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Review

From Local to Global Perspective in AI-Based Digital Twins in Healthcare

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Featured Application

Potential applications of the described group of technologies include the implementation of a patient's digital twin for general practitioners and specialized digital twins in specific medical disciplines (e.g., psychiatry, neurology, physiotherapy).

Abstract

Digital twins (DTs) powered by artificial intelligence (AI) are becoming important transformational tools in healthcare, enabling real-time simulation and personalized decision support at the patient level. The aim of this review is to critically examine the evolution, current applications, and future potential of AI-based DTs in healthcare, with a particular focus on their role in enabling real-time simulation and personalized patient-level decision support. Specifically, the review aims to provide a comprehensive overview of how AI-based DTs are being developed and implemented in various clinical domains, identifying existing scientific and technical gaps and highlighting methodological, regulatory, and ethical issues. Taking a "local to global" perspective, the review aims to explore how individual patient-level models can be scaled and integrated to inform population health strategies, global data networks, and collaborative research ecosystems. This will provide a structured foundation for future research, clinical applications, and policy development in this rapidly evolving field. Locally, DTs allow medical professionals to model individual patient physiology, predict disease progression, and optimize treatment strategies. Hospitals are implementing AI-based DT platforms to simulate workflows, efficiently allocate resources, and improve patient safety. Generative AI further enhances these applications by creating synthetic patient data for training, filling gaps in incomplete records, and enabling privacy-respecting research. On a broader scale, regional health systems can use connected DTs to model population health trends and predict responses to public health interventions. On a national scale, governments and policymakers can use these insights for strategic planning, resource allocation, and increasing resilience to health crises. Internationally and globally, AI-based DTs can integrate diverse datasets across borders to support research collaboration and improve early pandemic detection. Generative AI contributes to global efforts by harmonizing heterogeneous data, creating standardized virtual patient cohorts,

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Academic Editors: Gang Wei and Zhonghua Sun

Received: 18 October 2025
Revised: 16 December 2025
Accepted: 17 December 2025
Published: 21 December 2025

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and supporting cross-cultural medical education. Combining local precision with global insights highlights DTs' role as a bridge between personalized and global health. Despite the efforts of medical and technical specialists, ethical, regulatory, and data governance challenges remain crucial to ensuring responsible and equitable implementation worldwide. In conclusion, AI-based DTs represent a transformative paradigm, combining individual patient care with systemic and global health management. These perspectives highlight the potential of AI-based DTs to bridge precision medicine and public health, provided ethical, regulatory, and governance challenges are addressed responsibly.

Keywords: artificial intelligence; healthcare information processing; digital twin; eHealth; digital twin of patient; cybersecurity

1. Introduction

The concept of digital twins (DTs) originated in engineering and manufacturing, where virtual replicas of physical assets were created to monitor performance, predict failures, and optimize operations [1]. Over time, the concept was adapted to healthcare, evolving from basic computational models toward dynamic, patient-specific virtual representations [2]. Early applications in healthcare focused on anatomical modeling and physiological simulations, often limited by computational power and static datasets [3]. The integration of artificial intelligence (AI) marked a turning point, enabling DTs to process complex, multimodal medical data and update it in real time [4]. AI-based DTs can now leverage data from sensors, imaging, electronic health records, and genomics to create highly personalized patient models [5,6]. These intelligent twins allow physicians to simulate disease progression, evaluate treatment scenarios, and optimize therapeutic strategies before implementing them in clinical practice [7,8]. The increasing availability of medical robots, mobile devices and Internet of Things (IoT) technologies, including the Internet of Medical Things (IoMT), has further increased the granularity and timeliness of the patient data feeding these models [9]. As a result, digital transformation technologies have expanded beyond experimental research to encompass clinical decision support, personalized medicine, and predictive health monitoring [10]. Their ability to integrate local patient-specific information with large-scale population data represents a significant paradigm shift [11]. AI-based digital transformation technologies are becoming transformative tools in modern healthcare, combining real-time clinical insights with global data intelligence [12].

The emergence of AI-based DTs represents a novel paradigm in healthcare, combining dynamic computational modeling with real-time clinical data. Unlike traditional predictive models, AI-based DTs continuously learn and adapt to individual patient characteristics, enabling highly personalized simulations of disease progression and treatment outcomes [13]. Integration of multimodal data—including physiological signals, imaging, genomics, and electronic health records—allows for a more holistic representation of a patient's condition [14]. This capability contributes to better clinical decision support, allowing clinicians to test "what-if" scenarios and optimize interventions before implementation. From a systems perspective, DTs enable the seamless connection of patient-specific models with population-level analyses, combining local care decisions with global medical intelligence [15]. This dual functionality increases predictive accuracy, supports proactive care strategies, and facilitates more efficient resource allocation. AI-based DTs are making a revolutionary contribution to precision medicine, moving from static data interpretation towards adaptive, patient-centric healthcare ecosystems [16].

Despite promising results, significant research gaps remain in the development and implementation of AI-based DTs in healthcare. A standardized data integration framework is lacking, hindering the efficient combination of heterogeneous clinical, sensor, imaging, and genomic datasets [17]. Most current DT models rely on limited or single-center datasets, limiting their generalization to diverse patient populations and clinical contexts. Acquiring and synchronizing data in real time remains a technical challenge, especially in resource-constrained or out-of-hospital settings [18]. The underlying AI algorithms often operate as "black boxes," raising concerns about interpretability and confidence in clinical decision-making. Sufficient longitudinal studies verifying the predictive effectiveness of DTs and their impact on patient outcomes over time are lacking [19]. Methodological gaps exist in simulating complex multi-organ interactions and comorbidities, which are essential for accurate patient-level modeling. Interoperability and scalability issues hinder the integration of DT systems with existing healthcare infrastructure and electronic health records systems [20,21]. Regulatory and ethical frameworks specific to DT systems are still emerging, leaving uncertainties regarding data ownership, accountability, and clinical responsibility. Limited evidence exists on how healthcare professionals and patients interact with DT systems in real-world workflows, which impacts their implementation [22]. Robust strategies for continuous model updating, validation, and management are also lacking, hindering their safe transition from research to clinical practice [23].

The aim of this review is to critically examine the evolution, current applications, and future potential of AI-based DTs in healthcare, with a particular focus on their role in enabling real-time simulation and personalized patient-level decision support. Specifically, the review aims to provide a comprehensive overview of how AI-based DTs are being developed and implemented in various clinical domains, identifying existing scientific and technical gaps, and highlighting methodological, regulatory, and ethical issues. Taking a "local to global" perspective, the review aims to explore how individual patient-level models can be scaled and integrated to inform population health strategies, global data networks, and collaborative research ecosystems. This will provide a structured foundation for future research, clinical applications, and policy development in this rapidly evolving field.

2. Materials and Methods

2.1. Data Set

This article presents a bibliometric analysis that examines the current state of scientifically relevant knowledge and practice in the application and implementation of AI-based DTs in healthcare at various levels, with the aim of optimising the use of knowledge and experience in the available and applied healthcare system. This approach addresses common limitations (of a single element or separate group of members) that prevent the use and implementation of this user group, usually from an interdisciplinary perspective. From this perspective, it is beneficial to shape DTs as bridges between individualised care and system-level planning and crisis resilience. To achieve this goal, we used bibliometric methods to analyse recently published (i.e., within the last 10 years) global scientific publications. We formulated the following research questions (RQ):

- RQ1: What is the most common origin of publications, broken down by affiliation/research unit and university, country and, if possible, sources of research and publication funding?
- RQ2: Can the most influential authors and their teams be identified?
- RQ3: What are the most popular research/publication topics and, if possible, how are they developing?

We also sought to answer the following question as comprehensively as possible:

- RQ4: Which Sustainable Development Goals (SDGs, formulated by the UN to be achieved by 2030) are most commonly associated with the publications covered by the review?

