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SURVEY

Revolutionizing Healthcare: A Review Unveiling the Transformative Power of Digital Twins

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ABSTRACT In the dynamic landscape of healthcare, Digital Twin (DT) technology has emerged as a transformative force, holding the promise of revolutionizing patient care and industry practices. This article surveys the literature over the period 2020 to 2023 on a comprehensive exploration of DT in healthcare, elucidating its roles, benefits, and implications for smart personalized healthcare. The study addresses fundamental questions concerning the transformative potential of DT, investigating its varied roles and benefits in healthcare, its revolutionary impact on the industry, and the essential requirements for crafting a DT system tailored to the demands of smart personalized healthcare. The research further unveils the key layers necessary for implementing a DT smart healthcare system, examining potential applications that extend from diagnostics to treatment strategies. Methodologically, the paper navigates through different model discussions, providing a structured approach to understanding the implementation of DT in healthcare. Despite the transformative potential, the research delves into the limitations and challenges faced by DT technology, offering a balanced perspective on its current state. In conclusion, the paper synthesizes key findings, outlines methodologies, discusses challenges, and sets the stage for future research, presenting a holistic overview of the potential, pitfalls, and pathways for integrating DT in the healthcare industry.

INDEX TERMS Digital twin, personalized healthcare, literature review.

I. INTRODUCTION

Digital Twin (DT), a concept rooted in the realm of advanced technology, serves as a virtual counterpart mirroring physical entities, processes, or systems in real-time [1], [2], [3]. In the context of healthcare, this technology has garnered increasing significance, offering transformative potential in reshaping patient care and industry practices [4], [5]. At its core, a DT creates a dynamic, digital replica that captures and represents the intricacies of its physical counterpart as shown in Figure 1. This article surveys the literature over the period 2020-2023 and provides a comprehensive exploration of the multifaceted landscape of DT technology in the healthcare sector, elucidating its fundamental definition, highlighting the critical role it plays, and delineating the challenges and opportunities in the DT domain.

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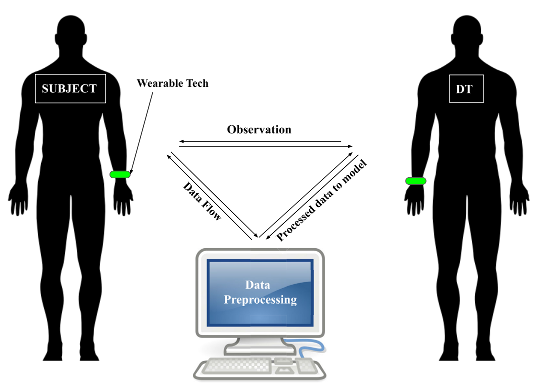

FIGURE 1. Schematic Representation of a DT.

The importance of DTs in healthcare lies in their ability to facilitate more personalized, intelligent, and proactive approaches to patient well-being [6], [7]. This transformative potential extends to various facets of healthcare, from

FIGURE 2. Word-cloud representation of Keywords adopted for searching through the literature.

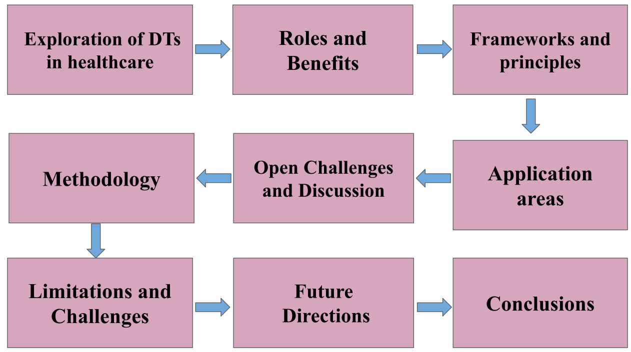

FIGURE 3. Roadmap of paper structure.

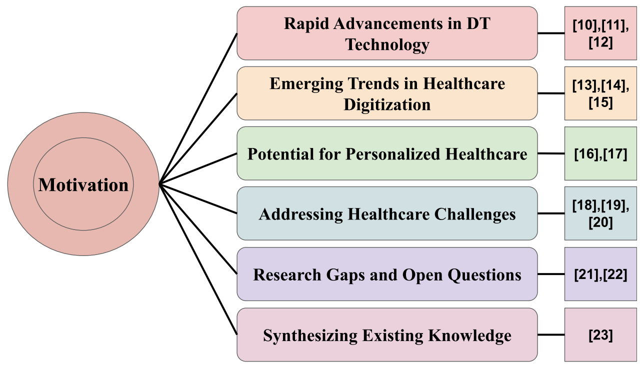

FIGURE 4. Key factors motivate the undertaking of this review paper.

diagnostics and treatment strategies to operational efficiency and resource allocation [8]. As healthcare systems worldwide grapple with the complexities of providing tailored and timely care, the integration of emerges as a promising solution to meet these evolving demands.

The scope of our research endeavours to dissect the intricacies of DT technology within the healthcare domain. This exploration involves a meticulous examination of its roles, benefits, and potential applications. As we embark on this investigative journey, the research aims to understand the conceptual underpinnings of as well as to discern its practical implications in enhancing healthcare outcomes.

Our research methodology involves a systematic and comprehensive approach to gathering, analysing, and interpreting data pertinent to the roles and applications of DTs in healthcare. We employ a combination of literature review, case studies, and empirical analyses to provide a nuanced understanding of the subject matter. To enhance the transparency of our research process, we incorporate a keyword search, highlighting specific search terms that guided our exploration of relevant material as shown in Figure 2. Furthermore, we meticulously classify the researched articles into distinct categories such as case studies, review articles, implementations, and modeling methods. This structured framework not only provides a nuanced understanding of the subject matter but also ensures a comprehensive and organized presentation of our findings

To guide the reader through the subsequent sections, the outlined paper structure provides a roadmap as shown in Figure 3.

A. MOTIVATION

The exploration of DTs in the context of healthcare stems from the pressing need for a comprehensive understanding of their potential impact on the industry [9]. The intersection of DT technology and healthcare holds promise for transformative advancements in patient care, operational efficiency, and medical research. Several key factors motivate the undertaking of this review paper as shown in Figure 4:

- **Rapid Advancements in DT Technology:** The field of DT has witnessed rapid advancements, driven by innovations in sensor technologies, data analytics, and artificial intelligence [10], [11]. Understanding how to harness these technological breakthroughs to optimize healthcare processes and outcomes is paramount [12].
- **Emerging Trends in Healthcare Digitization:** The healthcare sector is undergoing a significant shift towards digitization and smart healthcare solutions. Investigating the role of DT in this evolving landscape is crucial to staying abreast of emerging trends and harnessing the full potential of innovative technologies [13], [14], [15].
- **Potential for Personalized Healthcare:** The potential of DT to revolutionize personalized medicine and healthcare delivery is a compelling motivation. Examining the applications of DT in tailoring treatments based on individual patient characteristics aligns with the broader goal of improving patient outcomes and experiences [16], [17].
- **Addressing Healthcare Challenges:** Healthcare faces numerous challenges, including rising costs, resource constraints, and the need for more effective and patient-centric care models. This review aims to explore how DTs can address these challenges by offering innovative solutions for healthcare optimization, resource management, and enhanced patient care [18], [19], [20].
- **Research Gaps and Open Questions:** Despite the growing interest of DTs in healthcare, there exist

research gaps and open questions that warrant exploration. This review seeks to identify these gaps, offering a foundation for future research endeavours and guiding the development of more effective DT applications in healthcare [7], [21].
- **Synthesizing Existing Knowledge:** By synthesizing existing knowledge and research findings, this review aims to provide a comprehensive overview of the current state of DTs in healthcare. This synthesis will contribute to the establishment of a knowledge base that can guide practitioners, researchers, and policymakers in leveraging DT technology for improved healthcare outcomes [22].

In summary, the imperative to comprehensively explore and understand the roles, benefits, challenges, and potential applications of in the healthcare domain is what motivates this review paper. We anticipate the insights derived from this examination to inform future research directions and contribute to the ongoing transformation of healthcare through innovative technological solutions.

II. RESEARCH QUESTIONS AND OBJECTIVES

A. RESEARCH QUESTIONS

In this section, we will describe the research questions discussed in the paper and their purpose. The following are the research questions:

- **RQ1: Roles and Benefits of Introducing DT in Healthcare**
  - **Purpose:** This question aims to comprehensively explore and delineate the specific roles and benefits associated with the introduction of DT technology in the healthcare sector. The focus is on understanding how DTs contribute to various aspects of healthcare delivery, patient outcomes, and operational efficiency.
- **RQ2: What are the design principles for Building a DT System for a Smart Healthcare Industry?**
  - **Purpose:** The focus is on understanding the foundational components, technologies, and infrastructure necessary to build an adaptive and effective DT ecosystem in the healthcare domain.
- **RQ3: What are the key Layers for Implementing a DT Smart Healthcare System?**
  - **Purpose:** It focuses on understanding the foundational elements such as data acquisition, modeling, analytics, and communication that contribute to the successful deployment and operation of DT-based healthcare infrastructure.
- **RQ4: What are the existing tools and frameworks available to construct a DT for healthcare?**
  - **Purpose:** The focus is on understanding the technological landscape, identifying available resources, and guiding future developments to leverage DT technology for improved healthcare outcomes.

TABLE 1. Research questions and corresponding sections.

RQ no:	Research Question	Section
RQ1	What are the roles and benefits of introducing DT in Healthcare?	Sec III
RQ2	What are the design principles for Building a DT System for a Smart Personalized Healthcare Industry?	Sec IV
RQ3	What are the key layers for implementing a DT smart healthcare system?	Sec IV
RQ4	What are the existing tools and frameworks available to construct a DT for healthcare?	Sec IV
RQ5	What are the potential applications of using PDT for a smart personalized healthcare industry?	Sec V
RQ6	What are the open challenges to applying DT in smart personalized healthcare?	Sec VI

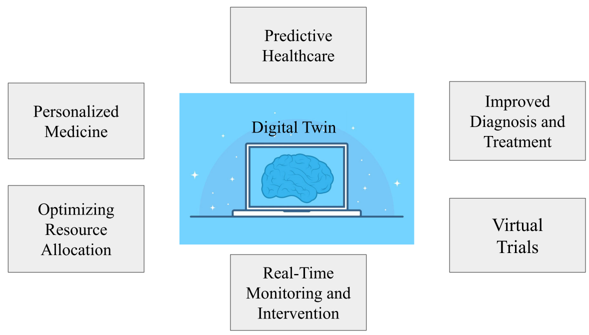

FIGURE 5. Benefits of DT.

- **RQ5: What are the potential Applications of Using DT for a Smart Healthcare Industry?**
  - **Purpose:** The focus is on identifying specific areas within healthcare where we can effectively use DTs, such as patient monitoring, treatment optimization, and healthcare facility management.
- **RQ6: What are the open Challenges to Applying DT in Personalized Healthcare?**
  - **Purpose:** It seeks to identify obstacles and research gaps that may hinder the seamless integration of DTs and personalized healthcare solutions.

III. THE CONCEPT OF DT AND IT'S BENEFITS

RQ1: What are the roles and benefits of introducing DT in Healthcare?

