Healthcare Digital Twins: Advances, Stakeholders, and Challenges

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Digital Twins (DT) have a huge potential for transforming both healthcare delivery and management. This review paper surveys the evolving landscape of DTs within the healthcare domain. First, we review different definitions of the term "digital twin" and ontologies containing related terms such as "digital model" and "digital shadow". Second, we identify groups of stakeholders with interests and/or roles in healthcare DT development and deployment. We then provide a review of recent developments regarding the application of DTs within the healthcare domain, which we divide into two main categories: clinical service applications which focus on the patient, and hospital management applications which focus on healthcare infrastructure and processes. Finally, we present an analysis of various challenges in healthcare DT development and deployment, as well as existing and/or potential solutions for each.

CCS Concepts: • **Applied computing → Health care information systems**; Consumer health; Command and control; Forecasting.

Additional Key Words and Phrases: Digital Twins, Hospital Management, Clinical Services, Healthcare, Survey

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1 Introduction

The digital twin (DT) is a cutting-edge technological concept that has emerged as a transformative force in various industries, including manufacturing, aerospace, healthcare, and more. At its core, a DT is a virtual dynamic representation of a physical system [110]. The digital counterpart is a dynamic and data-driven model that continuously updates in real-time (or near-real-time) to mirror the physical realities it represents, and is created by collecting and integrating real-time data from sensors, IoT devices, and other sources, allowing it to mimic the behaviour, characteristics, and status of its physical counterpart in a highly detailed and accurate manner.

The concept of a DT thus goes beyond mere simulation or modelling: it encompasses continuous monitoring [94], analysis, and feedback loops [123], enabling real-time insights and predictive capabilities. By creating a digital replica that mirrors (some aspect of) the physical world, organisations and industries can gain valuable insights, optimise processes, improve decision making, and enhance performance across various domains. DTs have the potential to revolutionise product development, maintenance, and operational efficiency, leading to significant advancements in innovation, sustainability, and overall productivity.

As technology continues to advance, the applications of DTs are expanding rapidly, driving innovation and transformation across diverse sectors. A 2022 global survey of 2,007 professionals [4], found that 69% of respondents' organisations currently leverage DT technology, with the majority of the remainder stating that their organisation planned to adopt DT technology within the next two years. On the other hand, of the 1,393 respondents which stated that their organisation currently leverages DT technology (at the time the survey was conducted), only eight percent claimed that their organisation begun doing so more than three years prior.

In particular, the field of healthcare is no exception to the rapid growth of DT applications. The global healthcare DT market is estimated to produce USD 1.6 billion in 2023, and is projected to grow to USD 21.1 billion by 2028, representing a remarkable compound annual growth rate of 67% during the forecast period [70]. Recent research [70] of industry trends within this market shows that this growth is being driven by increased demand for advanced technological solutions and the growing importance of DT technology in supporting various healthcare applications. Hence, it is essential to review all the recent advancements and factors associated with the use of DTs in the healthcare system.

This review paper aims to serve as a vital resource for researchers, practitioners, and decision-makers by gathering diverse perspectives on the definitions, advancements, stakeholders, challenges, and future prospects of DTs in healthcare. By offering a holistic understanding of this transformative technology, this paper aims to provide insights that not only contribute to current discourse on healthcare innovation but also guide future research, policy development, and strategic implementation in digital healthcare.

1.1 Organisation

In Section 2, we first review different **definitions** of the term "digital twin". Next, we identify a list of **stakeholders** in healthcare DT deployments and their respective needs in Section 3.

We then classify **applications** of DTs in healthcare into two main categories as shown in Fig. 1, and review recent advances in each. The *clinical and healthcare services* category, described in Section 4, relates primarily to the delivery of healthcare to individual patients, whereas the *hospital management* category, described in Section 5, relates primarily to the efficient use of hospital resources to maximise healthcare throughput. A summary of the identified applications is provided in Section 6.

Section 7 lists the **challenges** currently faced by healthcare DTs and describe existing and/or potential solutions for each. Finally, discussions and concluding remarks are provided in Section 8 and 9, respectively.

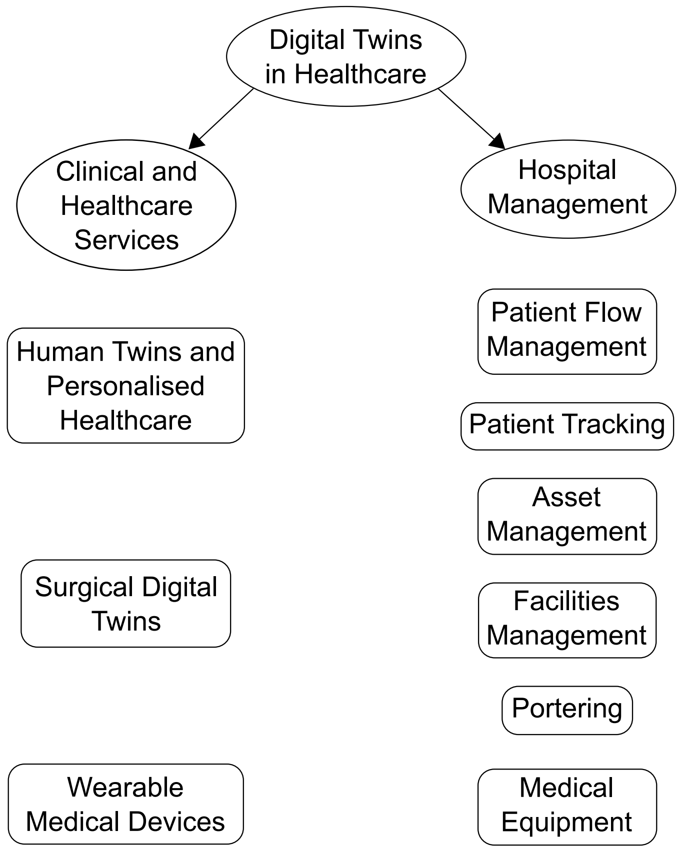

Fig. 1. Various applications of DTs in healthcare.

2 Definitions

White *et al.* [120] gave a very general definition of a DT: "A digital twin is a digital representation of a physical process, person, place, system or device." A similarly broad definition was given in [61]: "Digital twins are digital representations of things in the real world." From these two definitions, we can conclude that as virtual models, digital twins can be used to simulate, analyse, and optimise their real-world counterparts, enhancing understand and decision-making across various applications.

In contrast, Trauer *et al.* [110] added requirements on the relationship between the physical and digital systems:

> A Digital Twin is a virtual dynamic representation of a physical system, which is **connected** to it over the entire lifecycle for **bidirectional** data exchange.

In the above definition, bidirectional data exchange means that the DT can give feedback to the real system, which may include predictions of future state, control commands to directly alter the state of the real system, or suggestions for product or process-oriented improvements (to be reviewed by a human operator).

A more comprehensive list of DT definitions was compiled in [13]. Despite the extensiveness of this list, a few key terms were identified, including "virtual", "counterpart/replica", "simulation", and "prediction".

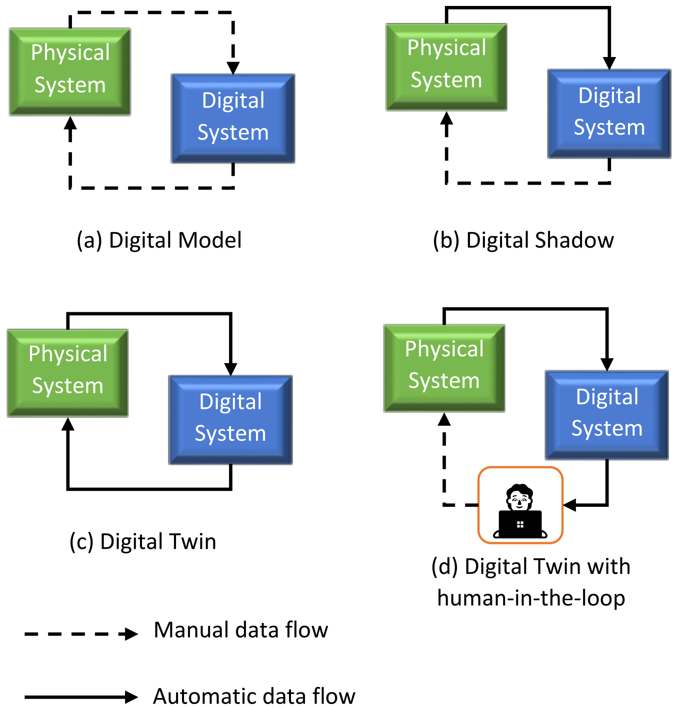

Fig. 2. Typology of physical-digital system pairs, adapted from [80].

2.1 Relationship between the physical and digital counterpart

Kritzinger *et al.* [60] define three separate terms according to the level of data integration between the physical and digital systems, as depicted in Fig. 2a–2c:

- In a *Digital Model* (DM), the physical and digital systems are separate and changes to one system have no direct effect on the other. Data of the physical system may be used to develop the digital system, and insights gained from the digital system may be used to improve the operation of the physical system; however, all data exchange between the systems is done manually. For example, a DM for surgical planning may be used to compare surgical approaches and analyse potential outcomes, thus providing insights to the surgeons and medical professionals involved in the surgery, but does not directly alter the state of the physical patient by itself. A major aspect of the digital system is the use of simulation to predict the future state of the physical system; for example, [129] provides a comprehensive review of discrete-event simulation in healthcare.
- In a *Digital Shadow* (DS), data flows automatically from the physical system to the digital system, but not vice versa. The primary purpose of DSs is simply to mimic/visualise the behaviour of the physical system. For example, a hospital patient may be connected to multiple sensors to monitor vital signs, with the information combined to form a DS of the patient, but any medical interventions are still decided upon and administered manually by medical staff.
- In a *DT*, automatic data flow is established in both directions, and the digital system might also act as a controller for the physical system. For example, a closed loop insulin delivery system, also known as an

artificial pancreas, continuously monitors a patient's glucose levels and adjusts insulin dosages accordingly, and can be thought of as a simple version of a medical DT. Data flow is established in both directions (glucose level as input to the digital system and ideal glucose flow rate as output back to the physical system), and the output is used to control the patient's glucose levels.

Additionally, [80] propose a fourth category as an evolution of DT which adds a human to the decision-making loop, as shown in Fig. 2d. The authors give three reasons for this:

(1) The digital system is necessarily a simplification of the physical system and thus may contain incorrect or missing events. Therefore, decisions made by the digital system may be incorrect and should be reviewed by a human operator first.
(2) The physical system must be maintained as the "master" system in the pair; adding a human-in-the-loop ensures this.
(3) A DT should be non-invasive: the human operators of the healthcare system should feel in control, with the digital system merely providing suggested actions. The human operators may choose to ignore a suggestion or implement an alternative course of action, upon which the digital system will update its state to reflect the actual state of the physical system.

Items 2 and 3 above are also reflected in the requirements stated in [110] that data "should only be transferred on demand." Additionally, Trauer *et al.* [110] also emphasise that the digital system need not be a full representation of the physical system: "only data required for the respective use case should be entailed." They also differentiate between "data" and "information": although the physical and digital systems both exchange data with each other, only the physical system generates information, which is then reflected in the digital space.

Notably, the distinction between a simple digital model and a DT, as defined by [60, 80], is not well-observed in some cases. Wright and Davidson [124] express concern that such vagueness may lead people to reject the concept of DTs as "just hype", limiting its final level of interest and use in the long run. This highlights the importance of a consistent typology of physical-digital system pairs such as that proposed in [80].

In summary, DTs can be used to capture and visualise a physical system's state, predict its future state, and suggest actions that impact upon the physical system, with or without automatic implementation, thus forming a critical role in healthcare management and delivery. Their continuous and automatic data flow allows them to cater to their users' unique and real-time needs and demands, thereby enhancing their effectiveness in healthcare applications.

3 Stakeholders in Healthcare DT Deployments

In the context of DT technology and its applications, stakeholders refer to individuals, groups, or entities that have a vested interest or role in the creation, operation, or outcomes of the DT system or project. In this section, we identify various stakeholders in healthcare DT deployments.

3.1 Healthcare administrators

As detailed in Section 5, healthcare administrators can use DTs for facilities and process management (e.g., maintaining inventory levels, setting staffing levels, identifying throughput bottlenecks, and predicting key performance metrics). Additionally, DT-driven improvements in healthcare can reduce patient lengths-of-stay, thus freeing up beds for additional patients, increasing revenue (in private healthcare systems), and reducing congestion/backlogs (especially in public healthcare systems). Improved healthcare efficiency may also reduce the need to hire additional staff, thus lowering operating expenditure. Finally, improved data management and networking systems can reduce communication barriers between hospitals and general practitioners (GPs).

3.2 Healthcare staff

DTs can be used by medical staff to pre-visualise certain medical procedures, assist in medical decision-making, and in some cases even perform certain medical tasks. For example, machines for robotic surgery can perform autonomous tissue manipulation, with the surgeon's role redefined primarily towards decision-making rather than physical tasks [99]. The featured system combined computer vision, machine learning, and simulation for validation of the machine learning framework.

In addition to advances in medical treatment, especially personalised treatment/surgery, and medical diagnosis, DTs also have the potential to change how patients are monitored and treated. For example, machine learning can be used to alert nursing staff to the unexpected deterioration of a patient's health or vitals, while reducing the number of false alarms caused by traditional patient monitoring systems [35, 36, 41]. This is useful for identifying patients at risk of septic shock, which requires urgent and timely intervention [48, 77]. On the other hand, increased automation in patient monitoring may lead to nursing staff being required to monitor an increased number of patients simultaneously; thus a balance must be found between staffing costs, staff burnout, and patient risk.

