



Article

Impactful Digital Twin in the Healthcare Revolution

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Abstract: Over the last few decades, our digitally expanding world has experienced another significant digitalization boost because of the COVID-19 pandemic. Digital transformations are changing every aspect of this world. New technological innovations are springing up continuously, attracting increasing attention and investments. Digital twin, one of the highest trending technologies of recent years, is now joining forces with the healthcare sector, which has been under the spotlight since the outbreak of COVID-19. This paper sets out to promote a better understanding of digital twin technology, clarify some common misconceptions, and review the current trajectory of digital twin applications in healthcare. Furthermore, the functionalities of the digital twin in different life stages are summarized in the context of a digital twin model in healthcare. Following the Internet of Things as a service concept and digital twining as a service model supporting Industry 4.0, we propose a paradigm of digital twinning everything as a healthcare service, and different groups of physical entities are also clarified for clear reference of digital twin architecture in healthcare. This research discusses the value of digital twin technology in healthcare, as well as current challenges and insights for future research.

Keywords: digital twin; healthcare; digital twin model; big data



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1. Introduction

Over the last decade, we have witnessed fast-paced digitalization transformation in almost every aspect of human life, not to mention the recent significant boost to digital technologies owing to the COVID-19 pandemic. Businesses and service providers had to adapt to digital changes quickly to overcome containment challenges and survive in an ever-changing world. Meanwhile, digital infrastructure has enjoyed a vast expansion, and shows no sign of slowing down [1]. Among the many prominent tech buzzwords, digital twin has received significant attention, as have closely related terms such as hyperautomation, digital shadows, digital threads, digital ghosts, and so on. Digital twin and its "derivative terms" share the same underlying technological concept and have featured on the Gartner top 10 strategic technology trends every year since 2017. According to ReportLinker [2], the value of the global digital twin market was estimated to be almost USD 8 billion in 2021, with a compound annual growth rate (CARG) of 39% between 2022 and 2030. Although one can challenge the accuracy of the valuation, and different market research sources may present different (albeit similar) valuations, they all indicate that digital twin technology is playing an essential role in digital transformation. The potential value it can contribute should not be overlooked [3]. The Google Trends index has been widely used in modelling and forecasting as a reliable indicator of public interests [4–6]. Therefore, the Google Trends index since 1 January 2019 was extracted from the Google Trends website along with another well-known emerging term - the UN SDGs (United Nations Sustainable Development Goals) for comparison. The trend of UN SDGs is used here, considering its global endorsement and increasing policy relevance in almost every country and sector. Both terms have increased Google Trends indices, at a global level, since

100Search Term

— Digital Twins (worldwide)

— UN SDGs (worldwide)

25
2019

2020

Date

2021

2022

2019 (see Figure 1). The digital twin index is fast approaching the peak value of 100, which indicates the highest possible search interest on Google.

Figure 1. UN SDGs and digital twins global google trends since 2019.

The public interest in digital twin technology is significantly inflated as the result of the boost from digitalization transformation in recent years, the enormous investment plans announced by a few tech giants, as well as the enabling environment of expanding digital infrastructure and advancing technology in today's fast and ever-changing world. Many industries/sectors have shown their emerging interest in embracing digital twin technology. Among those, a rapidly developing healthcare sector on the back of the COVID-19 pandemic indicates crucial needs for further investigation [7]. Therefore, this paper aims to promote a better understanding of digital twin technology and explore the current trajectory of interactions between it and healthcare to bring insightful contributions to interested parties.

Data source: Google Trends

The paper's organization and its contribution by section are summarized as follows. Section 2 aims to promote a better understanding of this fast-emerging technology. The history and development of digital twin is investigated, and common misconceptions of digital twin technology are addressed for a broader range of readers to prevent misunderstanding. Moreover, critical functionalities of digital twin in the emerging Metaverse are summarized. A specific focus on healthcare is presented in Section 3, where we extend the classic five-dimensional digital twin model [8] and propose a digital twin model in the healthcare context differentiated by the different life stages, which has not been conducted by previous literature to the best of our knowledge. It is also the first time the paradigm of digital twinning everything as a healthcare service has been proposed, which was grouped by different types of physical entities and remains consistent with digital twinning architecture to support Industry 4.0 [9]. Furthermore, the benefits and revolutions of digital twin technology for the healthcare sector are explored by reviewing relevant applications. The paper concludes in Section 4 with a discussion of the strengths and challenges concerning digital twin in healthcare. This section also proposes insights for fruitful future research.

2. Digital Twin: An Old Concept with a New Major Boost

Digital twin has emerged as a buzzword and trending topic recently. It is recognized as a "building block" of the Metaverse, another fast-emerging case representing an immersive digital world that allows real-life experiences and interactions. The general digitalization process across sectors/services, rapidly increasing data processing and analysis capacity enabled by fast-paced technological revolutions, and continuous advancements in cognition and artificial intelligence (AI), all of which have accelerated digital twin technology, began decades ago.

In this section, the definition of digital twin is reviewed along with common misconceptions that may have caused confusion and misunderstandings. It is of paramount importance to first understand the actual meaning and development history of digital twin technology so that researchers and practitioners can distinguish the wheat from the chaff and promising use cases from the numerous advertised cases, many of which are just hype, allowing them to glean valuable insights into likely future directions of research and implementation of this rapidly advancing technology.

2.1. Digital Twin: Development History

Digital twin as a term has been widely used to define a variety of models, systems, or technologies. Inflated expectations, lack of standardized definitions, and a poor understanding of the underlying technology, coupled with false or over-promising advertising by several short-term profit-oriented opportunists, have resulted in a significant boost to every aspect of digital twin. Closer scrutiny of the actual "player" behind this bustling "show" reveals that the concept of digital twin has existed for decades.

Although the label' digital twin' was first introduced by Michael Grieves in a 2003 presentation [10], it is generally accepted that the concept of digital twin was first applied by the National Aeronautics and Space Administration (NASA) in the 1960s to simulate and program spacecraft (i.e., the Apollo missions). In 2012, according to Glaessgen and Stargel (2012) [11], NASA formally defined digital twin technology as "an integrated multiphysics, multi-scale, probabilistic simulation of an as-built vehicle or system that uses the best available physical models, sensor updates, fleet history, etc., to mirror the life of its corresponding flying twin". Manufacturing and general industry quickly became and remain the primary domain for the application of digital twin technology, as the links between digital twin and cost reduction and production efficiency are straightforward.