DTs are virtual representations of physical objects or systems that can be used to simulate and analyse them. Reference [23] In the healthcare context, we can employ DTs to create personalized models of patients, enabling healthcare providers to gain deeper insights into their conditions and make informed treatment decisions [24]. offer a plethora of benefits that can enhance patient care and improve healthcare outcomes as shown in Figure 5:

- **Personalized Medicine:** DTs facilitate the development of personalized medicine by enabling the creation of detailed patient models that incorporate their unique genetic, medical, and lifestyle factors [25]. We can use these models to predict individual responses to treatments, allowing for the tailoring of therapies to

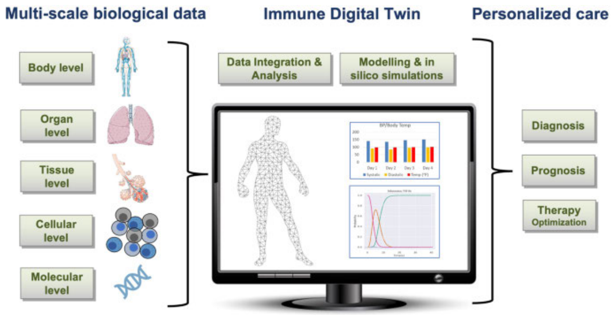

FIGURE 6. DT in personalized healthcare [174].

optimize patient outcomes as shown in Figure 6 [26]. In a landmark study published in 2020, researchers at Stanford University showcased the power of DTs for personalized diagnosis and treatment [27]. They created a DT of a patient with a rare liver disease, enabling them to identify a potential treatment that was previously unknown to be effective. The field of drug discovery and development also stands to benefit significantly from DTs. A research team at Novartis exemplifies this potential in their use of DTs to develop personalized cancer treatment [28]. By simulating the effects of various drugs and therapies on a virtual representation of the patient's tumour, they were able to design a more effective treatment than existing therapies. This personalized approach to drug development holds immense promise for accelerating the development of effective treatments tailored to individual patients' specific needs. DTs also empower patients to take control of their health and engage actively in their healthcare journey. A study by researchers at the University of California, San Francisco, found that patients using DTs were more likely to adhere to their medication regimens and achieve their health goals [29]. This demonstrates how DTs can foster patient engagement and self-management, ultimately leading to improved adherence, better outcomes, and a more empowered patient population. DTs offer significant benefits for optimizing clinical workflows and resource allocation within healthcare systems. A study by researchers at the Mayo Clinic demonstrated this potential by utilizing DTs to manage operating room schedules [30]. This resulted in reduced wait times for patients and improved overall efficiency, showcasing the ability of DTs to streamline clinical processes and optimize resource allocation for better healthcare delivery.

- **Predictive Healthcare:** DTs empower healthcare providers to transition from reactive to proactive care by enabling the identification of patients at risk of developing specific diseases [31]. By analysing patient data and identifying patterns, DTs can predict potential health issues before they manifest, allowing for timely interventions and preventive measures [32]. Moving beyond diagnosis, researchers at MIT utilized DTs for predictive analytics and risk assessment in personalized medicine [33]. In their 2021 study, they successfully predicted the risk of heart failure in patients with diabetes, allowing for early intervention and improvement in patient outcomes. This highlights the potential of DTs to anticipate future health issues for individual patients, enabling preventative measures and proactive healthcare management. Reference [34]developed a DT of a patient's heart to predict the progression of his heart failure and personalize his treatment plan. Their results demonstrate the feasibility of using DTs to improve outcomes for patients with chronic diseases. Similarly, [16] created a DT of a patient's tumour to predict its response to various treatments and personalized cancer therapy. These studies highlight the potential of DTs to provide personalized, data-driven insights into disease progression, enabling more effective treatment strategies. Reference [36] proposed a DT-based approach for analysing patient data to identify individuals at risk for suicide or self-harm. This work exemplifies the potential of DTs for early intervention and prevention of mental health crises. Reference [37] utilized DTs to identify patients at high risk for developing chronic diseases, offering opportunities for early detection and preventive intervention.
- **Improved Diagnosis and Treatment:** DTs can enhance diagnostic accuracy by analysing patient data from various sources, including electronic health records, medical images, and wearable devices [37]. By identifying subtle patterns and anomalies that traditional methods may overlook, DTs can assist in early detection and accurate diagnosis of diseases [25]. DTs facilitate early and accurate diagnoses as they, can analyse medical images with greater precision than traditional methods [38]. In silico modeling using DTs simulates individual patients' organs and systems, allowing doctors to predict disease development and response to treatments [34], [35]. Additionally,DTs can identify individuals at high risk for specific diseases, enabling early intervention and preventive measures [37].
- **Virtual Trials:** DTs can accelerate drug development and reduce costs by enabling the simulation of clinical trials [24]. By testing new drugs and treatments on virtual patient models, researchers can assess their efficacy and safety without the need for large-scale human trials [26].
- **Real-time Monitoring and Intervention:** DTs can be used to monitor patients' health in real-time, providing healthcare providers with early warning of potential health issues [26]. This can enable proactive interventions to prevent complications and optimize patient outcomes. The way patients are monitored and cared for is also being enhanced by .DTs enable remote patient monitoring, allowing for early detection of potential health problems and timely intervention [25], [38]. Patients with chronic diseases can better manage their

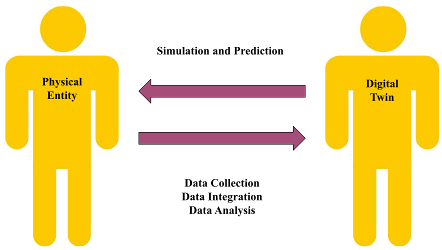

FIGURE 7. Overall working of DT.

conditions with personalized insights and recommendations provided byDTs [39], [40]. Communication and collaboration between doctors, patients, and other healthcare professionals are also facilitated by, leading to a more coordinated and comprehensive approach to care [41], [42].
- **Optimizing Resource Allocation:** We can employ DTs to optimize resource allocation in healthcare systems, such as staffing, equipment, and beds, to improve efficiency and reduce costs [23]. This can lead to better use of healthcare resources and improved patient experiences.

Overall, the potential of DTs to revolutionize the healthcare industry is vast. By enabling personalized medicine, predictive healthcare, and improved diagnostic accuracy, DTs can help to improve patient outcomes, reduce healthcare costs, and transform the way we provide healthcare.

IV. PRINCIPLES AND FRAMEWORKS FOR THE SMART HEALTHCARE INDUSTRY

A. HIGH-LEVEL DESIGN PRINCIPLES FOR SMART PERSONALISED HEALTHCARE

RQ2: What are the design principles for building a DT system for a smart personalized healthcare industry? Building a DT system for a smart personalized healthcare industry requires a comprehensive approach that encompasses various technical and non-technical considerations. Figure7 represents the overall working of DT. Here are the key requirements:

- **Data Collection and Integration:** A DT system must be able to collect and integrate data from a variety of sources, including electronic health records (EHRs), wearable devices, medical imaging data, and patient-generated data (e.g., social media posts, and fitness apps) [17].Figures 8 and 22 show an example.
  This requires the establishment of data pipelines and data governance frameworks to ensure data quality and security [43]. Building a comprehensive DT in healthcare relies heavily on establishing a robust data collection and integration framework, which necessitates addressing several key requirements (Figure 10) [44], [45]: Firstly, a diverse range of data sources, including clinical records, imaging data, sensor data (from wearables and implanted devices), genomic data, environmental data, and lifestyle information, must be holistically captured to support the DTs functionality. Secondly, interoperability and standardization are crucial for overcoming the fragmentation of healthcare data across various systems and formats, ensuring seamless integration and analysis [25], [38]. Thirdly, prioritizing data privacy and security is paramount, necessitating robust cybersecurity measures and adherence to ethical guidelines to protect patient data throughout its lifecycle [40], [46]. Ensuring data quality and consistency is the fourth requirement, where the implementation of data cleansing and validation procedures is critical for accurate and reliable simulations and predictions [39], [47]. The fifth requirement involves real-time data integration from various sources, facilitated by robust data streaming and processing pipelines, enabling continuous updates and dynamic decision-making within the DT [41], [42].
- **Data modeling and Simulation:** The DT system must be able to create and maintain accurate models of patients that it can use to simulate their behaviour and predict their outcomes [31]. This requires expertise in data modeling, machine learning, and artificial intelligence (AI) to develop sophisticated models that capture the complex dynamics of human physiology and disease progression. Data modeling and simulation are pivotal elements in the development and utilization of DTs for personalized healthcare [25]. Data continuously enriches, serving as virtual replicas of real-world entities, to emulate their behaviour and forecast future outcomes [45]. In the intricate process of constructing and leveraging, data modeling and simulation play a vital role as shown in Figure 11. First is, the meticulous modeling of the physical system, encompassing detailed representations of human anatomy, physiology, and disease mechanisms [44], [48]. These models, sourced from medical imaging data, anatomical databases, and scientific literature, facilitate simulations of disease progression, treatment response, and potential complications. Secondly, data integration and processing are imperative for maintaining the DTs currency, incorporating real-time data from diverse sources such as sensors, wearables, and medical records [38], [48]. It employs advanced algorithms, including machine learning and artificial intelligence, to derive meaningful insights and refine DT models for personalized predictions and recommendations. Thirdly, the power of DTs is harnessed through simulation and predictive analysis, enabling scenarios like treatment impact assessment, disease progression under varied conditions, and personalized treatment planning [47], [49]. In silico clinical trials expedite the testing of new drugs and therapies, fostering advancements in personalized medicine and enhancing patient outcomes [40], [50]. Lastly, a continuous improvement and feedback loop, utilizing data generated by the DT and patient input, refines models over time, ensuring their relevance

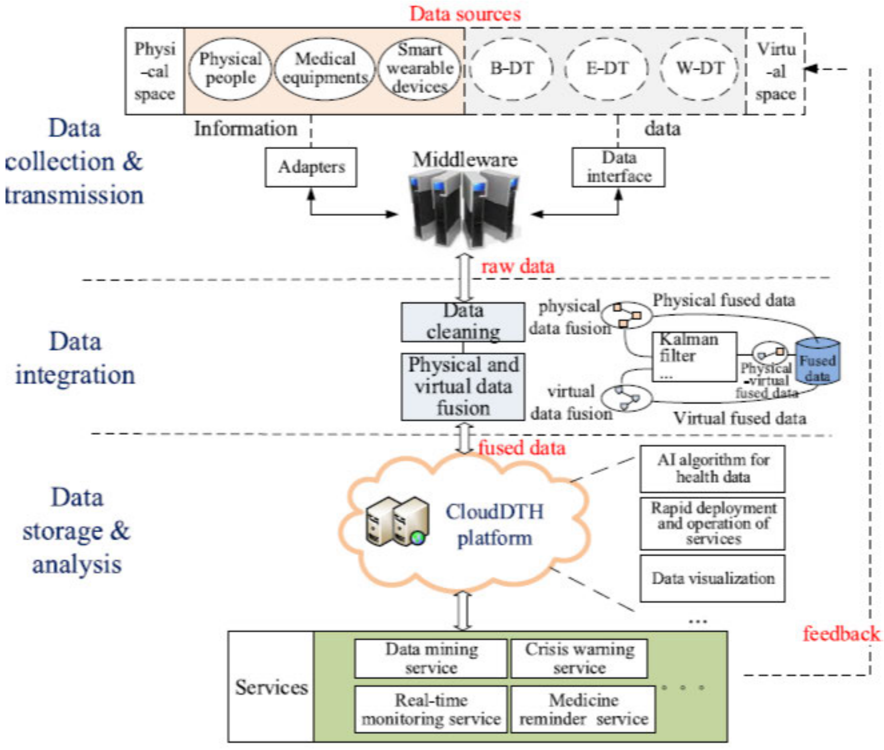

FIGURE 8. Data collection, integration, and analysis [27].