The approach to bibliographic analysis proposed above allows for a repeatable and comprehensive understanding of current trends, policies, strategies, and approaches to clinical research and business practices related to the planning, implementation, and use of AI-based DTs in healthcare at various levels, from local to global. To achieve the objective of this analysis, it was also necessary to understand and plan further research in this area that would significantly expand knowledge, integrate technical and organisational solutions, and increase their potential already at the planning and implementation stage. This approach to interpreting bibliometric data broadens the current discussions to include an interdisciplinary dimension and will provide a solid basis for formulating and implementing future research.

2.2. Methods

The analysis involved searching four major bibliographic databases: Web of Science (WoS), Scopus, PubMed, and dblp. These databases were selected to ensure the widest possible range of indexed publications (both technical and medical) and their rich metadata with global reach and significance (Figure 1). Filters built into these databases and keyword selection were used to focus on a carefully selected group of relevant publications in English. After filtering, each article was manually reviewed by three independent reviewers for inclusion criteria (decisions were made by a majority of at least two votes), which allowed the final sample size to be determined. Further analysis identified key features of the dataset, including the most frequent authors, their research groups/institutions/affiliations, countries, subject areas, and emerging trends. This allowed for a more accurate mapping of key terminology and its evolution, as well as the most important research achievements in the area under analysis. Where possible, temporal trends were tracked to help monitor changes observed over time in the research area under study. Publications were also grouped into thematic clusters, revealing links between different sub-fields of research. This process highlighted the most important research topics and sub-fields emerging in the research area under study.

The study used ten selected items from the PRISMA 2020 bibliographic review guidelines, focusing on the following aspects (Supplementary Materials):

- rationale (item 3);
- objectives (item 4);
- eligibility criteria (item 5);
- sources of information (item 6);
- search strategy (item 7);
- selection process (item 8);
- data collection process (item 9);
- synthesis methods (item 13a);
- synthesis results (item 20b);
- discussion (item 23a).

The focus on local and global perspectives likely stems from the article's contextualisation of AI-based DTs within broader socio-technical and industrial ecosystems. This broadening of the narrative also raises wider issues such as regional adoption patterns, policy implications, and sustainability trade-offs that have not been formally addressed in previous literature reviews and may not have been sufficiently clearly described before. This article is a review based on the results of the PRISMA 2020 study, but due to the use of only 10 items, it does not constitute a complete systematic review. However, the

discussion synthesises evidence from a number of previous studies and databases, allows for comparative regional analysis, and enhances the scientific credibility of the article.

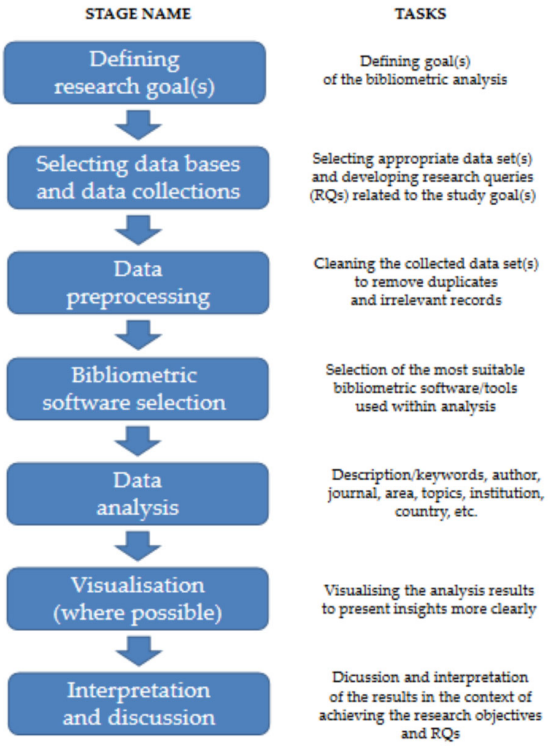


Figure 1. The bibliometric analysis procedure used (own work).

Using only the ten PRISMA 2020 items for a review may be more useful than a scoping or systematic review, as the field is rapidly evolving and lacks standard definitions and a solid evidence base. The current PRISMA-based review provides transparency and methodological rigor while avoiding the excessive limitations of full systematic reviews, which require exhaustive and often impractical data synthesis. Compared to scoping reviews, which prioritize scope over structure, a focused PRISMA subset provides clearer inclusion criteria, replicability, and critical appraisal tailored to specific research questions. This approach is particularly useful for capturing conceptual, architectural, and implementation trends for AI-based digital twins in local and global healthcare contexts. It also reduces the burden of time and resources while providing high analytical value for emerging technologies. Therefore, a concise PRISMA-based review better balances rigor and flexibility than scoping analyses or systematic reviews in this interdisciplinary and rapidly evolving field.

This bibliometric analysis uses analytical and visualisation tools directly embedded in the WoS, Scopus, PubMed and dblp databases. The methodology chosen for this review supports the replication of research (using the same publicly available analytical tools), enabling subsequent researchers to precisely classify results according to concepts, research areas, authors, documents and sources. The results are presented in tabular and graphical form, allowing for further flexible analysis and visualisation. The interdisciplinary scope and complexity of the topic led to the key findings of the review being summarised in a summary table.

3. Results

3.1. Data Sources

Eligible studies were identified using targeted search terms such as “artificial intelligence” OR “machine learning” AND “digital twin” AND “healthcare” in the WoS,

Scopus, PubMed, and dblp databases. The limited to ten items but transparent PRISMA framework ensures methodological transparency in the identification, screening, and selection of studies while avoiding the rigidity of full systematic reviews. Data extraction focused on predefined variables such as area of research, healthcare environment (local vs. global), data sources, and reported outcomes. Analysis was conducted using qualitative thematic synthesis and comparative mapping to highlight trends, gaps, and scalability challenges, rather than quantitative meta-analysis. A defined but flexible time window (the last 10 years: published between 31 January 2016 and 30 October 2025, but no articles meeting the criteria for inclusion were found between 2016 and 2018, all articles were published between 2019 and 2026, as the latest publications are already appearing with the date 2026) was appropriate for capturing recent advances while maintaining relevance, further supporting the validity of a concise PRISMA-based review over broader or fully systematic approaches.

To narrow down the search, advanced filters were applied immediately, thus limiting the results to articles in English. The search was conducted in each database in a separate manner specific to that database. In the WoS database, this was done using the 'Subject' field consisting of the title, abstract, keywords and other keywords. In the Scopus database, this was done using the article title, abstract and keywords. In the PubMed database, this was done using manually entered sets of keywords. Similarly, in the dblp database, manually entered sets of keywords were used to search for articles. Keywords such as 'artificial intelligence,' 'digital twin,' and 'healthcare' were used to search the databases (Figure 2).

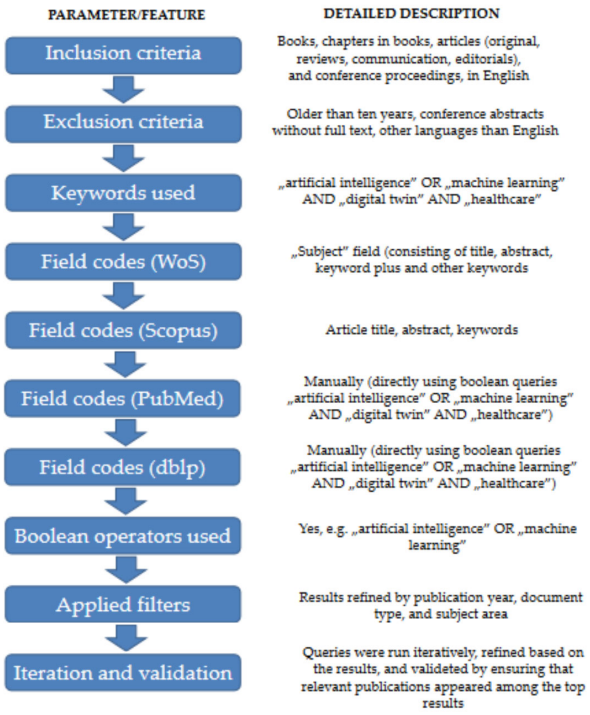


Figure 2. Detailed search in the database (own work).