Meanwhile, the definition of a digital twin has also been evolving as its use has spread beyond spacecraft and vehicular applications. Grieves (2014) [10] further clarified that a digital twin is a system of three elements: the physically existing product, its virtual representation, and the bi-directional data connections between them. Specifically, the physical product feeds data to the virtual "twin" while the virtual representation keeps returning information/processes back to the physical product. According to [8,12], "DT involves creating a virtual model for a physical entity in the digital form to simulate entity behaviours, monitor the ongoing status, recognize internal and external complexities, detect abnormal patterns, reflect system performance, and predict future trend". Digital twin fast became the "must have" technology among industrial companies. Considering its significant contribution towards product lifecycle management (PLM), Grieves (2017) [13] also presented more detailed definitions of some key terms closely related to the use of digital twin in PLM, for instance, digital twin prototype, digital twin instance, digital twin aggregate, and digital twin environment, among others. Those definitions are not reproduced here, but a summarized list can be found in [14]. Building on the three-dimensional digital twin model firstly introduced by Grieves [10], Tao et al. (2019) [15] proposed a five-dimension digital twin model, extending the initial three-dimension architecture by including digital twin data and services; this extended model addressed data fusion ("information capture") from both the physically existing product and its digital counterpart, as well as the functionalities of digital twin arising from embedding a service component. Liu et al. (2021) [16] argue that recent studies highlight the digital twin's dynamic, real-time, and bi-directional data connection features. That paper also provides a list of digital twin definitions that can be found in research articles.

The digital twin model advanced and became more sophisticated thanks to the continuous dedication of researchers and practitioners. The digital revolution and fast-paced advancements of IoT (Internet of Things), Big Data, and cloud computing also contributed as the general digital infrastructure experienced an exponential upgrade. Together, these factors combined to create a digitally enabling environment for implementing digital twin technologies, with fewer restrictions than had existed when the concept was first outlined. Today, in both the industrial and academic sectors, digital twin is considered a vital pillar of the Industrial Revolution 4.0 [8,17–20].

2.2. Digital Twin: Common Misconceptions

Almost half of the world's population has no access to the internet, and only a few countries are exploiting the frontier edge of technological advancement [1]. According to [21–23], a digital divide has been witnessed between developed and developing countries/regions, different income levels, genders, ages, digital divides, and exclusions further exacerbate already existing inequalities, especially for those digitally disadvantaged groups [1,24]. Despite the continuous efforts to bridge the digital divide [23], rapid technological advances, like the digital twin, may have further accelerated human vulnerability in technology evolution [1]. A lack of understanding, knowledge, and access to the frontier edge of developments increases the chances of possible misconceptions, false or inflated expectations of the public, adverse reputational outcomes, and misunderstandings, as well as more significant risks of the most digitally vulnerable groups being exploited. Therefore, this section aims to clarify the common misconceptions about the digital twin and discuss the reasons for those misconceptions to contribute to promoting a better understanding of this fast-growing technology.

There are some common misconceptions regarding digital twins (as can be seen in Table 1), and this paper aims to discuss the reasons for those misconceptions. It also seeks to clarify issues so that researchers and practitioners can refer to the correct technology and then reflect on the opportunities for their areas of expertise and work to bring more significant insights and drive future development. In brief, common digital twin misconceptions arise from the closely related technologies of digital twins, 2D/3D modelling, system simulation, validation computation, digital prototyping, and so on [25]. Without a comprehensive understanding of the digital twin and its related technologies, confusion with one of its rooting technologies is common, often confusing elements or steps of digital twin with the digital twin itself. Digital twin's dynamic, real-time, and bi-directional data connection features [16] are keys to distinguishing the digital twin, but also the most common source of misconception.

Table 1. Common misconceptions of the digital twin.

Term	Reasons and Differences	
Digital shadow	A digital shadow contains a physically existing product and its virtual twin, but it has only a unidirectional data connection from the physical entity to its virtual representative, meaning the virtual twin only digitally reflects the physical product [26–28].	
Digital modelling	Modelling is the essential aspect of a digital twin but is not an alternative term to represent digital twin as a whole. There are bi-directional data connections between the physical product and its virtual twin; however, the data is exchanged manually [27,28], meaning the virtual twin represents a certain status of the physical product with the manually controlled process of synthesis.	
Digital thread	The digital thread represents the continuous lifetime digital/traceable record of a physical product, starting from its innovation and designing stage to the end of its lifespan, and it plays an important role in the digitalisation process and functions as the enablers of interdisciplinary information exchange [29–31].	
Simulation	Simulation refers to the important imitating functionality of digital twin technology from the virtual twin's perspective, and simulation indicates a broader range of models; it is an essential aspect of the digital twin rather than an alternative term representing digital twin, as it does not consider the real-time data exchange in between the physically existing object [16,25].	

Table 1. Cont.

Term	Reasons and Differences
Fidelity model/ Simulation	Fidelity refers to the level of imitation state of a simulation model compared with the physical product it is reproducing. It is common to find terms like high/low/core/multi fidelity model/simulation, which describe different fidelity levels or considerations while building up the simulation model [16,32]. It is also frequently found that researchers use high fidelity or even ultrahigh fidelity to describe the common feature of the digital twin considering its real-time dynamic data exchange between the physical object and virtual twin [14,33,34].
Cyber twin	Some researchers referred to cyber twin and digital twin interchangeably as a result of understanding "cyber" as another alternative term for "digital". It is also common to see terms like cyber digital twin, cyber twin simulation, cyber-physical system, and so on. The key aspect the cyber twin or cyber-physical system would like to address is a network (internet architecture), closely related to the advancements and implementations of IoE (Internet of Everything) [35–38]. It is also common to mix the cyber twin or cyber-physical system network architecture with a digital thread.
Device shadow	It is common to find research on device shadow in areas of cloud computing platforms and the Internet of Things (IoT). Device shadow highlights the virtual representation of the physically existing object; in brief, it refers to the service of maintaining a copy of information extracted from the physical object, which is connected to IoT [39–42].

2.3. Digital Twin Functionalities in the Emerging Metaverse

In this section, the key functionalities of digital twins are summarized to assist readers in understanding how it works "behind the scenes" to identify insightful implementation possibilities in their areas of expertise. As highlighted in the previous section, digital twin technologies include the features of being dynamic and real-time, and bi-directionally exchanging data between a physical object and its virtual representative or avatar. These key characteristics, along with the support of advancing digital infrastructures, make the digital twin an enabler for some complex functionalities [27], which can be grouped into a few categories: simulation, validation, monitoring, and analytics (including but not limited to visualization, documentation, prediction, valuation, and optimization).

As already noted, digital twin technologies have been adopted mainly by manufacturing and industry in general, where their functionalities have been closely embedded in PLM. It is used to digitally simulate the whole product lifecycle (including every physically existing product/process), monitor physical objects and feed real-time data to the digital representative, digitally record and visualize the whole lifecycle and associated data, simulate, validate operations/processes digitally, and optimize them for the physical entity by providing both real-time and forward-looking analytics (i.e., performance validation and forecasting, status tracking, and adjusting, among others. Extending these PLM-related functionalities of a digital twin to a more general context, Rasheed et al. (2020) [43] summarized eight possible additional implementations of the digital twin: "real-time remote monitoring and control, greater efficiency and safety, predictive maintenance and scheduling, scenario and risk assessment, better intra- and inter-team synergy and collaborations, more efficient and informed decision support system, personalization of products and services, better documentation and communication". These functionalities of digital twins are applicable regardless of the use case.