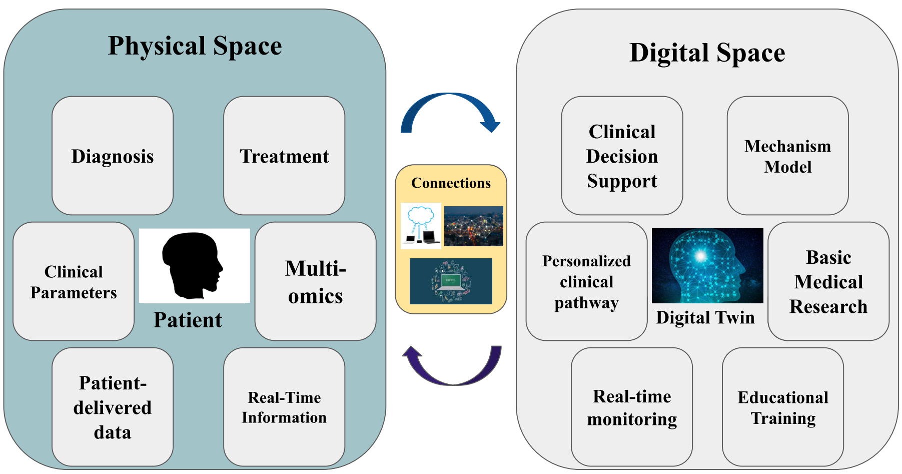

FIGURE 9. Data collection, integration, and analysis.

and value in personalized healthcare decisions [41], [42]. This holistic approach, integrating data modeling and simulation, underscores the transformative potential of DTs in revolutionizing healthcare delivery, ultimately resulting in improved patient care, optimized treatment plans, and a more patient-centric approach to medicine.

- **Real-time Analysis and Decision Support:** The DT system must be able to analyse patient data in real-time and provide decision support to healthcare providers [75]. This involves developing algorithms and tools that can detect anomalies, identify patterns, and predict potential health risks (Figure 12. The system should also provide clear and actionable insights to healthcare providers, enabling them to make informed decisions about patient care. Real-time analysis within DTs involves the continuous processing of data from an array of sources such as wearable sensors, medical devices, and health records. Employing advanced algorithms and machine learning techniques, it promptly analyses this data to discern trends, predict potential complications, and generate personalized alerts and recommendations [44], [48]. Noteworthy instances

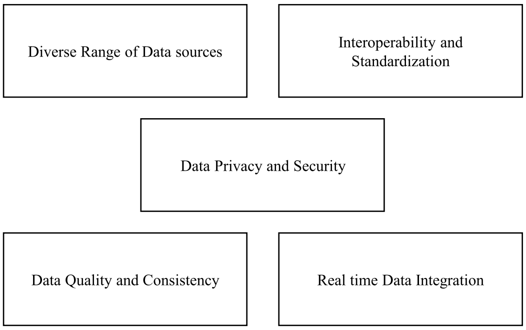

FIGURE 10. Requirements for data collection and integration framework.

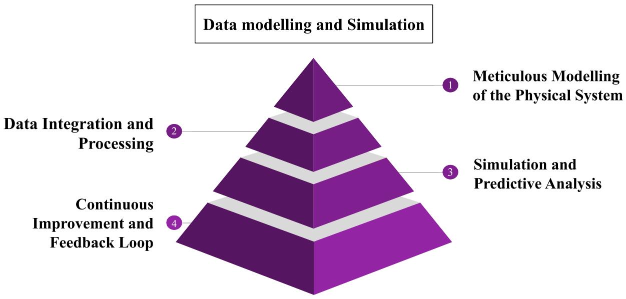

FIGURE 11. Intricate process of constructing and leveraging, data modeling and simulation.

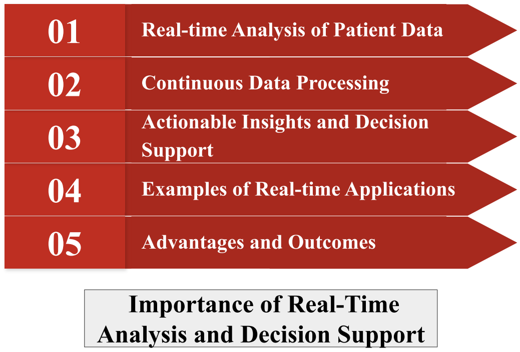

FIGURE 12. Real-time analysis and decision support.

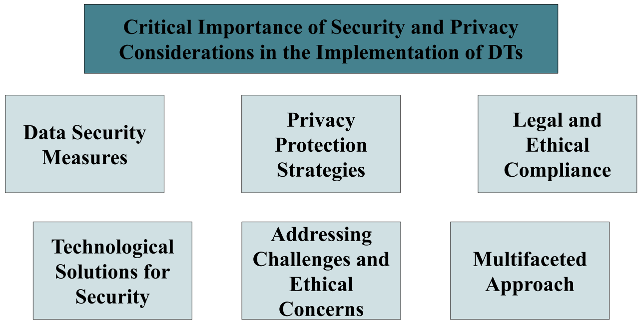

FIGURE 13. Critical importance of security and privacy considerations in the implementation of.

encompass the real-time monitoring of vital signs in critical care, the analysis of wearable sensor data for early detection of disease progression, and the tracking of medication adherence. Concurrently, DTs furnish decision support tools that offer clinicians personalized assistance by amalgamating diverse data sources and expert knowledge. These tools assist clinicians in crafting individualized treatment plans, simulating potential treatment outcomes, and prioritizing resources based on real-time risk assessments [34], [40]. Exemplary instances include AI-powered algorithms predicting patient responses to medications, virtual reality simulations facilitating surgical planning, and personalized dashboards providing clinicians with real-time overviews of a patient's health status. The advantages encompass not only improved clinical outcomes but also heightened patient experiences through active participation and increased efficiency and productivity achieved through task automation and streamlined workflows.

- **Security and Privacy:** Establishing robust security and safeguarding patient privacy are fundamental prerequisites for the transformative potential of DTs in healthcare. In the pursuit of this, we need to address several critical aspects (Figure 13. In terms of data security, [9] stresses the importance of data encryption at rest and in transit, alongside stringent access control measures highlighted by [38], and the adoption of established security frameworks such as the NIST Cybersecurity Framework as proposed by [48]. Furthermore, [34] advocates for data anonymization and pseudonymization to balance privacy protection with the need for research and analysis. Privacy considerations include [36] emphasis on obtaining informed patient consent, [37] call for transparency and patient control over their data, and [40] recommendation for data minimization and clear data governance policies. Underscoring legal and ethical compliance is the necessity of adhering to relevant data privacy regulations, including HIPAA and GDPR. Technological considerations, as proposed by [39], suggest the use of block chain for secure data storage, while [47] advocates for federated learning to enable collaborative analysis without compromising patient privacy, and [49] proposes homomorphic encryption for enhanced privacy protection during data computations. It remains crucial to address challenges and ethical concerns, such as the delicate balance between data accessibility and privacy, algorithmic biases, and equitable access across populations. Building trust and transparency through open communication, patient involvement, and independent oversight mechanisms, as recommended by [36], [39], and [41], respectively, further solidifies the foundation for deploying DTs as powerful tools in advancing personalized healthcare. This multifaceted approach integrates technical measures, governance frameworks, and ethical considerations, envisioning a future where data-driven healthcare optimizes patient outcomes while upholding individual rights and privacy.
- **Interoperability:** Interoperability, defined as the seamless exchange of data between diverse systems, emerges as a foundational prerequisite for the development and

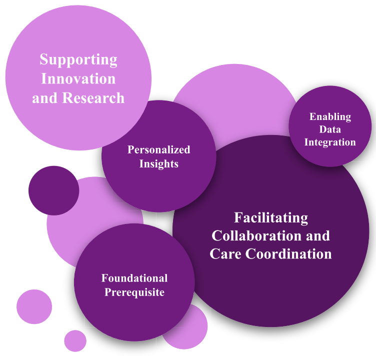

FIGURE 14. Critical importance of interoperability in the development and utilization of DTs.

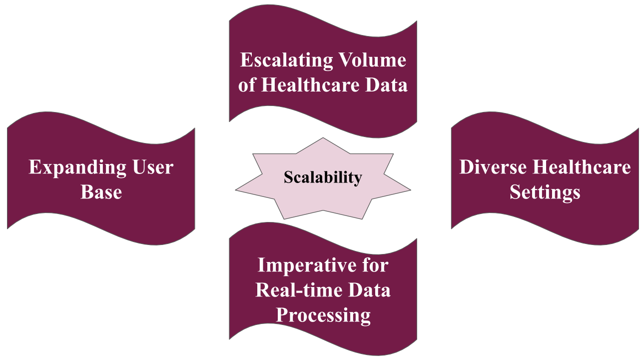

FIGURE 15. Key considerations for scalability.

utilization of DTs in healthcare. Devoid of interoperability, DTs remain isolated entities, incapable of accessing and integrating data from diverse sources such as medical records, imaging data, sensors, and genomics, consequently constraining their potential to deliver personalized care and enhance health outcomes. Interoperability empowers DTs in several crucial ways as shown in Figure 14. Firstly, it facilitates data integration, allowing DTs to collect and integrate information from various sources and thereby construct a comprehensive profile of an individual's health [38], [49]. Secondly, it fosters collaboration and care coordination among healthcare professionals by providing access to shared patient data and insights, leading to improved decision-making and more effective care coordination [41], [42]. Thirdly, interoperability enables the generation of personalized insights and recommendations within, tailored to the unique needs and health conditions of individuals, thereby paving the way for more efficient personalized medicine approaches [41], [45]. Finally, it supports innovation and research by allowing data sharing and collaboration across institutions, expediting research and innovation in healthcare, and contributing to the swift development of new treatments, therapies, and diagnostic tools [47].

- **Scalability:** The DT system must be scalable to accommodate the growing volume of patient data and the increasing demand for personalized care [26]. This requires designing the system with cloud-based architecture and distributed computing capabilities to handle the computational demands of data analysis and modeling. Ensuring scalability is a pivotal requirement for unleashing the transformative potential of DTs in healthcare. Despite their capacity to offer personalized insights and predictive capabilities, the true revolution lies in their ability to efficiently handle and process data amidst the ever-growing demands of the healthcare landscape. Key considerations underscore the significance of scalability (Figure 15): the escalating volume of healthcare data, the expanding user base, diverse healthcare settings, and the imperative for real-time data processing. Strategies to achieve scalability encompass leveraging cloud computing for elastic resources, employing data optimization techniques, adopting a micro-services architecture for modular scaling, and exploring edge computing for improved real-time performance. Prioritizing scalability, as elucidated by [34], [47], and [48] among others, is fundamental for developing robust DTs capable of meeting the burgeoning demands of the healthcare industry.
- **User-centric Design:** We need to design the DT system keeping the needs of healthcare providers in mind, providing a user-friendly interface that is easy to learn and use [32]. The system should also incorporate feedback from healthcare providers to ensure that it meets their clinical needs and workflow preferences.

These requirements highlight the complexity and multifaceted nature of building a DT system for a smart personalized healthcare industry. Addressing these requirements will require collaboration among healthcare providers, technology experts, data scientists, and policymakers to ensure effective and ethical implementation of DTs and to transform patient care and improve healthcare outcomes.