In subsequent stages of the selection process, the selected set of publications was further refined by manually selecting articles and removing irrelevant publications and duplicates in order to determine the final sample size (Figure 3).

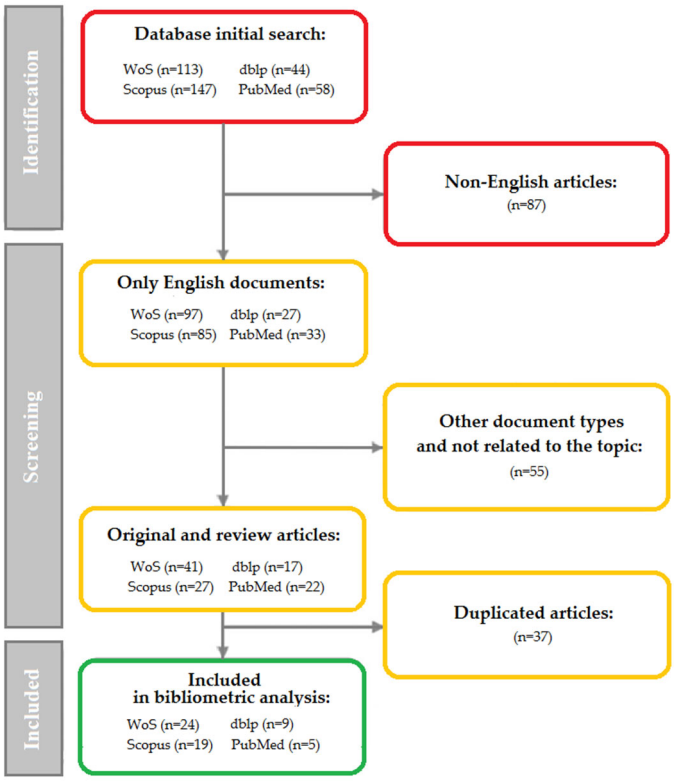


Figure 3. The process used in the review was based on the ten items of PRISMA 2020.

3.2. General Results of Analysis

A summary of the overall results of the bibliographic analysis is presented below in Table 1 and Figures 4–8. A total of fifty-seven articles published over the last ten years were analysed. As no articles meeting the criteria for inclusion in this review were found between 2016 and 2018, all articles were published between 2019 and 2026. Articles older than 10 years were rejected as not included in the review due to the rapid obsolescence of the older knowledge and practice in the field of AI digital technologies contained therein. In addition, the search included 2026 because, although 2025 is still ongoing, the latest publications are already appearing with the date 2026 due to the end of the publication of 2025 journal issues.

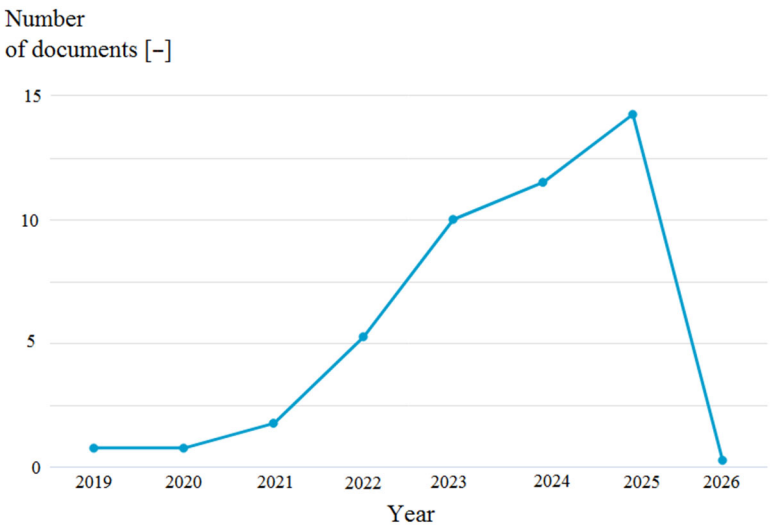


Figure 4. Publications by year.

Table 1. General summary of the results of the bibliographic analysis (own study based on the analysis of data from all four bibliographic databases: WoS, Scopus, PubMed and dblp).

Parameter/Feature	Value
Leading types of publication	Article (41.6%), review (39.9%), Conference paper (14.6%)
Leading areas of science	Computer science (25.6%), Engineering (17.3%), Medicine (15.7%)
Leading countries	USA, Italy, China, UK
Leading scientists	Wicramasinghe N., Zelcer J., Fuchs B., Heesen P., Shuakat N., Ulapane N.
Leading affiliations	Harvard Medical School, La Trobe University, Zurich University, Consiglio Nazionale delle Recerche, Universita degli Studi della Campagna Luigi Vanvitelli, Massachusetts General Hospital, Swinburne University of Technology
Leading funders (where information available)	Horizon 2020 Framework Programme, Ministero dell'Instrucione, dell'Universita e della Ricerca, National Natural Science Foundation of China, UK Research and Innovation
Sustainable development goals	Industry innovation and infrastructure, Responsible consumption and production, Good health and well being

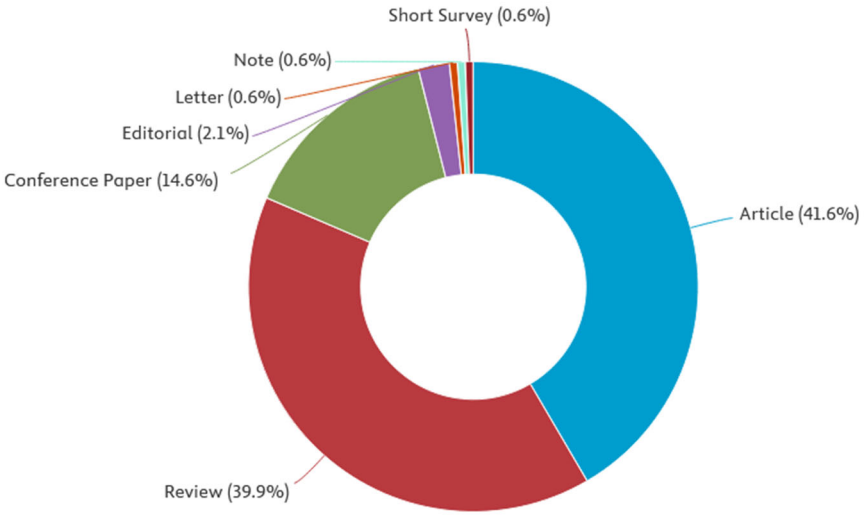


Figure 5. Publications by type.

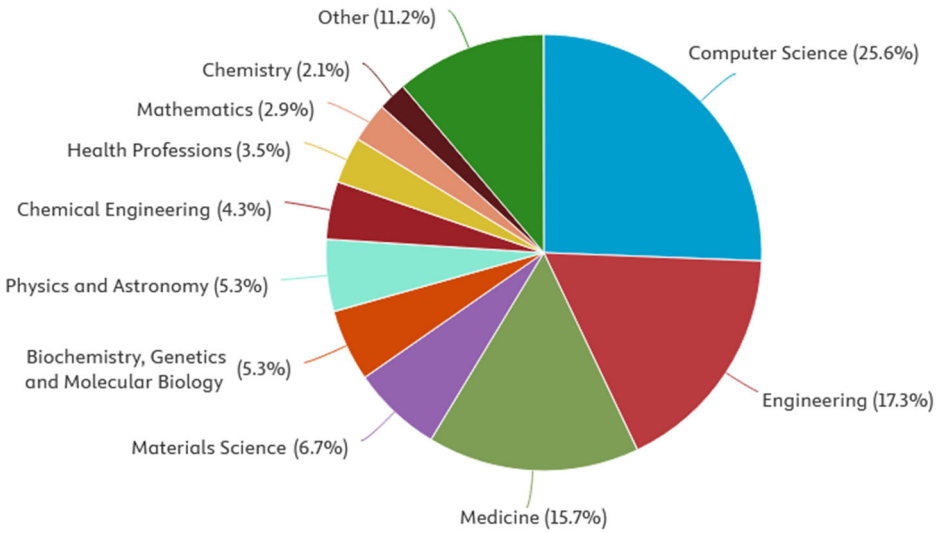


Figure 6. Publications by area of science.