In this fast-changing world, the concept of the Metaverse has become another emerging topic as people are seeking an ultra-immersive digital world experience, which allows real-life experiences and interactions. The Metaverse is considered "the post-reality universe, a perpetual and persistent multiuser environment merging physical reality with digital virtuality" [44]. While digitalization is rapidly forming a bridge between the real world

and the Metaverse, digital twin technology is considered as the building block of the Metaverse, as the Metaverse can be considered as digital twinning everything around everyone on the scale, thus understanding the value proposition of digital twin will be an important first step for anyone interested in exploiting the next phase of this digital evolution. Although the functionalities of digital twin technologies are being exploited by manufacturing and industry, the applications in the Metaverse, especially considering the challenges of scalability, regulation, data/system/platform uniformity, composability, and so on, are still in relatively early stages. Applications in routine daily life where people can experience the benefits include, for instance, virtual shopping, immersive virtual events/meetings, immersive learning, virtual travelling, and so on; however, the digital twin is frequently teamed up with virtual reality, artificial reality, or immersive reality. It is important to note that not every case being publicly promoted as a digital twin is technically a digital twin. It may simply be an uncompleted product or a progressing project using part of a digital twin technology and enriched by virtual reality. To distinguish the difference, the best strategy is to identify the most important or defining features of digital twins, which are the dynamic, real-time, and bi-directionally exchange of data between a physical object and its virtual representative. Using these criteria, it is clear that despite the increasing attention being given to the Metaverse, there is still a long way to go before a truly dynamic, real-time, immersive, bidirectionally influential experience has been achieved. However, even if the adoption is not yet "completed", the values and possibilities are already so impactful they have empowered advances in many industries, companies, areas of scientific research, and various aspects of human life.

From a more technical perspective, Liu et al. (2021) [16] conducted a literature review to identify critical technologies and software for digital twins. They grouped those key technologies into three categories: data-related technologies, high fidelity modelling technologies, and model-based simulation technologies. Using this classification, the authors also proposed a technology architecture for digital twins, decomposing the digital twin into different stages and mapping critical technologies to each of the elements. Similarly, Qi et al. (2021) [12] listed a comprehensive framework of relevant technologies and technical tools required for enabling the digital twin, which can be referred to as the one-stop directory for identifying the specific technologies/software/technological tools needed to apply a digital twin.

3. Healthcare Upgrading via a Digital Twin

3.1. Five Dimensions of the Digital Twin Model in Healthcare

Manufacturing industries have achieved significant developments by embedding digital twin technology into every stage of PLM, and it has been recognized as one of the most important pillars of Industry 4.0 [8,17]. Interest in digital twins across many different industries/sectors is evident, particularly in a rapidly developing healthcare sector on the back of the COVID-19 pandemic [45–47]. Referring to the five-dimensional model of the digital twin outlined in Section 2.1 [15] (and see Table 2), the details of the five-dimension model are summarized for a healthcare context. Although it is theoretically straightforward to embed the general five-dimensional model into a healthcare context, in practice, it is far more complex and challenging as healthcare caters for humans rather than dealing with "products", and contains a high level of variety and complexity, which requires sophisticated domain-specific knowledge at every stage of the process. Furthermore, there are often complex ethical concerns, regulation, privacy, and security challenges to be taken into consideration [48].

Digital Twin Model Element	Description in the Healthcare Context
Physical entity	Human/patient in the healthcare context
Virtual twin	Digital representative of human/patient
Digital twin data	Fusion of information including data collected from the patient (both historical and real-time), analytical data from a digital model, simulation, validation and prediction supported by research, computational modelling, Big Data mining, and machine learning.
Services	Collective functionalities and services provided via applying the digital twin, i.e., monitoring, modelling, simulation, validation, optimisation, and analytics, in the healthcare context; for instance, monitoring patient health status, timely diagnosis, effective and personalised treatment, operational efficiency improvement of healthcare institutions, and so on.
Data connection	The data exchanging channels between humans and the digi-representative; the fusion of digital twin data and services.

Table 2. Five dimensions of the digital twin model in healthcare.

3.2. Digital Twin: Supporting Healthcare in Different Life Stages

In Figure 2, a digital twin model for the healthcare context is proposed. With humans/patients as the physically existing entity and inspired by the product lifecycle management infrastructure, several healthcare stages are suggested: preconception care, lifetime healthcare, and afterlife stage. Each stage is associated with its relevant digital twin data and the corresponding functionalities of the digital twin. The digital representative or avatar is the virtual twin of the human/patient and supports the fusion of information and model digital twin data. The bidirectional connections between the key elements of the model are consistent with the well-established five-dimensional digital twin model set out in [15]. Using this extended model incorporating different life cycle healthcare stages, the objective is to demonstrate an easy-to-understand model of a digital twin for general readers who are interested in this developing area, outline the different types of information contained in digital twin data as a whole, and showcase some of the functionalities digital twins can have in supporting healthcare. The remainder of this subsection elaborates on the model in detail, sequentially following the different life cycle stages.

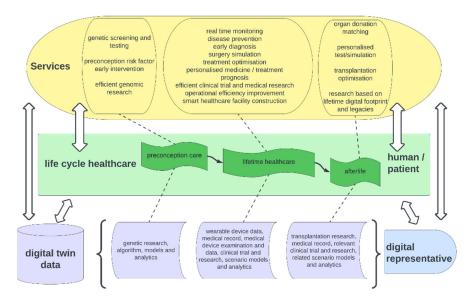


Figure 2. Digital twin model in healthcare.

3.2.1. Preconception Care

Many maternal health and child mortality risk factors are preventable [49]. Proper and timely preconception care could significantly reduce adverse maternal and infant outcomes at a population level, promote healthier pregnancies for women, and improve the general health of everyone of reproductive age. Although the preconception stage is specifically discussed here, many aspects are closely connected with lifetime healthcare, for instance, healthier lifestyle, nutrition, fitness, mental health, and so on. Here, the focus is on applications relevant only to the preconception care stage, but overlapping implementation will be evident in the lifetime healthcare section.

A paper by Gardiner et al. (2013) [50] systematically highlighted the importance of adopting fast-growing health information technology (i.e., virtual patient advocate) to support implementing preconception care measures via clinical services. They proposed using the widely adopted Gabby preconception care system [50,51]. Later, a personal mHealth smart pregnancy programme was developed by [52], which shared similar aims of promoting individual preconception care information and coaching in order to prevent unhealthy behaviours. Davidson and Boland (2020, 2021) [53,54] reviewed relevant studies and addressed the current trajectory of empowering pregnant women's decision-making and improving reproductive health using advanced information technology like artificial intelligence and machine learning. A comprehensive intelligent system was recently proposed by Oprescu et al. (2022) [55], which is being tested now as part of a pregnancy health study.

Apart from the intelligent digital systems noted above, advanced ultrasound empowered by virtual reality technology could provide a more accurate visualization of embryonic and placental structures to support early diagnosis and identification of complications during pregnancy [56,57]. The results presented in [58] suggest that an immersive virtual reality experience could reduce the negative emotional impacts on women undergoing in vitro fertilization (IVF) before embryo transfer.

Although only in their infancy, there are also genomes projects exploring the secrets of our genes [59–61], collecting detailed molecular data from individual patients [59,60], as well as newborns [61], which can be used not only to construct digital genetic models in order to assist genetic studies, testing, and early interventions, but will also contribute to the development of a wide breadth of other healthcare products and services in the future; for instance, this can be the beginning of enabling the lifetime genomic record, promoting a better understanding of diseases, discovering new methods of diagnostics and treatments, among others [59–62].