B. LAYERS OF THE REFERENCE FRAMEWORK

RQ3: What are the key layers for implementing a DT smart healthcare system? Implementing a DT smart healthcare system involves a multi-layered approach as shown in Figure 16 that encompasses various technical and non-technical considerations. The four key layers for implementing a DT smart healthcare system are [51]:

- **Layer 1: Device Layer** The device layer consists of the physical devices that collect and transmit data to the DT system. This includes wearable devices, medical imaging devices, patient-generated data (e.g., social media posts, fitness apps), and other sources of patient data. The device layer plays a crucial role in ensuring the quality and consistency of data input into the DT system. In the realm of, ensuring the accuracy and reliability of sensor data through proper calibration and noise-filtering techniques is imperative. Reference [53] propose a novel machine learning-based calibration method for wearable sensors, employing supervised learning

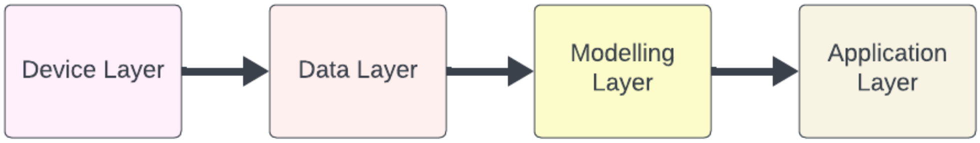

FIGURE 16. Layers of a DT framework.

algorithms to dynamically correct biases and drifts by analysing sensor data alongside reference measurements from gold standard devices. Reference [54] present a framework for automatic calibration of medical imaging devices using deep learning, ensuring consistent data quality by automatically correcting distortions and inconsistencies in images from uncalibrated devices. Noise filtering techniques are crucial [55], suggesting a hybrid approach combining Kalman filter and wavelet transform for wearable sensor data, offering robust noise filtering. Reference [56] explores adaptive filtering and deep learning-based image denoising techniques for medical images used in, ensuring noise reduction without compromising important details. Reference [57] addresses establishing gold standards and baselines through a wearable sensor, dataset benchmarked against laboratory-grade equipment, providing a valuable reference for evaluating sensor technologies, calibration methods, and noise filtering techniques. Reference [58] emphasizes the importance of reference standards in medical imaging, advocating for established phantoms and standardized protocols to ensure the accuracy and reliability of data used in, thereby enhancing the validity of insights for clinical decision-making.

- **Layer 2: Data Layer** The data layer collects, stores, and manages patient data. This includes electronic health records (EHRs), medical images, laboratory results, and other types of clinical data. The data layer also transforms and cleans data to ensure its quality and consistency. Additionally, the data layer integrates data from different sources, such as wearable devices and patient-generated data, to create a comprehensive view of each patient's health. DTs Essential data processing techniques encompass cleaning and pre-processing, addressing inconsistencies and errors through outlier detection, data imputation, and normalization, as advocated by [59] and [60]. Transformation and feature engineering, a pivotal step, involve converting raw data into an analysable format, utilizing techniques such as feature selection and dimensionality reduction, as emphasized by [61] and [62] Integration and fusion of data from disparate sources, including EHRs, medical images, sensors, and patient-generated data, create a holistic view of a patient's health, involving techniques like data alignment and merging, according to [63] and [64]. Real-time data processing, facilitated by streaming algorithms, distributed processing, and edge computing, ensures immediate insights and decision-making in dynamic healthcare environments, aligning with the insights of [17] and [65]. In terms of storage and transmission, data warehouses and lakes, cloud storage, block chain technology, and robust encryption measures collectively provide secure and scalable solutions for centralized and decentralized storage, guaranteeing patient privacy and data integrity, as elucidated by [66], [68], [69], and [70]. This comprehensive orchestration, situated within layer 2 of the DT architecture, establishes the data layer as the linchpin in the seamless operation and effectiveness of DT applications in smart healthcare systems
- **Layer 3: modeling Layer** The modeling layer acts a pivotal role in the DT architecture, shaping and sustaining precise patient models essential for simulating behaviours and predicting outcomes. In addressing the inherent complexities of healthcare systems, such as nonlinear dynamics, data heterogeneity, and individual variances, robust modeling techniques become imperative. Acknowledging the intricate interplay between physiological systems, nonlinear dynamics necessitates modeling approaches beyond linear paradigms, as emphasized by [17] and [71]. The presence of diverse data sources, including wearable sensors, medical images, and genomics, contributing to data heterogeneity, mandates adept feature engineering and integration techniques, as outlined by [63] and [64]. Moreover, individual variations in treatment responses underscore the need for personalized modeling approaches, a facet emphasized by [72] and [73]. Within the arsenal of modeling techniques, machine-learning methods, spanning supervised and unsupervised learning, and deep learning strategies, exemplified by convolutional and recurrent neural networks, enable intricate analyses of complex datasets, catering to diverse healthcare applications. Agent-based modeling captures emergent behaviours within specific environments, illustrating complex system dynamics, as highlighted by [67]. Artificial intelligence (AI) models, such as Explainable AI (XAI) techniques, generative adversarial networks (GANs), and federated learning, further contribute to the modeling layer's versatility. Existing exemplary models, including DeepMind's AlphaFold, IBM's Watson Oncology, and NVIDIA's Clara AI platform, showcase the practical implementation of these techniques in predicting protein structures, recommending personalized cancer treatment plans, and providing tools for AI-powered healthcare applications. In summary, the

modeling layer not only encapsulates the multifaceted techniques and methodologies addressing the intricacies of healthcare systems but also serves as the linchpin for ushering in personalized medicine, predictive healthcare, and virtual trials within the DT framework.

- **Layer 4: Application Layer** The application layer, situated at Layer 4 of the DT in healthcare (DTH) architecture, serves as the interface between the DT system and healthcare providers, offering a suite of tools for effective analysis and interpretation of complex datasets. Central to this layer are diverse data visualization techniques that play a pivotal role in presenting insights to healthcare providers in a clear, concise, and actionable manner. Dashboards, as highlighted by [59] and [74], provide a consolidated view of key metrics and indicators, empowering healthcare providers to monitor health trends and make informed decisions. Various chart types, such as bar charts, line graphs, and scatter plots, serve to visualize temporal trends and correlations, as discussed by [70] and [73]. Heat maps, a technique noted by [66] and [58], employ colour gradients for the quick identification of areas of interest within complex datasets. Additionally, interactive 3D models and technologies like Virtual Reality (VR) and Augmented Reality (AR), as advocated by [67], [68], and [75], facilitate realistic visualization of anatomical structures, disease progression, and treatment outcomes.
  To enable these visualizations, the DTH ecosystem employs various methods, tools, and frameworks. Unity3D, a game engine with capabilities for interactive 3D environments [72], [76], Microsoft Azure DTs (integrating with Azure services), Eclipse Ditto (an open-source DTH platform) [53], [54], and NVIDIA Clara AI platform (providing tools for medical data visualization and simulations) [55], [56] are instrumental in creating immersive and informative user interfaces. Together, these visualization techniques and tools empower healthcare providers to glean actionable insights, fostering seamless interactions and decision-making within the DTH system.

These four layers work together to create a comprehensive DT smart healthcare system that can support personalized medicine, predictive healthcare, improved diagnosis and treatment, virtual trials, and real-time monitoring and intervention. As DT technology continues to develop, we can expect to see even more sophisticated and integrated DT systems transforming healthcare delivery and improving patient outcomes.

C. EXISTING TOOLS AND FRAMEWORKS FOR DT

RQ 4: What are the different tools and frameworks available to construct a DT for healthcare? This section addresses the essential tools needed for constructing a DT in the healthcare sector, outlining the specific tools layer by layer. Additionally, it provides insights into end-to-end tools that encompass the entire DT development process.

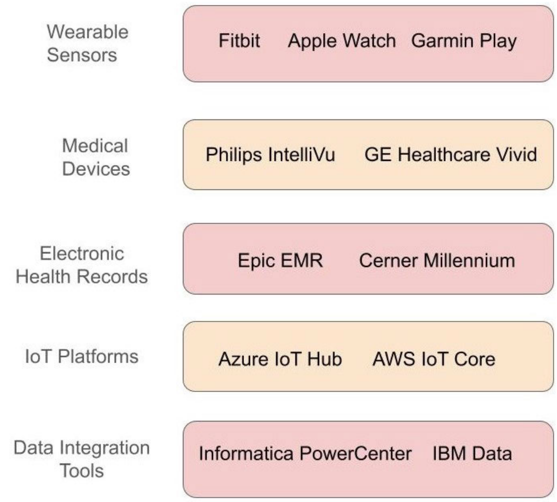

FIGURE 17. **Tools used in data acquisition and integration layer.**

1) DATA ACQUISITION AND INTEGRATION LAYER

Wearable sensors from Fitbit, Apple Watch, and Garmin play a pivotal role in collecting real-time health data, including metrics such as heart rate, activity levels, and sleep patterns. This data is valuable for creating a dynamic and personalized digital representation of an individual's health. Wearable sensors contribute to the continuous monitoring aspect of the DT, providing rich and timely data for analysis and modeling [59].

Medical devices like Philips IntelliVue MX800 [77] and GE Healthcare Vivid S6 are critical for acquiring detailed clinical data. These devices capture information such as vital signs, imaging data, and patient-specific measurements. Integrating this data into the DT allows for a comprehensive representation of a patient's physiological status. This layer ensures that the digital replica aligns closely with the real-time condition of the patient.

Electronic Health Records (EHRs) are fundamental in providing a historical context to a patient's health. Systems like Epic EMR [79], Cerner Millennium [79], and Allscripts TouchWorks store and manage patient information, medical history, and treatment plans. Integrating EHR data into the DT ensures a holistic view, enabling the consideration of past health records and facilitating a more accurate representation of the patient's health over time.

IoT platforms, including Azure IoT Hub, AWS IoT Core, and Google Cloud IoT Core [80], offer scalable solutions for managing and processing data from diverse sources. These platforms are instrumental in handling the large volumes of data generated by wearable sensors and medical devices. They provide the infrastructure needed to securely transmit and store data, facilitating the seamless integration of real-time information into the DT.

Data integration tools like Informatica PowerCenter, IBM DataStage [81], and Talend Open Studio play a crucial role in aggregating and harmonizing data from heterogeneous sources. These tools can effectively integrate data from wearable sensors, medical devices, and EHRs into a cohesive dataset for the DT. They streamline the process of transforming raw data into actionable insights, contributing to the accuracy and reliability of the digital representation.

2) MODEL DEVELOPMENT AND SIMULATION

Modeling and simulation tools such as AnyLogic [82], Simulink [83], and COMSOL Multiphysics provide a foundation for creating dynamic models that mimic real-world healthcare scenarios. These tools are crucial for developing the core structure of the DT, allowing for the representation of complex systems, physiological processes, and medical interventions.

Machine-learning libraries, including TensorFlow, PyTorch, and sci-kit-learn, play a vital role in enhancing DTs capabilities. By incorporating machine learning algorithms, the DT can learn and adapt based on evolving health data, enabling predictive analytics and personalized treatment recommendations. TensorFlow and PyTorch, in particular, offer versatile frameworks for implementing advanced machine learning models tailored to healthcare applications.

Artificial intelligence platforms such as Google AI Platform, AWS AI Services, and Microsoft Azure AI bring cutting-edge AI capabilities to the DT. These platforms empower the DT to analyse large datasets, identify patterns, and derive meaningful insights. Through AI integration, the DT gains the ability to interpret complex medical data, providing valuable decision support for healthcare professionals and contributing to personalized medicine initiatives.

In the context of high-performance computing (HPC), platforms like NVIDIA DGX A100 and Google Cloud TPUs offer accelerated computational capabilities. These platforms are instrumental in handling computationally intensive tasks, such as complex simulations and large-scale data processing, thereby enhancing the performance and efficiency of the DT. The integration of HPC ensures that the DT can handle the computational demands of real-time simulations and analyses in healthcare scenarios.

3) VISUALIZATION AND USER INTERFACE

3D visualization software, including Unity [84], Unreal Engine, and Blender [85], facilitates the creation of lifelike representations of medical environments and anatomical structures. These tools are instrumental in building a visually rich DT, allowing healthcare professionals to interact with and explore intricate medical scenarios in three dimensions. Unity and Unreal Engine, enable the development of realistic and dynamic visualizations that enhance the understanding of complex healthcare data.

Augmented Reality (AR) and Virtual Reality (VR) hardware such as Microsoft HoloLens, Meta Quest 2, and HTC Vive Pro introduce an interactive dimension to the DT. These platforms offer immersive experiences, enabling healthcare practitioners to engage with virtual representations of patient data, medical procedures, and healthcare environments. AR and VR technologies enhance training, surgery planning, and medical education by providing realistic simulations in a virtual environment.

Data visualization libraries, including Tableau [86], Power BI, and Plotly [87], contribute to the effective communication of complex healthcare data. These tools enable the creation of interactive and insightful visualizations, aiding healthcare professionals in interpreting and analysing patient data within the DT. Tableau and Power BI, for instance, empower users to create dashboards and reports that convey critical information in a comprehensible manner.