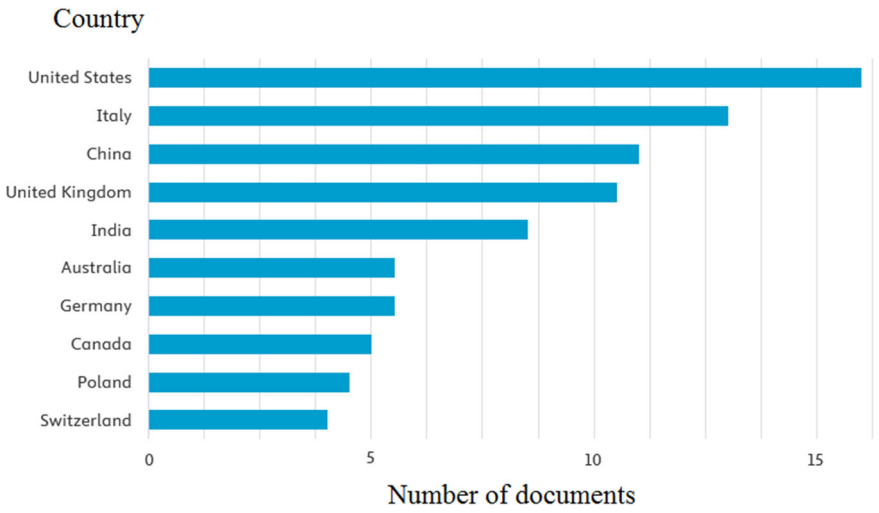


Figure 7. Publications by affiliation location (country).

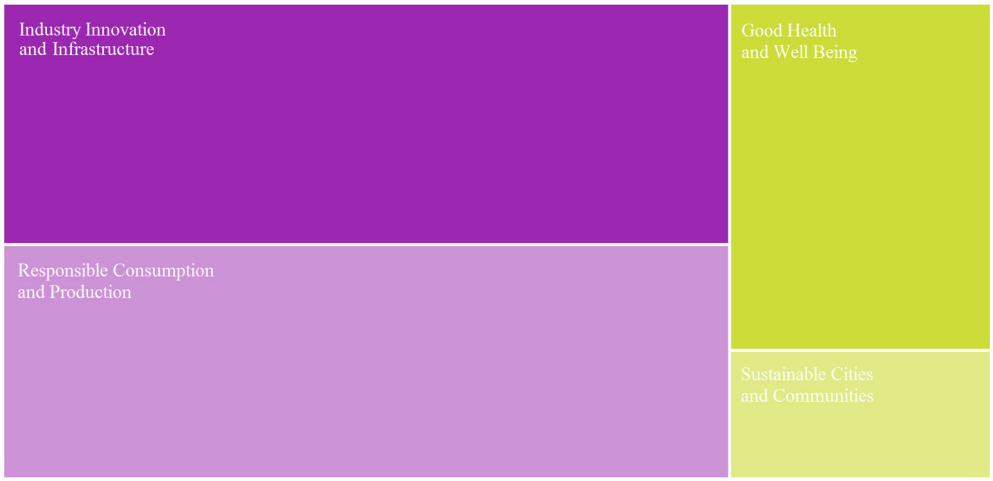


Figure 8. Publications by SDGs.

The results of this review of publications indicate that by combining AI, Big Data and IoT technologies, DT will enable the creation of high-resolution patient and process models facilitating earlier, precise diagnosis and personalized treatment and care [24]. However, each level of analysis and implementation requires a distinct approach and research perspective. In the medical context, a DT is a dynamic, high-fidelity digital replica of a specific patient's physiological and pathological state, continuously updated using multimodal data (biometric, clinical, imaging, genomic, and behavioral) to simulate, predict, and optimize individual health outcomes. Unlike generic AI-based DTs, a true medical DT is bidirectionally connected to its physical counterpart. This means it both receives patient data in real time and can simulate or recommend interventions, the results of which are fed back to improve the model. Systems that exclusively focus on data collection (IoMT), predictive analysis, or hospital-level process simulations without individualized feedback loops should be labeled as not fully meeting the full classification of AI-based DTs in healthcare. Inclusion criteria for true healthcare DTs should include representation (at the individual level), dynamic updating, real-time feedback, and the ability to perform counterfactual experiments or scenario testing. A future coding guide will need to explicitly classify DTs in healthcare only if they combine continuous physiological reflection and personalized predictive adaptation, ensuring a clear distinction from general frameworks of AI, IoT, or simulation in healthcare.

3.3. Local Perspective

Locally, AI-based DTs enable medical professionals to create detailed virtual replicas of individual patients, capturing unique physiological, anatomical, and behavioral characteristics (Figure 9).

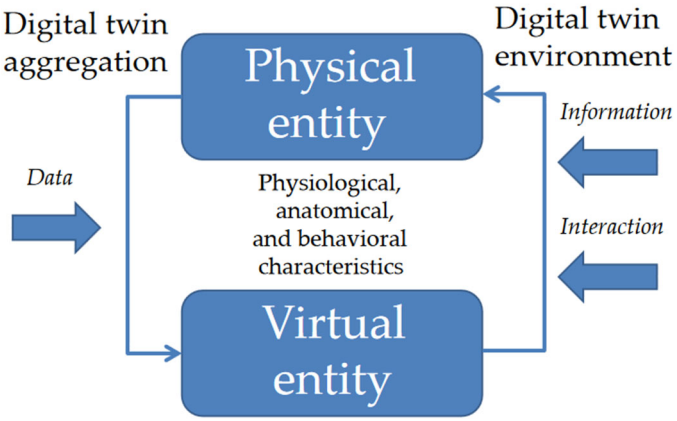


Figure 9. Collection and monitoring of the patient/process state within DT infrastructure (own version based on [2]).

These personalized models allow healthcare professionals to simulate disease progression, test treatment responses, and predict complications before they occur. By integrating real-time data from electronic medical records, wearable devices, and imaging systems, DTs provide a dynamic and constantly evolving picture of a patient's health status (Figure 10) [25].

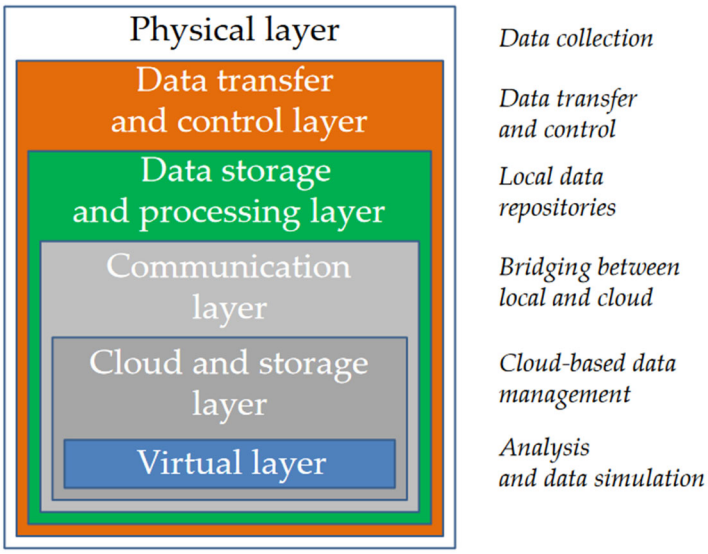


Figure 10. Architecture of DT in healthcare (own version based on [11]).