3.2.2. Lifetime Healthcare

There are innumerable ways that advanced information technologies can contribute to healthcare, ranging from the most straightforward multimedia channels to facilitate health information sharing [63], processing social media information for healthcare modelling [64,65], and customized features that help draw attention to individual healthcare [66], optimization and personalized precision medicine, treatment, and equipment, in order to improve the construction and operational efficiency of healthcare professionals/institutions/systems/facilities and so on. The value of digitalization and advanced technologies like the digital twin in healthcare is immeasurable [67]. Applications that incorporate part or whole digital twin technology in the general lifetime healthcare stage are identified. It is worth noting that applications empowered by hybrid or selective combinations of technologies are increasingly common, and this is typical both in healthcare settings as well as in almost every other aspect of human life.

Promoting healthcare education, knowledge sharing, and personalized healthcare information tailored to individual needs has an important role, where technology can assist as it integrates with the healthcare sector [44]. Digital innovations assisting healthcare education and training are systematically summarized in [68], including but not limited to simulations [69], virtual patients [70], and virtual reality learning platforms/environments [71–73],

as well as other multimedia channels, chat-bots, big data analytics, and so on. While witnessing the values of general digital twin technologies in educating healthcare students, professionals, and patients, raising awareness of healthcare and healthier lifestyles is also emerging as an increasingly significant field of incorporating technologies. Digital twins have been widely applied in coaching physical activities [74], giving personalized and precise nutrition advice [75], assisting with fitness management [76], and improving self-management of ergonomic risks [77], all thanks to advances in sensors, smart devices, and expanding IoT infrastructures.

Similarly, enabling technological infrastructures to benefit patients too, especially those with chronic diseases, by providing them with real-time health monitoring to detect early warning signs and prevent adverse outcomes [78]. Shamanna et al. (2020, 2021) [79,80] discussed precision nutrition and treatment for diabetes patients supported by digital twin technologies. Apart from providing continuous and real-time life monitoring for patients with chronic diseases, it could also be applied to training athletes [74], critical patient care in intensive care units [81], elderly healthcare [82], and everyday care for patients with multiple sclerosis [83], and the detection of abdominal aortic aneurysms [84], among others. These types of functionalities, which efficiently detect risk factors or early warning signals of changes in key health indicators [85,86], could prevent severe outcomes and help healthcare professionals with their decision-making and diagnostics. For example, a digital twin patient model was applied in [87] to predict treatment response and assist decision-making in clinical settings. Mourtzis et al. (2021) [88] have embraced digital twin technology for oncology patient diagnosis, data analysis, and prediction. Other research by Corral et al. (2020) [89] focused on precision cardiology and highlighted the value of digital twin technology in assisting diagnosis, evaluating prognosis, optimizing treatments, and accelerating regulatory decision-making. The lung cancer diagnosis was specifically discussed by Zhang et al. (2020) [90], along with techniques to improve the cyber vulnerability and resilience of digital twin models [91]. These digital-twin-related advances continue to strengthen the links between healthcare and the digital world, which in time should encourage more progress towards improved personalized medicine and treatment.

The applications of digital twin could also help in providing more accurate immersive surgery simulation [92], building up comprehensive digital databases for certain types of surgery [93], enabling remote surgery [94], and improving less invasive surgery [95]. This would allow better access to efficient surgery training, more accurate surgery planning and evaluation, more accessible medical resources, and reduced constraints arising from geographic location. By learning from digital twin applications in the industrial sector, hospitals and other healthcare institutions have also embraced this technology to optimize their own operational and management efficiency. The HospiT'Win framework supported by digital twin technology was proposed in [96] to optimize patient pathways and hospital operation, and to predict the operational impact of unexpected events. A recent paper by Lu et al. (2021) [97] proposed a hospital digital twin prototype aimed at assuring efficient hospital operations while responding to the COVID-19 pandemic. Peng et al. (2020) [98] presented an implementation use case for a hospital building digital twin in China, which can mirror real-time visual management and provide operational improvement suggestions. A digital twin can also play an important role in building smart cities [99,100] and smart construction projects [101–103]. The construction and planning of hospitals could also benefit from incorporating digital twin technology in its design, planning, construction, maintenance, and facility management [104–106].

3.2.3. Afterlife Stage

There are limited studies and public interest in this stage; however, we believe it is still an important aspect to consider. The potential of digital twin technology has already been outlined above, and it could also be used to simulate organ transplantation and associated cost-benefit or decision matrices [45,107]. Better prediction of survival for individual liver transplantation grafts is explored in [108], and a recent study in [109] discussed

the optimization of donor-recipient pairing in liver transplantation. If the digital twin database of an organ donor collected during the lifetime healthcare stage were available, it would significantly improve the testing and matching process with more personalized and accurate simulations. As digital twins have also been applied to the development of smart transportation infrastructure [99,110,111], the technology is also transferable to assist in the logistics of organ transportation.

Living in this digitalized era, it is impossible to avoid leaving a lifetime trail of digital footprints and legacies [112]. Research has focused on digital identity, ethics, grief, and remembrance [113,114]. However, as digital twin databases expand, the immortality of digitalized information will attract greater attention. However, no relevant research is identified discussing the solution or values appropriate to those digital legacies left behind in healthcare.

3.3. Digital Twinning Everything as a Healthcare Service

The expanding digital twin architecture in the healthcare sector highlights a paradigm with complex integration levels. In accordance with the digital twin as a service in Industry 4.0 [9], digital twinning everything as a healthcare service paradigm is proposed in Figure 3. Here, the complex integration levels are clarified by summarizing the different types of physical entities for digital twinning, as well as by listing key healthcare services that could benefit most from the emerging digitalization transformation of the healthcare sector.

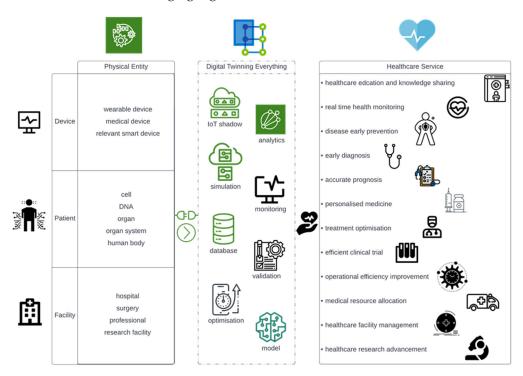


Figure 3. Digital twinning everything as a healthcare service.

Based on the digital twin applications reviewed for this paper, healthcare-related physical entities for digital twinning are grouped into three categories: device, patient, and facility. The first group, devices, includes wearable fitness or health monitoring devices, any medical device, and other relevant smart devices used for healthcare-related purposes. The data collected and stored by these devices, along with the potential analytics, make these devices important parts of the physical entities we observed. They are continuously making a significant contribution to healthcare delivery [115].

