	2	0	0	2	100%
	Capacity	0	0	0	0	—
	Human factors	0	0	0	0	—
	Safety/Quality	0	0	0	0	—
	Sustainability	0	0	0	0	—
ICU	Flow	2	0	0	2	100%
	Safety/Quality	0	0	0	0	—
	Other (non-KPI)	0	1	0	1	0%
OR	Flow	2	0	0	2	100%
	Capacity	1	0	1	2	50%
	Human factors	1	0	1	2	50%
Ward	Flow	2	0	0	2	100%
	Capacity	0	1	0	1	0%
	Human factors	0	0	0	0	—
	Safety/Quality	3	0	0	3	100%
	Sustainability	1	0	0	1	100%
CCU	Flow	1	0	0	1	100%
	Safety/Quality	1	0	0	1	100%
Totals Operational	—	16	2	2	20	≈80% Overall Improvement

In this review, each KPI reported in Table 10 was classified into one of three categories presented in Table 11: Improved (+1), No Effect (0), or Worse (−1), based on the direction of change reported in the original study. These classifications were subsequently grouped according to hospital setting (e.g., ED, ICU, OR, Ward, and CCU) and KPI category (Flow, Capacity, Human Factors, Safety/Quality, and Sustainability) to identify recurring operational patterns across clinical environments. The Share Improved (%) column reports the proportion of positive outcomes within each category, thereby providing

a normalized measure of how frequently HDT implementations were associated with operational improvements.

The vote-counting synthesis indicates that the majority of reported KPIs demonstrate positive outcomes, with approximately 80% classified as improvements following HDT implementation. This aggregate proportion should, however, be interpreted together with the evidence-quality information reported in Table 10. The reviewed evidence spans simulation-only studies, simulation combined with retrospective calibration, and prospective prototype evaluations, with corresponding differences in Evidence Strength. The setting-specific results in Table 11 further show that flow-related KPIs were consistently positive across ED, ICU, OR, Ward, and CCU applications, whereas capacity and human-factor indicators showed greater variability, particularly in OR and Ward settings. Thus, the 80% overall improvement rate provides a descriptive summary of reported KPI direction rather than a robustness-adjusted estimate of treatment effect, and the observed positive pattern should not be interpreted as evidence of uniform effectiveness across evidence tiers or clinical settings.

By comparison, capacity utilization and human-factor outcomes exhibit greater variability, reflecting potential trade-offs between operational efficiency and staff workload. Sustainability indicators are comparatively limited in the current literature, although the available evidence suggests potential benefits related to resource utilization and operational robustness. Overall, these findings suggest that HDT implementation is generally associated with favourable operational outcomes across multiple hospital settings, although the magnitude and consistency of these effects vary according to application context.

Overall, the evidence synthesized in this theme supports the operational potential of Human Digital Twins in hospital environments. Across the reviewed studies, HDTs are associated with improvements in several aspects of healthcare delivery, particularly patient flow, operational efficiency, and selected safety outcomes. However, the variability in study design, evaluation methodology, and implementation context indicates that further empirical validation is needed to establish the generalizability of these findings across diverse healthcare settings.

3.2.2. Bridge Narrative: Linking I4.0 Rails to I5.0 Values

This section synthesizes the findings from the preceding analyses to illustrate how HDTs can bridge the technological capabilities of I4.0, including IoT, data integration, and real-time synchronization, with the human-centered principles of I5.0, such as explainability, collaboration, and well-being. It integrates the architectural, governance, and operational perspectives discussed in the previous themes to provide a system-level understanding of how HDTs combine technological capabilities with human-centered values in hospital operations.

To answer RQ4 of the content analysis, a bridge matrix was developed by integrating the findings from the three thematic analyses to examine the relationships between the technological foundations of I4.0 and the value-oriented principles of I5.0 within hospital-based HDT implementations. Seven analytical dimensions were considered (see Table 12), comprising three technological dimensions (IoT/CPS integration, analytics and optimization, and twin synchronization) and four human-centered dimensions (HIL, XAI, privacy and governance, and sustainability and resilience). Each study was coded according to the presence (✓), partial implementation (–), or absence (blank) of each dimension. The resulting matrix was visualized as a heatmap to illustrate the distribution and co-occurrence of I4.0 and I5.0 characteristics across the reviewed studies.

The analysis indicates that the reviewed studies predominantly emphasize the technological capabilities associated with Industry 4.0. Most HDT implementations incorpo-

rate IoT/CPS integration by connecting sensorized assets, clinical information systems (EHR/HIS), or real-time tracking technologies with analytical and optimization models that support predictive decision-making. Similarly, synchronization between physical and virtual entities is widely reported, ranging from continuous telemetry in ICUs and EDs to periodic synchronization in simulation-based operational models. Collectively, these findings indicate that real-time monitoring, predictive analytics, and operational optimization constitute the primary technological focus of current HDT research.

Table 12. Bridge matrix between I4.0 and I5.0 values through core HDT research (✓ = present, – = partial, blank = not mentioned).