3.3 Citizens/Patients

In the envisioned future, all citizens will have their own personal full-body DTs. Benefits of personal DTs for healthcare include personalised treatment, rapid diagnoses, and personalised prediction of treatment outcomes (e.g., response to surgical interventions) [96]. One effort towards a whole-body DT implementation is the EDITH consortium [31].

However, the generation and consolidation of vast amounts of personal data generates concerns about security and privacy. For example, in additional to the theft of classical personal information such as phone numbers, email addresses, and physical addresses, health information collected for personalised treatment may be illegally sold to insurance providers, who may raise premiums based on the patient's predicted future health, or to potential employers, who may reject an applicant based on predicted future inability to work. Personal health data may also include information on spending habits, which may be sold to advertisers (e.g., whether/how often the individual smokes or drinks). In countries with both public and private healthcare, health data may be used by advertisers to sell the latter by targeting those on waiting lists for specific treatments at public hospitals. Therefore, to maintain trust between citizens and healthcare providers, rigorous privacy laws and enforcement mechanisms are required, creating a compliance challenge for healthcare administrators.

3.4 Pathology and radiology laboratories

As with hospital management, process DTs can be used to optimise operations and reduce costs in pathology [78] and radiology labs. Additionally, DT technologies can be use to assist in making diagnoses, reducing human error and effort. Finally, medical image databases can reduce the need for on-site slide/image storage as well as enabling remote diagnosis work. Medical images can also be quickly shared between different labs, allowing medical expertise to be more easily shared.

3.5 Pharmaceutical companies

As mentioned in Section 4.1, DTs of organ systems (or even the entire human body) can be used to study interactions between the human body and potential new drugs, thus reducing costs for research and development. For example, simulations can be conducted to select only the most promising drugs for clinical trials. Furthermore, personal DTs could potentially be used to customise drug treatments, e.g. cancer treatments, via genetic profiling of cancer cells.

3.6 Medical equipment manufacturers

In addition to the development and manufacture of pharmaceuticals, DTs also play a role in the design and manufacture of medical equipment. In the design plane, DTs are used to simulate and optimise the design of medical devices, allowing their performance and longevity to be predicted and optimised against device cost. DTs can also be used to tune such medical devices to individual patients to optimise diagnoses and treatments [63].

In the manufacturing plane, the design of a new assembly line can be first performed in the digital space, allowing the design to be optimised before being realised in the physical world. Process DTs can also be used to optimise the efficiency of existing manufacturing process chains. Finally, DTs can also be used to monitor the health of manufacturing equipment in order to conduct preventative maintenance, and to track inventory levels and the flow of parts through the assembly processes.

3.7 Software providers

With the "D" in DT standing for "digital", it follows that software development plays a crucial role in healthcare DT deployment. Therefore, software providers stand to receive significant amounts of revenue through the DTs that they deploy, as well as the provisioning of ongoing software support.

To increase adoption, software providers need to ensure interoperability with existing medical software, using standards such as Digital Imaging and Communications in Medicine (DICOM) [15, 38, 83] and Fast Healthcare Interoperability Resources (FHIR) [14]. They must also fulfil all obligations regarding data security and privacy, which may require significant expenditure for compliance experts. Any tightening of privacy laws may reduce the value of collected patient data, thus introducing risks to the implementation of commercial patient DT projects. Additionally, any security breaches may have major financial consequences, which may be passed on as penalties to the service provider; for example, the WannaCry ransomware attack was estimated to have caused £3.6 to 8.2 million in damages to the UK's NHS through lost admissions/A&E activity and cancelled appointments [39].

3.8 Insurance providers

Personal DTs could potentially be used by insurance providers to predict future illnesses and adjust insurance policies at the individual level, e.g., premium payments and payout structures. Naturally, this potential use of patient data is subject to limitations caused by patients' right to privacy; however, commercial healthcare providers may require certain privacy rights to be waived as part of their terms of service. This approach could motivate individuals to maintain a healthier lifestyle to reduce their insurance premiums, benefiting both the individual by encouraging better health and the insurance agency by reducing the risk they bear.

3.9 Public agencies

Government agencies are responsible for legal oversight of healthcare DT deployments, particularly in creating laws to protect data privacy. They are also a major source of funding research, and can also grant patents to protect the financial interests of commercial entities in healthcare DT development. Additionally, both government and non-governmental organisations can be tasked with setting industry standards, thus ensuring interoperability between DT implementations; examples include the National Institute of Standards and Technology (NIST) in the United States, the British Standards Institution, and the International Organization for Standardization (ISO) [50–52].

In India, The National Health Authority (NHA) is executing the Ayushman Bharat Digital Mission (ABDM), uniting diverse stakeholders within the healthcare ecosystem by utilising cutting-edge technologies like artificial intelligence, the Internet of Things, blockchain, and cloud computing. This mission ensures continuous care by creating and establishing a digital health infrastructure, which is linked to citizens through a unique health identification ID (UHID).

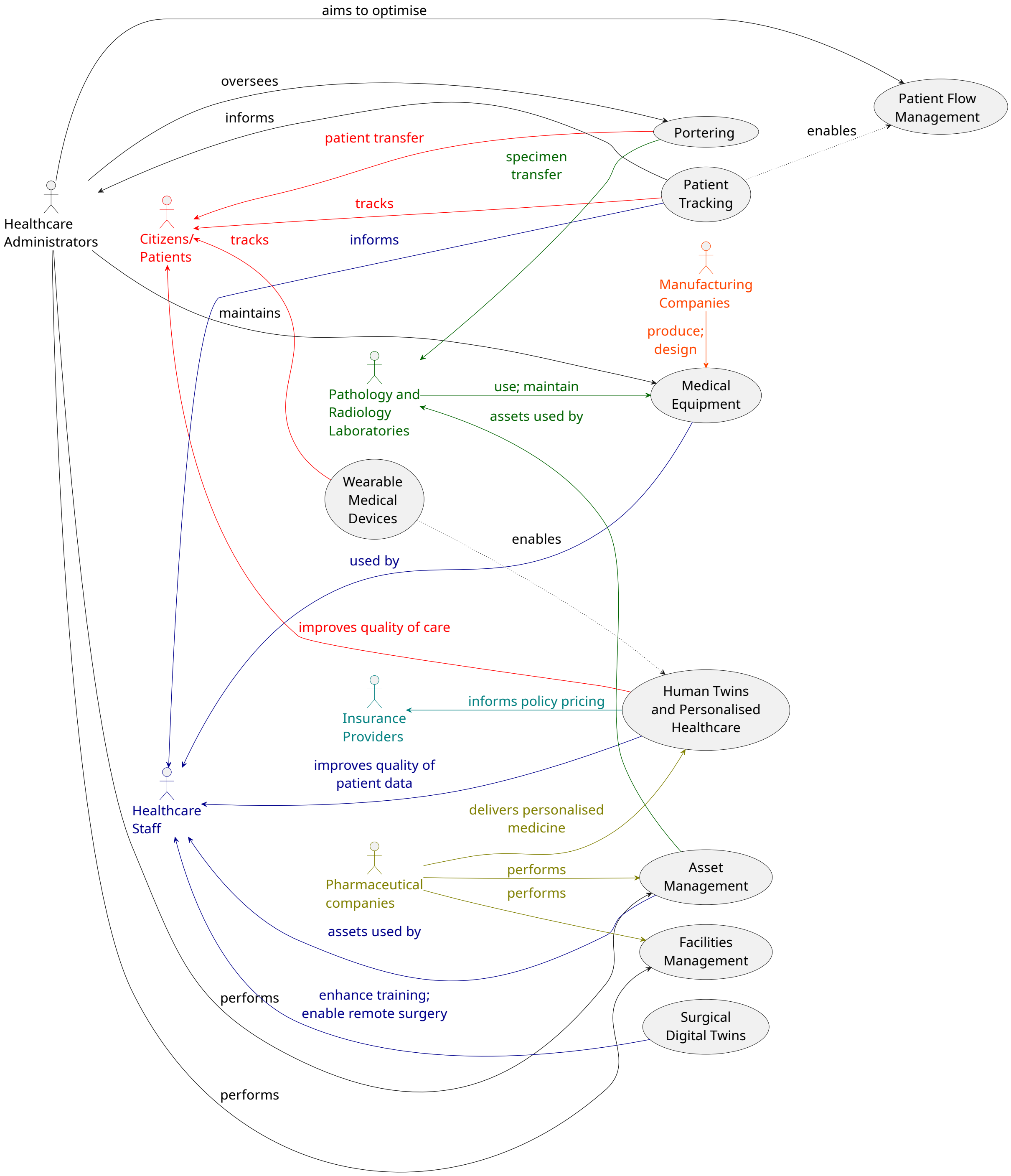

Fig. 3. Mapping of stakeholders to healthcare DT applications.

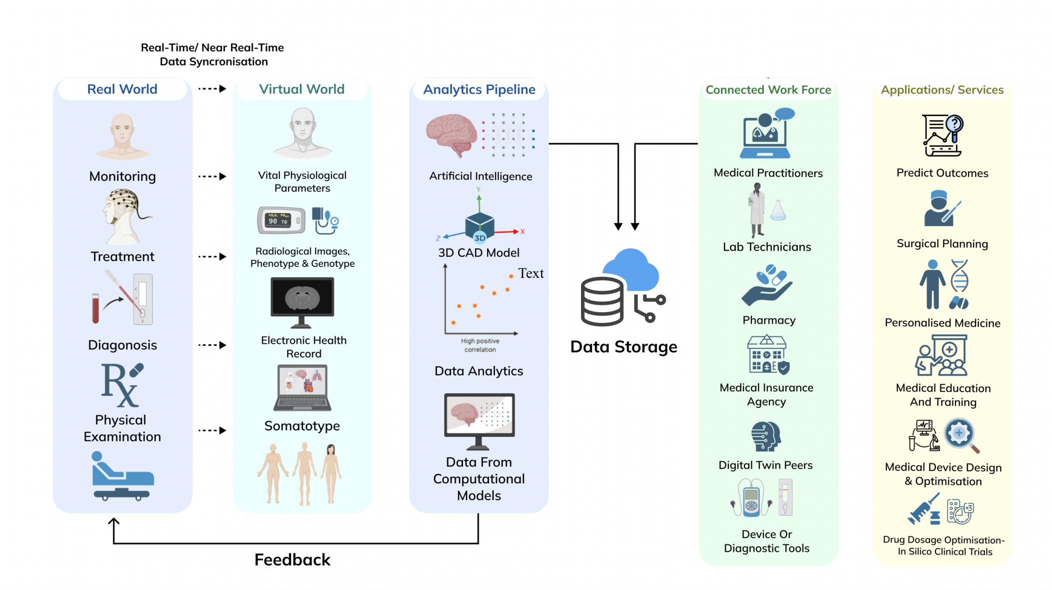

Fig. 4. Graphical depiction of a human DT, including its components, users, and applications/services provided.

3.10 Mapping of stakeholders to Healthcare DT applications

Figure 3 shows a mapping of stakeholders identified in this section to the applications of healthcare DTs as identified in Fig. 1. Several applications are shown to involve multiple stakeholders; additionally, some applications enable other applications, e.g., wearable medical devices are an important component towards the implementation of human twins and personalized healthcare. Note that software providers and public agencies are not shown in the graph, as their potential involvement includes all of the applications shown. The complex web of interactions between stakeholders and healthcare applications demonstrates why a holistic view of healthcare DTs is required to maximize their benefit.

4 DT Applications: Clinical and Healthcare Services

In this section, we summarise recent developments in DTs for clinical and healthcare services. With regard to Section 3 regarding healthcare DT stakeholders, this section focuses on applications where the patient is the primary stakeholder. However, healthcare administrators and staff can also benefit — improved diagnosis procedures mean that patients' medical problems can be detected quicker, earlier, and more accurately, and thus can, in combination with improved treatment methods, improve patient outcomes and reduce hospital stay times (therefore increasing throughput capacity and decreasing congestion).

4.1 Human twins and personalised healthcare

In the context of personalised healthcare, a DT refers to a virtual replica of a living (e.g., a human or part thereof) or non-living object (drugs, medical equipment), system (a hospital department), or process. They provide real-time insights and enable simulation for better understanding, prediction, and decision-making. In particular, human DTs encompass a wide range of scales, from the complete human body to individual organs, cells, sub-cellular components, and even molecular structures [18]. A "human twin" can thus be used to provide targeted and tailored treatments for specific illnesses or disorders, for example cancer, where no two cases are exactly the same [42]. They may also involve interactions with non-human elements, for example viruses, proteins, or pharmaceuticals. Furthermore, the concept of human twins has evolved from taking a gene-centric view to encompass patient lifestyle and biological data [108].

Figure 4 shows the components and features of a potential human DT. Data is collected from various real-world sources and used to build multiple representations in the virtual world, which are then processed by various data analytics pipelines. The processed data is then interpreted by various parties to deliver a number of applications or services.

4.1.1 *Oncology.*

- In 2019, a consortium of government, academic, and industrial partners formed the Envisioning Computational Innovations for Cancer Challenges (ECCIC) community, from which formed the idea of cancer patient digital twins [45] for predictive oncology. Another such consortium, based in Europe, is the PRIMAGE project [72], whose primary objective is to provide precise clinical assistance in the areas of diagnosis, treatment allocation, and patient endpoints (prognosis) for childhood cancers.
- Mourtzis *et al.* [79] proposed a human twin platform for cancer diagnosis (oncology) based on the Internet of Things (IoT), artificial intelligence (AI), and augmented reality (AR).
- Borau *et al.* [17] describe a multi-scale model for neuroblastoma spanning “nine orders of magnitude in space and time”, from molecular interactions at the microsecond level to overall tumor evolution over years.