Following the expanding IoT and its increasingly strong integration in healthcare [116], this first group of physical entities have the most straightforward access to the digital twinning process. In the second group, patients, where more ethical considerations exist

and owing to the highly complex nature of human physiology, it is a more challenging path towards complete digital twinning. Nevertheless, several projects are underway to digitalize cell and DNA level data. Other applications have also been identified for specific organs [117], i.e., the heart [118,119] and liver [120], among others, as well as organ systems like the cardiovascular system [121]. Although there is still a long way to go before the human body can be fully digitalized, there is increasing public interest and research [1,122,123] in this field. All healthcare-related facilities are then grouped into the last category, namely, facilities, which includes hospitals [96–98,124], other healthcare institutions, surgery [92,94], healthcare services/operations within these facilities [104–106], and professionals who carry out those operations [50–52], as well as labs, trials, and other research relevant facilities.

Digital twinning of those physical entities creates a monumental IoE-like architecture for providing improved healthcare service. The valuable information and models contained by the digital twin and its mixed functionalities all contribute to the advancing healthcare service in this ever-changing and digitally expanding world. As can be seen in Figure 3, the critical beneficial aspects for healthcare from digital twin technologies according to the applications reviewed are summarized for convenience as improvements in the following: information sharing, education, monitoring, diagnosis, precision medicine/treatment, medical resource management, facility operation management, and research advancement.

4. Discussion

4.1. Strengths and Challenges

This section discusses the current trajectory of digital twin implementation supporting healthcare by looking into current achievements, existing challenges, and possible concerns.

4.1.1. Digital Twin Helps to Combat Healthcare Inequality

The expanding IoT and digitalization process is enabling more and more people to have equal access to valuable information that exists digitally [125–127]. Similarly, digital twinning processes in healthcare can promote better access to healthcare education, self-healthcare management information, and other remote healthcare services without restrictions associated with the graphical location. More people now have convenient access to fitness devices, medical devices for real-time health monitoring, early adverse signal identification, and early diagnosis without imposing a considerable burden on already limited healthcare resources.

4.1.2. Digital Twin Assists with Achieving Sustainable and Efficient Healthcare Facility Management

The operational efficiency of healthcare facilities could benefit substantially from digital twin technology and achieve more sufficient operations and improved healthcare services with the same level of resources. For instance, hospitals could optimize their resource allocations and patient pathway arrangements to provide patients with better healthcare experiences. Furthermore, energy planning and usage, logistics of resources, administration process, facility maintenance, and so on could all be empowered with digital twin technology to support a more sustainable future [128].

4.1.3. Digital Twin Accelerates Advances in Healthcare Research

The digitalization of genomic, organ, and organ system level data, as well as surgery, provides holistic access to researchers and healthcare professionals to a digital world for modelling, simulating, validating, and predicting, with greatly reduced costs and improved accuracy and performance.

4.2. Conclusions and Future Research Directions

The enhanced value and benefits that digital twin technologies bring to healthcare are accompanied by some challenges. There has been a comprehensive discussion on digital

poverty, the digital divide, and how digital twinning may exacerbate the situation for digitally disadvantaged groups [1]. The faster digitalization advances, the bigger the digital divide may become. It is essential to ask whether more people are being left behind or are being brought along by today's fast-paced digital transformations.

In addition to concerns associated with the digital divide, considering the fast development of AI technology across sectors, there are also concerns regarding the equality of access, privacy, ethics, security, and suitability for diverse needs. Often, these concerns are overlooked, especially at the early stages of new technological development when public interest and expectations may be inflated. Research has also highlighted the importance of compatibility for future integration between virtual entities, platforms, systems, IT infrastructure, and so on [14], as the development of the digital twin begins to scale. Mixed ownership, varying standards, and possibly contradictory interests may dilute the initial impact and functionalities of the digital twin. Forward-thinking, unified, compatible, and future-proofed standard/legislation is the most important pillar for the sustainable development of the digital twin in healthcare. Without it, the risk is that applications may prioritize short-term profits over long-term benefits, resulting in misunderstandings and reputational damage as public expectations are not realized. This in turn may negatively impact the availability of crucial resources for any future long-term development.

This research aimed to build a bridge between two different interest groups—digital twin and healthcare—and present the current trajectory of digital twin applications in the healthcare sector, and bring insights to enable future development in research and application. Compared with the existing literature about digital twins in healthcare, to the best of our knowledge, this is the first paper presenting the digital twin model in the healthcare context across the different life stages; it is also the first time the paradigm of digital twinning everything as a healthcare service has been proposed, which would extend the digital twinning architecture in Industry 4.0 to healthcare. This model and proposed architecture can assist researchers and practitioners in better understanding the framework of the digital twin in healthcare, identify research gaps, and discover valuable applications in specific life stages or healthcare services to contribute to further perfecting the digital twin in the healthcare model/architecture in practice. Future research will focus on healthcare aspects currently being overlooked, but where the potential exists for integrating advanced technologies like a digital twin. Inevitably, digital twin technologies are also joining forces with other trending technological advancements, i.e., AI, which has already shown its significant value in numerous areas [64,65,129,130]. Future research will investigate the interactions of digital twins and AI in general and their joint impact in specific sectors like healthcare.

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References

- 1. Hassani, H.; Huang, X.; Silva, E. The human digitalisation journey: Technology first at the expense of humans? *Information* **2021**, 12, 267. [CrossRef]
- 2. ReportLinker. Global Digital Twin Market, By Type, By Technology, By Application, By End User, By Region, Competition, Forecast Opportunities, 2017–2027F. Available online: https://www.reportlinker.com/p05778901/Global-Digital-Twin-MarketBy-Application-By-End-User-Sector-By-Region-Competition-Forecast-Opportunities.html (accessed on 27 April 2022).
- 3. Tao, F.; Qi, Q. Make more digital twins. *Nature* **2019**, 573, 490–491. [CrossRef]