This helps physicians optimize treatment plans, such as adjusting medication doses, planning interventions, or selecting the most effective rehabilitation strategies. Hospitals are increasingly implementing AI-based DTs platforms to model and simulate clinical processes within their facilities. Such simulations enable administrators to forecast patient flow, anticipate bottlenecks, and allocate staff and equipment more efficiently [26]. In critical care, DTs can predict the need for ICU beds or ventilators, allowing for better preparedness during surges or emergencies as far as need for rehabilitation equipment for better performance purposes [27,28]. These systems also play a key role in improving

patient safety, as virtual testing can identify potential risks and procedural errors before they impact real-world patients. In addition to patient-specific modeling, personalized diagnosis systems support department optimization by allowing hospitals to test "what-if" scenarios for new protocols or infrastructure changes [29,30]. Generative AI (genAI) extends these capabilities by creating synthetic patient data that reflects real-world clinical complexity without revealing sensitive information. This synthetic data can be used to expand training datasets, helping AI models achieve high performance even with limited real-world data. It also enables filling gaps in incomplete medical records, improving the accuracy and robustness of patient twin studies [31]. By ensuring privacy protection through data anonymization and the generation of synthetic data, generative AI supports ethical research and model development [32,33]. Locally, these technologies enable hospitals to advance personalized medicine while maintaining operational efficiency. The local integration of AI-based personalized diagnosis systems fosters smarter clinical decision-making, resource optimization, and data-driven innovation in healthcare settings [33–35].

In healthcare, AI-based DTs are used in a variety of areas, each tailored to local clinical needs and data infrastructure:

- Patient-specific DTs simulate a person's physiological processes—such as cardiac dynamics, tumor growth, or metabolic regulation—allowing hospitals to test treatment response before implementing them in practice;
- DTs in hospital operations model patient flow, bed allocation, and staff utilization to optimize resource utilization and reduce wait times, particularly in regional healthcare systems under pressure;
- DTs for medical devices, including prostheses, exoskeletons, and implantable sensors, utilize AI-driven feedback loops to adapt device performance in real time to the patient's biomechanical or neurological status;
- DTs for training and rehabilitation are leveraging the integration of AI and VR/BCI to create personalized therapeutic environments that improve recovery outcomes and support clinical education within locally available digital infrastructures.

3.4. Regional Perspective

Furthermore, in public health, population-level DTs support epidemic modeling and vaccination strategies by integrating local epidemiological data with predictive AI simulations. At the regional level, AI-based data centers extend beyond individual patients and hospitals to represent entire communities and healthcare systems [36]. By connecting local data centers across multiple hospitals, clinics, and public health agencies, regional networks can create aggregated, anonymized population health models [37]. These connected data centers enable governments to analyze population-level trends, such as the incidence of chronic diseases, hospitalization rates, and vaccination coverage [38]. Through predictive modeling, regional health systems can forecast the spread of infectious diseases, assess the demand for healthcare resources, and evaluate the potential impact of policy changes [39]. For example, data centers can simulate the impact of vaccination campaigns or screening programs on disease prevalence in cities or provinces. Regional data center platforms help coordinate healthcare delivery by identifying underserved areas and more effectively managing resources such as personnel, medications, and equipment. This allows health authorities to quickly respond to emerging health threats, such as epidemics, environmental disasters, or seasonal spikes in demand [40]. AI algorithms integrated with regional digital development systems can detect patterns and anomalies that may not be apparent at the local level, supporting earlier interventions [41]. Data-sharing agreements and secure interoperability frameworks enable the aggregation of data from different institutions while protecting patient privacy. This regional integration improves continuity of care because

patient data is accessible and modeled across facilities, enabling better follow-up and referral [42]. GenAI can complement these efforts by simulating synthetic populations, allowing researchers to test public health strategies without relying on identifiable data. Regional DTs also support capacity planning, such as predicting ambulance demand or emergency department utilization [43]. By providing real-time situational awareness, regional DTs enable more coordinated decision-making between hospitals, public health agencies, and policymakers [44]. They bridge the gap between individual care and system-level planning, ensuring targeted and scalable interventions (Figure 11) [45,46]. Regional AI-based DTs strengthen health systems by aligning local activities with broader public health goals, leading to more efficient, equitable, ethical, and proactive healthcare delivery [47,48].

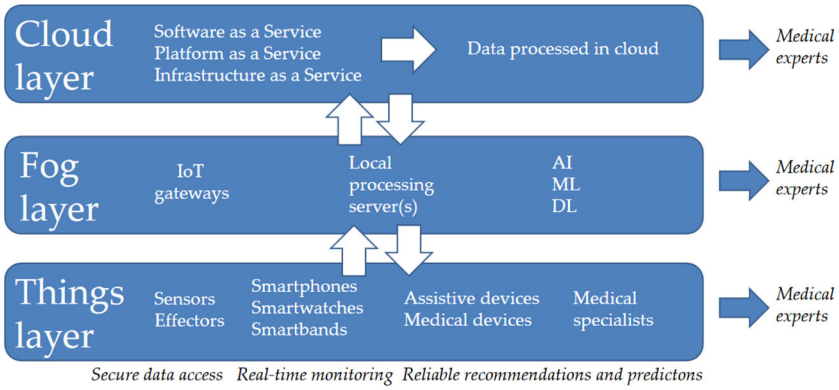


Figure 11. Edge-to-cloud architecture dedicated to Internet of Healthcare Things (IoHT) (own version based on [2,22]).

3.5. National Level

At the national level, AI-based DTs are powerful tools for strategic health planning and policymaking. Governments can integrate data from regional DT networks to create comprehensive virtual representations of the entire healthcare system [49]. These national-scale models allow decision-makers to simulate long-term population health trends, track disease burden, and assess the impact of proposed interventions across regions [50]. By analyzing aggregated data, authorities can identify systemic gaps such as healthcare workforce shortages, unequal access to care, or disparities in outcomes [51]. AI-based DTs enable evidence-based resource allocation, ensuring that funding, infrastructure, and medical supplies go where they are most needed [52]. In times of crisis—such as pandemics, natural disasters, or large-scale emergencies—national DTs provide real-time situational awareness, enabling rapid and coordinated responses. For example, they can model vaccine distribution strategies, optimize the national supply chain for essential medical equipment, and forecast hospital bed capacity in individual provinces. These models also support policy scenario testing, allowing governments to virtually test interventions (e.g., isolation measures, screening programs), even based on synthetic data, before implementation [53]. National DTs platforms promote data standardization and interoperability, ensuring seamless information flow between local, regional, and central health authorities. GenAI can refine these models by creating representative, synthetic national datasets that help fill data gaps for rural or underrepresented populations [54,55]. This improves the inclusiveness and robustness of national health strategies. Furthermore, DTs contribute to long-term resilience planning, helping governments prepare for future health crises by identifying gaps in the health system. They enable proactive decision-making, shifting national health policy from reactive crisis management to strategic anticipation [56]. By unifying local and regional data within a national framework, governments can support coherent health strategies that align clinical innovations with public health goals (Figure 12) [57].

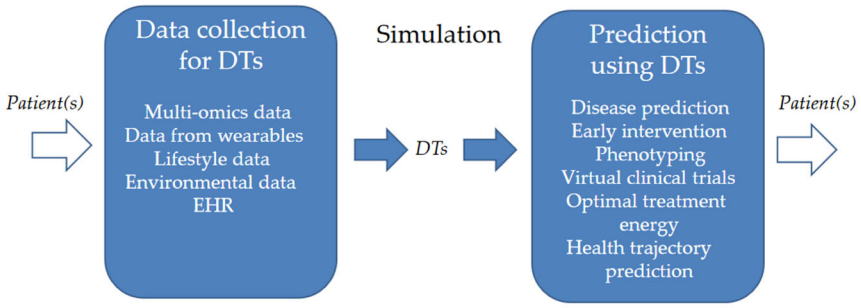


Figure 12. Integration of multi-omics data, wearable device data, lifestyle and environmental data in DTs ecosystem (own version based on [11]).