Study	IoT/CPS	Analytics (ML/AI)	Twin Sync	HIL	XAI	Privacy	Sustainability	Resilience
[19]	✓	✓	✓	✓	✓	✓	✓	✓
[47]	✓	✓	✓		–	–		
[59]	✓	✓	✓	–	–	✓	–	✓
[54]	✓		✓	✓		–		–
[60]	✓	✓	✓	✓	✓	✓	–	–
[61]	✓	✓	✓	–		✓		–
[62]	✓	✓		✓	–	✓	✓	
[20]	✓	✓	✓	✓		✓	–	–
[18]	✓	✓	✓	–		✓	–	✓
[56]	✓	✓	✓	✓		✓		
[48]	–	✓	✓	–		✓	–	✓
[49]	–	✓	✓	–		–	–	✓
[28]	✓	✓	✓	–		✓	–	✓
[42]	✓	✓	✓	–		✓	–	✓
[52]	–	✓	✓	–		–	–	✓
[53]	–	✓	–	–	✓		–	✓
[55]	–	✓	✓	–		–	–	✓
[63]	✓	✓	✓	–		✓	–	✓
[64]	✓	✓	–	–	✓	✓		–
[50]	–	✓	–	✓		✓	–	✓
[65]	✓	✓	–	✓		✓	–	✓
[57]	–	✓	✓	–		–	–	✓

In contrast, the human-centered dimensions associated with Industry 5.0 appear to be less extensively implemented. XAI is only occasionally operationalized, with relatively few studies reporting the application of interpretability techniques such as SHAP, LIME, or causal explainers. Human-in-the-Loop mechanisms are primarily implemented in managerial or scheduling applications, where users typically interact with advisory dashboards rather than participating in fully integrated collaborative decision-making processes. Privacy and governance receive comparatively greater attention through discussions of GDPR, HIPAA, encryption, and related regulatory or security mechanisms; however, relatively few studies report comprehensive implementations incorporating auditable consent management or complete data lineage. Sustainability and resilience receive the least attention, with only limited references to energy efficiency, resource optimization, or system resilience within hospital operational contexts.

The bridge matrix further suggests an uneven distribution between technological capabilities and human-centered characteristics across the reviewed studies. While many HDT implementations focus on operational efficiency, automation, and predictive analytics, comparatively fewer studies integrate transparency, explainability, governance, and sustainability within the same framework. Nevertheless, applications in emergency departments, ORs, and ICUs demonstrate the potential to combine continuous data acquisition and predictive models with clinical decision support, thereby enhancing operational safety and supporting healthcare professionals through adaptive decision-making. Similarly,

patient-level HDTs, including rehabilitation and chronic care applications, demonstrate substantial capabilities for sensing and personalized monitoring, although explainability, Human-in-the-Loop mechanisms, and sustainability assessments remain comparatively underdeveloped.

Addressing these limitations will require future HDT frameworks to incorporate Industry 5.0 principles more explicitly. In particular, future developments should integrate (i) Human-in-the-Loop intervention protocols, (ii) explainability-by-design through interpretable AI models, (iii) privacy-by-design supported by auditable governance mechanisms, and (iv) sustainability and resilience indicators as integral components of system performance evaluation.

Overall, this synthesis addresses RQ4 by indicating that current hospital-based HDT implementations largely reflect the technological orientation of Industry 4.0, while the integration of Industry 5.0 principles remains comparatively limited. Advancing toward human-centered, sustainable hospital operations will therefore require HDT frameworks that systematically combine technological capabilities with explainability, participatory decision-making, governance, and sustainability assessment. The proposed framework (see section 4) represents one possible direction by incorporating interpretability, participatory control, and sustainability assessment to support the development of accountable, human-centered decision-support systems for intelligent hospital environments.

4. Conceptual Framework

This study proposes a conceptual framework (see Figure 8) to support future research and the implementation of HDTs in hospital operations. Before describing the framework and its components, it is important to clarify the types of data required by an HDT, their potential sources, and the roles of historical and real-time data in supporting HDT functionality. The following section provides this background.