- 4. Angulo, C.; Ortega, J.A.; Gonzalez-Abril, L. Towards a Healthcare Digital Twin. In *Artificial Intelligence Research and Development*; IOS Press: Amsterdam, The Netherlands, 2019; pp. 312–315.
- 5. Van Deursen, A.J.; Van Dijk, J.A. The first-level digital divide shifts from inequalities in physical access to inequalities in material access. *New Media Soc.* **2019**, *21*, 354–375. [CrossRef]
- 6. Scheerder, A.; Van Deursen, A.; Van Dijk, J. Determinants of Internet skills, uses and outcomes. A systematic review of the second-and third-level digital divide. *Telemat. Inform.* **2017**, *34*, 1607–1624. [CrossRef]
- 7. Rogers, S.E. Bridging the 21st century digital divide. TechTrends 2016, 60, 197–199. [CrossRef]
- 8. Qi, Q.; Tao, F. Digital twin and big data towards smart manufacturing and industry 4.0: 360-degree comparison. *IEEE Access* **2018**, 6, 3585–3593. [CrossRef]
- 9. Aheleroff, S.; Xu, X.; Zhong, R.Y.; Lu, Y. Digital Twin as a Service (DTaaS) in Industry 4.0: An Architecture Reference Model. *Adv. Eng. Inform.* **2020**, 47, 101225. [CrossRef]
- 10. Grieves, M. Digital twin: Manufacturing excellence through virtual factory replication. White Pap. 2014, 1, 1–7.
- 11. Glaessgen, E.; Stargel, D. The digital twin paradigm for future NASA and US Air Force vehicles. In Proceedings of the 53rd AIAA/ASME/ASCE/AHS/ASC Structures, Structural Dynamics and Materials Conference, Honolulu, HI, USA, 23–26 April 2012; p. 1818.
- 12. Qi, Q.; Tao, F.; Hu, T.; Anwer, N.; Liu, A.; Wei, Y.; Wang, L.; Nee, A.Y.C. Enabling technologies and tools for digital twin. *J. Manuf. Syst.* **2021**, *58*, 3–21. [CrossRef]
- 13. Grieves, M.; Vickers, J. Digital twin: Mitigating unpredictable, undesirable emergent behavior in complex systems. In *Transdisci- plinary Perspectives on Complex Systems*; Springer: Cham, Switzerland, 2017; pp. 85–113.
- 14. Jones, D.; Snider, C.; Nassehi, A.; Yon, J.; Hicks, B. Characterising the Digital Twin: A systematic literature review. *CIRP J. Manuf. Sci. Technol.* **2020**, 29, 36–52. [CrossRef]
- 15. Tao, F.; Liu, W.; Zhang, M.; Hu, T.; Qi, Q.; Zhang, H.; Sui, F.; Wang, T.; Xu, H.; Huang, Z. Five-dimension digital twin model and its ten applications. *Comput. Integr. Manuf. Syst.* **2019**, 25, 1–18.
- 16. Liu, M.; Fang, S.; Dong, H.; Xu, C. Review of digital twin about concepts, technologies, and industrial applications. *J. Manuf. Syst.* **2021**, *58*, 346–361. [CrossRef]
- 17. Tao, F.; Zhang, H.; Liu, A.; Nee, A.Y. Digital twin in industry: State-of-the-art. *IEEE Trans. Ind. Inform.* **2018**, *15*, 2405–2415. [CrossRef]
- 18. Pires, F.; Cachada, A.; Barbosa, J.; Moreira, A.P.; Leitão, P. Digital twin in industry 4.0: Technologies, applications and challenges. In Proceedings of the 2019 IEEE 17th International Conference on Industrial Informatics (INDIN), Helsinki, Finland, 22–25 July 2019; IEEE: Piscataway, NJ, USA, 2019; Volume 1, pp. 721–726.
- 19. Fuller, A.; Fan, Z.; Day, C.; Barlow, C. Digital twin: Enabling technologies, challenges and open research. *IEEE Access* **2020**, *8*, 108952–108971. [CrossRef]
- 20. Pang, T.Y.; Pelaez Restrepo, J.D.; Cheng, C.T.; Yasin, A.; Lim, H.; Miletic, M. Developing a digital twin and digital thread framework for an 'Industry 4.0' Shipyard. *Appl. Sci.* **2021**, *11*, 1097. [CrossRef]
- 21. Yu, L.; Zhao, Y.; Tang, L.; Yang, Z. Online big data-driven oil consumption forecasting with Google trends. *Int. J. Forecast.* **2019**, 35, 213–223. [CrossRef]
- 22. Silva, E.S.; Hassani, H.; Madsen, D.Ø.; Gee, L. Googling fashion: Forecasting fashion consumer behaviour using google trends. *Soc. Sci.* **2019**, *8*, 111. [CrossRef]
- 23. Yang, D.; Karimi, H.R.; Kaynak, O.; Yin, S. Developments of digital twin technologies in industrial, smart city and healthcare sectors: A survey. *Complex Eng. Syst.* **2021**, *1*, 3. [CrossRef]
- 24. Van Dijk, J. The Digital Divide; John Wiley Sons: Hoboken, NJ, USA, 2020.
- 25. Boschert, S.; Rosen, R. Digital twin—the simulation aspect. In Mechatronic Futures; Springer: Cham, Switzerland, 2016; pp. 59–74.
- 26. Sepasgozar, S.M. Differentiating digital twin from digital shadow: Elucidating a paradigm shift to expedite a smart, sustainable built environment. *Buildings* **2021**, *11*, 151. [CrossRef]
- 27. Singh, M.; Fuenmayor, E.; Hinchy, E.P.; Qiao, Y.; Murray, N.; Devine, D. Digital twin: Origin to future. *Appl. Syst. Innov.* **2021**, 4, 36. [CrossRef]
- 28. Kritzinger, W.; Karner, M.; Traar, G.; Henjes, J.; Sihn, W. Digital Twin in manufacturing: A categorical literature review and classification. *IFAC-PapersOnLine* **2018**, *51*, 1016–1022. [CrossRef]
- 29. Siedlak, D.J.; Pinon, O.J.; Schlais, P.R.; Schmidt, T.M.; Mavris, D.N. A digital thread approach to support manufacturing-influenced conceptual aircraft design. *Res. Eng. Des.* **2018**, 29, 285–308. [CrossRef]
- 30. Miskinis, C. What Does a Digital Thread Mean and How It Differes from Digital Twin. Challenge Advisory. Available online: https://www.challenge.org/insights/digital-twin-anddigital-thread/ (accessed on 1 May 2022).
- 31. West, T.D.; Blackburn, M. Is digital thread/digital twin affordable? A systemic assessment of the cost of DoD's latest manhattan project. *Procedia Comput. Sci.* **2017**, *114*, 47–56. [CrossRef]
- 32. Zhang, Z.; Guan, Z.; Gong, Y.; Luo, D.; Yue, L. Improved multi-fidelity simulation-based optimisation: Application in a digital twin shop floor. *Int. J. Prod. Res.* **2022**, *60*, 1016–1035. [CrossRef]
- 33. Chetan, M.; Yao, S.; Griffith, D.T. Multi-fidelity digital twin structural model for a sub-scale downwind wind turbine rotor blade. *Wind. Energy* **2021**, *24*, 1368–1387. [CrossRef]