User Interface (UI) development frameworks, such as React, Angular, and Vue.js, are essential for creating intuitive and responsive interfaces for interacting with the DT. These frameworks enable the development of user-friendly applications that facilitate seamless navigation and interaction with the digital representation of healthcare scenarios. React, Angular, and Vue.js are widely utilized for building dynamic and engaging user interfaces, ensuring an optimal user experience in healthcare applications.

D. END TO END DT FRAMEWORKS

1) ECLIPSE 3D

Eclipse 3D [88] is a potent open-source platform designed specifically for building DTs in healthcare, offering a comprehensive suite of features that cater to the unique needs of healthcare professionals. Beyond conventional 3D modeling, Eclipse 3D excels in creating intricate models of organs, tissues, medical devices, and healthcare facilities. It stands out by enabling the development of interactive simulations for physiological processes, and medical device behaviours, and visualizing potential surgical procedures and treatment plans. It integrates real-time data into 3D models, facilitating dynamic visualization and empowering healthcare professionals to communicate complex information effectively through insightful dashboards and charts. For collaboration and training, Eclipse 3D supports collaborative work on shared 3D models among medical professionals. It also provides immersive training experiences for medical procedures and surgeries. The platform's open-source nature ensures accessibility, making it cost-effective and available to a broad range of healthcare institutions and researchers. Its extensible and customizable architecture allows developers to tailor functionalities, creating highly specialized solutions for diverse healthcare applications. Eclipse 3D's compatibility with various 3D formats streamlines data integration, eliminating the need for costly conversions. Supporting AR and VR technologies, Eclipse 3D enhances training and patient communication with immersive experiences. Compliance with standardized frameworks ensures interoperability and seamless communication between different DT applications.

2) Unity3D DT

Unity 3D [89] stands as a transformative force in healthcare by serving as a leading real-time 3D development platform,

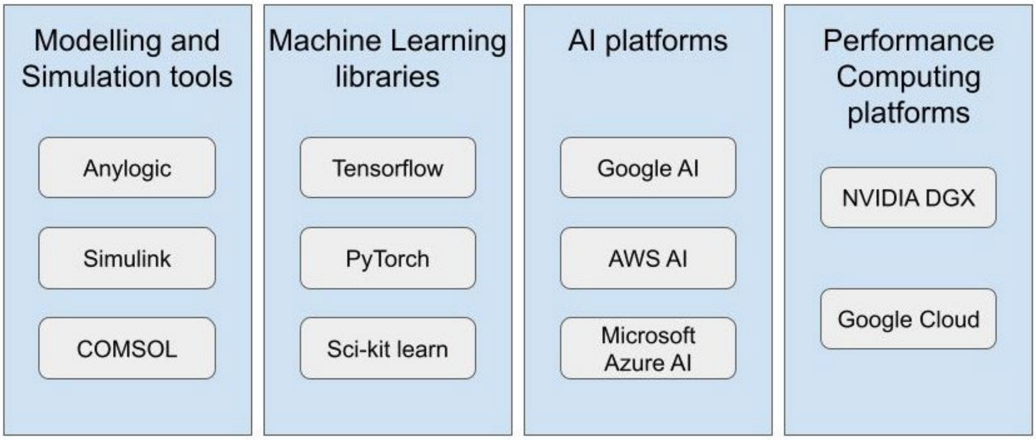

FIGURE 18. Tools used in model development.

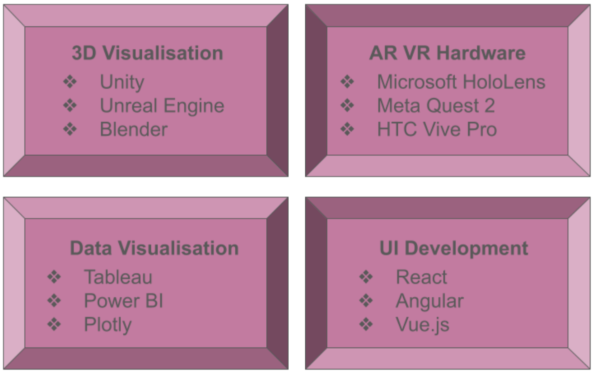

FIGURE 19. Tools used in visualization and user interface.

FIGURE 20. End to end frameworks.

uniquely equipped for constructing advanced. This dynamic tool excels in creating virtual replicas of healthcare environments, medical devices, and human anatomy, offering a multitude of benefits across the healthcare spectrum. Unity's prowess lies in its advanced data ingestion capabilities, seamlessly integrating data from diverse sources such as BIM, CAD, PLM, ERP, and IoT [89] systems. This integration results in accurate and dynamic DTs that faithfully reflect real-world healthcare assets. The platform's user-friendly interface and robust creation tools streamline the development process, enabling the rapid deployment of interactive DTs with features like real-time rendering, physics simulation, and scripting. Unity's multi-user functionality extends collaboration beyond design and engineering teams, allowing various stakeholders such as healthcare professionals, researchers, patients, and students to interact with DTs across devices. The platform's visual scripting tools and real-time data visualization capabilities facilitate in-depth analysis of complex healthcare data, empowering professionals to gain deeper insights into patient conditions, treatment effectiveness, and overall healthcare operations. Unity's AR/VR capabilities further contribute to immersive training and educational experiences, enhancing skill acquisition and knowledge retention among healthcare practitioners. By incorporating individual patient data, Unity enables the creation of personalized treatment plans and care pathways, ultimately improving patient care and reducing complication risks. Healthcare administrators and policy-makers benefit from improved decision-making through the platform's data-driven insights into resource needs, facility design, and workflow optimization. Unity's scalability and open-source nature provide adaptability to various project sizes and requirements, allowing for extensive customization and integration with other software tools and technologies. In essence, Unity 3D emerges as a powerful and versatile tool, empowering healthcare professionals to harness the potential of DTs for enhanced patient care, advanced medical research, and optimizing healthcare operations.

3) MICROSOFT AZURE DT

Microsoft Azure DTs [90] emerges as a robust and versatile platform tailored for creating and managing, particularly within the healthcare domain. Offering a comprehensive suite of tools and services, this platform empowers organizations to model, connect, visualize, and analyse various healthcare assets. The Azure DTs Definition Language (DTDL) allows the definition of custom DT models, facilitating the creation of detailed representations of medical equipment, facilities, patients, and even the human body. Integration with IoT Hub and other data integration services ensures real-time data flow, maintaining accurate DT representations. The platform's capabilities extend to creating interactive 3D visualizations of healthcare environments, employing powerful data analytics tools for insights into patient conditions, treatment effectiveness, and resource utilization. Azure DTs support the development of personalized treatment plans based on individual patient data and facilitate the optimization of hospital operations through data analysis. Collaboration and innovation thrive as the platform enables seamless information exchange across healthcare teams and encourages the development of innovative solutions on top of its core features. Azure DTs stands out for its open modeling language, live execution environment, comprehensive data integration and output capabilities, and advanced visualization and analytics tools. Overall, it proves instrumental in empowering healthcare organizations to enhance patient care, improve operational efficiency, and drive innovation in the healthcare industry through the implementation of.

V. APPLICATION AREAS

RQ5: What are the potential applications of using DT for a smart healthcare industry? The presented Figure 21 encapsulates a comprehensive overview of DT applications in healthcare, categorized into four principal domains. In the sphere of Personalized Medicine and Patient Care, DTs assume a crucial role in Precision Medicine, where they generate virtual models of individual patients by integrating genetic, biological, and environmental data. This process enables the tailoring of treatment plans, the advancement of drug development, and the prediction of potential health risks. Additionally, DTs play a vital role in Predictive Diagnostics and Disease Monitoring, utilizing real-time data from wearable sensors to continuously monitor health status and predict potential disease outbreaks. Furthermore, in Virtual Surgery and Surgery Planning, we can utilize DTs of organs and anatomical structures for pre-operative planning, simulating surgical procedures, and facilitating risk-free surgeon training.

Transitioning to Hospital Operations and Resource Management, DTs are instrumental in Optimizing Patient Flow and Resource Allocation. They simulate patient flow, predict resource needs, and optimize staffing and equipment allocation to enhance operational efficiency and minimize wait times. Additionally, DTs support the Predictive Maintenance of Medical Equipment, leveraging real-time data to monitor performance, predict potential failures, and facilitate preventative maintenance, thereby reducing downtime. In Virtual Commissioning and Training, DTs of new hospital facilities virtualize construction and commissioning processes, identify potential issues, and optimize layout before physical construction.

In Drug Development and Clinical Trials, DTs significantly contribute to Virtual Drug Testing and Safety Evaluation, creating virtual representations of organs and physiological systems to reduce reliance on animal testing and expedite the drug development process. Furthermore, the application of Personalized Drug Dosage Optimization involves using patient DTs to predict individual responses to medication, optimizing drug dosage for enhanced efficacy and minimized side effects. The utilization of DTs in Virtual Clinical Trials allows for faster and more cost-effective testing of new treatments and medical devices.

Lastly, within the domain of Public Health and Disease Prevention, DTs facilitate Predicting and Mitigating Outbreaks of Infectious Diseases by modeling the spread of diseases among populations. This aids public health officials in anticipating outbreaks and implementing preventive measures. Monitoring Chronic Diseases and Environmental Risks involves the use of DTs to monitor and manage chronic diseases, identify individuals at risk, and enable early intervention. Additionally, DTs contribute to the development of Personalized Health Interventions and Behavioural Change, promoting healthy behaviours at both individual and population levels, thereby enhancing overall public health.

VI. OPEN CHALLENGES AND DISCUSSION

RQ6: What are the open challenges to applying DT in personalized healthcare? have emerged as a transformative technology with the potential to revolutionize the healthcare industry. DTs are virtual representations of physical objects or systems that we can use to simulate and analyse their behaviour [1]. In the healthcare context, we can employ DTs to create personalized models of patients, enabling healthcare providers to gain deeper insights into their conditions and make informed treatment decisions [24].

Despite the many potential benefits of DTs in personalized healthcare, several open challenges need to be addressed before they can be widely adopted as shown in figure 22. These challenges include:

A. DATA QUALITY AND INTEGRATION

Ensuring the quality and consistency of patient data is essential for creating accurate DT models [17]. However, healthcare data is often fragmented and siloed, making it difficult to integrate and analyse. This is due to several factors, including the use of different electronic health record (EHR) systems, the lack of standardized data formats, and the reluctance of healthcare providers to share data.

Challenges and Solutions:

- Standardization of data formats and communication protocols: Establishing standards for data formats and communication protocols is crucial to facilitate seamless data exchange between different healthcare systems

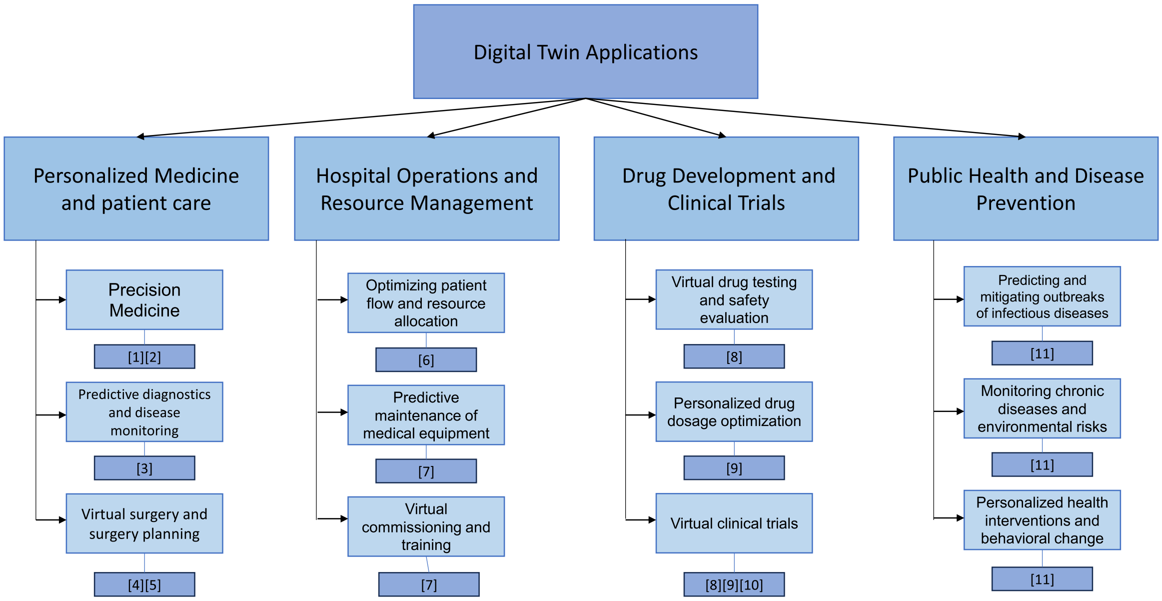

FIGURE 21. Various applications of DT.

and [17]. This will enable the integration of data from various sources, such as EHRs, wearable devices, and patient-generated data, into DT models.