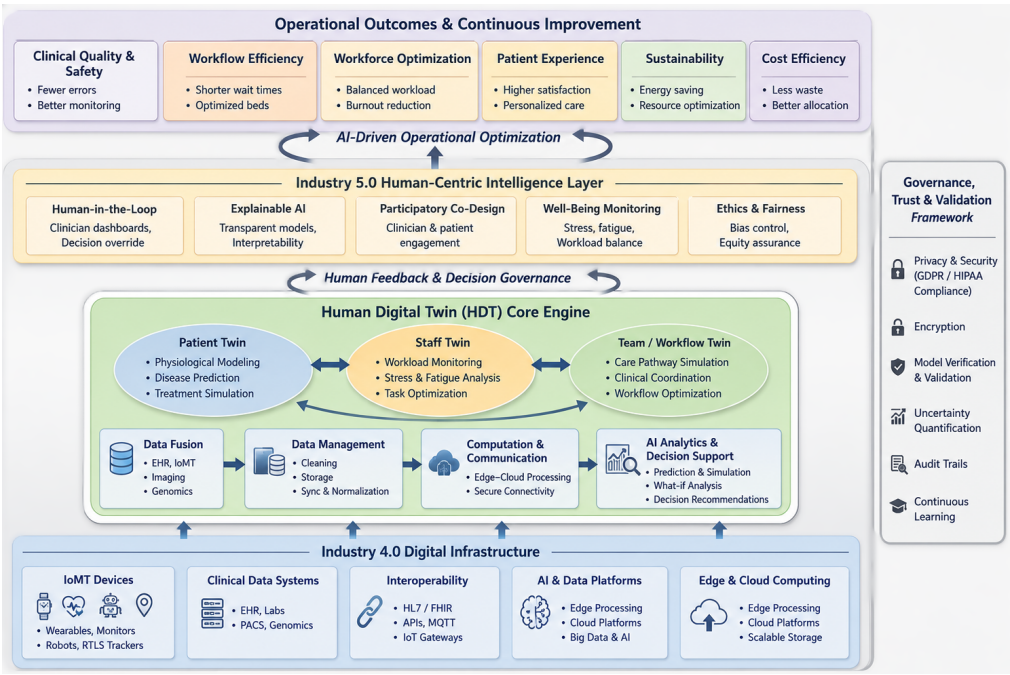

Figure 8. Conceptual framework for HDT-enabled smart hospital operations. The Human Digital Twin is represented in the central "HDT Core Engine" layer, comprising patient, staff, and team/workflow twins. The lower layer represents enabling I4.0 digital infrastructure, the upper human-centric layer represents Industry 5.0 oversight and value mechanisms, and the outer layers indicate governance and operational outcomes surrounding HDT deployment.

An HDT requires the integration of heterogeneous patient data to represent and predict an individual's health status accurately. This requirement is consistent with Afshar et al. [7], who note that healthcare digital twins integrate diverse datasets, including genetic information, wearable-device outputs, and real-time physiological data, to support predictive modelling and personalized interventions. In practice, this involves combining structured clinical records (demographics, diagnoses, laboratory results, medical imaging, and genomics from EHRs) with continuous physiological signals (e.g., heart rate, blood pressure, and respiration) and patient-reported information such as symptoms, physical activity, and sleep patterns [56]. Environmental context (e.g., air quality, temperature, and noise) and behavioural information obtained from smartphones or wearable devices can further enrich the digital representation. Together, these multimodal inputs establish a personalized baseline and enable the HDT to detect deviations from expected health trajectories in near real time [56]. Consequently, historical clinical data define the patient's baseline health profile, whereas live sensor streams continuously synchronize the digital twin with the patient's current condition.

The acquisition of these data relies on a combination of clinical and consumer sensing technologies. Related umbrella-review evidence also highlights the importance of wearable devices, IoT/IoMT connectivity, and AI-enabled multimodal data processing in supporting healthcare digital twins [7]. Core clinical information is obtained from hospital information systems, including EHRs, laboratory information systems, and picture archiving and communication systems (PACSs), which provide patient histories and diagnostic information [56]. Physiological measurements are collected using clinical equipment (e.g., ECG devices, blood pressure monitors, pulse oximeters, and ventilators) together with wearable and implantable biosensors that continuously transmit vital signs [29]. Lifestyle information and patient-reported outcomes are collected through mobile health applications and electronic surveys, while ambient IoT sensors capture contextual information such as environmental conditions and location. These heterogeneous data streams are subsequently integrated through cloud-based platforms or middleware that standardize data formats, synchronize timestamps, and fuse multiple data sources. Such integration is essential because it enables the HDT to combine historical and real-time information while addressing challenges associated with data silos and interoperability [56].

A practical HDT therefore combines both static (historical) and dynamic (real-time) data. Retrospective information, including EHRs, medical imaging, and genomic data, establishes the patient's baseline model and supports the training of predictive algorithms [56]. In contrast, continuous streams of physiological measurements and sensor data maintain synchronization between the physical patient and the digital representation. For example, continuous heart-rate and activity monitoring allow the HDT to function as a dynamic representation of the individual's current condition [56], thereby supporting the early identification of clinical deterioration. By integrating historical and real-time information within a temporally consistent framework, the HDT can continuously update its predictions and support timely clinical interventions, provided that robust data pipelines ensure accurate synchronization across heterogeneous data sources [56].

Based on the thematic synthesis, Figure 8 presents a conceptual technical taxonomy of HDT architectures for hospital operations, comprising interconnected data infrastructure, digital modelling, AI analytics and decision-support, human interaction and control, and governance layers.

To integrate the technological capabilities of Industry 4.0 with the human-centered principles of Industry 5.0 in hospital operations, this study proposes a conceptual framework in which the HDT serves as the central mediating component. It should be noted that the surrounding layers are not intended to represent the HDT itself. Rather, the HDT corre-

sponds to the central core engine, whereas the infrastructure, governance, and outcome layers represent the enabling ecosystem within which the HDT operates. As illustrated in Figure 8, the framework consists of four interconnected layers that extend from data infrastructure to operational outcomes. It is designed to combine Industry 4.0 technologies with the human-centered objectives of Industry 5.0 by using continuous data streams and AI-driven analytics from the "I4.0 rails" (IoMT devices, interoperability standards, and edge–cloud computing) to construct continuously updated digital representations of patients and healthcare professionals while explicitly incorporating human oversight, well-being, and ethical considerations [22,63].

The "I4.0 rails" layer collects data from wearable devices, smart medical equipment, medical robots, and real-time location systems (RTLSs). These heterogeneous data streams are integrated through interoperability technologies such as HL7/FHIR, MQTT, and application programming interfaces (APIs), while AI and machine-learning algorithms operate within edge and cloud computing environments supported by large-scale data storage and high-performance computing resources. The integrated data are subsequently transferred to the HDT core engine, where the data acquisition and fusion layer combines multimodal information from EHRs, medical imaging, genomic data, and IoMT streams [63]. A dedicated data-management layer performs data cleaning, normalization, and synchronization, while the underlying computational infrastructure supports AI inference, simulation, and communication processes. The analytics and decision-support module applies predictive machine-learning models and scenario-based analyses to support clinical and operational decision-making. At the centre of the framework, the digital-modelling layer constructs virtual representations of individual patients and healthcare personnel, including physiological, workload, and workflow models, thereby supporting individualized monitoring and operational analysis [22,67]. Human-in-the-Loop mechanisms, including clinician dashboards and override controls, together with explainable AI techniques such as rule-based reasoning and SHAP, support human oversight and facilitate the interpretation of model outputs [22,63].