- 34. Huang, S.; Wang, G.; Yan, Y. Building blocks for digital twin of reconfigurable machine tools from design perspective. *Int. J. Prod. Res.* **2022**, *60*, 942–956. [CrossRef]
- 35. Yu, Q.; Ren, J.; Fu, Y.; Li, Y.; Zhang, W. Cybertwin: An origin of next generation network architecture. *IEEE Wirel. Commun.* **2019**, 26, 111–117. [CrossRef]
- 36. Rodrigues, T.K.; Liu, J.; Kato, N. Application of cybertwin for offloading in mobile multiaccess edge computing for 6G networks. *IEEE Internet Things J.* **2021**, *8*, 16231–16242. [CrossRef]
- 37. Adhikari, M.; Munusamy, A.; Kumar, N.; Srirama, S.N. Cybertwin-Driven Resource Provisioning for IoE Applications at 6G-Enabled Edge Networks. *IEEE Trans. Ind. Inform.* **2021**, *18*, 4850–4858. [CrossRef]
- 38. Liu, C.; Jiang, P.; Jiang, W. Web-based digital twin modeling and remote control of cyber-physical production systems. *Robot. Comput. Manuf.* **2020**, *64*, 101956. [CrossRef]
- 39. Ammar, M.; Russello, G.; Crispo, B. Internet of Things: A survey on the security of IoT frameworks. *J. Inf. Secur. Appl.* **2018**, 38, 8–27. [CrossRef]
- 40. Bhatnagar, A.; Sharma, V.; Raj, G. IoT based car pollution detection using AWS. In Proceedings of the 2018 International Conference on Advances in Computing and Communication Engineering (ICACCE), Paris, France, 22–23 June 2018; IEEE: Piscataway, NJ, USA, 2018; pp. 306–311.
- 41. Fagbola, F.I.; Venter, H.S. Smart Digital Forensic Readiness Model for Shadow IoT Devices. Appl. Sci. 2022, 12, 730. [CrossRef]
- 42. Pierleoni, P.; Concetti, R.; Belli, A.; Palma, L. Amazon, Google and Microsoft Solutions for IoT: Architectures and a Performance Comparison. *IEEE Access* **2019**, *8*, 5455–5470. [CrossRef]
- 43. Rasheed, A.; San, O.; Kvamsdal, T. Digital Twin: Values, Challenges and Enablers from a Modeling Perspective. *IEEE Access* **2020**, *8*, 21980–22012. [CrossRef]
- 44. Mystakidis, S. Metaverse. Encyclopedia 2022, 2, 486–497. [CrossRef]
- 45. Erol, T.; Mendi, A.F.; Dogan, D. The Digital Twin Revolution in Healthcare. In Proceedings of the 2020 4th International Symposium on Multidisciplinary Studies and Innovative Technologies (ISMSIT), Istanbul, Turkey, 22–24 October 2020; IEEE: Piscataway, NJ, USA, 2020; pp. 1–7.
- 46. Croatti, A.; Gabellini, M.; Montagna, S.; Ricci, A. On the Integration of Agents and Digital Twins in Healthcare. *J. Med. Syst.* **2020**, 44, 1–8. [CrossRef]
- 47. Laubenbacher, R.; Sluka, J.P.; Glazier, J.A. Using digital twins in viral infection. Science 2021, 371, 1105–1106. [CrossRef]
- 48. Bruynseels, K.; Santoni de Sio, F.; Van den Hoven, J. Digital twins in healthcare: Ethical implications of an emerging engineering paradigm. *Front. Genet.* **2018**, *9*, 31. [CrossRef]
- 49. Pentecost, M.; Meloni, M. "It's Never Too Early": Preconception Care and Postgenomic Models of Life. Front. Sociol. 2020, 5, 21. [CrossRef]
- 50. Gardiner, P.; Hempstead, M.B.; Ring, L.; Bickmore, T.; Yinusa-Nyahkoon, L.; Tran, H.; Paasche-Orlow, M.; Damus, K.; Jack, B. Reaching Women through Health Information Technology: The Gabby Preconception Care System. *Am. J. Health Promot.* 2013, 27, eS11–eS20. [CrossRef]
- 51. Jack, B.; Bickmore, T.; Hempstead, M.; Yinusa-Nyahkoon, L.; Sadikova, E.; Mitchell, S.; Gardiner, P.; Adigun, F.; Penti, B.; Schulman, D.; et al. Reducing Preconception Risks Among African American Women with Conversational Agent Technology. *J. Am. Board Fam. Med.* 2015, 28, 441–451. [CrossRef] [PubMed]
- 52. Van Dijk, M.R.; Oostingh, E.C.; Koster, M.P.H.; Willemsen, S.P.; Laven, J.S.E.; Steegers-Theunissen, R.P.M. The use of the mHealth program Smarter Pregnancy in preconception care: Rationale, study design and data collection of a randomized controlled trial. BMC Pregnancy Childbirth 2017, 17, 1–7. [CrossRef] [PubMed]
- 53. Davidson, L.; Boland, M.R. Enabling pregnant women and their physicians to make informed medication decisions using artificial intelligence. *J. Pharmacokinet. Pharmacodyn.* **2020**, *47*, 305–318. [CrossRef]
- 54. Davidson, L.; Boland, M.R. Towards deep phenotyping pregnancy: A systematic review on artificial intelligence and machine learning methods to improve pregnancy outcomes. *Briefings Bioinform.* **2021**, 22, bbaa369. [CrossRef]
- 55. Oprescu, A.M.; Miro-Amarante, G.; Garcia-Diaz, L.; Rey, V.E.; Chimenea-Toscano, A.; Mart 'inez-Martinez, R.; Romero-Ternero, M.C. Towards a data collection methodology for Responsible Artificial Intelligence in health: A prospective and qualitative study in pregnancy. *Inf. Fusion* **2022**, *83*, 53–78. [CrossRef]
- 56. Rousian, M.; Koster, M.P.H.; Mulders, A.G.; Koning, A.H.J.; Steegers-Theunissen, R.P.M.; Steegers, E.A.P. Virtual reality imaging techniques in the study of embryonic and early placental health. *Placenta* **2018**, *64*, S29–S35. [CrossRef]
- 57. Rousian, M.; Schoenmakers, S.; Eggink, A.J.; Gootjes, D.V.; Koning, A.H.J.; Koster, M.P.; Mulders, A.G.M.G.J.; Baart, E.B.; Reiss, I.K.M.; E Laven, J.S.; et al. Cohort Profile Update: The Rotterdam Periconceptional Cohort and embryonic and fetal measurements using 3D ultrasound and virtual reality techniques. *Int. J. Epidemiol.* 2021, 50, 1426–1427l. [CrossRef]
- 58. Di Guardo, F.; Palumbo, M. Immersive virtual reality as tool to reduce anxiety during embryo transfer. *J. Obstet. Gynaecol.* **2022**, 4, 1–7. [CrossRef]
- 59. The Human Genome Project. (n.d.); The Human Genome Project. National Human Genome Research Institute. Available online: https://www.genome.gov/human-genomeproject (accessed on 12 May 2022).
- 60. 100,000 Genomes Project. (n.d.) 100,000 Genomes Project. Genomics England. Available online: https://www.genomicsengland.co.uk/initiatives/100000-genomes-project (accessed on 14 May 2022).