AI-based national DTs enable decision-makers to optimize healthcare systems, ensure equitable distribution of resources, and strengthen resilience to future challenges (e.g., Metaverse—Figure 13) [58–61].

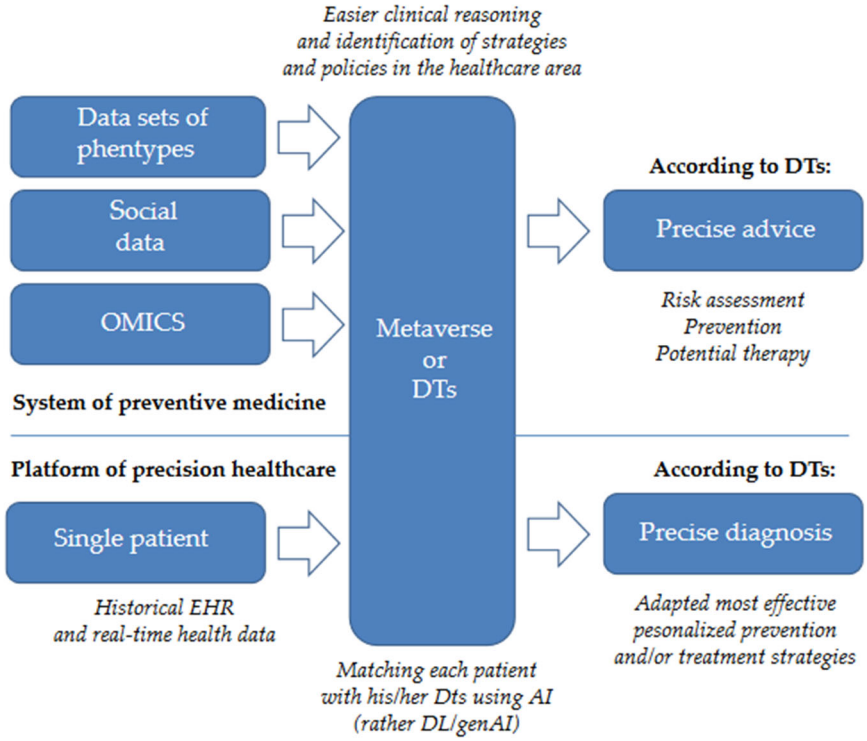


Figure 13. Integrated DTs data repository as a Metaverse (own version based on [2]).

3.6. International and Global Level

At the international level, AI-based DTs have the potential to integrate diverse datasets across borders, fostering unprecedented global collaboration in healthcare [62]. By connecting national and regional networks of transformative technologies, scientists and health authorities can create global virtual ecosystems that reflect the real-world dynamics of health [63,64]. These international transformative technology infrastructures support early pandemic detection by analyzing patterns of disease emergence and spread within countries in real time. Cross-border data integration enables the creation of shared surveillance systems, improving the ability to identify and respond to emerging health threats before they escalate globally [65–67]. GenAI, federated learning, and even quantum computing play a key role in this process by harmonizing heterogeneous datasets from different countries, healthcare systems, and cultural contexts [68,69]. It can generate standardized virtual patient cohorts, ensuring that models trained in one region can be effectively adapted and validated in others. This fosters research collaboration, enabling international teams

to share insights, validate algorithms, and accelerate medical innovation. Furthermore, AI-based DTs platforms support cross-cultural medical education and training by enabling clinicians to learn from virtual cases representing diverse populations and disease presentations [70–72]. International DTs also facilitate comparative policy simulations, allowing countries to assess the potential outcomes of common public health strategies. By combining local precision with global knowledge, DTs bridge the gap between personalized medicine and global health governance [73]. They provide a common framework for addressing transnational health challenges such as the impacts of climate change, antimicrobial resistance, and global pandemics, as far as societal changes [74]. However, international implementation of DTs poses significant ethical, regulatory, and governance challenges. Issues such as data sovereignty, varying privacy regulations, and unequal technological capabilities must be carefully addressed to ensure responsible and equitable implementation. Developing common standards for data interoperability and the ethical use of AI is essential for successful global implementation, especially in chronic care (Figure 14) [75,76].

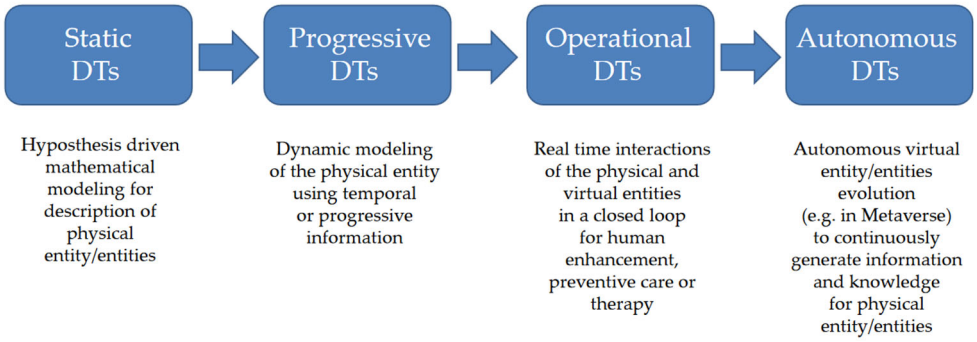


Figure 14. DTs development (own version based on [2]).

Despite these challenges, international collaboration through AI-based DTs represents a groundbreaking step toward a more connected and resilient global health ecosystem (Figure 15).

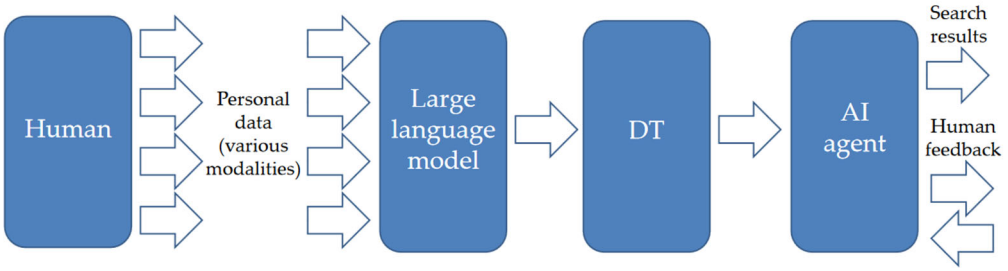


Figure 15. Building DTs in Metaverse (own version based on [2].

Aforementioned approach concludes current local, regional, national, and international/global perspective on AI-based DTs in healthcare. Next step will include applications of AI-based DTs beyond Earth—in space.

4. Discussion

DTs enable real-time patient-level simulation and decision support, while scaling to hospital operations, population health modeling, and international research networks. The article highlights the role of genAI as a catalyst for synthesizing data, filling gaps, and harmonizing heterogeneous sources. Furthermore, it highlights persistent obstacles in validation, ethics, regulation, and governance. The value of the article lies in presenting

decision technologies as a bridge between personalized care, system-level planning, and crisis resilience.

The current literature on DTs in healthcare is dominated by proof-of-concept (PoC) and pilot studies, rather than large-scale prospective clinical trials, reflecting the early translational stage of this technology. Most available studies focus on process optimization and diagnostic endpoints—such as predicting disease progression, response to therapy, or ICU resource utilization. So-called hard clinical endpoints, such as mortality, length of stay (LOS), and adverse event rates, are rarely prospectively validated. In many cases, DTs are evaluated using retrospective modeling or synthetic patient cohorts, demonstrating the feasibility of real-time simulation and decision support, but not the clinical impact on patient outcomes. Consequently, claims regarding real-time decision support in much of the existing literature thus far primarily refer to simulation-based testing or offline prediction, rather than verified live clinical implementation. No systematic formal extraction and meta-analysis of endpoint types and study design categories was attempted, and the conclusions are consistent with the methodological scope reported in the underlying studies, emphasizing feasibility rather than efficacy of the results.