Above the HDT core, the Industry 5.0 human layer introduces participatory and ethical components. Clinicians and patients contribute to the design of user interfaces and feedback mechanisms, while the framework incorporates human-factor indicators such as stress, fatigue, and user satisfaction as additional inputs. An ethical and social context layer considers inclusivity and social determinants of health, whereas dedicated bias and fairness monitoring aims to identify potential sources of algorithmic bias and promote equitable decision-making. A continuous human–machine feedback loop enables user feedback to support iterative model refinement. Collectively, these components are intended to maintain alignment between HDT functionality and human-centered values.

The upper outcome layer defines the operational objectives of the framework, including improved patient flow, reduced waiting times, optimized staff scheduling, balanced workloads, enhanced clinical quality and safety, greater operational sustainability and resilience, improved patient experience, and cost efficiency. Operational indicators such as throughput, error rates, and user satisfaction can be continuously monitored to evaluate system performance and support iterative model improvement. An overarching governance layer complements the framework by incorporating privacy and security mechanisms (e.g., GDPR/HIPAA compliance and encryption), model verification and validation, uncertainty quantification (VVUQ), and audit trails to enhance transparency and trustworthiness.

Overall, the proposed framework establishes a close interaction between technological infrastructure and human participation. Continuous IoMT data streams support AI-driven analytics that update individual digital twins, while clinicians remain involved throughout the decision-making process. Consequently, the framework is intended to support predic-

tive hospital operations, such as the early identification of patient deterioration or staff workload risks, while maintaining human oversight and ethical governance [22,63]. More broadly, the framework integrates the sensing, communication, cloud–edge computing, and AI capabilities associated with Industry 4.0 with the human-centered principles of Industry 5.0 to support hospital operations without overlooking transparency, safety, or ethical considerations. For example, patient-specific digital twins provide comprehensive virtual representations that can support predictive modelling for applications such as readmission or mortality risk assessment in precision medicine settings [67]. In summary, each layer of the proposed framework—from IoMT infrastructure to human-centered governance—has a clearly defined role in supporting more efficient, reliable, and patient-centered hospital operations while promoting privacy, fairness, and continuous validation.

Illustrative Use Case in Emergency Department Operations

To demonstrate the practical relevance of the proposed framework, this section presents an illustrative use case in the context of ED operations. This example is intended to demonstrate the potential application of the framework and does not constitute empirical validation.

Consider an ED experiencing a sudden increase in patient arrivals, leading to longer waiting times, bed shortages, and uneven staff workload. In this scenario, the proposed four-layer HDT framework supports monitoring, coordination, and decision-making across patients, staff, and clinical workflows.

At the I4.0 infrastructure layer, data are acquired from hospital information systems, EHRs, bedside monitors, wearable devices, and bed-management systems. These data include patient vital signs, triage status, admission and discharge records, staff allocation, and bed availability.

Within the HDT core engine, these data are transformed into three interconnected digital representations. The patient twin represents the patient's physiological condition and anticipated care pathway. The staff twin models workload distribution, task allocation, and potential fatigue or stress indicators. The team/workflow twin represents patient flow, care coordination, and operational bottlenecks across the ED and inpatient departments.

At the Industry 5.0 human-centric intelligence layer, the framework supports human oversight rather than replacing clinical decision-making. Predictive analytics estimate patient arrival patterns, waiting times, and workload levels, while clinicians and managers remain responsible for reviewing and adjusting recommendations. Explainable AI improves the interpretability of model outputs, and governance mechanisms support privacy, accountability, and fairness.

At the operational outcomes layer, the expected benefits include reduced waiting times, improved bed allocation, more balanced staff workload, enhanced monitoring of high-risk patients, and better coordination among clinical teams. This example illustrates how HDTs can integrate technical infrastructure with human-centered decision support in hospital operations.

This use case is intended solely to demonstrate the operational applicability of the proposed framework. Future research should evaluate the framework through retrospective analyses and real-world implementation in hospital environments.

5. Discussion

The reviewed literature indicates that HDTs have the potential to improve hospital operations. Across pilot studies and simulation-based investigations, HDT-enabled interventions have been associated with improvements in patient flow and resource utilization. For example, digital twins for patient flow, bed management, and operating room

scheduling report reductions in waiting times, shorter lengths of stay, and fewer operational bottlenecks. Approximately 80% of the reported performance indicators were classified as improvements in the descriptive vote-counting synthesis; however, this proportion should be interpreted in light of the heterogeneous evidence types and methodological strengths represented in the reviewed studies. High-acuity settings, such as ICUs and ORs, also report improvements in monitoring accuracy and communication reliability. These findings are consistent with previous studies highlighting the potential of digital twins to improve coordination and operational efficiency in healthcare [20,21]. Similar conclusions are reported by Afshar et al. [7], whose umbrella review identified the potential of DTs for personalized care, predictive maintenance, resource allocation, and healthcare system optimization. In addition, several HDT prototypes have undergone prospective evaluation in clinical environments, providing initial evidence of their practical feasibility [3].