- Data governance and sharing policies: Implementing robust data governance policies and encouraging data sharing among healthcare providers can enhance data quality and accessibility [17]. This will involve establishing clear guidelines for data collection, storage, and sharing, ensuring patient privacy and security while enabling the aggregation of rich patient data for DT modeling.

B. MODEL DEVELOPMENT AND VALIDATION

Developing accurate and reliable DT models requires expertise in data science, machine learning, and AI [31]. Additionally, we need to validate DT models against real-world data to ensure their accuracy and generalizability. This is a complex and time-consuming process, and it requires the involvement of experts from a variety of disciplines.

Challenges and Solutions:

- Development of robust modeling methodologies: Advancements in data science, machine learning, and AI techniques are necessary to create robust DT models that can capture the complex dynamics of human physiology and disease progression [31]. This includes developing algorithms that can handle large, heterogeneous datasets and adapt to new data as it becomes available.
- Rigorous validation and testing: Stringent validation methods and testing procedures are essential to ensure the accuracy, generalizability, and reliability of DT models [31]. This involves evaluating models against real-world clinical data and patient outcomes, identifying potential biases or limitations, and refining models accordingly.

C. SECURITY AND PRIVACY

handle sensitive patient data, making security and privacy paramount [24]. DT systems must implement robust cybersecurity measures to protect patient data from unauthorized access, breaches, and misuse. This includes measures such as encryption, access controls, and data governance policies.

Challenges and Solutions:

- Cybersecurity threats and mitigation strategies: Healthcare organizations face increasing cybersecurity threats, including data breaches, ransomware attacks, and phishing scams [24]. Implementing robust cybersecurity measures, such as multi-factor authentication, data encryption, and intrusion detection systems, is crucial to protect patient data from unauthorized access and misuse.
- Privacy-preserving data sharing and analysis: Balancing the need for data sharing for DT modeling with patient privacy is a critical challenge [24]. Secure data-sharing mechanisms, such as federated learning and anonymization techniques, can enable data collaboration while safeguarding patient privacy.

D. INTERPRETABILITY AND EXPLAINABILITY

DT models are often complex and opaque, making it difficult for healthcare providers to understand how the models make decisions [32]. This can lead to distrust and reluctance to adopt in clinical practice. Healthcare providers need to be able to understand how DT models work to trust them and to make informed decisions based on their outputs.

Challenges and Solutions:

- Explainable AI techniques: Developing and incorporating explainable AI (XAI) techniques into DT models can enhance their interpretability [32]. XAI methods provide insights into how DT models arrive at their

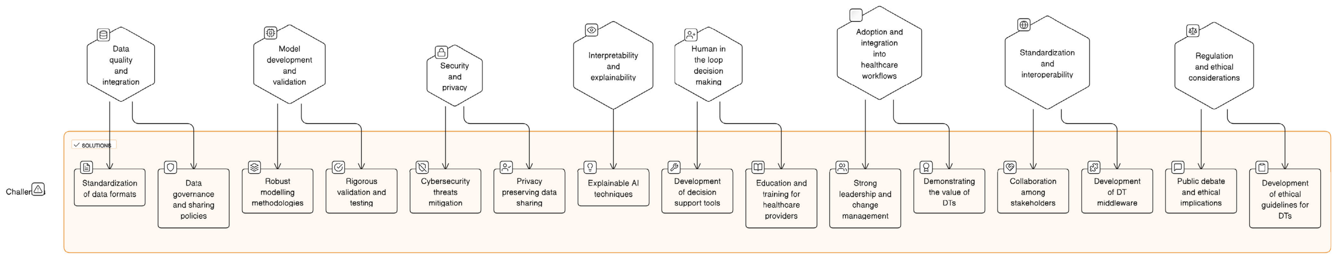

FIGURE 22. **Various challenges.**

decisions, allowing healthcare providers to understand the underlying logic and reasoning behind the model's predictions or recommendations.

E. HUMAN-IN-THE-LOOP DECISION-MAKING

should augment clinical judgment, not replace it. Healthcare providers need to be able to understand and interpret DT insights and make informed decisions based on all available information [75].

Challenges and Solutions:

- Development of decision support tools: Developing decision support tools that integrate DT insights with clinical judgment can help healthcare providers make informed decisions in real-time. These tools can provide personalized recommendations, risk assessments, and treatment plans based on the patient's individual DT.
- Education and training for healthcare providers: We need to educate and train healthcare providers on how to interpret and use DT insights effectively in their practice. This includes understanding the limitations of DTs and the importance of clinical judgment.

F. ADOPTION AND INTEGRATION INTO HEALTHCARE WORKFLOWS

Implementing DTs into existing healthcare workflows can be challenging due to organizational inertia, cultural resistance, and the need for training and education [26].

Challenges and Solutions:

- Strong leadership and change management: Healthcare organizations need strong leadership to champion DT adoption and address any cultural resistance. This includes creating a supportive environment for DT use and providing training and education for healthcare providers.
- Demonstrating the value of: Sharing success stories and demonstrating the value of DTs can help overcome scepticism and encourage wider adoption. Pilot projects, case studies, and other initiatives that showcase the benefits of DTs in clinical practice can help achieve this.

G. STANDARDIZATION AND INTEROPERABILITY

Establishing standards for data formats, communication protocols, and APIs is essential for interoperability between DT systems and other healthcare systems [1].

Challenges and Solutions:

- Collaboration among healthcare providers, technology vendors, and standards organizations: Collaboration among stakeholders is crucial to developing and implementing standards for DT interoperability. This includes establishing clear guidelines for data exchange, ensuring interoperability with existing healthcare systems, and developing open-source tools and platforms.
- Development of DT middleware: DT middleware can play a key role in facilitating interoperability by providing a layer of abstraction between different DT systems and healthcare systems. This can help to simplify data exchange and integration.

H. REGULATION AND ETHICAL CONSIDERATIONS

raise many ethical considerations, such as patient autonomy, informed consent, and the potential for discrimination. We need clear guidelines and regulations to ensure the ethical and responsible use of DTs in healthcare [17].

Challenges and Solutions:

- Public debate and discussion about the ethical implications of: There needs to be a public debate and discussion about the ethical implications of DTs in healthcare. This can help to raise awareness of the potential risks and benefits of DTs and to develop guidelines for ethical use.
- Development of ethical guidelines for: Clear ethical guidelines for the development, use, and governance of DTs need to be developed. These guidelines should address issues such as patient privacy, data security, bias, and discrimination.

Despite the challenges, DTs have the potential to revolutionize healthcare by providing personalized insights and decision support for healthcare providers. By addressing the challenges outlined above, we can integrate DTs into clinical practice and help to improve patient outcomes.

VII. METHODOLOGY

virtual representations of physical assets or systems as shown in figure 23, have emerged as a transformative technology with the potential to revolutionize various industries. By continuously synchronizing data from the physical counterpart, DTs enable real-time monitoring, predictive analysis, and optimization of physical systems. To effectively implement, a well-defined methodology is crucial. Several methodologies have been proposed for developing and implementing. These methodologies typically encompass four key phases [10] as shown in figure 24:

- Problem Definition and Requirements Gathering: The initial phase involves clearly defining the problem or challenge that the DT aims to address. This includes understanding the stakeholder needs, the specific use cases, and the data requirements.
- Data Collection and Analysis: The second phase focuses on gathering and analysing relevant data from the physical asset or system. This may involve sensor data, historical records, and engineering models. Pre-processing, cleaning, and structuring ensures its usability for the DT.
- DT Development: The third phase involves the development of the DT model. This may involve creating physics-based models, machine-learning models, or a combination of both. The model should accurately represent the behaviour of the physical asset or system under various conditions.
- Deployment and Validation: The final phase involves deploying the DT and validating its performance. This may involve testing the model's accuracy, responsiveness, and integration with existing systems.

A. DYNAMIC AND MODULAR ARCHITECTURE OF A DIGITAL MEDICAL TWIN (DMT) FOR ADAPTIVE HEALTHCARE INFORMATION INTEGRATION AND DECISION SUPPORT

The implemented Digital Medical Twin (DMT) in the paper [10]. adopts a dynamic approach to data handling, avoiding the persistence of case-related data to prevent unnecessary duplication and update challenges. Instead, it dynamically loads and caches only the necessary data to respond to the current application's request. Interfaces of the DMT seamlessly integrate with established standards, preserving existing information systems' data representations and ontologies through references. They embed case-related data into an extendable internal data structure, MPMResource, based on the Resource Description Framework (RDF). Each resource contains DMT-specific metadata and an RDF representation of the original data resource or a reference, facilitating semantic linkage across various modalities. The DMT concept encompasses modules for trend analyses and abstractions based on different model types. The architecture is agnostic to analysis methods, with specialized collector modules aggregating patient data from primary clinical information systems. RDF module descriptions define modules, enabling on-demand compilation of a module call hierarchy for complex requests. They calculate an execution fingerprint for each successful module call, enhancing reusability. The DMT offers a GraphQL endpoint for third-party applications to request information for assistance tasks. The response, provided as an MPMResource, includes data from clinical information systems and abstracted information from modules. They link MPMResources, particularly data computed from modules to all resources used for calculation, ensuring traceability for constructing argument chains. This traceability is crucial in computer-aided clinical decision-making. The modular architecture accommodates both knowledge-based and data-driven methods, allowing the extension of the DMT implementation to incorporate new clinical knowledge, and treatment strategies, or address additional diseases. The design promotes adaptability, traceability, and integration of evolving medical information and methodologies.

B. COMPOSITION AND FEATURES OF DT

1) COMPOSITION OF DT TECHNOLOGY

In the paper by [11] the DT is structured in five dimensions: physical entity, virtual model, connections, DT data, and service. The physical entity represents real-world objects, and the Internet of Things (IoT) facilitates data collection through methods like two-dimensional codes, data acquisition cards, and sensors. The virtual model is a digital representation of the physical entity, enhanced by technologies like Virtual Reality (VR), Augmented Reality (AR), and Mixed Reality (MR). Connections enable intercommunication between different parts of DT models, utilizing 5G communication technology. DT data encompasses diverse information categories, benefiting from Big Data for valuable insights and block chain for data security. The DT service model serves both the physical entity and virtual model, employing AI for data analysis, fusion, and deep learning to enhance various services.

2) SIMULATION CHARACTERISTICS OF

High fidelity is a crucial characteristic of the DT, ensuring accurate simulations and real-time data collection. Validation of data as a benchmark, continuous calibration, and the integration of sensor data and numerical simulations contribute to accurate results. Standardization, lightweight design, robustness, and modularization are essential for an effective virtual model. Standardization in communication protocols and encodings improves information sharing, while modularity enhances flexibility by recombining or separating individual models. These technical features pave the way for mapping patient data in the medical process into a predictive framework, aiding in precision medicine.