4.1.2 *Cardiac/Cardiovascular.*

- An early effort to build a digital simulation model (albeit not a full DT) of the human heart was the Living Heart Project, which published such a model in 2014 [11].
- Jung *et al.* [55] developed a cardiac DT, focusing on the study of cardiac contraction and relaxation in patients with aortic coarctation (narrowing). The produced DT is highly detailed, focusing on the cellular scale.
- Gillette *et al.* [40] describe a cardiac DT model with a focus on the His-Purkinje system (HPS), which governs the conduction of electrical signals in the heart. They claim that this breakthrough is important due to two major factors hindering previous efforts to model the system: limited knowledge about the actual topology of the HPS and the computational cost of simulating such a spatially complex network.
- Chakshu *et al.* [21] use inverse analysis [19] to build a cardiovascular DT for estimating blood pressure waveforms in internal blood vessels, e.g. the aorta, based on readings from more accessible blood vessels. One application cited is the detection of abdominal aortic aneurysms.
- Another product for the fast and robust detection of abdominal aortic aneurysms is PRAEVAorta, by the French company Nurea [20].
- PrediSurge have developed a predictive simulation tool for the deployment of stent grafts in cases of aortic arch aneurysms, with close agreement reported between simulations and post-operative CT scans [27].
- Nova Heart is a collaboration between UK-based AIBODY and the German Heart Center at Charite (DHZC) to produce a cardiac DT for both clinical practice and medical instruction [105]. AIBODY has also published an full-human virtual model named Luke, with a focus on educational purposes.
- Volpato *et al.* [118] describe a automated, machine-learning-based software platform by Philips for determination of left ventricular mass, an important predictor of adverse cardiovascular events. The authors found the method to be fast and accurate, and a feasible addition into clinical practice.

Other reviews of digital twins in cardiology include [24, 25].

4.1.3 *Orthopaedics and Kinesiology.*

- He *et al.* [44] developed a system combining motion capture technology with biological models of the human spine for real-time biomechanic prediction. This system may be used to predict risk factors towards lumbar disc herniation and chronic lower back pain.
- Aubert *et al.* [9] used finite element analysis and 3D radiography to model treatments and estimate repeated fracture risks for tibial plateau (the knee end of the shinbone) fractures.
- Alsubai *et al.* [3] propose an IoT-based framework for analysing real-time health data during exercises, specifically the training and exercise sessions of athletes.

4.1.4 Neurological.

- The Blue Brain Project [71] is a long-running project since 2006 focused on constructing biologically detailed simulation models of the mouse brain. The project covers all scales from an atlas of the entire mouse brain [33] to the study of molecular processes at the neuron level [23]. Discussions on the suitability of mice brains as a human analogue have also been made [56].
- Gazerani [37] describes the use of DT for personalised migraine care, including the identification of migraine-associated biomarkers and lifestyle factors.

4.1.5 General/Other.

- A consortium of European partners, EDITH, aims to build a roadmap from human organ DTs to a full human *whole-body* DT, which they call a "virtual human twin" (VHT), with a target of September 2024. A first draft of this roadmap was published in July 2023 [31].
- Wei [119] lists ten characteristics of a potential human DT, and describes the differences between a human DT and other types of DTs. Among these are the high variety among human beings and the high level of interaction with the environment. Wei also describes a layer protocol for the implementation of a human DT, as well as a potential implementation approach.
- Laubenbacher *et al.* [65] describe a four-stage roadmap towards a DT of the immune system, which is further divided into eleven steps. The four stages can be summarised as application definition, personalisation, testing, and ongoing data collection and improvement. The roadmap is designed to tackle the major challenges of complexity in the human immune system and the difficulty of taking *in vivo* measurements.
- The Anatomage Virtual Dissection Table [2] is a software platform containing virtual human organs for medical and anatomical instruction. Comparisons against physical cadaverous dissection as a means of instruction shows comparable or favourable results for the Anatomage system [12].
- The CharakDT human DT platform, developed by IIT Indore and DRISHTI CPS Foundation (a Technology Innovation Hub of IIT Indore under the National Mission of Interdisciplinary Cyber Physical Systems), emphasises individual-centric and pathy-agnostic digital healthcare support, aiming to use technology to deliver personalised and preventive care. It focuses on predictive, preventive, and personalised healthcare by offering holistic modelling and the creation of individual, family, and community health profiles [62].

4.2 Surgical DTs

Various research has delved into the usage of DTs for pre-operative planning and surgical training [1, 28, 93, 98, 100]. Such DTs can also play a crucial role during the actual surgery by providing real-time guidance to surgeons, enhancing situational awareness and aiding in making informed surgical decisions. They thus form an advancement compared to static models constructed using preoperative data or teaching models that do not correspond to a real human. A key challenge for surgical DTs is the ability to model soft-body deformations in real-time [1]; however, multiple publications suggest that this challenge has been well-addressed in current surgical DTs. One application of surgical DTs is minimally invasive laparoscopic surgery, due to the increased complexities of such surgeries caused by limited access to and visibility of the surgical site [93].

- Shu *et al.* [100] present Twin-S, a digital twin for skull base surgery that can update its virtual model at 28 frames per second, with a mean error of 1.39mm.
- Shi *et al.* [98] show how a DT for minimally invasive liver surgery, with augmented reality (AR) for real-time navigation, can account for internal motion and deformation caused by respiration.
- Bonne *et al.* [16] show how a DT-based telesurgery framework can be made robust against network instability and delays. This allows surgeons to serve remote, sparsely populated, or otherwise inaccessible locations.

4.3 Wearable medical devices

Wearable medical devices allow for remote monitoring of patients (a "virtual ward" [68, 88, 117]), thus enabling some patients to be discharged from hospital that may otherwise take up valuable space, e.g. those will chronic diseases. They can also be used to build patient DTs for early diagnosis and preventive medicine.

- Hutchings *et al.* [49] describe the use of wearable temperature monitors for the remote management of COVID-19 patients in Australia. Each temperature monitoring patch lasted 72 hours and three were used for each patient's monitoring period. The automatic temperature recordings were supplemented with video consultations to visually assess patients and confirm vital sign readings.
- Chen *et al.* [22] describe "Wearable 2.0", with an emphasis on comfort and durability (wearable devices should be embedded into traditional clothing and be machine-washable). A supporting cloud platform is also described in the paper.

5 DT Applications: Hospital Management

In this section, we summarise recent developments in DTs for hospital management, i.e., applications where the primary stakeholders are hospital administrators. Other key stakeholders include specific hospital departments (e.g. pathology and radiology), hospital staff, and medical equipment manufacturers.

5.1 Patient flow management

- Karakra *et al.* [57] consider a simple fictional hospital department with emulated sensor data, and construct a series of models from a simple digital model to a full predictive DT with regular data updates from the emulator.
- England *et al.* [32] demonstrate a DT for short-term bed planning, with automatic daily updates from the physical system and a one-week forecast horizon. The model was applied to a Trauma & Orthopaedic department and shown to accurately predict admission numbers and occupancy within the one-week window. A similar predictive model is presented by [10] for Covid-19 bed occupancy. This is especially important due to the time delay involved in converting a regular ward to an isolation ward for Covid-19 patients, if extra capacity is required.
- Moyaux *et al.* [80] describe a "very first step" towards a full DT for an ED. The DT describes a simple ED with a single patient arrival stream, a triage nurse, a waiting room, several "boxes" for patient care, and an X-ray room. Patient attributes include a severity score from 1 to 5 (1 being the most severe); with path branching depending on whether the severity is 2 or less and whether an X-ray is required.
- Mater Private Hospital in Dublin, Ireland partnered with Siemens Healthineers to create a digital twin of its radiology operations, yielding a nearly half-hour reduction in patient waiting time and significantly reduced staff overtime costs [103].

5.2 Patient tracking, asset management, and facilities management

- Phua *et al.* [91] describe an NFC-based system for hospital discharge tracking and bed management. When a patient is due for discharge, they are given an NFC card to deposit in a box when they leave. An NFC reader in the box will detect the deposited card and automatically notify cleaning staff of a bed to be cleaned. In turn, a simple button press in a mobile app will notify the admission and ward staff that the bed is ready for the next patient. The NFC-based system was shown to reduce average bed turnaround time and admission wait time.
- Yoo *et al.* [126] demonstrated a locating system for mobile assets, using a combination of Bluetooth and WiFi and covering 400 medical instruments. Despite limitations, largely caused by battery life issues, survey data indicated that the asset tracking system was more helpful than manual management, with ICU staff more likely than emergency department staff to agree that the system provided up-to-date information.
- A ultra-wideband radio (UWB) based tracking system was trialled in [101], achieving an precision of 10cm or less. A major advantage of the UWB-system is that items do not need to be manually scanned. Although the trial was limited to a single hospital room, the authors plan to conduct a full-hospital trial in the next stage.
- Peng *et al.* [90] describe a hospital DT for building information modelling (BIM) and facilities management. Cited use cases include space management (i.e., monitoring/controlling room allocations), energy management, repair/maintenance scheduling and tracking, and AI-enhanced security.
- Another example of a DT for hospital facilitates management is given in [106], with listed applications including environmental monitoring (e.g., temperature, CO_2 concentration, and PM2.5), location tracking of patients and medical equipment, and fire and safety management.

Additionally, the following works focus on DTs for specific hospital departments and laboratories:

- Two robot dispensaries were described in [95, 115]. Although neither work used the term "digital twin", the combination of a robot dispensary with a real-time stock management system could be considered an example of a DT. Rodriguez-Gonzalez *et al.* [95] reported reduced dispensing error and stock-out rates and high staff satisfaction with the robotic system, with most remaining errors due to residual manual dispensing (due to limitations of the robotic system). The time required for stock management was also significantly reduced. However, one area in which staff showed a desire for improvement was the dispensing speed of the robotic system. Vekaria *et al.* [115] also reported longer overall dispensing times (although not significant) but improved accuracy.
- Mukherjee *et al.* [82] describe a roadmap towards building a hospital DT, with an initial focus on the histopathology lab at a regional hospital in the United Kingdom.
- Zhong *et al.* [130] present a DT model for an intensive care units, incorporating patient tracking, staff management, and asset/equipment management.

5.3 Portering

Within the context of a hospital, portering is the act of delivering materials, equipment, and patients between different departments and locations.

- Liu *et al.* [69] describe a logistics system with automated guided vehicles and robotic porters for the delivery of food, medication, and linens within a hospital.
- Law *et al.* [66] discuss the use of robot porters in hospitals, with focus on sample collection (blood and urine) and food delivery. Respondents from both sites said that the robots could be a good addition to their facilities.
- Lee *et al.* [67] add location monitoring to their robotic porter management system, thus approaching a *true* portering DT, unlike the previous two examples. In addition to providing a real-time tracking system,

porters' traces were collected for five months and analysed to find ways to improve the efficiency of the system.

5.4 Advances in medical equipment

- Phillips [114] describe how DTs for medical equipment can be used for device diagnostics, design and performance improvements, predictive maintenance, and optimised operations. In particular, predictive maintenance allows equipment maintenance to be scheduled at a time when the equipment is not in use, thus minimising disruption to service delivery. They also describe how DT technology can be used in for prototyping new products, reducing the time and number of physical iterations required. One use case cited was the development of a portable oxygen generator for patients with breathing problems.
- Ang *et al.* [7, 8] describe the development of a "virtual patient framework" for testing designs for mechanical ventilation, in which patient data needs to be continuously monitored to optimise pressure and flow settings.

6 Summary of Healthcare DT Applications

Based on our review of healthcare DTs in the preceding sections, we identify a number of applications of DT technology in healthcare systems, as listed below.

(1) **Enhanced patient care**: DTs are transforming personalised medicine and patient care by creating virtual human and organ replicas, enabling better prediction of patient outcomes and responses to various medical interventions (e.g., drug treatments or surgery) and allowing such treatments to be personalised for each individual patient. They have also led to new innovations in surgery by allowing surgeons to better visualise the body parts/organ systems being operated on. By simulating the results of medical procedures, patient risks can be reduced.

(2) **Research and development**: DTs have the potential to revolutionise clinical research by swiftly identifying research directions, virtually modelling trial participants, enhancing compliance, and expanding trial diversity through IoT and telemedicine integration. Patient-specific DTs continuously collect medical data, predicting future health issues with machine learning.
DTs also have the potential to transform the design and production of new medical equipment by virtually modelling manufacturing processes, enhancing product designs and eliminating inefficiencies. The virtual models can be used to predict the lifetime of manufactured components as well as identifying the most likely failure modes.

(3) **Medical training**: Human DTs will allow medical trainees to practice medical procedures on a virtual body, allowing greater opportunities for hands-on experience and a potentially higher level of realism compared to practising on cadavers. Simulation designers can also emulate medical emergencies to enhance the training experience. Artificially generated medical images and other patient data can be used for medical diagnosis training.

(4) **Risk identification**: At the personal level, DTs use patient data, machine learning, and early health indicators to assess risks, guide healthy behaviours, and design preventive programs. At the hospital level, DTs consolidate data from various sources to forecast bed demand, which is vital for enhanced patient care amid workforce challenges and rising healthcare demand.

(5) **Personalised insurance**: By utilising human DTs, individuals can access customised and cost-effective medical insurance. Healthy individuals with low-risk lifestyles may be offered cheaper insurance policies compared to generic plans, based on a predicted lower risk of future disease or injury.