Despite these encouraging findings, the reviewed studies also identify important trade-offs and implementation challenges. Optimizing operational efficiency without considering human factors may increase staff workload and contribute to fatigue, even when throughput improves. For example, maximizing OR utilization may unintentionally increase scheduling pressure and reduce staff recovery time [23]. These findings highlight the importance of balancing efficiency with caregiver well-being, a central principle of Industry 5.0. Early hospital DT implementations primarily emphasized operational optimization, with limited consideration of clinician workload or patient experience. More recent studies increasingly incorporate human-centered indicators, such as staff workload and patient satisfaction, alongside conventional efficiency metrics [22,23]. This emerging trend reflects the transition toward Industry 5.0, where technological advancement is expected to support both operational performance and human well-being.

This review contributes theoretically by synthesizing fragmented HDT research into a unified perspective that integrates I4.0 technologies with Industry 5.0 human-centered principles within the context of hospital operations. The proposed four-layer conceptual framework provides a structured foundation for future HDT research and highlights important research directions related to governance, explainability, sustainability, and human-centered system design. From a practical perspective, the findings provide hospital managers, healthcare professionals, and technology developers with a comprehensive overview of HDT applications, implementation challenges, and enabling technologies. The proposed framework and illustrative use case may support the planning and deployment of HDT solutions for improving patient flow, resource utilization, staff workload management, and decision support in smart and sustainable hospital environments.

6. Limitations and Future Recommendations

6.1. Gaps in Explainability and Trust

A major limitation of current HDT systems is the limited integration of XAI. Transparent decision support is essential in healthcare, yet most HDT applications provide only limited explainability. Only a few studies report concrete XAI techniques, primarily rule-based methods or SHAP values, while most acknowledge the importance of explainability without implementing practical solutions. Consequently, AI outputs often remain difficult for clinicians to interpret [68].

Several studies identify explainability as essential for user trust and ethical deployment. For example, Gaffinet et al. state that clinicians "need to understand the reason behind a given output", highlighting explainability as a prerequisite for HDT acceptance [19]. Addressing this gap requires integrating interpretable models or post-hoc explanation methods (e.g., LIME, SHAP) into HDT pipelines and evaluating their impact on clinician

trust through user studies. Without stronger investment in XAI, HDTs may face limited clinical acceptance [24]. Beyond explainability, broader HDT adoption will also depend on clinician acceptance, patient trust, effective ethical governance, and clear responsibility allocation, where AI supports decision-making while clinicians retain responsibility for clinical decisions.

6.2. Data Privacy and Security Challenges

The integration of HDTs into hospitals raises significant privacy and security challenges. Afshar et al. [7] similarly identify data privacy and security as major barriers to healthcare DT adoption, particularly when integrating real-time personal health data across digital systems. Most reviewed studies recognize the sensitivity of patient information and emphasize compliance with regulations such as GDPR and HIPAA. Several reviews identify privacy-preserving design as a prerequisite for healthcare HDTs [16,17]. Hasan et al. further describe security and privacy as "crucial" for successful HDT implementation [60]. Some prototypes implement encryption, authentication, role-based access control, or blockchain-based audit trails, demonstrating the feasibility of secure data management. For example, Bongomin et al. propose combining edge computing with blockchain to maintain hospital control over sensitive data while ensuring traceability [9].

Despite this awareness, many studies discuss privacy conceptually without describing concrete implementation mechanisms. Secure deployment environments, consent management, and end-to-end data provenance are rarely reported. As a result, privacy is often treated as a compliance requirement rather than a design principle. Future research should adopt privacy-by-design approaches and stronger governance mechanisms [19,28]. Techniques such as federated learning and differential privacy could enable collaborative learning while protecting sensitive patient information.

6.3. Sustainability and Energy Considerations

Sustainability remains one of the least explored aspects of HDT development. Although Industry 5.0 emphasizes environmentally sustainable technologies alongside human-centricity, few healthcare DT studies explicitly address energy efficiency or environmental impact [4,68]. In this review, sustainability received only limited attention. Existing studies provide only occasional references to energy efficiency or resource optimization, such as reduced cloud communication through edge computing or improved patient flow that may reduce resource waste [47,69]. However, quantitative sustainability indicators, including energy consumption and carbon footprint, are rarely reported.

Where sustainability benefits are discussed, the evidence remains preliminary. For example, edge-based HDTs reduce communication overhead, potentially lowering energy consumption, while improved operating room scheduling may reduce equipment idle time [21]. Nevertheless, sustainability is rarely evaluated systematically.

Future research should integrate sustainability into HDT design and evaluation. Green HDT frameworks could monitor resource consumption while optimizing operational performance. Sustainability indicators should complement clinical and operational metrics to support Industry 5.0 objectives of efficient and environmentally responsible healthcare [3,70].

6.3.1. Sustainability KPIs for HDT-Based Hospital Operations

Although sustainability is increasingly recognized, most studies do not define measurable evaluation indicators. To support future research and implementation, sustainability should be assessed using standardized KPIs.

Relevant KPIs include operational measures (patient throughput, waiting time), environmental measures (energy consumption of medical equipment and digital infrastructure), workforce measures (staff workload and utilization), and patient-centered measures (treat-

ment response time and quality of care). Integrating these KPIs into HDT monitoring systems would support continuous sustainability assessment while maintaining a human-centered perspective consistent with Industry 5.0. Future studies should validate these indicators empirically and incorporate them into HDT dashboards for real-time monitoring. Table 13 summarizes the proposed sustainability KPIs, their dimensions, descriptions, and example measurement units.