3) TECHNICAL CHARACTERISTICS IN THE MEDICAL FIELD

In the medical field, DTs offer precise diagnosis through virtual fractional flow reserve, replacing invasive catheters for monitoring arterial blood pressure. Computational models and statistical models play a role in data acquisition, diagnosis, and therapy planning stages. They create virtual human organs using high-fidelity simulation data, enabling the establishment of efficient AI models. Technologies like motion capture systems, Inverse Kinematics (IK), and AI models work together for real-time position and pose tracking

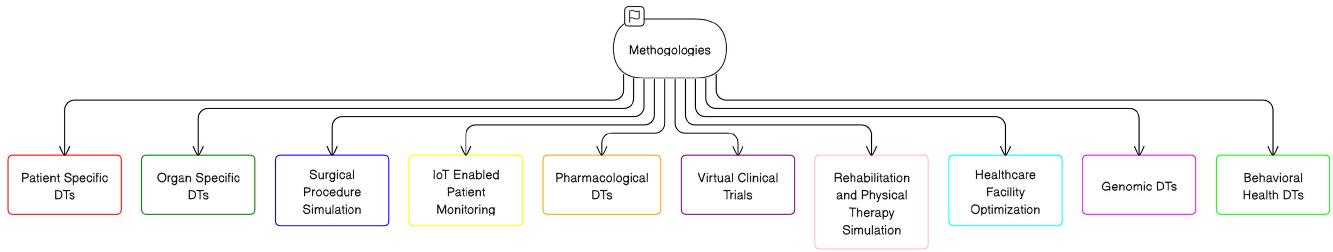

FIGURE 23. Different methodologies of DT.

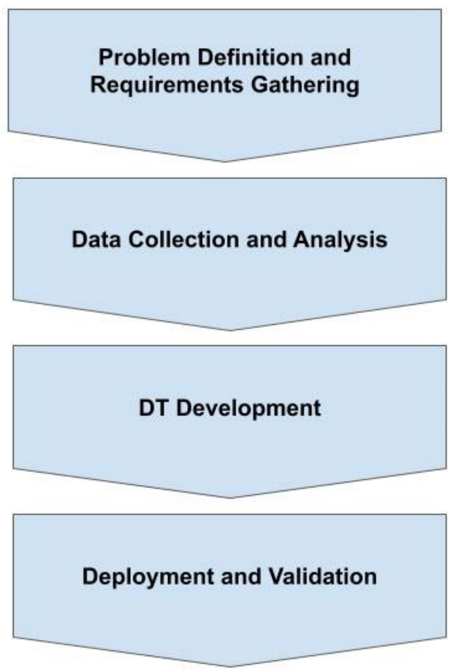

FIGURE 24. Key phases of methodology.

of the human body. DT technology, with its sophisticated composition and simulation characteristics, has promising applications in healthcare, particularly in precise diagnosis and personalized medicine. The integration of AI and advanced technologies enhances the capabilities of DTs in the medical field.

C. ONTOLOGY-BASED DTs FOR PERSONALIZED MEDICINE

Personalized medicine aims to tailor healthcare interventions to the unique characteristics of each patient. DTs can facilitate personalized medicine by providing a structured framework for representing and integrating a patient's complex medical data, including genetic, clinical, and phenotypic information. Ontologies provide a structured and standardized way to represent knowledge, enabling the integration of various data sources without compromising data integrity or interoperability. In the context of personalized medicine, ontologies can capture the patient's genetic profile, clinical history, and phenotypic characteristics, forming a comprehensive representation of the patient's health status. The paper by [16] proposes an ontology-based personalized medicine DT platform for cancer treatment decision support. The platform utilizes a comprehensive ontology to capture the patient's genetic profile, clinical history, and phenotypic characteristics. This structured representation enables the platform to identify patterns and relationships within the patient's data, facilitating the development of personalized treatment recommendations.

D. FEDERATED LEARNING-BASED DTs FOR SECURE HEALTHCARE DATA SHARING

Healthcare data privacy is a critical concern, as we must protect sensitive patient information from unauthorized access or misuse. Traditional data-sharing practices often involve transferring patient data to centralized repositories, increasing the risk of data breaches. Federated learning provides a secure solution for sharing healthcare data while preserving patient privacy. Federated learning algorithms enable the training of machine learning models on distributed healthcare data without directly accessing or sharing the underlying patient data. They train models on local data sources, and share only the aggregated model parameters, ensuring that sensitive patient data remains protected. The paper by [13] proposes a federated learning framework for privacy-preserving DTs in healthcare. The framework enables the training of machine learning models on distributed healthcare data without compromising patient privacy. This approach allows for the secure aggregation of knowledge and insights while protecting patient privacy.

E. EXPLAINABLE AI-ENHANCED DTs FOR CLINICAL DECISION SUPPORT

Explainable AI (XAI) techniques provide transparency and interpretability for machine learning models. By explaining the reasoning behind their predictions, XAI enhances trust and understanding in machine learning models. We can enhance DTs with XAI to provide clinicians with clear explanations for their recommendations and predictions. This transparency facilitates informed clinical decision-making by empowering clinicians to understand the factors influencing the DTs outputs. The paper by [14] proposes an XAI-enhanced DT for clinical decision support in sepsis management. The DT integrates XAI techniques to explain its predictions for patient deterioration and treatment recommendations. This transparency enables clinicians to understand the factors influencing the DTs decisions, fostering trust and collaboration between clinicians and the DT.

F. REAL-TIME DTs FOR PATIENT MONITORING AND SURVEILLANCE

Real-time DTs enable continuous monitoring and surveillance of patient health status. They continuously update these DTs with real-time data from various sensors and monitoring devices, providing a comprehensive view of the patient's condition. This real-time monitoring facilitates early detection of changes in patient conditions and enables timely interventions to prevent adverse events. For instance, we can use real-time DTs to monitor vital signs, detect subtle changes in electrocardiograms, and identify early signs of sepsis or other critical conditions. The paper by [96] proposes real-time DTs for patient monitoring and surveillance in the intensive care unit (ICU). They update the DTs continuously updated with real-time data from vital signs monitors, electrocardiograms, and other ICU devices. This real-time monitoring enables clinicians to identify subtle changes in patient conditions and make timely interventions to prevent complications.

G. DIFFERENT METHODOLOGIES OF DT

1) PATIENT-SPECIFIC

- Patient-specific DTs in healthcare involve the creation of highly personalized virtual replicas of individual patients. As shown in Figure 25 these DTs integrate comprehensive patient data, including medical history, genetic information, and real-time physiological data. This methodology facilitates precise treatment planning, personalized medicine, and the prediction of patient responses to different interventions. By tailoring healthcare strategies to the unique characteristics of each patient, this approach holds significant promise for improving treatment outcomes and patient satisfaction
- "An Ontology-Based Personalized Medicine DT Platform for Cancer Treatment Decision Support" by [35]: This paper presents an ontology-based DT platform to aid in cancer treatment decision support. It utilizes ontologies to integrate a patient's genetic, clinical, and phenotypic data into a structured and interoperable format, enabling personalized treatment plans.

2) ORGAN-SPECIFIC

- Organ-specific DTs focus on replicating the structure and function of specific organs or organ systems in a virtual environment. This methodology as shown in Figure 26enables detailed modeling and simulation, providing valuable insights into organ behaviour and response to various stimuli. In healthcare, organ-specific DTs are particularly useful for preoperative planning, understanding disease progression, and optimizing treatment strategies. Surgeons and healthcare professionals can leverage these DTs to enhance their understanding of complex anatomical structures and plan interventions with greater precision.

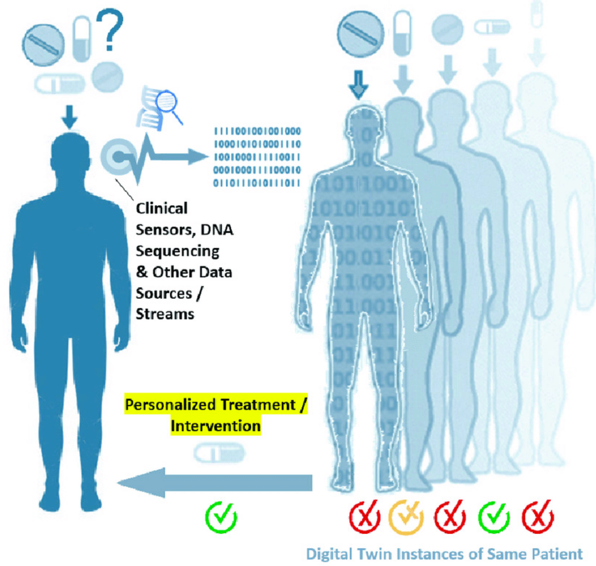

FIGURE 25. Patient-specific DT.

- "A DT Approach for Personalized Aortic Valve Disease Management" by [17]: This paper explores a DT approach for personalized aortic valve disease management. It constructs DTs of an individual's aortic valves to simulate their functionality under various conditions, facilitating personalized treatment decisions and risk assessment.

3) SURGICAL PROCEDURE SIMULATION

- The surgical procedure simulation methodology utilizes DTs to create virtual environments for practicing and simulating surgical procedures. This approach allows surgeons to hone their skills in a risk-free and controlled setting before performing actual surgeries. By providing a realistic platform for training and rehearsal, surgical procedure simulation DTs contribute to improved surgical outcomes, reduced risks, and enhanced patient safety.
- "A DT Approach for Personalized Surgery Planning and Simulation in Total Knee Arthroplasty" by [50]: This paper proposes a DT approach for personalized surgery planning and simulation in total knee arthroplasty. It generates DTs of patients' knees, allowing surgeons to simulate and optimize surgical procedures virtually before actual surgery.

4) IoT-ENABLED PATIENT MONITORING

- IoT-enabled patient monitoring integrates Internet of Things devices to continuously collect and transmit real-time data from patients. DTs created through this methodology offer a dynamic representation of a patient's health status. Remote patient monitoring, enabled by these, facilitates early detection of health

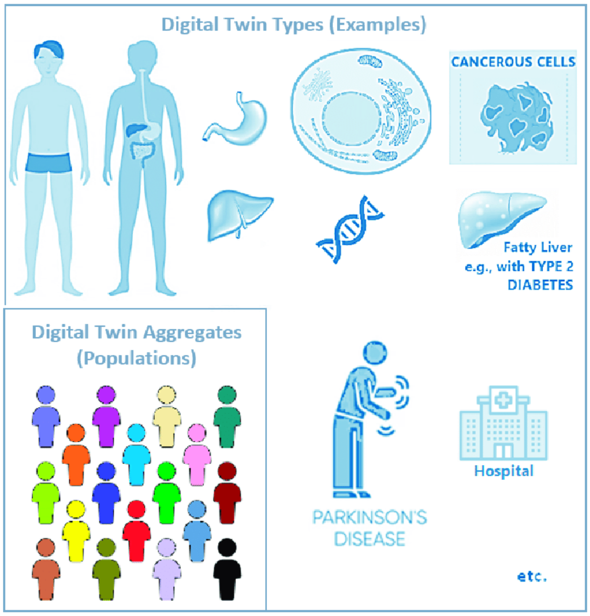

FIGURE 26. **Organ-specific DT [47].**

issues, timely intervention, and ongoing care management. This approach is especially valuable for patients with chronic conditions, allowing healthcare providers to monitor and respond to changes in health proactively.

- "A Real-Time IoT-Enabled DT Framework for Patient Monitoring in the Intensive Care Unit" [18]: This paper introduces a real-time IoT-enabled DT framework for patient monitoring in the intensive care unit (ICU). It continuously updates DTs with real-time patient data from various sensors and monitoring devices, enabling early detection of changes in patient conditions and timely interventions.