(6) **Enhanced inventory management**: DTs can be used to track stock levels in pharmacies, as well as general inventory management in hospitals and laboratories. Spare inventory targets can be adjusted

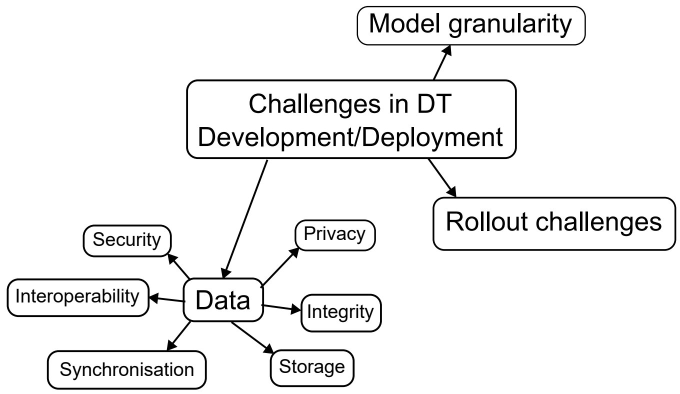

Fig. 5. A categorization of challenges in Healthcare DT Development/Deployment.

according to seasonal changes in demand. This proactive approach helps prevent shortages of essential medicines and medical kits during emergency situations.

7 Challenges in Healthcare DT Development/Deployment

In this section, we examine a number of challenges in healthcare DT development/deployment as well as existing and potential solutions for each. A summary of challenges considered in this section is provided in Fig. 5.

7.1 Data security and privacy

As healthcare data can have high value, it is important to prevent its unauthorised access/use. The WannaCry ransomware attack of May 2017 is a strong example demonstrating the importance of data security in healthcare. In the United Kingdom, 34 NHS trusts were infected, becoming locked out of their digital systems and medical devices, whereas 46 other trusts reported disruption due to either preventative action or additional overflow demand from the infected organisations [39]. Disruption continued over the next week [39]. Moreover, it was found that the reason why the attack was possible was due to unpatched versions of Microsoft Windows — while a patch for the exploit was made freely available for newer versions of Windows, the NHS would have had to pay for extended support for machines still running Windows XP, and funding for this was terminated in 2015 by then-Secretary of Health Jeremy Hunt [75].

Lack of funding was also listed as a major challenge towards healthcare data security in [53], especially for rural hospitals. Outsourcing was listed as a solution [75], but it was noted that while enabling hospitals to do more with less, outsourcing also led to a sense of complacency as the responsibility for cybersecurity was "offloaded" to someone else. Research institutions using healthcare data obtained from hospitals are also a target for cyberattacks: in 2023, one such attack led to the leaking of over a million NHS patients' details [109].

Closely related to the issue of data security is that of privacy: to prevent unauthorised access to healthcare data, one must first define what are the appropriate use cases for the data in the first place. The United Kingdom's National Data Guardian defines eight Caldicott Principles, named after the late Dame Fiona Caldicott [84]:

(1) Justify the purpose(s) for using confidential information.
(2) Use confidential information only when it is necessary.
(3) Use the minimum necessary confidential information.
(4) Access to confidential information should be on a strict need-to-know basis.
(5) Everyone with access to confidential information should be aware of their responsibilities.

(6) Comply with the law.
(7) The duty to share information for individual care is as important as the duty to protect patient confidentiality.
(8) Inform patients and service users about how their confidential information is used.

Technologies for data security include cryptography and biometrics [104]. However, one major factor in data security and privacy is the human factor, i.e., the unauthorised sharing of data in its unencrypted form by individuals with access [104]. Therefore, regular staff training is required to imprint the importance of proper security and privacy practices (while also balancing the risk of training fatigue if training is conducted too often).

7.2 Data integrity

Whereas data security and privacy relate to the accessibility of data, data integrity relates to its trustworthiness, e.g., ensuring that data originates from its claimed source and has not been tampered with. The importance of data integrity has increased in recent years due to the emergence of generative AI, making it easier for data to be faked. Faked health data may be used to obtain cheaper medical insurance, or to cause harm to others (by hiding medical conditions requiring treatment or suggesting the need for medical interventions that would otherwise not be recommended).

Technologies to protect data integrity include digital signatures, digital watermarking, and blockchain [104]. Digital signatures are used to authenticate the identity of a data item's creator; for example, the Pretty Good Privacy (PGP) protocol provides digital signing as well as encryption. Digital watermarking uses steganography to hide additional metadata within an image, e.g. a digital signature, while minimising its effects on visual quality, and can be used to prevent image tampering or the generation of fake medical images. Finally, blockchain is a technology for implementing an *append-only* distributed ledger, i.e., a dataset with embedded and immutable history, such that all changes to the data are permanently recorded within the chain. However, blockchain is subject to concerns over high energy consumption, and is generally not needed in many use cases. The National Institute of Standards and Technology (NIST) has published Fig. 6 to highlight alternatives to blockchain [125], e.g., a centrally managed encrypted database.

7.3 Big-data-related challenges

With medical data in the U.S. expected to reach the yottabyte (1000^8 bytes) scale [34], new solutions are required for the storage and analysis of this data. In the literature, aspects of big data have been traditionally catalogued as a set of V's: for example, the initial 3V taxonomy included *volume*, *velocity*, and *variety*, whereas newer taxonomies typically include additional V's. An example 7V taxonomy [112] is shown in Table 1.

7.3.1 Data storage.

In addition to the challenges of data security, privacy, and integrity as described in the previous subsections, data storage itself is a major challenge for big data. A likely solution for this will be to rent storage capacity from a third-party provider, such as AWS, Google Cloud, or Azure. Two main options for healthcare providers are **(a)** Software as a Service (SaaS), where the cloud provider provides a software interface to the underlying hardware, e.g. a database management system, and **(b)** Infrastructure as a Service (IaaS), where the cloud provider provides direct access to storage and compute resources. Regardless of the type of service provided, using external service providers means that hospitals can outsource the problems of scalability and data security to specialised experts.

Since generally only the most recent data will need to be accessed frequently, data storage providers will need to use different storage technologies to optimise the trade-off between storage costs and data latency. Such technologies include solid-state storage, magnetic disc storage, magnetic tape storage, optical disc storage, holographic data storage [6], and DNA-based storage [29]. Other concerns that data storage providers must consider include energy consumption [58, 74], datacenter cooling [128], data redundancy and loss protection, equipment procurement, maintenance and replacement, networking capacity management, and load balancing.

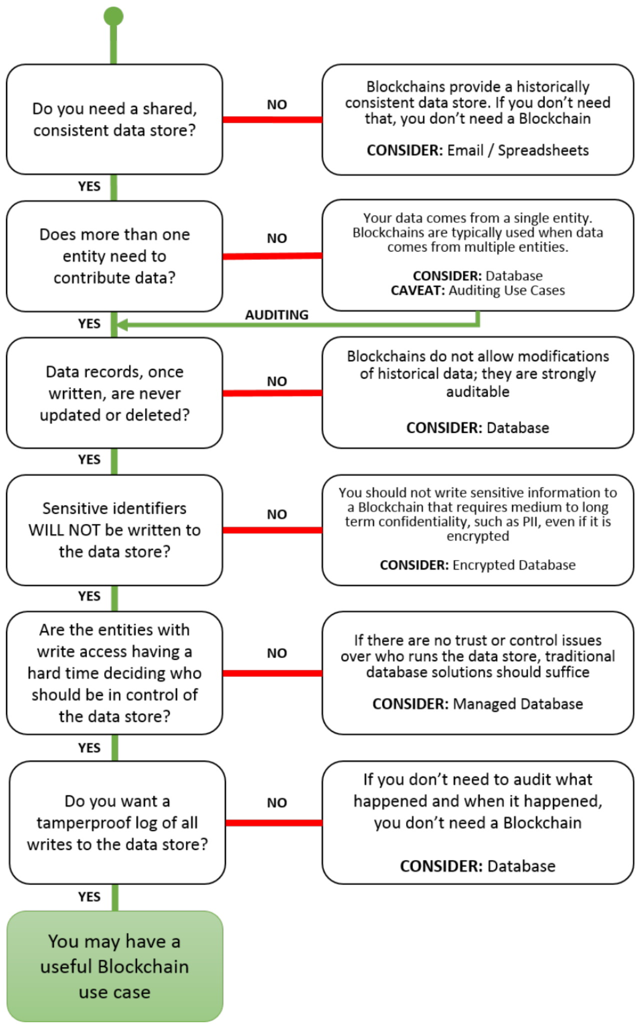

Fig. 6. NIST flowchart on blockchain suitability and alternatives [125].

7.3.2 Data analytics. The large amount of data generated by healthcare systems will require novel big data analytics tools to maximise the generated value of this data. One proposed solution is using edge or fog computing [64] to filter out unimportant data, thus reducing the storage and communication bandwidth requirements of the network. For example, a location tracker might only send an update to the central server when a change in location is detected, rather than providing periodic location updates. Edge and fog computing has also been proposed as a solution for fall detection, for example in hospitals and residential care homes [81, 92].

Another aspect of the big-data challenge is that a large portion of medical data, especially clinician notes, is unstructured. Natural language processing is a machine learning tool that may help to identify patterns in clinical diagnoses [59]. However, such tools are known to posses a number of problems such as amplification of existing

Table 1. A 7V taxonomy of big data attributes [112]

V	Definition
Volume	The size of the data, e.g. in petabytes or exabytes.
Velocity	The frequency at which new data is generated; the speed of the feedback loop from data input to decision (stale data leads to improper decisions).
Variety	The many formats in which data can appear, including unstructured data.
Veracity	The reliability (truthfulness) of the data.
Validity	The correctness of accuracy of the data with respect to its intended use.
Volatility	Data can be invalidated by new data or by natural expiry after a given timeframe.
Value	The desired outcome of big data processing.

biases in the training data and lack of explainability with respect to decisions made by the model. Furthermore, the data entry and validation required to train a such machine learning algorithm can be substantial [85].

7.4 Data synchronisation

As a DT contains both a physical and virtual component, frequent data synchronisation is required to maintain high fidelity between the two. Additionally, where the virtual component is used for prospective/predictive purposes, it is necessary to be able to restart a model simulation from the newly input state. This can be done using the following series of steps:

1. Serialise the physical system state into a machine-readable format, e.g. JSON, YAML, or BSON (binary JSON).
2. Update the state of each entity in the virtual system based on the serialised state.
3. Recompute the current resource usage based on the entity states.
4. Recompute the estimated remaining time of each entity in their current state.
5. Continue simulation of the virtual system based on the updated system state.

7.4.1 Survival functions. In particular, Step 4 above requires an estimate of the survival function of a particular process' duration, namely the probability $S(x)$ that a task will take at least x time units. From there, a *conditional* survival function $S(x+t;t) = S(x+t)/S(t)$ can be defined as the probability that a task will take at least x additional units of time, given that t time units have already elapsed. The remaining times of simulation entities in a given state can then be sampled using these conditional survival functions.

Note that for exponentially distributed task durations, $S(x+t;t) = S(x)$; analytical methods for computing $S(x)$ also exist for the Gamma and Weibull distributions [102]. However, in other cases, empirical methods may be required to estimate $S(x)$.

7.4.2 Real-time computing. In certain cases, a DT may be used to control the physical system in real-time. In such cases, *real-time computing* techniques are required to ensure timeliness of responses. Martin [73] defines a real-time computer system as "one which controls an environment by receiving data, processing them, and returning the results sufficiently quickly to affect the environment at that time." Note that, when evaluating the value produced by a real-time system, the value of a late result is often *zero*; for example, prediction of the future state of a DT is useless if the moment in time to be predicted has already occurred. Real-time computing thus generally requires that certain operations are completed in a fixed number of computer clock cycles — this involves not only CPU computation but also the management of memory access and network delays. One method proposed for reducing latency in healthcare systems is edge computing [64, 116], which moves computation and data storage in a networked system as close to the sources of data as possible.

7.5 Data interoperability

One major challenge when different medical institutions work together is data interoperability. For example, hospitals and general practitioners may need to share patient data, and hospitals may outsource certain services (e.g., pathology) to other hospitals in the region or to external consultants. On the other hand, recent surveys on interoperability in the UK medical system (the NHS) revealed that less than a quarter of surveyed NHS Trusts share care records digitally with non-primary care providers, and a third of Trusts could not digitally access outside patient data [127]. Even within a single hospital, there may exist a variety of software systems that need to communicate with each other, often with incompatible data formats. According to Sullivan [107], the average hospital runs 16 distinct electronic health records platforms! This results in the need for data to be duplicated across systems and introduces many vectors through which errors can be introduced. For example:

- Many medical service requests (e.g., pathology) still rely on paper forms [122]. This means that digital data often needs to be re-entered manually when transferred between systems. This is a waste of time for the staff tasked with re-entering the data, and errors can be introduced at this step. Additionally, the transfer of paper forms was noted during the Covid-19 pandemic to be a possible infection risk [122].
- Paper forms can also be lost. This is particularly problematic if the recipient of the data does not typically acknowledge receipt of the data immediately, as relevant processes cannot proceed until the data loss is detected.
- Dates may be corrupted, for example if a date in DD/MM/YYYY format is interpreted using the MM/DD/YYYY format or vice versa. This can often occur when data is copied as plaintext rather than using an internal representation, e.g. Unix timestamps. However, standardised plaintext formats such as ISO 8601 can prevent such issues while remaining human-readable.
- Units may be confused, which may lead to incorrect dosages of medication.