Table 13. Sustainability KPIs for Healthcare System Performance.

Sustainability Dimension	KPI	Description	Measurement Example
Operational Efficiency	Patient Throughput	Number of patients processed per unit time	Patients/hour
Environmental Impact	Energy Consumption of Medical Equipment	Energy usage during patient monitoring and treatment	kWh per patient
Workforce Sustainability	Clinician Workload Balance	Distribution of workload across staff	Patients per clinician
Patient-Centered Care	Average Waiting Time	Time between patient arrival and treatment	Minutes
Resource Utilization	Bed Occupancy Rate	Percentage of available beds occupied during a given period	%
System Resilience	Response Time to Critical Events	Time required to detect and respond to emergencies	Minutes

6.4. Need for Validation and Real-World Trials

Another important limitation is the lack of prospective validation of HDT solutions. Afshar et al. [7] similarly note that many healthcare DT applications remain at the pilot or small-scale stage and require broader clinical validation across diverse healthcare settings. Although numerous proof-of-concept studies and simulation-based investigations have been published, few report large-scale implementation in real hospital environments. Most healthcare DT studies focus on conceptual development or retrospective analysis, while real-world integration and validation remain at an early stage [3,46]. Xames and Topcu identify implementation research as a major gap, noting that many studies demonstrate technical feasibility without addressing deployment in clinical practice [30]. Likewise, Katsoulakis et al.[3] describe healthcare digital twins as "still in its infancy," emphasizing the need for collaborative research to advance the field. To date, only a limited number of HDT systems have undergone pilot evaluation with patients or healthcare professionals.

Some encouraging examples have emerged. A small number of studies have evaluated HDTs in clinical settings. For example, one study implemented an HDT-based decision-support system in an emergency department and reported improvements in operational performance [51]. Another integrated a digital twin into ICU patient monitoring and collected clinician feedback [15,56]. These studies provide initial evidence supporting the practical feasibility of HDTs, although they remain limited to single institutions or short evaluation periods. Long-term and multi-center evaluations are still largely absent.

As a result, evidence regarding the long-term reliability, clinical adoption, and organizational impact of HDTs remains limited. Questions regarding performance under high-demand conditions, sustained clinician trust, and integration into routine clinical workflows have yet to be adequately addressed. Future research should prioritize rigorous prospective validation through collaboration among academia, hospitals, and industry to evaluate HDTs under real-world conditions and establish best practices for clinical implementation [3,42].

6.5. Human-Centric Design and Integration

A defining characteristic of Industry 5.0 is its human-centric perspective, and the HDT paradigm places humans at the center of the digital twin ecosystem. However, many early DT applications did not adequately incorporate human factors. Studies on I4.0, DTs, particularly in manufacturing, primarily focus on machines, sensors, and automation while treating humans as external to the system. This approach is insufficient for healthcare, where clinicians and caregivers play a central role in decision-making. Karnoub et al. emphasize that "the role of humans is particularly important in the context of human-centric…I5.0" and argue that human elements should be tightly integrated into future DT systems [54]. Accordingly, they propose a "digital triplet" framework that explicitly incorporates the human alongside the physical and virtual entities, demonstrating the value of human integration in DT systems.

This reflects a broader trend toward incorporating HIL mechanisms into HDTs for healthcare. Xames and Topcu identify the limited consideration of clinicians' roles in decision-making as a major gap in current DT research [30]. Similarly, our review found that only a small number of studies enable active human oversight, such as allowing clinicians or managers to adjust model parameters or override AI recommendations. In most cases, human involvement remains supervisory rather than interactive.

Future HDT development should integrate HIL principles more systematically. This includes designing interfaces that enable healthcare professionals to interact with the HDT throughout its operation. For example, an HDT-based scheduling system could present multiple optimized scenarios for human evaluation rather than automatically enforcing a single solution [21]. User-centered design approaches that involve clinicians, nurses, and hospital managers throughout development may also improve usability and acceptance [60]. Accordingly, HDTs should be designed as collaborative decision-support systems rather than autonomous decision-makers. Some studies have already moved in this direction by providing staff training [16] or incorporating clinician feedback to refine the HDT over time [17].

Future research should also evaluate human factors associated with HDT use, including cognitive workload, situation awareness, and user trust. Early evidence suggests that appropriately designed HDTs can reduce routine workload while enhancing decision support, thereby complementing rather than replacing human expertise [22]. Overall, strengthening human-centered design remains essential for realizing the Industry 5.0 vision in healthcare.

6.6. Practical Implementation Challenges and Governance

Translating HDT concepts into hospital practice presents both technical and organizational challenges. A major technical challenge is data integration and interoperability. This observation is consistent with Afshar et al. [7], who identify data integration, interoperability, implementation cost, and limited real-world validation as major barriers to the broader adoption of DTs in healthcare. Hospitals generate large volumes of heterogeneous data (EHRs, laboratory results, medical devices, and IoT sensors) that are distributed across multiple systems. An HDT must aggregate and synchronize these data continuously to maintain an accurate representation of hospital operations. Achieving this requires addressing incompatible data standards, legacy IT infrastructure, and data quality issues [3]. Additional challenges include achieving semantic interoperability across heterogeneous clinical information systems, handling incomplete or missing data, maintaining reliable real-time synchronization, and enabling secure cross-institutional data sharing while preserving privacy, regulatory compliance, and patient confidentiality. Pellegrino et al. emphasize the need for harmonized and standardized reference architectures for healthcare DTs [28].