Table 2 below provides a structured comparison across four levels (local, regional, national, international), incorporating SWOT analysis elements to highlight realistic strengths and threats. It also includes risk mitigation strategies, which are often missing from conceptual discussions. This data is useful for policy reports, strategic planning, or research discussions on scaling an AI-based DTs development strategy.

Table 2. SWOT analysis and risk mitigation strategies across local, regional, national, international perspectives of AI-based DTs in healthcare (own elaboration).

Perspective	Strengths	Weaknesses	Opportunities	Threats	Risk Mitigation Strategies
Local (hospitals, clinics, individual patients)	High personalization of care through patient-specific modeling Real-time data integration (EHR, wearables, imaging) Improvement of workflow efficiency and patient safety Predictive treatment planning	Limited data volume and diversity High implementation costs for infrastructure Staff training requirements Potential for local data silos	Enhancing personalized medicine Testing new clinical protocols virtually Generating synthetic data to overcome data gaps Building internal capacity for innovation	Data privacy breaches Technical failure affecting patient care Resistance to adoption by clinicians Overreliance on models.	Strong cybersecurity and anonymization measures Clinician-in-the-loop systems Regular audits and technical validation Staff training and change management programs
Regional (health systems, networks, provinces)	Aggregated population-level modeling Improved coordination between facilities Resource optimization across a broader area Early detection of regional health trends	Interoperability challenges between institutions Uneven data quality across sites Dependence on regional data-sharing agreements	Coordinated response to outbreaks - Better planning for emergency preparedness Targeted interventions in underserved communities Capacity forecasting	Data governance inconsistencies Political or administrative fragmentation - Infrastructure disparities between urban and rural areas	Standardized data-sharing protocols Establishment of regional governance frameworks Investing in interoperability and infrastructure upgrades Regular joint training and drills

Table 2. *Cont.*

Perspective	Strengths	Weaknesses	Opportunities	Threats	Risk Mitigation Strategies
National (government, policy, national health agencies)	Strategic planning at a system-wide level Evidence-based resource allocation National policy scenario testing Standardized data collection and interoperability	Bureaucratic delays in implementation Risk of centralization limiting flexibility High cost of nationwide deployment Data gaps in marginalized populations	Improving health system resilience National capacity planning (e.g., pandemics) Aligning policy with clinical innovation Large-scale AI research initiatives	Political shifts affecting continuity - Cybersecurity risks at national scale. Inequitable distribution of resources - Public mistrust or misuse of data	Robust legal and ethical frameworks Investment in cybersecurity and data infrastructure Inclusive national data strategies - Transparent public communication and stakeholder engagement
International/global (cross-border, global health networks, multinational research)	Integration of diverse datasets across borders Early global pandemic detection International research collaboration Harmonization of medical education and research	Differences in regulatory and ethical standards Data sovereignty issues Technological disparities between countries Language and cultural barriers	Global disease surveillance Accelerated AI innovation through shared knowledge Development of global health standards Cross-cultural training and research	Unequal access and benefits between high- and low-resource countries Data misuse or geopolitical tensions Lack of global governance mechanisms Privacy concerns at international scale.	Development of global ethical and interoperability standards. International treaties or agreements on data use Capacity building in low-resource settings Transparent and equitable data-sharing frameworks

4.1. Limitations

Previous research on AI-based DTs has provided a valuable conceptual and technical foundation, but it suffers from several significant limitations. Many studies rely on small or single-center datasets, limiting the generalizability of their findings to broader and more diverse patient populations [77]. Most existing studies focus on proof-of-concept models rather than large-scale clinical validation, leaving unanswered questions about their effectiveness in practice. Most DT implementations are disease- or organ-specific and cannot model the complex interactions between multiple systems that often occur in clinical practice. Data integration remains incomplete, with limited integration of real-time sensor data, behavioral information, and longitudinal medical records. Limitations are often independent of the disease, e.g., in the area of dementia care, data availability, cost considerations and the efficiency of AI algorithms have been identified as barriers to implementing AI-based DTs [78]. Previous studies often use retrospective data, limiting the ability to evaluate model performance in dynamic, real-world environments. AI methods used are often "black-box" models with limited interpretability, hindering clinical acceptance and trust—there is need for a more post hoc explainable artificial intelligence (XAI) solutions [79]. Few studies address interoperability with existing health information systems, hindering clinical implementation. Ethical, legal, and regulatory issues are often superficially addressed, leaving key management issues unanswered [80]. Furthermore, research on physician and patient interactions with health information systems is lacking, resulting in gaps in usability and workflow integration [81]. The lack of a standardized reporting and benchmarking framework hinders comparison of results across studies and the building of cumulative scientific knowledge.

DTs, as virtual representations of health and disease processes, can integrate data and simulations (including real-time or near-real-time) for prevention, prediction, and personalization of diagnostics, therapy, and care. Previous applications of DTs have demonstrated

their potential in oncology, cardiology, artificial organ design, and hospital workflow optimization. However, further transformation of healthcare delivery and improved patient outcomes require an even more predictive, preventive, and personalized approach. This presents a number of challenges, including:

- more precise description of the mechanisms of dynamic molecular changes in DTs at various biological scales;
- prioritization of disease mechanisms and therapeutic targets;
- mutual learning of interoperable DTs systems;
- VR/AugR-based interfaces to DTs for medical professionals and patients/their families;
- global scaling of DTs technology to ensure equal access to healthcare;
- consideration of ethical and regulatory issues [82].

In AI-based DTs in healthcare, synthetic data generated by genAI is increasingly being used to overcome privacy constraints and data scarcity, enabling model training and validation without revealing real-world patient records. However, such data must be subject to strict validation and provenance protocols, ensuring representativeness, lack of bias amplification, and clinical relevance through comparison with real-world cohorts. Regulatory bodies such as the EU AI Act, GDPR, and national health data authorities recommend transparent documentation of data generation processes, the use of differential privacy, and a formal re-identification risk assessment before deployment. Safeguards include the use of federated learning, edge data generation, and synthetic data quality metrics (e.g., statistical accuracy, diversity, utility scores) to monitor whether the generated data maintains population-level realism without the possibility of tracing personal data. The governance framework should therefore incorporate ethical review, ongoing bias audits, and compliance certification mechanisms to ensure that GenAI-based synthetic datasets in healthcare medical transformations remain secure, irreversible, and verifiably compliant with medical and regulatory standards.

4.2. Technological Implications

The manuscript's primary focus on AI-based DTs required the definition of a healthcare-specific DT framework, including those derived from previous IoMT and 3D printing applications in medicine, emphasizing patient-centric modeling, validation, and clinical relevance. The shift from a local to a global perspective in AI-based DTs has profound technological implications for healthcare. It requires the development of scalable architectures capable of integrating data from individual patients, institutions, and global healthcare networks in real time. Robust interoperability standards and secure data exchange protocols are essential to enable seamless communication between different clinical systems and DT platforms [83]. A combination of cloud and edge computing is necessary to support both high-performance computing and low-latency point-of-care applications. Federated learning and privacy-preserving AI methods will play a key role in enabling collaborative model training without compromising patient confidentiality [84,85]. Advanced data harmonization and semantic interoperability frameworks are essential to unify heterogeneous datasets from different regions and healthcare systems. Integrating Internet of Things (IoT) devices and wearable sensors will enable continuous patient monitoring and enrich DT models with real-time data streams.AI algorithms must adapt to handle massive, distributed, and multimodal data sources while maintaining accuracy and explainability. Cybersecurity measures must be strengthened to protect sensitive medical information as it flows across local and international networks [86,87]. Creating common platforms and digital infrastructure will support collaborative research, model benchmarking, and rapid knowledge dissemination. Leveraging these technological advances will enable AI-

based digital transformation technologies to function as interconnected systems, combining individual patient care with global medical intelligence.