To avoid the above problems, data transfer between systems should be paperless and fully automated, with a common data format understood by all systems. Health Level 7 is a set of international standards for the transfer of clinical and administrative data between systems. In particular, the Fast Healthcare Interoperability Resources (FHIR) standard defines a RESTful (REpresentational State Transfer) interface for the exchange of medical information [14]. Within the UK NHS, examples of services with FHIR APIs include the Personal Demographics Service [86] and the Summary Care Record [87].

7.6 Model granularity

A major challenge in DT construction is achieving a high enough level of detail to adequately represent the real system. For example, an analysis of a patient's journey through the Majors unit in an emergency department in a UK hospital revealed 73 different processes and ten different roles [5]. At this level of detail, a process model of an entire emergency department is likely to be overly complex, requiring large amounts of human resources to develop and maintain. This issue is magnified when constructing models of even greater scale such as an entire hospital, a regional network of hospitals, or even a national healthcare network. To avoid this, *multi-scale models* are required, such that at larger scales, finer details of the model are abstracted away and replaced with simplified versions. Multi-scale models are even more important for human DTs. For example, [17] describe a model for neuroblastoma (a form of cancer) spanning "nine orders of magnitude in space and time", from molecular interactions to metastasis (the migration of cancer cells within the human body).

Table 2. Free and/or open-source software for information systems

Application	Example software tools
Database management	MySQL, PostgreSQL, Redis, Citus
Electronic health record	GNU Health, OpenEMR [97]
DICOM/PACS server	Orthanc [54]
Database visualisation and design	MySQL Workbench, DBeaver, Visual Paradigm Community Edition
Data processing	tidyverse [121], pandas
Data visualisation	tidyverse (ggplot2), matplotlib, seaborn, Plotly [26]
Dashboarding	Dash [26], Genie [89]
Discrete event simulation	simpy, salabim [113], simmer [111], JaamSim, Warteschlangensimulator [47]

For more detailed models, or finer levels of a multi-scale model, one major challenge may be the lack of available data. For example, for process simulations, not only may timestamps for various steps in the process be unavailable, but the steps in the process may themselves be poorly defined. In the context of emergency department modelling, [30] provide an algorithm for estimating missing patient timestamps (i.e., *imputation*) and correcting errors due to delayed or duplicate timestamp entry. They also demonstrate a method for extracting patient trajectories from this corrected list of patient activities.

7.6.1 Enhancement of monitoring and information systems. In addition to data imputation, additional monitoring systems can be installed to increase the amount of data available for digital twinning of a system. However, this poses a challenge due to tight financial constraints in many hospital systems. To reduce costs, one can borrow the "Shoestring" approach from digital manufacturing [43], which is based on the assembly of low-cost, off-the-shelf components and software to meet companies and organisations' digital needs [76]. For example:

- Edge computing can be provided using low-cost single-board microcontroller kits such as Arduino or Raspberry Pi.
- Seeed Studio produces the Grove series of low-cost sensors, compatible with both Arduino or Raspberry Pi micro-controllers.
- Open-source software can be used for various aspects of the information system as shown in Table 2. The use of free and/or open-source software prevents vendor lock-in, e.g., due to proprietary file formats or communications protocols. However, some free software may have limited functionality compared to the commercial edition of the same product.

7.7 Roll-out challenges

The rollout of a new hospital information system, such as one used by a DT, can be disruptive. This is especially true for 'big-bang' rollouts, in which the new system goes live all at once rather than in stages. For example, when the Electronic Medical Record (EMR) software Epic went live at Cambridge University Hospitals (CUH) on 26

October 2014, a number of problems immediately occurred [46], culminating in a 20 percent drop in emergency department performance, large productivity decreases in outpatient clinics, and the eventual resignation of CUH's executive director. Similar problems were reported in a Danish case [46], with rushed deadlines set by Epic cited as a factor:

- When the designated clinician team failed to make configuration decisions in time, Epic would forge ahead with a 'default' functionality instead.
- When the completion of training materials was delayed, the training schedule was compressed rather than pushing back the go-live date.
- Reconfiguration of the Epic system continued during training, causing such training to immediately become obsolete. Only one of 149 survey respondents felt comfortable using Epic one month after go-live, compared to a target of 80 percent.

Most of the problems associated with Epic's initial rollout at CUH have been resolved, and CUH has now reached EMRAM (Electronic Medical Record Adoption Model) Stage 6 [46]. However, the initial rollout problems experienced by CUH and others may discourage new hospitals from launching similar digitalisation projects.

8 Discussion

DTs have emerged as a transformative force within the healthcare sector, poised to revolutionise various facets of the industry. Advancements in DT technology, complemented by progress in IoT and sensor technology, big data analytics, and artificial intelligence, have led to a surge in the diversity and number of DT applications. For example, healthcare management DTs play a pivotal role in optimising operations, encompassing tasks such as patient monitoring and flow management in emergency departments, operating theatres, and wards, process and inventory management in pharmacies and laboratories, and overall facilities management in healthcare buildings. Such optimisations offer the potential to streamline healthcare services, enhance resource allocation, and reduce patient waiting times, benefiting both patients and healthcare professionals. DT technologies may also lead to improved automation opportunities, such as drug dispensing at pharmacies and portering in hospitals.

Moreover, DTs facilitate personalised healthcare via the construction of human DTs, with treatments, interventions, and even drugs specifically tailored to each individual for improved patient outcomes. They also allow better visualisation of the human interior, with potential benefits in laparoscopy, thus minimising the invasiveness of surgical procedures. Multi-scale DTs can even model the human body at different scales from the entire human to molecular level, with potential applications in drug development — researchers can predict both how drugs interact with individual cells and their effect on the human body as a whole. Another application of human DTs is to provide simulated training environments for surgical trainees, reducing patient risk during real surgical procedures by improving training effectiveness.

Finally, improved sensing technology, such as wearable medical sensors, will lead to advancements in remote medicine, where patients will chronic illnesses can be monitored and possibly even treated at home. This will reduce the demand for scarce hospital space, reducing congestion in hospitals and care homes and improving patient outcomes.

9 Conclusion

In this survey, we first examined various existing **definitions** of a DT. In particular, we emphasise automatic bidirectional data exchange as a property of full DTs, as opposed to digital models and digital shadows where such data flows may be missing or manually triggered. Next, we examined various existing **applications** of DTs in healthcare, based on the two main categories of hospital management and healthcare services. Next, we identified a list of **stakeholders** in healthcare DT deployments, as well as their roles and interests in DT creation, operation, and outcomes. Finally, we examined a number of **challenges** in healthcare DT development and deployment, as well as existing and potential solutions for each.

Many of the challenges mentioned in this paper for hospital DTs are related to complexity and scale. To extract maximum value, hospital activities and assets need to be modelled with high fidelity and fine granularity, generally requiring additional data collection, which may add to a hospital's operating costs. Furthermore, the interactions between large numbers of hospital systems require data interoperability and big data solutions to combine multiple subsystem DTs into a hospital-wide DT. Additionally, the scale required for a full-hospital DT can pose major rollout challenges.

Integrating various digital healthcare solutions from academia and industry is essential for creating a holistic DT-based healthcare system. This can be achieved by incorporating diverse technology elements contributed by multiple developers, thereby enhancing the system's capabilities through a range of integrated solutions. Ensuring interoperability of these solutions and devices is crucial for seamless functionality. For a sustainable DT-based system, it is vital to connect technology developers with hospitals and data sources for validation, while also linking hospitals and practitioners to the available technology. This not only ensures the commercial viability of the system but also fosters a collaborative ecosystem. The focus on predictive, preventive, and personalised healthcare is central to this approach, involving holistic modelling and the creation of health profiles at individual, family, and community levels. This comprehensive integration will drive advancements in personalised care and improve overall healthcare outcomes.

Although technical solutions are described or proposed for most of the challenges mentioned in this paper, one challenge that remains is that of funding. As shown by the WannaCry cyberattack example [39] (which was caused by a security flaw patched in later versions of Microsoft Windows but not Windows XP), digital security is often a victim of lack of funding, with potentially major consequences. While "Shoestring" solutions can help to reduce costs in other areas, ensuring digital security requires solution providers to prioritise it, even if this limits the value that can be extracted from the data. While outsourcing digital security to third-party experts can reduce cost and reduce the risk of poor security implementations, healthcare providers should still be responsible for ensuring that the services rendered meet all security and privacy requirements. Additionally, when selecting Shoestring solutions, healthcare providers need to balance the cost benefits of open-source software versus the benefits of commercial software with paid ongoing vendor support and the possibility of feature customisation to best suit the healthcare provider's needs (while open-source software, by their very nature, can also be customised, most healthcare providers will lack the necessary expertise to do so).

Acknowledgments

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References

[1] Hanad Ahmed and Laurence Devoto. 2020. The Potential of a Digital Twin in Surgery. *Surgical Innovation* 28, 4 (Dec. 2020), 509–510. https://doi.org/10.1177/1553350620975896

[2] Melanie A. Allen, Niki Kirkpatrick, and Elizabeth R. Agosto. 2019. Anatomage Table 6. *Journal of Electronic Resources in Medical Libraries* 16, 2 (April 2019), 59–66. https://doi.org/10.1080/15424065.2019.1638866

[3] Shtwai Alsubai, Mohemmed Sha, Abdullah Alqahtani, and Munish Bhatia. 2023. Hybrid IoT-Edge-Cloud Computing-based Athlete Healthcare Framework: Digital Twin Initiative. *Mobile Networks and Applications* (Aug. 2023), 20 pages. https://doi.org/10.1007/s11036-023-02200-z

[4] Altair. 2022. *2022 Digital Twin Global Survey Report.* Technical Report. Altair Engineering Inc. https://altair.com/docs/default-source/pdfs/altair_dt-global-survey-report_web.pdf

[5] Marian Amissah and Sudakshina Lahiri. 2022. Modelling Granular Process Flow Information to Reduce Bottlenecks in the Emergency Department. *Healthcare* 10, 5 (May 2022), 942. https://doi.org/10.3390/healthcare10050942

[6] Ken Anderson, Mark Ayres, Fred Askham, and Brad Sissom. 2014. Holographic data storage: science fiction or science fact?. In *Optical Data Storage 2014*, Ryuichi Katayama and Thomas D. Milster (Eds.). SPIE, San Diego, 8 pages. https://doi.org/10.1117/12.2061402

[7] Christopher Yew Shuen Ang, Yeong Shiong Chiew, Xin Wang, Ean Hin Ooi, Mohd Basri Mat Nor, Matthew E. Cove, and J. Geoffrey Chase. 2023. Virtual patient with temporal evolution for mechanical ventilation trial studies: A stochastic model approach. *Computer Methods and Programs in Biomedicine* 240 (Oct. 2023), 107728. https://doi.org/10.1016/j.cmpb.2023.107728

[8] Christopher Yew Shuen Ang, Jay Wing Wai Lee, Yeong Shiong Chiew, Xin Wang, Chee Pin Tan, Matthew E Cove, Mohd Basri Mat Nor, Cong Zhou, Thomas Desaive, and J. Geoffrey Chase. 2022. Virtual patient framework for the testing of mechanical ventilation airway pressure and flow settings protocol. *Computer Methods and Programs in Biomedicine* 226 (Nov. 2022), 107146. https://doi.org/10.1016/j.cmpb.2022.107146

[9] Kévin Aubert, Arnaud Germaneau, Michel Rochette, Wenfeng Ye, Mathieu Severyns, Maxime Billot, Philippe Rigoard, and Tanguy Vendeuvre. 2021. Development of Digital Twins to Optimize Trauma Surgery and Postoperative Management. A Case Study Focusing on Tibial Plateau Fracture. *Frontiers in Bioengineering and Biotechnology* 9, Article 920102 (Oct. 2021), 11 pages. https://doi.org/10.3389/fbioe.2021.722275

[10] Stef Baas, Sander Dijkstra, Aleida Braaksma, Plom van Rooij, Fieke J. Snijders, Lars Tiemessen, and Richard J. Boucherie. 2021. Real-time forecasting of COVID-19 bed occupancy in wards and Intensive Care Units. *Health Care Management Science* 24, 2 (June 2021), 402–419. https://doi.org/10.1007/s10729-021-09553-5

[11] Brian Baillargeon, Nuno Rebelo, David D. Fox, Robert L. Taylor, and Ellen Kuhl. 2014. The Living Heart Project: A robust and integrative simulator for human heart function. *European Journal of Mechanics - A/Solids* 48 (Nov. 2014), 38–47. https://doi.org/10.1016/j.euromechsol.2014.04.001

[12] Guy Baratz, Amy L. Wilson-Delfosse, Bryan M. Singelyn, Kevin C. Allan, Gabrielle E. Rieth, Rubina Ratnaparkhi, Brenden P. Jenks, Caitlin Carlton, Barbara K. Freeman, and Susanne Wish-Baratz. 2019. Evaluating the Anatomage Table Compared to Cadaveric Dissection as a Learning Modality for Gross Anatomy. *Medical Science Educator* 29, 2 (March 2019), 499–506. https://doi.org/10.1007/s40670-019-00719-z

[13] Barbara Rita Barricelli, Elena Casiraghi, and Daniela Fogli. 2019. A Survey on Digital Twin: Definitions, Characteristics, Applications, and Design Implications. *IEEE Access* 7 (Nov. 2019), 167653–167671. https://doi.org/10.1109/access.2019.2953499

[14] Duane Bender and Kamran Sartipi. 2013. HL7 FHIR: An Agile and RESTful approach to healthcare information exchange. In *Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems*. IEEE, Porto, Portugal, 6 pages. https://doi.org/10.1109/cbms.2013.6627810