In practice, successful implementations have adopted interoperability standards such as HL7/FHIR together with middleware to connect heterogeneous systems [15]. Some architectures also incorporate edge computing. For example, Bozkaya-Aras et al. propose a four-layer HDT in which wearable sensor data are preprocessed at the edge to reduce latency and bandwidth before transmission to the central twin model [47]. Such architectures can improve responsiveness and reduce network load, which is particularly important for real-time operational twins. Nevertheless, large-scale deployment requires robust IT infrastructure, including high-speed networks, cloud–edge resources, and reliable data management platforms. Cybersecurity also remains essential, requiring encryption, network segmentation, intrusion detection, and related safeguards [60]. Overall, successful HDT implementation requires substantial technical investment and careful integration with existing hospital IT systems.

Beyond technical considerations, governance and organizational readiness are equally important. Several studies recommend establishing governance frameworks before deployment [23,68]. These frameworks should define ethical principles, institutional policies, and oversight mechanisms. Data ownership and sharing policies should clearly specify access rights and usage conditions, while hospitals may require dedicated data stewardship roles to oversee HDT data management. When patient data are involved, formal consent procedures and audit mechanisms are necessary, although auditable consent provenance remains uncommon in current implementations. Ethics committees and institutional review boards should also be involved when HDTs influence clinical decision-making [3]. For example, one HDT implementation incorporated ethics approval and governance oversight throughout deployment to safeguard privacy and patient benefit [16]. Clear accountability is equally important, ensuring that clinicians understand how recommendations are generated and who retains responsibility for clinical decisions.

Meijer et al. argue that responsible AI in healthcare should integrate explainability, privacy protection, and regulatory oversight [68]. In practice, governance frameworks may include compliance assessments (GDPR/HIPAA), security evaluations, ethics reviews covering fairness and explainability, usability assessments, and contingency procedures for conflicts between HDT recommendations and clinical judgment. Establishing these governance mechanisms early can support responsible deployment and improve coordination among clinical, administrative, and technical stakeholders [3].

Finally, organizational readiness and staff training should not be overlooked. Implementing HDTs requires effective change management, including training healthcare professionals and fostering confidence in AI-supported systems. Early resistance has been reported when users lacked understanding of AI-generated recommendations. Involving end users throughout system design and evaluation, together with clear education on HDT functionality, can improve acceptance. A human-centered implementation that incorporates user feedback is therefore more likely to succeed than a purely technology-driven approach. Overall, while technical infrastructure is essential, governance, training, and human-centered implementation are equally critical for successful HDT adoption in hospitals [3,24]. This conclusion is consistent across recent reviews, which emphasize that appropriate governance and ethical safeguards are necessary for HDTs to achieve their full potential [19,28].

6.7. Limitations of Current Research

Although this review highlights the potential of HDTs, several limitations in the current literature should be acknowledged. First, most studies remain at the proof-of-concept or conceptual stage. Many rely on limited datasets or simplified assumptions about patient volumes and hospital workflows [55]. Consequently, findings may not generalize

across hospitals with different processes, infrastructures, or patient populations. Moreover, many HDT implementations target specific settings (e.g., a single ICU or patient group), limiting evidence of scalability [21]. Comparisons across studies are also challenging because architectures, evaluation methods, and performance metrics vary considerably. This lack of standardized evaluation hinders evidence synthesis. Pellegrino et al. propose a conceptual framework covering functional, technological, and operational dimensions to support more consistent evaluation [28]. Wider adoption of such frameworks would improve comparability and reduce methodological inconsistency.

A further limitation is that the review did not employ a formal standardized risk-of-bias assessment tailored to healthcare digital twin studies. Although the Quality Flag and Evidence Strength classifications in Table 10 provide structured information on evidence type, comparator availability, methodological robustness, and validation status, they do not constitute a comprehensive domain-specific risk-of-bias appraisal. Consequently, methodological issues such as unvalidated simulation assumptions, incompletely reported comparators or baselines, limited statistical testing, and potential lack of blinding may not have been captured systematically. The reported performance improvements should therefore be interpreted in light of the heterogeneous methodological quality and limited prospective validation of the available evidence. Future reviews should incorporate standardized risk-of-bias criteria adapted to healthcare digital twin research.

A further methodological limitation concerns the classification of the included studies. Although predefined criteria were applied to classify architectural characteristics, human-centric and governance dimensions, and operational KPI outcomes, independent duplicate coding and formal inter-rater reliability assessment were not performed. Therefore, some degree of subjectivity in coding decisions cannot be excluded. Future evidence syntheses should incorporate independent duplicate coding of a predefined subset of studies and report an appropriate inter-rater reliability statistic to improve reproducibility.

A further limitation concerns the cross-comparative synthesis of operational outcomes. Although Table 10 summarizes evidence type, comparator status, Quality Flag, and Evidence Strength, and Table 11 summarizes KPI directions across clinical settings and categories, the available data do not permit a fully cross-stratified assessment of outcome robustness. Accordingly, the approximately 80% overall improvement rate should be interpreted as a descriptive vote-counting result rather than an evidence-strength- or risk-of-bias-adjusted estimate. Future reviews should stratify KPI outcomes by evidence type, methodological strength, and clinical setting to better assess the generalizability and robustness of reported improvements.