4.3. Economic Implications

The shift from a local to a global perspective in AI-based decision-making technologies has significant economic implications for healthcare systems worldwide [88]. The initial investment required for infrastructure development, including data platforms, sensor networks, and computing resources, can be significant. Once implemented, DT technologies have the potential to reduce long-term healthcare costs by enabling earlier diagnosis, personalized treatment planning, and more efficient resource allocation. Real-time simulation and predictive capabilities can help minimize unnecessary procedures, hospital readmissions, and adverse events, thereby improving cost-effectiveness. Global data sharing and federated learning models can reduce duplication of research and accelerate innovation, generating economic value through resource sharing. DT technologies can support value-based care models by linking clinical outcomes to financial outcomes, encouraging preventative and personalized interventions [89]. Economic differences between high- and low-resource settings must be considered, as unequal access to DT technologies can exacerbate global gaps in healthcare coverage and financing. New business models related to data markets, digital infrastructure services, and AI-based clinical decision support may emerge, transforming the economics of healthcare [90]. The scalability of DT platforms allows for economies of scale, as global collaboration can reduce the unit costs of data storage, model development, and validation. A thorough economic assessment, including cost–benefit and cost-effectiveness analyses, is essential to guide sustainable implementation. By transforming both clinical effectiveness and innovation pathways, AI-based DT technologies have the potential to transform healthcare from reactive treatment to proactive, economically sustainable care models, both locally and globally.

4.4. Societal Implications

Integrating AI-based DTs into healthcare systems, both locally and globally, has far-reaching societal implications. At the individual level, DTs can empower patients by providing personalized insights, promoting self-care, and improving health literacy [91]. They also have the potential to enhance equity in healthcare delivery, enabling more precise and timely interventions, even in remote or underserved areas, thanks to digital connectivity [92]. Widespread implementation could foster greater patient engagement and shared decision-making, strengthening the patient-physician relationship. Social trust will play a crucial role, as people need to be confident that their medical data is protected and used ethically. Unequal access to DT technologies can lead to disparities, potentially exacerbating existing digital divides between high- and low-resource communities. Global DT networks can facilitate rapid information sharing during health crises, improving collective preparedness and response [93]. The use of real-time, population-level health analytics can support more responsive and evidence-based public health policies. These technologies can influence cultural perceptions of health as individuals increasingly interact with digital representations of their bodies and states. Maintaining social acceptance will require addressing ethical issues around autonomy, consent, and data ownership. By combining personalized care with global health intelligence, AI-based transformational technologies could reshape the social contract between individuals, healthcare systems, and societies, fostering a more collaborative and proactive approach to health.

4.5. Ethical and Legal Implications

The expansion of AI-based DTs in healthcare, from local to global contexts, raises complex ethical and legal implications. The collection and integration of sensitive patient

data require a robust framework for ensuring privacy, confidentiality, and informed consent. Key ethical aspects include informational self-determination, confidence, privacy, data security, and reliability [94]. Data ownership remains unclear, as patients, healthcare providers, and technology companies may have conflicting claims on digital representations. Ethical questions arise regarding how DT-generated predictions should be communicated and used in clinical decision-making, particularly in life-changing situations. Ensuring algorithm transparency and explainability is essential to prevent bias and maintain patient trust [95]. Inequalities can deepen if DT technologies are unevenly implemented, raising ethical concerns about fairness and equity in access to advanced care. Cross-border use of DT raises legal issues related to differing data protection regulations, such as the GDPR in Europe compared to less stringent frameworks in other countries. Liability for medical errors or adverse effects resulting from decisions based on AI-based therapeutic strategies is not yet clearly defined in legal systems. Regulatory frameworks have not yet fully adapted to the dynamic, constantly learning nature of AI-based therapeutic strategies, raising concerns about oversight and compliance. Ethical governance structures will need to balance innovation with patient rights, ensuring transparency, safety, and equity. International cooperation will be essential to harmonize ethical standards and legal regulations, supporting the responsible global implementation of AI-based therapeutic strategies in healthcare, and early warning [96,97].

4.6. Directions for Further Research

A novel DTs model based on computed tomography and data presents a new approach to containing emerging infectious diseases by leveraging the potential of the Metaverse as a convergence of physical and cyber domains. This demonstrates the usefulness and scalability of AI-based DTs in precisely protecting public health while taking into account data security and privacy protection [98].

Future research on AI-based DT should focus also on increasing data diversity and quality to enhance model robustness and generalizability. There is a need for large, multicenter, and longitudinal datasets that encompass diverse patient populations and clinical scenarios. Developing a standardized framework for data integration and interoperability will be essential to seamlessly combine multimodal data, including genomics, imaging, sensor data, and electronic health records [99]. Future research should prioritize real-time data acquisition and synchronization methods to support dynamic, continuously updated DT in clinical practice [100]. Research should emphasize explainable and transparent AI methods to improve interpretability and build clinical confidence [101]. Development of multi-organ and multi-system modeling will enable DT to more accurately reflect the complex pathophysiology of many diseases [102]. Rigorous, prospective clinical trials are necessary to validate DT's effectiveness and demonstrate measurable impact on patient outcomes, workflow efficiency, and healthcare costs [103]. Exploring user-centered design approaches will help optimize physician and patient interactions with DT platforms [104]. Research must consider ethical, legal, and regulatory frameworks, including data governance, accountability, and equitable access. Integrating DT with population health and global data-sharing networks will create opportunities for collaborative research and early detection of public health trends [105]. Sustained interdisciplinary collaboration between physicians, data scientists, engineers, and policymakers will be crucial to translating the potential of AI-based DT into routine healthcare practice [106].

In addition to AI-based DTs, large language models (LLMs) aid in data processing, reporting, reasoning, and support for improved clinical decision-making. They generate comprehensive reports that integrate multiple sources and layers of diagnostic information [107]. However, the challenge remains to increase transparency and interpretability

in AI-based DTs using XAI. This will maintain trust between medical professionals and patients [79].

The next breakthrough in AI-based DTs is the launch of sixth generation (6G) communication networks, planned for 2030 [108–110]. Internet of Nano-Things (IoNT) is considered to be the next future technology as more advanced and miniature version of IoT [108–110]. Intelligent healthcare will then move to globally available real-time Internet of Healthcare Things (IoHT) solutions [24,111–113].

5. Conclusions

AI-based DTs represent a transformative paradigm, combining individual patient care with systemic and global health management. At the local level, DTs enable personalized modeling, clinical workflow optimization, and real-time decision support. Regional integration extends these benefits to population health monitoring, resource coordination, and early detection of health trends. Nationally, DTs support strategic planning, equitable resource allocation, and resilience building in response to health crises. Internationally, connected DTs support research collaboration, pandemic preparedness, and the harmonization of global health strategies. These perspectives highlight the potential of AI-based DTs to bridge precision medicine and public health, provided ethical, regulatory, and governance challenges are addressed responsibly.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app16010083/s1, PRISMA 2020 Checklist (partial only). Reference [114] are cited in the supplementary materials.

Author Contributions: Conceptualization, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; methodology, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; software, M.P., D.M. and I.R.; validation, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; formal analysis, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; investigation, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; resources, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; data curation, M.P., D.M. and I.R.; writing—original draft preparation, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; writing—review and editing, M.P., A.G., E.P., J.M., D.M., I.R. and E.M.; visualization, M.P., D.M. and I.R.; supervision, E.M.; project administration, E.M.; funding acquisition, D.M. All authors have read and agreed to the published version of the manuscript.

Funding: The work presented in this paper was financed by a grant to maintain the research potential of Kazimierz Wielki University.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

AI	Artificial intelligence
DL	Deep learning
DT	Digital twin
EHR	Electronic health record
GenAI	Generative AI
IoHT	Internet of Healthcare Things
IoMT	Internet of Medical Things
IoNT	Internet of Nano-Things
IoT	Internet of Things

ML	Machine learning
SDG	Sustainable Development Goal
WoS	Web of Science
XAI	eXplainable AI

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