[15] W. D. Bidgood, S. C. Horii, F. W. Prior, and D. E. Van Syckle. 1997. Understanding and Using DICOM, the Data Interchange Standard for Biomedical Imaging. *Journal of the American Medical Informatics Association* 4, 3 (May 1997), 199–212. https://doi.org/10.1136/jamia.1997.0040199

[16] Sophea Bonne, Will Panitch, Karthik Dharmarajan, Kishore Srinivas, Jerri-Lynn Kincade, Thomas Low, Bruce Knoth, Cregg Cowan, Danyal Fer, Brijen Thananjeyan, Justin Kerr, Jeffrey Ichnowski, and Ken Goldberg. 2022. A Digital Twin Framework for Telesurgery in the Presence of Varying Network Quality of Service. In *2022 IEEE 18th International Conference on Automation Science and Engineering (CASE)*. IEEE, Mexico City, 8 pages. https://doi.org/10.1109/case49997.2022.9926585

[17] C. Borau, K.Y. Wertheim, S. Hervas-Raluy, D. Sainz-DeMena, D. Walker, R. Chisholm, P. Richmond, V. Varella, M. Viceconti, A. Montero, E. Gregori-Puigjané, J. Mestres, M. Kasztelnik, and J.M. García-Aznar. 2023. A multiscale orchestrated computational framework to reveal emergent phenomena in neuroblastoma. *Computer Methods and Programs in Biomedicine* 241 (Nov. 2023), 107742. https://doi.org/10.1016/j.cmpb.2023.107742

[18] Maged N. Kamel Boulos and Peng Zhang. 2021. Digital Twins: From Personalised Medicine to Precision Public Health. *Journal of Personalized Medicine* 11, 8 (July 2021), 745. https://doi.org/10.3390/jpm11080745

[19] Vladimir Buljak. 2011. Inverse Analysis: Introduction. In *Computational Fluid and Solid Mechanics*. Springer Berlin Heidelberg, Berlin, Chapter 1, 1–18. https://doi.org/10.1007/978-3-642-22703-5_1

[20] Caroline Caradu, Anna-Louise Pouncey, Emilie Lakhlifi, Céline Brunet, Xavier Bérard, and Eric Ducasse. 2022. Fully automatic volume segmentation using deep learning approaches to assess aneurysmal sac evolution after infrarenal endovascular aortic repair. *Journal of Vascular Surgery* 76, 3 (Sept. 2022), 620–630.e3. https://doi.org/10.1016/j.jvs.2022.03.891

[21] Neeraj Kavan Chakshu, Igor Sazonov, and Perumal Nithiarasu. 2020. Towards enabling a cardiovascular digital twin for human systemic circulation using inverse analysis. *Biomechanics and Modeling in Mechanobiology* 20, 2 (Oct. 2020), 449–465. https://doi.org/10.1007/s10237-020-01393-6

[22] Min Chen, Yujun Ma, Yong Li, Di Wu, Yin Zhang, and Chan-Hyun Youn. 2017. Wearable 2.0: Enabling Human-Cloud Integration in Next Generation Healthcare Systems. *IEEE Communications Magazine* 55, 1 (Jan. 2017), 54–61. https://doi.org/10.1109/mcom.2017.1600410cm

[23] Weiliang Chen, Tristan Carel, Omar Awile, Nicola Cantarutti, Giacomo Castiglioni, Alessandro Cattabiani, Baudouin Del Marmol, Iain Hepburn, James G. King, Christos Kotsalos, Pramod Kumbhar, Jules Lallouette, Samuel Melchior, Felix Schürmann, and Erik De Schutter. 2022. STEPS 4.0: Fast and memory-efficient molecular simulations of neurons at the nanoscale. *Frontiers in Neuroinformatics*

16 (Oct. 2022), 26 pages. https://doi.org/10.3389/fninf.2022.883742

[24] Genevieve Coorey, Gemma A. Figtree, David F. Fletcher, Victoria J. Snelson, Stephen Thomas Vernon, David Winlaw, Stuart M. Grieve, Alistair McEwan, Jean Yee Hwa Yang, Pierre Qian, Kieran O'Brien, Jessica Orchard, Jinman Kim, Sanjay Patel, and Julie Redfern. 2022. The health digital twin to tackle cardiovascular disease—a review of an emerging interdisciplinary field. *npj Digital Medicine* 5, 1 (Aug. 2022), 12 pages. https://doi.org/10.1038/s41746-022-00640-7

[25] Jorge Corral-Acero, Francesca Margara, Maciej Marciniak, Cristobal Rodero, Filip Loncaric, Yingjing Feng, Andrew Gilbert, Joao F Fernandes, Hassaan A Bukhari, Ali Wajdan, Manuel Villegas Martinez, Mariana Sousa Santos, Mehrdad Shamohammdi, Hongxing Luo, Philip Westphal, Paul Leeson, Paolo DiAchille, Viatcheslav Gurev, Manuel Mayr, Liesbet Geris, Pras Pathmanathan, Tina Morrison, Richard Cornelussen, Frits Prinzen, Tammo Delhaas, Ada Doltra, Marta Sitges, Edward J Vigmond, Ernesto Zacur, Vicente Grau, Blanca Rodriguez, Espen W Remme, Steven Niederer, Peter Mortier, Kristin McLeod, Mark Potse, Esther Pueyo, Alfonso Bueno-Orovio, and Pablo Lamata. 2020. The 'Digital Twin' to enable the vision of precision cardiology. *European Heart Journal* 41, 48 (March 2020), 4556–4564. https://doi.org/10.1093/eurheartj/ehaa159

[26] Elias Dabbas. 2021. *Interactive Dashboards and Data Apps with Plotly and Dash.* Packt Publishing, Limited.

[27] L. Derycke, D. Perrin, F. Cochennec, J.-N. Albertini, and S. Avril. 2019. Predictive Numerical Simulations of Double Branch Stent-Graft Deployment in an Aortic Arch Aneurysm. *Annals of Biomedical Engineering* 47, 4 (Jan. 2019), 1051–1062. https://doi.org/10.1007/s10439-019-02215-2

[28] Laurence Devoto, Sam Muscroft, and Manish Chand. 2019. Highly Accurate, Patient-Specific, 3-Dimensional Mixed-Reality Model Creation for Surgical Training and Decision-making. *JAMA Surgery* 154, 10 (Oct. 2019), 968. https://doi.org/10.1001/jamasurg.2019.2546

[29] Yiming Dong, Fajia Sun, Zhi Ping, Qi Ouyang, and Long Qian. 2020. DNA storage: research landscape and future prospects. *National Science Review* 7, 6 (Jan. 2020), 1092–1107. https://doi.org/10.1093/nsr/nwaa007

[30] Davide Duma and Roberto Aringhieri. 2018. An ad hoc process mining approach to discover patient paths of an Emergency Department. *Flexible Services and Manufacturing Journal* 32, 1 (Dec. 2018), 6–34. https://doi.org/10.1007/s10696-018-9330-1

[31] EDITH Consortium. 2023. *EDITH CSA Deliverable 3.2: first draft of the VHT roadmap.* Technical Report. EDITH Consortium. https://doi.org/10.5281/ZENODO.8200955

[32] Tracey England, Daniel Gartner, Edward Ostler, Paul Harper, Doris Behrens, John Boulton, Dilwyn Bull, Claire Cordeaux, Ian Jenkins, Fiona Lindsay, Rhys Monk, and Leanne Watkins. 2021. Near real-time bed modelling feasibility study. *Journal of Simulation* 15, 4 (Dec. 2021), 261–272. https://doi.org/10.1080/17477778.2019.1706434

[33] Csaba Erö, Marc-Oliver Gewaltig, Daniel Keller, and Henry Markram. 2018. A Cell Atlas for the Mouse Brain. *Frontiers in Neuroinformatics* 12 (Nov. 2018), 16 pages. https://doi.org/10.3389/fninf.2018.00084

[34] Ruogu Fang, Yao Xiao, Jianqiao Tian, Samira Pouyanfar, Yimin Yang, Shu-Ching Chen, and S. S. Iyengar. 2019. Big Data in Computational Health Informatics. In *Big Data in Multimodal Medical Imaging*, Ayman El-Baz and Jasjit S. Suri (Eds.). Chapman and Hall/CRC, New York, Chapter 5, 103–142. https://doi.org/10.1201/b22410

[35] Chrystinne Fernandes, Simon Miles, and Carlos José Pereira Lucena. 2020. Detecting False Alarms by Analyzing Alarm-Context Information: Algorithm Development and Validation. *JMIR Medical Informatics* 8, 5 (May 2020), e15407. https://doi.org/10.2196/15407

[36] Chrystinne Oliveira Fernandes, Simon Miles, Carlos José Pereira De Lucena, and Donald Cowan. 2019. Artificial Intelligence Technologies for Coping with Alarm Fatigue in Hospital Environments Because of Sensory Overload: Algorithm Development and Validation. *Journal of Medical Internet Research* 21, 11 (Nov. 2019), e15406. https://doi.org/10.2196/15406

[37] Parisa Gazerani. 2023. Intelligent Digital Twins for Personalized Migraine Care. *Journal of Personalized Medicine* 13, 8 (Aug. 2023), 1255. https://doi.org/10.3390/jpm13081255

[38] Brad W. Genereaux, Donald K. Dennison, Kinson Ho, Robert Horn, Elliot Lewis Silver, Kevin O'Donnell, and Charles E. Kahn. 2018. DICOMweb™: Background and Application of the Web Standard for Medical Imaging. *Journal of Digital Imaging* 31, 3 (May 2018), 321–326. https://doi.org/10.1007/s10278-018-0073-z

[39] S. Ghafur, S. Kristensen, K. Honeyford, G. Martin, A. Darzi, and P. Aylin. 2019. A retrospective impact analysis of the WannaCry cyberattack on the NHS. *npj Digital Medicine* 2, 1 (Oct. 2019), 7 pages. https://doi.org/10.1038/s41746-019-0161-6

[40] Karli Gillette, Matthias A. F. Gsell, Julien Bouyssier, Anton J. Prassl, Aurel Neic, Edward J. Vigmond, and Gernot Plank. 2021. Automated Framework for the Inclusion of a His–Purkinje System in Cardiac Digital Twins of Ventricular Electrophysiology. *Annals of Biomedical Engineering* 49, 12 (Aug. 2021), 3143–3153. https://doi.org/10.1007/s10439-021-02825-9

[41] José A. González-Nóvoa, Laura Busto, Juan J. Rodríguez-Andina, José Fariña, Marta Segura, Vanesa Gómez, Dolores Vila, and César Veiga. 2021. Using Explainable Machine Learning to Improve Intensive Care Unit Alarm Systems. *Sensors* 21, 21 (Oct. 2021), 7125. https://doi.org/10.3390/s21217125

[42] Susanne B. Haga. 2022. No Two Cancers the Same. In *The Book of Genes and Genomes.* Springer, New York, Chapter 8, 83–95. https://doi.org/10.1007/978-0-387-70916-1_8

[43] Gregory Hawkridge, Anandarup Mukherjee, Duncan McFarlane, Yedige Tlegenov, Ajith K. Parlikad, Nicholas J. Reyner, and Alan Thorne. 2021. Monitoring on a shoestring: Low cost solutions for digital manufacturing. *Annual Reviews in Control* 51 (2021), 374–391. https://doi.org/10.1016/j.arcontrol.2021.04.007

[44] Xiwang He, Yiming Qiu, Xiaonan Lai, Zhonghai Li, Liming Shu, Wei Sun, and Xueguan Song. 2021. Towards a shape-performance integrated digital twin for lumbar spine analysis. *Digital Twin* 1 (Nov. 2021), 8. https://doi.org/10.12688/digitaltwin.17478.1

[45] Tina Hernandez-Boussard, Paul Macklin, Emily J. Greenspan, Amy L. Gryshuk, Eric Stahlberg, Tanveer Syeda-Mahmood, and Ilya Shmulevich. 2021. Digital twins for predictive oncology will be a paradigm shift for precision cancer care. *Nature Medicine* 27, 12 (Nov. 2021), 2065–2066. https://doi.org/10.1038/s41591-021-01558-5

[46] Morten Hertzum and Gunnar Ellingsen. 2019. The implementation of an electronic health record: Comparing preparations for Epic in Norway with experiences from the UK and Denmark. *International Journal of Medical Informatics* 129 (Sept. 2019), 312–317. https://doi.org/10.1016/j.ijmedinf.2019.06.026

[47] Alexander Herzog. 2021. *Simulation mit dem Warteschlangensimulator: Mathematische Modellierung und Simulation von Produktions- und Logistikprozessen.* Springer Gabler, Wiesbaden. https://doi.org/10.1007/978-3-658-34668-3

[48] Jiang Hu, Xiao-hui Kang, Fang-fang Xu, Ke-zhi Huang, Bin Du, and Li Weng. 2022. Dynamic prediction of life-threatening events for patients in intensive care unit. *BMC Medical Informatics and Decision Making* 22, 1 (Oct. 2022), 10 pages. https://doi.org/10.1186/s12911-022-02026-x

[49] Owen Rhys Hutchings, Cassandra Dearing, Dianna Jagers, Miranda Jane Shaw, Freya Raffan, Aaron Jones, Richard Taggart, Tim Sinclair, Teresa Anderson, and Angus Graham Ritchie. 2021. Virtual Health Care for Community Management of Patients With COVID-19 in Australia: Observational Cohort Study. *Journal of Medical Internet Research* 23, 3 (March 2021), e21064. https://doi.org/10.2196/21064

[50] International Organization for Standardization. 2023. *Digital twin — Concepts and terminology.* Standard 30173:2023. ISO. https://www.iso.org/standard/88799.html

[51] International Organization for Standardization. 2023. *Internet of Things (IoT) — Digital twin — Use cases.* Standard 30172:2023. ISO. https://www.iso.org/standard/88799.html

[52] International Organization for Standardization. 2024. *Internet of Things (IoT) and digital twin — Vocabulary.* Standard 20924:2024. ISO. https://www.iso.org/standard/88799.html

[53] Mohammad S Jalali and Jessica P Kaiser. 2018. Cybersecurity in Hospitals: A Systematic, Organizational Perspective. *Journal of Medical Internet Research* 20, 5 (May 2018), e10059. https://doi.org/10.2196/10059

[54] Sébastien Jodogne. 2018. The Orthanc Ecosystem for Medical Imaging. *Journal of Digital Imaging* 31, 3 (May 2018), 341–352. https://doi.org/10.1007/s10278-018-0082-y

[55] Alexander Jung, Matthias A. F. Gsell, Christoph M. Augustin, and Gernot Plank. 2022. An Integrated Workflow for Building Digital Twins of Cardiac Electromechanics — A Multi-Fidelity Approach for Personalising Active Mechanics. *Mathematics* 10, 5 (March 2022), 823. https://doi.org/10.3390/math10050823

[56] Lida Kanari, Ying Shi, Alexis Arnaudon, Natali Barros Zulaica, Ruth Benavides-Piccione, Jay S. Coggan, Javier DeFelipe, Kathryn Hess, Huib D. Mansvelder, Eline J. Mertens, Idan Segev, Henry Markram, and Christiaan P.J. de Kock. 2023. Of Mice and Men: Increased dendritic complexity gives rise to unique human networks. (Sept. 2023). https://doi.org/10.1101/2023.09.11.557170 bioRχiv preprint..