5) PHARMACOLOGICAL

- Pharmacological DTs focus on modeling the effects of drugs at a molecular level, simulating drug interactions, and predicting individual responses. By integrating genetic and physiological data, these DTs contribute to drug development and personalized medicine. Virtual testing within the DT environment helps identify potential adverse effects and optimize drug regimens, ultimately enhancing the efficacy and safety of pharmaceutical interventions
- "Pharmacological DTs for Personalized Medicine: A Review" by [19]: This paper provides a comprehensive review of pharmacological DTs for personalized medicine. It discusses the potential applications of DTs in drug development, personalized medicine, and minimizing adverse effects through virtual testing.

6) VIRTUAL CLINICAL TRIALS

- Virtual clinical trials leverage DTs to simulate and predict the outcomes of clinical trials. This methodology accelerates the drug development process by allowing researchers to virtually test new treatments and interventions. By reducing costs, shortening timelines, and minimizing the need for physical participants, virtual clinical trials contribute to more efficient and streamlined drug development, potentially bringing innovative therapies to market faster.
- "Virtual Clinical Trials in the Era of DTs and Predictive modeling" by [20]: This paper explores the potential of virtual clinical trials in the era of DTs and predictive modeling. It highlights how we can use DTs to simulate and predict the outcomes of clinical trials, accelerating the drug development process and reducing costs.

7) REHABILITATION AND PHYSICAL THERAPY SIMULATION

- Rehabilitation and physical therapy simulation methodologies involve the creation of digital representations of patients to simulate rehabilitation exercises and track progress. Physical therapists can use these DTs to design personalized rehabilitation plans, monitor patient recovery, and adjust interventions based on real-time feedback. This approach enhances the efficiency and effectiveness of rehabilitation programs, supporting patients in their recovery journey.
- "A DT Approach for Personalized Rehabilitation Planning and Guidance in Stroke Patients" by [7]: This paper presents a DT approach for personalized rehabilitation planning and guidance in stroke patients. It utilizes DTs to simulate patient-specific responses to various rehabilitation exercises, facilitating personalized treatment plans and monitoring patient progress.

8) HEALTHCARE FACILITY OPTIMIZATION

- Healthcare facility optimization DTs model the entire healthcare ecosystem, including facilities, equipment, and staff. This methodology aims to optimize resource allocation, enhance operational efficiency, and improve overall healthcare delivery. By simulating various scenarios and analysing workflow data, healthcare administrators can make informed decisions to reduce wait times, improve patient care, and ensure optimal utilization of resources.
- "A DT Framework for Healthcare Facility Optimization: A Simulation-Based Approach" by [21]: This paper proposes a DT framework for healthcare facility optimization. It utilizes simulation-based optimization techniques to improve hospital workflows, reduce wait times, and ensure optimal utilization of resources.

9) GENOMIC

- Genomic DTs integrate genetic information to create virtual representations of an individual's genomic profile. This methodology aids in disease risk assessment, precision medicine, and treatment decision-making based on genetic predispositions. By understanding the unique genetic characteristics of each patient, healthcare professionals can tailor interventions and therapies,

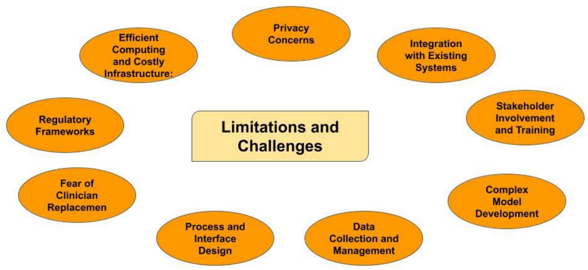

FIGURE 27. Limitations and challenges of DT.

paving the way for more personalized and effective healthcare strategies

- "Genomic DTs: A New Frontier in Precision Medicine" by [22]: This paper discusses the concept of genomic DTs and their potential in precision medicine. It emphasizes how genomic DTs can integrate genetic information to create personalized models of an individual's health, aiding in disease risk assessment and treatment decisions.

10) BEHAVIOURAL HEALTH

- Behavioural health DTs involve modeling and simulating behavioural patterns, mental health conditions, and the impact of interventions on psychological well-being. This methodology supports mental health professionals in treatment planning, intervention strategies, and understanding patient responses. By creating a virtual environment to explore behavioural health dynamics, DTs contribute to improved mental health care, personalized interventions, and better patient outcomes
- "Behavioural Health: A Conceptual Framework for Mental Health Assessment and Intervention" by [23]: This paper introduces a conceptual framework for behavioural health. It discusses how DTs can model and simulate behavioural patterns, mental health conditions, and the impact of interventions, supporting mental health professionals in treatment planning and understanding patient responses.

VIII. LIMITATIONS, CHALLENGES AND FUTURE DIRECTIONS

Despite the considerable advancements and research efforts dedicated to incorporating DTs into healthcare, several challenges persist, shaping the future trajectory of this technology as shown in figure 27. The following sections outline key challenges and possible directions for addressing them.

A. EFFICIENT COMPUTING AND COSTLY INFRASTRUCTURE

A primary obstacle in deploying DTs within healthcare lies in the sheer volume of generated data. To operate effectively, DTs demand substantial data, leading to potential issues in storage, processing, and bandwidth capacities. Addressing this challenge requires the development of efficient storage and computing systems capable of managing and processing extensive datasets. Cloud computing offers scalable and flexible resources, enhancing the efficiency and cost-effectiveness of DT systems. Additionally, emerging technologies like edge computing show promise by processing data closer to its source, thereby minimizing data transfer and reducing latency. Building and maintaining the infrastructure for DTs can be financially demanding, requiring substantial investments in computational resources, storage, and expertise. Smaller healthcare providers or resource-constrained settings may encounter challenges in implementing and sustaining DTs due to financial limitations.

B. PRIVACY AND SECURITY CONCERNS

Privacy emerges as a critical challenge when integrating DTs into healthcare, given the sensitivity of healthcare data. Unauthorized disclosure could have severe consequences, necessitating robust privacy measures. block chain technology is explored as a means to enhance data security and privacy. Furthermore, federated learning, a decentralized approach to training machine learning models, ensures data privacy while building global models. Techniques such as differential privacy, multiparty differential privacy, homomorphic encryption, multiparty computation, and detection of data and model poisoning in federated learning contribute to safeguarding data security and privacy. Additionally, potential model manipulation and systemic vulnerabilities within the digital twin ecosystem pose significant security challenges.

C. INTEGRATION WITH EXISTING SYSTEMS

Integrating digital twins with existing healthcare systems presents a significant challenge due to the widespread presence of legacy systems. These older systems often lack standardized data formats, which makes seamless communication and data exchange with newer technologies like digital twins difficult. Additionally, incompatibility with modern communication protocols further hinders smooth integration, creating roadblocks for real-time data exchange and updates. The sheer volume of legacy medical equipment still in use also contributes to data silos, limiting access to historical and real-time data and preventing the full potential of digital twins from being realized. This lack of interoperability between digital twins and legacy systems poses a major hurdle to achieving seamless and efficient healthcare delivery. Upgrading these systems can be costly and disruptive, while continued reliance on them creates limitations on the potential benefits of digital twins in healthcare.

D. REGULATORY FRAMEWORKS

The development of ethical guidelines and regulations is imperative for the responsible use of DTs in healthcare. Establishing standards for data security, data sharing, and informed consent is crucial to protecting patient rights and privacy.

E. STAKEHOLDER INVOLVEMENT AND TRAINING

Successful development and implementation of DT tools for healthcare necessitate active involvement from stakeholders, including healthcare providers, patients, policymakers, and governments. Input from these stakeholders ensures that DT tools meet practical requirements and exhibit high usability. Additionally, education and training programs for healthcare professionals and patients are vital for the successful adoption of DT technology. Healthcare professionals must comprehend and utilize DT data to provide personalized and effective care, while patients need training to navigate and interpret DT information.

F. COMPLEX MODEL DEVELOPMENT

Creating accurate models for complex physiological systems or diseases requires an in-depth understanding of underlying biological processes. Representing these processes effectively in virtual models is a challenging task that demands expertise in both healthcare and technology [25].

G. DATA COLLECTION AND MANAGEMENT

Human DTs require deep and detailed datasets, but existing Electronic Health Records (EHR) designs are heterogeneous and challenging to navigate. Extracting information from unstructured formats requires manual effort or the implementation of natural language processing technologies. The quality of data from hospital data collection processes, often reliant on blood tests and imaging systems, presents challenges, with data collection being expensive and time-consuming.

H. PROCESS AND INTERFACE DESIGN

Despite being labelled as fully autonomous, DT applications require interdisciplinary knowledge due to the complexity of human beings. User-friendly interfaces for DTs in healthcare are lacking, hindering effective communication among software, patients, and physicians. Mistrust on Decision Points: Physicians'. Mistrust of decisions derived from algorithms and big data stems from the lack of transparent explanations. Scepticism arises due to concerns about misdiagnosis and improper treatment.

I. FEAR OF CLINICIAN REPLACEMENT

The broader use of DTs in clinical tasks may evoke fears of clinician replacement. While DTs may outperform clinicians in certain scenarios, concerns about decision points and the need for adaptation to clinicians' needs and workflows are prevalent.

In summary, while there has been notable progress in integrating DTs into healthcare, we should systematically address these challenges to facilitate widespread adoption and maximize the benefits for patients and society [39]. Involving healthcare professionals, data scientists, technologists, policymakers, and regulatory bodies is crucial. Investment in research, standardization initiatives, and the establishment of robust governance frameworks are essential steps to unlock the full potential of DTs in healthcare while mitigating these concerns. It is imperative to address these challenges systematically to ensure the successful integration and sustainable use of DHTs in healthcare settings.

IX. CONCLUSION

In conclusion, this paper has provided a comprehensive review of the current applications of DTs in healthcare, shedding light on their immense potential while acknowledging existing barriers that hinder widespread adoption. The integration of DTs into medical decision-making is impeded by computational, ethical, and cultural concerns impede the integration of DTs into medical decision-making, underscoring the importance of simultaneous evolution in technological capacity and cultural acceptance, fostering an environment of trust.

The recommendations put forth include the incorporation of DTs in education programs and national pilot-diffusion projects to prevent entropy and miscoordination. We emphasize that while DTs can significantly support medical decision-making, they should not replace clinical decision-making, and caution against excessive reliance on technology alone is warranted.

Addressing challenges such as data bias and the ethical implications of genetic profiling, along with building trust in decision points derived from algorithms, remains pivotal. The paper underscores the need for developing ad-hoc methods to incorporate DTs into clinical trials and evidence generation, emphasizing the evolving nature of support within the scientific community.

Moreover, DT applications in construction and healthcare are gaining traction. In construction, DTs aid in representing the as-built versus as-designed project, minimizing errors, and improving information flow. In healthcare, DTs contribute to the discovery of illnesses, experimentation with treatments, and enhancement of surgery preparation by creating accurate full-dimensional human body models.

The technological advancements in AI, IoT, and cloud computing have propelled the rapid evolution of DT solutions, finding applications across various industries. The paper highlights AI-enabled ' ability to simulate complex real-world systems, continuously identify improvement areas, and optimize systems design to increase efficiency.

In essence, as we move into the future, DTs are positioned to expand their reach, combining with emerging technologies for a more immersive experience and unlocking novel applications that have the potential to make a significant positive impact on diverse sectors.

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AUTHOR CONTRIBUTIONS

Adithya Balasubhramanyam and Prasad B. Honnavalli: mentorship, coneptualization, review, drafting, funding aquision; Rhea Sudheer and Richa Ramesh: drafting, review, visualization, data curation.

DECLARATION OF COMPETING INTERESTS

The authors affirm that they have no known financial or interpersonal conflicts that might have influenced the research presented in this study.

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