Another limitation is the fragmented nature of current research. HDTs span multiple disciplines, including medicine, data science, engineering, and human factors, yet most studies address only part of the overall system. Some focus on IoT and data integration, others on AI methods, while others emphasize governance or user interaction. Few studies consider these aspects within a unified framework. Gaffinet et al. observe that multiple architectures have been proposed for specific applications, but consensus on common standards remains limited [19]. As a result, technical advances are often disconnected from human-centered design or governance considerations. Addressing this gap will require closer collaboration among clinicians, engineers, data scientists, and ethicists. Shared research infrastructures and collaborative initiatives, as advocated by Katsoulakis et al. [3], could support more integrated HDT development.

Finally, publication and selection bias should be considered. Positive findings and successful implementations are more likely to be published than unsuccessful deployments or negative outcomes. Consequently, the current literature may overrepresent the benefits of HDTs while underreporting implementation challenges. In addition,

this review covers studies published between 2020 and 2025 and may not capture the latest developments or unpublished industrial applications. Despite these limitations, the review identifies consistent research trends and important gaps. Addressing these limitations through standardized evaluation, broader validation, transparent reporting, and interdisciplinary collaboration will support the development of more robust and generalizable HDT systems.

7. Conclusions

This review shows that HDTs have strong potential to support hospital operations by extending the technological capabilities of I4.0 toward the human-centric objectives of I5.0. The reviewed studies report improvements in operational efficiency, patient flow, and workflow management, indicating that HDTs can support hospital decision-making and resource optimization. However, important challenges remain before their broader adoption. These include improving AI explainability, strengthening privacy and security mechanisms, incorporating sustainability measures, and, most importantly, moving beyond simulation-based studies toward prospective clinical validation. Addressing these challenges is essential to establish trustworthy, safe, and effective HDT systems aligned with I5.0 principles.

The proposed HDT framework supports this transition by integrating technological capabilities with human-centered design principles. By combining IoT, AI, and simulation with human oversight, ethical governance, and continuous learning, HDTs have the potential to support more transparent, adaptive, and accountable hospital operations. Realizing this potential will require interdisciplinary collaboration, appropriate governance, and iterative development and evaluation. As these challenges are progressively addressed, HDTs are expected to become an important component of intelligent, resilient, and human-centered healthcare systems.

This review also has several limitations. Some are discussed in Section 6, while others should be acknowledged here. First, only 22 studies were included, and future reviews should consider a larger evidence base. Second, the review covers publications from 2020 to 2025, excluding earlier studies that may provide additional insights. Third, most existing studies lack prospective real-world validation, highlighting the need for implementation and evaluation in operational hospital settings. Fourth, the findings depend on the predefined search strategy, and variations in keywords or terminology may affect the studies retrieved. Finally, the proposed framework is conceptual and has not yet been implemented or validated, which will be the focus of future research.

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Abbreviations

The following abbreviations are used in this manuscript.

ABS	Agent-Based Simulation
AI	Artificial Intelligence
API	Application Programming Interface
AR	Augmented Reality
BLE	Bluetooth Low Energy
CCU	Critical Care Unit
CPSs	Cyber–Physical Systems
DES	Discrete Event Simulation
DT	Digital Twin
DTD/DTM/DTP	Digital Twin Data/Digital Twin Monitoring/Digital Twin Prediction
DTDL	Digital Twin Definition Language
ECG	Electrocardiogram
ECO	Emergency Call Operator
ED	Emergency Department
EHR	Electronic Health Record
EMCC	Emergency Medical Communication Center
EMR	Electronic Medical Record
EVS	Environmental Services (Hospital Cleaning Staff)
FHIR	Fast Healthcare Interoperability Resources
FPS	Frames Per Second
GDPR	General Data Protection Regulation
GPU	Graphics Processing Unit
HDT	Human Digital Twin
HIL	Human-in-the-Loop
HIPAA	Health Insurance Portability and Accountability Act
HIS	Hospital Information System
HL7	Health Level Seven
HRC	Human–Robot Collaboration
HR	Heart Rate
IAM	Identity and Access Management
ICU	Intensive Care Unit
IDS	Intrusion Detection System
I4.0	Industry 4.0
I5.0	Industry 5.0
IMU	Inertial Measurement Unit
IoMT	Internet of Medical Things
IoT	Internet of Things
ISO	International Organization for Standardization
JSON	JavaScript Object Notation
KPI	Key Performance Indicator
LAN	Local Area Network
LIME	Local Interpretable Model-Agnostic Explanations
LOS	Length of Stay
ML	Machine Learning
MQTT	Message Queuing Telemetry Transport
OR	Operating Room
PACS	Picture Archiving and Communication System
PGHD	Patient-Generated Health Data
PINNs	Physics-Informed Neural Networks
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QoS30	Quality of Service ($\leq$30-second Call Answer Rate)

RBAC	Role-Based Access Control
RTLS	Real-Time Location System
SEM	Structural Equation Modeling
SHAP	SHapley Additive exPlanations
SMOL	Satisfiability Modulo Logic
SOP	Standard Operating Procedure
TAT	Turnaround Time
TLS	Total Link Strength
TRL	Technology Readiness Level
UA	Unit Assistant (Hospital Operational Role)
UI/UX	User Interface/User Experience
USB	Universal Serial Bus
VR	Virtual Reality
VVUQ	Verification, Validation, and Uncertainty Quantification
XAI	Explainable Artificial Intelligence

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