[57] A. Karakra, E. Lamine, F. Fontanili, and J. Lamothe. 2020. HospiT'Win: a digital twin framework for patients' pathways real-time monitoring and hospital organizational resilience capacity enhancement. In *Proceedings of the 9th International Workshop on Innovative Simulation for Healthcare (IWISH 2020)*. CAL-TEK srl, Virtual conference, 62-71 pages. https://doi.org/10.46354/i3m.2020.iwish.012

[58] Avita Katal, Susheela Dahiya, and Tanupriya Choudhury. 2022. Energy efficiency in cloud computing data centers: a survey on software technologies. *Cluster Computing* 26, 3 (Aug. 2022), 1845–1875. https://doi.org/10.1007/s10586-022-03713-0

[59] Bardia Khosravi, Pouria Rouzrokh, and Bradley J. Erickson. 2022. Getting More Out of Large Databases and EHRs with Natural Language Processing and Artificial Intelligence. *Journal of Bone and Joint Surgery* 104, Suppl 3 (Oct. 2022), 51–55. https://doi.org/10.2106/jbjs.22.00567

[60] Werner Kritzinger, Matthias Karner, Georg Traar, Jan Henjes, and Wilfried Sihn. 2018. Digital Twin in manufacturing: A categorical literature review and classification. *IFAC-PapersOnLine* 51, 11 (June 2018), 1016–1022. https://doi.org/10.1016/j.ifacol.2018.08.474

[61] Thomas Kuhn. 2017. Digitaler Zwilling. *Informatik-Spektrum* 40, 5 (July 2017), 440–444. https://doi.org/10.1007/s00287-017-1061-2

[62] Bhupesh Kumar Lad and Atreyee Ghosh. 2023. CHARAK DT: Human Digital Twin (DT) Healthcare Platform. *DRISHTIKON* 2, 3 (Oct. 2023), 20–21. https://drishticps.iiti.ac.in/3d-flip-book/drishtikon-vol2-issue3/#drishtikon-vol2-issue3/20/

[63] Mincai Lai, Haochen Yang, Jicheng Gu, Xinye Chen, and Zhihao Jiang. 2022. Digital-twin-based Online Parameter Personalization for Implantable Cardiac Defibrillators. In *2022 44th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*. IEEE, Glasgow, 3007–3010. https://doi.org/10.1109/embc48229.2022.9871142

[64] Mohammed Laroui, Boubakr Nour, Hassine Moungla, Moussa A. Cherif, Hossam Afifi, and Mohsen Guizani. 2021. Edge and fog computing for IoT: A survey on current research activities & future directions. *Computer Communications* 180 (Dec. 2021), 210–231. https://doi.org/10.1016/j.comcom.2021.09.003

[65] R. Laubenbacher, A. Niarakis, T. Helikar, G. An, B. Shapiro, R. S. Malik-Sheriff, T. J. Sego, A. Knapp, P. Macklin, and J. A. Glazier. 2022. Building digital twins of the human immune system: toward a roadmap. *npj Digital Medicine* 5, 1 (May 2022), 5 pages. https://doi.org/10.1038/s41746-022-00610-z

[66] Mikaela Law, Ho Seok Ahn, Elizabeth Broadbent, Kathy Peri, Ngaire Kerse, Eve Topou, Norina Gasteiger, and Bruce MacDonald. 2021. Case studies on the usability, acceptability and functionality of autonomous mobile delivery robots in real-world healthcare settings. *Intelligent Service Robotics* 14, 3 (July 2021), 387–398. https://doi.org/10.1007/s11370-021-00368-5

[67] Chia-Rong Lee, Edward T.-H. Chu, Hong-Cheng Shen, Juin Hsu, and Hui-Mei Wu. 2023. An indoor location-based hospital porter management system and trace analysis. *Health Informatics Journal* 29, 2 (April 2023), 15 pages. https://doi.org/10.1177/14604582231183399

[68] Ann-Chatrin Linqvist Leonardsen, Ann Karin Helgesen, Andreas Stensvold, Jannik Magnussen, and Vigdis A. Grøndahl. 2022. Cancer patients' perspectives on remote monitoring at home during the COVID-19 pandemic- a qualitative study in Norway. *BMC Health Services Research* 22, 1 (April 2022), 9 pages. https://doi.org/10.1186/s12913-022-07897-4

[69] Weibo Liu, Wei Zhang, Bapi Dutta, Zhenyong Wu, and Mark Goh. 2020. Digital Twinning for Productivity Improvement Opportunities with Robotic Process Automation: Case of Greenfield Hospital. *International Journal of Mechanical Engineering and Robotics Research* 9, 2 (Feb. 2020), 258–263. https://doi.org/10.18178/ijmerr.9.2.258-263

[70] Markets and Markets. 2023. *Digital Twins in Healthcare Market by Component (Software, Services), Application (Personalized Medicine, Drug Discovery, Medical Education, Workflow Optimization), End User (Providers, Research & Academia, Payers), and Region - Global Forecast to 2028*. Tech Report HIT8675. Markets and Markets. https://www.marketsandmarkets.com/Market-Reports/digital-twins-in-healthcare-market-74014375.html

[71] Henry Markram. 2006. The Blue Brain Project. *Nature Reviews Neuroscience* 7, 2 (Feb. 2006), 153–160. https://doi.org/10.1038/nrn1848

[72] Luis Martí-Bonmatí, Ángel Alberich-Bayarri, Ruth Ladenstein, Ignacio Blanquer, J. Damian Segrelles, Leonor Cerdá-Alberich, Polyxeni Gkontra, Barbara Hero, J. M. García-Aznar, Daniel Keim, Wolfgang Jentner, Karine Seymour, Ana Jiménez-Pastor, Ismael González-Valverde, Blanca Martínez de las Heras, Samira Essiaf, Dawn Walker, Michel Rochette, Marian Bubak, Jordi Mestres, Marco Viceconti, Gracia Martí-Besa, Adela Cañete, Paul Richmond, Kenneth Y. Wertheim, Tomasz Gubala, Marek Kasztelnik, Jan Meizner, Piotr Nowakowski, Salvador Gilpérez, Amelia Suárez, Mario Aznar, Giuliana Restante, and Emanuele Neri. 2020. PRIMAGE project: predictive in silico multiscale analytics to support childhood cancer personalised evaluation empowered by imaging biomarkers. *European Radiology Experimental* 4, 1 (April 2020), 11 pages. https://doi.org/10.1186/s41747-020-00150-9

[73] James Martin. 1965. *Programming Real Time Computer Systems*. Prentice Hall, Englewood Cliffs.

[74] Eric Masanet, Arman Shehabi, Nuoa Lei, Sarah Smith, and Jonathan Koomey. 2020. Recalibrating global data center energy-use estimates. *Science* 367, 6481 (Feb. 2020), 984–986. https://doi.org/10.1126/science.aba3758

[75] Tobias A. Mattei. 2017. Privacy, Confidentiality, and Security of Health Care Information: Lessons from the Recent WannaCry Cyberattack. *World Neurosurgery* 104 (Aug. 2017), 972–974. https://doi.org/10.1016/j.wneu.2017.06.104

[76] Duncan McFarlane, Svetan Ratchev, Alan Thorne, Ajith Kumar Parlikad, Lavindra de Silva, Benjamin Schönfuß, Greg Hawkridge, German Terrazas, and Yedige Tlegenov. 2019. Digital Manufacturing on a Shoestring: Low Cost Digital Solutions for SMEs. In *9th International Workshop on Service Oriented, Holonic and Multi-agent Manufacturing Systems for Industry of the Future*. Springer International Publishing, Valencia, 40–51. https://doi.org/10.1007/978-3-030-27477-1_4

[77] Maximiliano Mollura, Stefano Romano, Giulio Mantoan, Li-wei Lehman, and Riccardo Barbieri. 2020. Prediction of Septic Shock Onset in ICU by Instantaneous Monitoring of Vital Signs. In *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*. IEEE, Montreal, 2768–2771. https://doi.org/10.1109/embc44109.2020.9176276

[78] N. Moretti, A. Mukherjee, Y. C. Chan, G. Yilmaz, J. Merino, M. Sasidharan, Z. Rosun, C. Carr, D. McFarlane, and A. K. Parlikad. 2023. Low-cost digitalisation opportunities in healthcare: a histopathology department case study. In *Low-Cost Digital Solutions for Industrial Automation (LoDiSA 2023)*. Institution of Engineering and Technology, Cambridge, 7 pages. https://doi.org/10.1049/icp.2023.1735

[79] Dimitris Mourtzis, John Angelopoulos, Nikos Panopoulos, and Dimitrios Kardamakis. 2021. A Smart IoT Platform for Oncology Patient Diagnosis based on AI: Towards the Human Digital Twin. *Procedia CIRP* 104 (2021), 1686–1691. https://doi.org/10.1016/j.procir.2021.11.284

[80] Thierry Moyaux, Yinling Liu, Guillaume Bouleux, and Vincent Cheutet. 2023. An Agent-Based Architecture of the Digital Twin for an Emergency Department. *Sustainability* 15, 4 (Feb. 2023), 3412. https://doi.org/10.3390/su15043412

[81] Nassim Mozaffari, Javad Rezazadeh, Reza Farahbakhsh, Samaneh Yazdani, and Kumbesan Sandrasegaran. 2019. Practical fall detection based on IoT technologies: A survey. *Internet of Things* 8 (Dec. 2019), 100124. https://doi.org/10.1016/j.iot.2019.100124

[82] Anandarup Mukherjee, Nicola Moretti, Yin-Chi Chan, Gokcen Yilmaz, Manu Sasidharan, Jorge Merino, Zahrah Rosun, Colin Carr, Duncan McFarlane, and Ajith Parlikad. 2023. Healthcare process and variable mapping for identifying digitalisation opportunities and building a hospital digital twin. In *Computing in Construction*. European Council for Computing in Construction, Heraklion, 8 pages. https://doi.org/10.35490/ec3.2023.270

[83] Mario Mustra, Kresimir Delac, and Mislav Grgic. 2008. Overview of the DICOM standard. In *2008 50th International Symposium ELMAR*. IEEE, Zadar, 39–44.

[84] National Data Guardian. 2020. The Eight Caldicott Principles. https://www.gov.uk/government/publications/the-caldicott-principles

[85] Gemma Newlands. 2021. Lifting the curtain: Strategic visibility of human labour in AI-as-a-Service. *Big Data & Society* 8, 1 (Jan. 2021), 205395172110160. https://doi.org/10.1177/20539517211016026

[86] NHS Digital. 2023. Personal Demographics Service – FHIR API. https://digital.nhs.uk/developer/api-catalogue/personal-demographics-service-fhir

[87] NHS Digital. 2023. Summary Care Record – FHIR API. https://digital.nhs.uk/developer/api-catalogue/summary-care-record-fhir

[88] Gill Norman, Paula Bennett, and Emma R L C Vardy. 2023. Virtual wards: a rapid evidence synthesis and implications for the care of older people. *Age and Ageing* 52, 1 (Jan. 2023), 12 pages. https://doi.org/10.1093/ageing/afac319

[89] Hendrik Nunner, Katinka Feltes, Pius Gutsche, Helen Kuswik, Erik Luda, Leonard Stellbrink, and André Calero Valdez. 2023. *Adapting the "Networking During Infectious Diseases Model" (NIDM) for Science Communication Using Julia and Genie.* Springer Nature Switzerland, Cham, 355–370. https://doi.org/10.1007/978-3-031-35927-9_25

[90] Yang Peng, Ming Zhang, Fangqiang Yu, Jinglin Xu, and Shang Gao. 2020. Digital Twin Hospital Buildings: An Exemplary Case Study through Continuous Lifecycle Integration. *Advances in Civil Engineering* 2020 (Nov. 2020), 1–13. https://doi.org/10.1155/2020/8846667

[91] Wei Jie Phua, Malcolm Yoke Hean Low, Neelakantam Venkatarayalu, and Jared Koh. 2018. NFC-based Smart Notification System for Hospital Discharge Process and Bed Management. In *2018 IEEE International Conference on Service Operations and Logistics, and Informatics (SOLI)*. IEEE, Singapore, 143–147. https://doi.org/10.1109/soli.2018.8476736

[92] Osvaldo Ribeiro, Luis Gomes, and Zita Vale. 2022. IoT-Based Human Fall Detection System. *Electronics* 11, 4 (Feb. 2022), 592. https://doi.org/10.3390/electronics11040592

[93] Paul Riedel, Michael Riesner, Karsten Wendt, and Uwe Assmann. 2022. Data-Driven Digital Twins in Surgery utilizing Augmented Reality and Machine Learning. In *2022 IEEE International Conference on Communications Workshops (ICC Workshops)*. IEEE, Seoul, 580–585. https://doi.org/10.1109/iccworkshops53468.2022.9814537

[94] Luis F. Rivera, Miguel Jiménez, Prashanti Angara, Norha M. Villegas, Gabriel Tamura, and Hausi A. Müller. 2019. Towards continuous monitoring in personalized healthcare through digital twins. In *29th Annual International Conference on Computer Science and Software Engineering (CASCON '19)*. IBM Corp., Toronto, 329–335. https://doi.org/10.5555/3370272.3370310

[95] Carmen Guadalupe Rodriguez-Gonzalez, Ana Herranz-Alonso, Vicente Escudero-Vilaplana, Maria Aranzazu Ais-Larisgoitia, Irene Iglesias-Peinado, and Maria Sanjurjo-Saez. 2019. Robotic dispensing improves patient safety, inventory management, and staff satisfaction in an outpatient hospital pharmacy. *Journal of Evaluation in Clinical Practice* 25, 1 (Feb. 2019), 28–35. https://doi.org/10.1111/jep.13014

[96] Radhya Sahal, Saeed H. Alsamhi, and Kenneth N. Brown. 2022. Personal Digital Twin: A Close Look into the Present and a Step towards the Future of Personalised Healthcare Industry. *Sensors* 22, 15 (Aug. 2022), 5918. https://doi.org/10.3390/s22155918

[97] Mohsin Shaikh, Arshad HM Vayani, Sabina Akram, and Nafees Qamar. 2022. Open-source electronic health record systems: A systematic review of most recent advances. *Health Informatics Journal* 28, 2 (Jan. 2022), 146045822210998. https://doi.org/10.1177/14604582221099828

[98] Yangyang Shi, Xuesong Deng, Yuqi Tong, Ruotong Li, Yanfang Zhang, Lijie Ren, and Weixin Si. 2022. Synergistic Digital Twin and Holographic Augmented-Reality-Guided Percutaneous Puncture of Respiratory Liver Tumor. *IEEE Transactions on Human-Machine Systems* 52, 6 (Dec. 2022), 1364–1374. https://doi.org/10.1109/thms.2022.3185089

[99] Changyeob Shin, Peter Walker Ferguson, Sahba Aghajani Pedram, Ji Ma, Erik P. Dutson, and Jacob Rosen. 2019. Autonomous Tissue Manipulation via Surgical Robot Using Learning Based Model Predictive Control. In *2019 International Conference on Robotics and Automation (ICRA)*. IEEE, Montreal, 3875–3881. https://doi.org/10.1109/icra.2019.8794159

[100] Hongchao Shu, Ruixing Liang, Zhaoshuo Li, Anna Goodridge, Xiangyu Zhang, Hao Ding, Nimesh Nagururu, Manish Sahu, Francis X. Creighton, Russell H. Taylor, Adnan Munawar, and Mathias Unberath. 2023. Twin-S: a digital twin for skull base surgery. *International Journal of Computer Assisted Radiology and Surgery* 18, 6 (May 2023), 1077–1084. https://doi.org/10.1007/s11548-023-02863-9

[101] Shilpa Shyam, Sujitha Juliet, and Kirubakaran Ezra. 2022. Tracking and Monitoring of Medical Equipments using UWB for Smart Healthcare. In *2022 6th International Conference on Computing Methodologies and Communication (ICCMC)*. IEEE, Erode, 631–637. https://doi.org/10.1109/iccmc53470.2022.9753719

[102] M.M. Siddiqui and M. Çağlar. 1994. Residual lifetime distribution and its applications. *Microelectronics Reliability* 34, 2 (Feb. 1994), 211–227. https://doi.org/10.1016/0026-2714(94)90104-x

[103] Siemens Healthineers. 2021. *The value of digital twin technology.* Technical Report. Siemens Healthcare GmbH. https://marketing.webassets.siemens-healthineers.com/1800000007115634/143ec96042c1/Siemens-Healthineers_Whitepaper_Digital-Twin-Technology3_1800000007115634.pdf

[104] A. K. Singh, A. Anand, Z. Lv, H. Ko, and A. Mohan. 2021. A Survey on Healthcare Data: A Security Perspective. *ACM Transactions on Multimedia Computing, Communications, and Applications* 17, 2s (May 2021), 1–26. https://doi.org/10.1145/3422816

[105] Aaron Smith. 2023. Introducing Nova Heart: A Milestone Innovation for Cardiology Care. https://aibody.io/introducing-nova-heart-a-milestone-innovation-for-cardiology-care/

[106] Ying Song and Yongkui Li. 2022. Digital Twin Aided Healthcare Facility Management: A Case Study of Shanghai Tongji Hospital. In *Construction Research Congress 2022*. American Society of Civil Engineers, Arlington, 1145–1155. https://doi.org/10.1061/9780784483961.120

[107] Tom Sullivan. 2018. Why EHR data interoperability is such a mess in 3 charts. https://www.healthcareitnews.com/news/why-ehr-data-interoperability-such-mess-3-charts

[108] Tianze Sun, Xiwang He, Xueguan Song, Liming Shu, and Zhonghai Li. 2022. The Digital Twin in Medicine: A Key to the Future of Healthcare? *Frontiers in Medicine* 9 (July 2022), 9 pages. https://doi.org/10.3389/fmed.2022.907066

[109] Rebecca Thomas. 2023. More than a million NHS patients' details compromised after cyberattack. https://www.independent.co.uk/news/health/nhs-patient-data-attack-b2364202.html

[110] J. Trauer, S. Schweigert-Recksiek, C. Engel, K. Spreitzer, and M. Zimmermann. 2020. What is a Digital Twin? – Definitions and insights from an industrial case study in technical product development. *Proceedings of the Design Society: DESIGN Conference* 1 (May 2020), 757–766. https://doi.org/10.1017/dsd.2020.15

[111] Iñaki Ucar, Bart Smeets, and Arturo Azcorra. 2019. simmer: Discrete-Event Simulation for R. *Journal of Statistical Software* 90, 2 (2019), 30 pages. https://doi.org/10.18637/jss.v090.i02

[112] M. Ali ud-din Khan, Muhammad Fahim Uddin, and Navarun Gupta. 2014. Seven V's of Big Data — understanding Big Data to extract value. In *Proceedings of the 2014 Zone 1 Conference of the American Society for Engineering Education*. IEEE, Bridgeport, 5 pages. https://doi.org/10.1109/aseezone1.2014.6820689

[113] Ruud van der Ham. 2018. salabim: discrete event simulation and animation in Python. *Journal of Open Source Software* 3, 27 (July 2018), 767. https://doi.org/10.21105/joss.00767

[114] Henk van Houten. 2018. The rise of the digital twin: how healthcare can benefit. https://www.philips.com/a-w/about/news/archive/blogs/innovation-matters/20180830-the-rise-of-the-digital-twin-how-healthcare-can-benefit.html

[115] Shaylee Vekaria, Glenn Boardman, Kenneth Tam, Janice Kho, Barry Jenkins, and Matthew Rawlins. 2021. Implementation of robotics in the Australian hospital pharmacy dispensary: adding to the evidence. *Journal of Pharmacy Practice and Research* 51, 6 (Dec. 2021), 552–553. https://doi.org/10.1002/jppr.1764

[116] Parul Verma and Shahnaz Fatima. 2020. *Smart Healthcare Applications and Real-Time Analytics Through Edge Computing*. Springer International Publishing, Cham, 241–270. https://doi.org/10.1007/978-3-030-37526-3_11

[117] Cecilia Vindrola-Padros, Kelly E Singh, Manbinder S Sidhu, Theo Georghiou, Chris Sherlaw-Johnson, Sonila M Tomini, Matthew Inada-Kim, Karen Kirkham, Allison Streetly, Nathan Cohen, and Naomi J Fulop. 2021. Remote home monitoring (virtual wards) for confirmed or suspected COVID-19 patients: a rapid systematic review. *eClinicalMedicine* 37 (July 2021), 100965. https://doi.org/10.1016/j.eclinm.2021.100965

[118] Valentina Volpato, Victor Mor-Avi, Akhil Narang, David Prater, Alexandra Gonçalves, Gloria Tamborini, Laura Fusini, Mauro Pepi, Amit R. Patel, and Roberto M. Lang. 2018. Automated, machine learning-based, 3D echocardiographic quantification of left ventricular mass. *Echocardiography* 36, 2 (Dec. 2018), 312–319. https://doi.org/10.1111/echo.14234

[119] Shengli Wei. 2021. Is Human Digital Twin possible? *Computer Methods and Programs in Biomedicine Update* 1 (2021), 100014. https://doi.org/10.1016/j.cmpbup.2021.100014

[120] Gary White, Anna Zink, Lara Codecá, and Siobhán Clarke. 2021. A digital twin smart city for citizen feedback. *Cities* 110 (March 2021), 103064. https://doi.org/10.1016/j.cities.2020.103064

[121] Hadley Wickham, Mara Averick, Jennifer Bryan, Winston Chang, Lucy McGowan, Romain François, Garrett Grolemund, Alex Hayes, Lionel Henry, Jim Hester, Max Kuhn, Thomas Pedersen, Evan Miller, Stephan Bache, Kirill Müller, Jeroen Ooms, David Robinson, Dana Seidel, Vitalie Spinu, Kohske Takahashi, Davis Vaughan, Claus Wilke, Kara Woo, and Hiroaki Yutani. 2019. Welcome to the Tidyverse. *Journal of Open Source Software* 4, 43 (Nov. 2019), 1686. https://doi.org/10.21105/joss.01686

[122] G. Winzor, A. Bosworth, C. Whalley, A.D. Beggs, and S.F. Atabani. 2021. Detection of SARS-CoV-2 on laboratory paper request forms: a potential source of infection for laboratory personnel. *Journal of Hospital Infection* 108 (Feb. 2021), 207–208. https://doi.org/10.1016/j.jhin.2020.11.003

[123] Eugene Y. C. Wong, Daniel Y. Mo, and Stuart So. 2020. Closed-loop digital twin system for air cargo load planning operations. *International Journal of Computer Integrated Manufacturing* 34, 7-8 (June 2020), 801–813. https://doi.org/10.1080/0951192x.2020.1775299

[124] Louise Wright and Stuart Davidson. 2020. How to tell the difference between a model and a digital twin. *Advanced Modeling and Simulation in Engineering Sciences* 7, 1 (March 2020), 13 pages. https://doi.org/10.1186/s40323-020-00147-4

[125] Dylan Yaga, Peter Mell, Nik Roby, and Karen Scarfone. 2018. *Blockchain technology overview.* Report NISTIR 8202. National Institute of Standards and Technology. https://doi.org/10.6028/nist.ir.8202

[126] Sooyoung Yoo, Seok Kim, Eunhye Kim, Eunja Jung, Kee-Hyuck Lee, and Hee Hwang. 2018. Real-time location system-based asset tracking in the healthcare field: lessons learned from a feasibility study. *BMC Medical Informatics and Decision Making* 18, 1 (Sept. 2018), 10 pages. https://doi.org/10.1186/s12911-018-0656-0

[127] Joe Zhang, Harpreet Sood, Oliver Thomas Harrison, Ben Horner, Nikhil Sharma, and Sanjay Budhdeo. 2020. Interoperability in NHS hospitals must be improved: the Care Quality Commission should be a key actor in this process. *Journal of the Royal Society of Medicine* 113, 3 (Jan. 2020), 101–104. https://doi.org/10.1177/0141076819894664

[128] Qingxia Zhang, Zihao Meng, Xianwen Hong, Yuhao Zhan, Jia Liu, Jiabao Dong, Tian Bai, Junyu Niu, and M. Jamal Deen. 2021. A survey on data center cooling systems: Technology, power consumption modeling and control strategy optimization. *Journal of Systems*

Architecture 119 (Oct. 2021), 102253. https://doi.org/10.1016/j.sysarc.2021.102253

[129] Xiange Zhang. 2018. Application of discrete event simulation in health care: a systematic review. *BMC Health Services Research* 18, 1 (Sept. 2018), 11 pages. https://doi.org/10.1186/s12913-018-3456-4

[130] Xiang Zhong, Farnaz Babaie Sarijaloo, Aditya Prakash, Jaeyoung Park, Chanyan Huang, Amelia Barwise, Vitaly Herasevich, Ognjen Gajic, Brian Pickering, and Yue Dong. 2022. A multidisciplinary approach to the development of digital twin models of critical care delivery in intensive care units. *International Journal of Production Research* 60, 13 (Feb. 2022), 4197–4213. https://doi.org/10.1080/00207543.2021.2022235