- 61. Newborn Genomes Programme. (n.d.) Newborn Genomes Programme. Genomics England. Available online: https://www.genomicsengland.co.uk/initiatives/newborns (accessed on 14 May 2022).
- 62. Project Baseline. (n.d.) Project Baseline. Available online: https://www.projectbaseline.com/ (accessed on 15 May 2022).
- 63. Kuwabara, A.; Su, S.; Krauss, J. Utilizing Digital Health Technologies for Patient Education in Lifestyle Medicine. *Am. J. Lifestyle Med.* **2020**, *14*, 137–142. [CrossRef]
- 64. Comito, C.; Pizzuti, C. Artificial intelligence for forecasting and diagnosing COVID-19 pandemic: A focused review. *Artif. Intell. Med.* 2022, 128, 102286. [CrossRef]
- 65. Comito, C. How COVID-19 Information Spread in U.S.? The Role of Twitter as Early Indicator of Epidemics. *IEEE Trans. Serv. Comput.* **2021**, *15*, 1193–1205. [CrossRef]
- 66. De Moraes Lopes, M.H.B.; Ferreira, D.D.; Ferreira, A.C.B.H.; da Silva, G.R.; Caetano, A.S.; Braz, V.N. Use of artificial intelligence in precision nutrition and fitness. In *Artificial Intelligence in Precision Health*; Academic Press: Cambridge, MA, USA, 2020; pp. 465–496.
- 67. Boulos, M.K.; Zhang, P. Digital Twins: From Personalised Medicine to Precision Public Health. *J. Pers. Med.* **2021**, *11*, 745. [CrossRef] [PubMed]
- 68. Konstantinidis, S.; Bamidis, P.D.; Zary, N. (Eds.) *Digital Innovations in Healthcare Education and Training*; Academic Press: Cambridge, MA, USA, 2020.
- 69. Bracq, M.S.; Michinov, E.; Jannin, P. Virtual reality simulation in nontechnical skills training for healthcare professionals: A systematic review. *Simul. Healthc.* **2019**, *14*, 188–194. [CrossRef]
- 70. Dolianiti, F.; Tsoupouroglou, I.; Antoniou, P.; Konstantinidis, S.; Anastasiades, S.; Bamidis, P. Chatbots in healthcare curricula: The case of a conversational virtual patient. In *International Conference on Brain Function Assessment in Learning*; Springer: Cham, Switzerland, 2020; pp. 137–147.
- 71. Kyaw, B.M.; Saxena, N.; Posadzki, P.; Vseteckova, J.; Nikolaou, C.K.; George, P.P.; Divakar, U.; Masiello, I.; Kononowicz, A.A.; Zary, N.; et al. Virtual reality for health professions education: Systematic review and meta-analysis by the digital health education collaboration. *J. Med. Internet Res.* 2019, 21, e12959. [CrossRef]
- 72. Pottle, J. Virtual reality and the transformation of medical education. Future Health J. 2019, 6, 181. [CrossRef] [PubMed]
- 73. Chavez, O.L.; Rodríguez, L.F.; Gutierrez-Garcia, J.O. A comparative case study of 2D, 3D and immersive-virtual-reality applications for healthcare education. *Int. J. Med. Inform.* **2020**, *141*, 104226. [CrossRef]
- 74. Gamez Diaz, R.; Yu, Q.; Ding, Y.; Laamarti, F.; El Saddik, A. Digital twin coaching for physical activities: A survey. *Sensors* **2020**, 20, 5936. [CrossRef]
- 75. Gkouskou, K.; Vlastos, I.; Karkalousos, P.; Chaniotis, D.; Sanoudou, D.; Eliopoulos, A.G. The "virtual digital twins" concept in precision nutrition. *Adv. Nutr.* **2020**, *11*, 1405–1413. [CrossRef]
- 76. Barricelli, B.R.; Casiraghi, E.; Gliozzo, J.; Petrini, A.; Valtolina, S. Human digital twin for fitness management. *IEEE Access* **2020**, *8*, 26637–26664. [CrossRef]
- 77. Ogunseiju, O.R.; Olayiwola, J.; Akanmu, A.A.; Nnaji, C. Digital twin-driven framework for improving self-management of ergonomic risks. *Smart Sustain. Built Environ.* **2021**, *10*, 403–419. [CrossRef]
- 78. Rivera, L.F.; Jimenez, M.; Angara, P.; Villegas, N.M.; Tamura, G.; Müller, H.A. Towards continuous monitoring in personalized healthcare through digital twins. In Proceedings of the 29th Annual International Conference on Computer Science and Software Engineering, Markham, ON, Canada, 4–6 November 2019; pp. 329–335.
- 79. Shamanna, P.; Saboo, B.; Damodharan, S.; Mohammed, J.; Mohamed, M.; Poon, T.; Kleinman, N.; Thajudeen, M. Reducing HbA1c in Type 2 Diabetes Using Digital Twin Technology-Enabled Precision Nutrition: A Retrospective Analysis. *Diabetes Ther.* **2020**, 11, 2703–2714. [CrossRef] [PubMed]
- 80. Shamanna, P.; Dharmalingam, M.; Sahay, R.; Mohammed, J.; Mohamed, M.; Poon, T.; Kleinman, N.; Thajudeen, M. Retrospective study of glycemic variability, BMI, and blood pressure in diabetes patients in the Digital Twin Precision Treatment Program. *Sci. Rep.* **2021**, *11*, 1–9. [CrossRef] [PubMed]
- 81. Zhong, X.; Sarijaloo, F.B.; Prakash, A.; Park, J.; Huang, C.; Barwise, A.; Herasevich, V.; Gajic, O.; Pickering, B.; Dong, Y. A multidisciplinary approach to the development of digital twin models of critical care delivery in intensive care units. *Int. J. Prod. Res.* 2022, 60, 4197–4213. [CrossRef]
- 82. Liu, Y.; Zhang, L.; Yang, Y.; Zhou, L.; Ren, L.; Wang, F.; Liu, R.; Pang, Z.; Deen, M.J. A Novel Cloud-Based Framework for the Elderly Healthcare Services Using Digital Twin. *IEEE Access* **2019**, *7*, 49088–49101. [CrossRef]
- 83. Voigt, I.; Inojosa, H.; Dillenseger, A.; Haase, R.; Akgun, K.; Ziemssen, T. Digital twins for multiple sclerosis. *Front. Immunol.* **2021**, 12, 1556. [CrossRef]
- 84. Chakshu, N.K.; Sazonov, I.; Nithiarasu, P. Towards enabling a cardiovascular digital twin for human systemic circulation using inverse analysis. *Biomech. Modeling Mechanobiol.* **2021**, 20, 449–465. [CrossRef]
- 85. Barbiero, P.; Torne, R.V.; Lio, P. Graph Representation Forecasting of Patient's Medical Conditions: Toward a Digital Twin. *Front. Genet.* **2021**, *12*, 1289. [CrossRef]
- 86. Elayan, H.; Aloqaily, M.; Guizani, M. Digital twin for intelligent context-aware iot healthcare systems. *IEEE Internet Things J.* **2021**, 8, 16749–16757. [CrossRef]

- 87. Lal, A.; Li, G.; Cubro, E.; Chalmers, S.; Li, H.; Herasevich, V.; Dong, Y.; Pickering, B.W.; Kilickaya, O.; Gajic, O. Development and verification of a digital twin patient model to predict specific treatment response during the first 24 hours of sepsis. *Crit. Care Explor.* 2020, 2, e0249. [CrossRef]
- 88. Mourtzis, D.; Angelopoulos, J.; Panopoulos, N.; Kardamakis, D. A Smart IoT Platform for Oncology Patient Diagnosis based on AI: Towards the Human Digital Twin. *Procedia CIRP* **2021**, *104*, 1686–1691. [CrossRef]
- 89. Corral-Acero, J.; Margara, F.; Marciniak, M.; Rodero, C.; Loncaric, F.; Feng, Y.; Gilbert, A.; Fernandes, J.F.; Bukhari, H.A.; Wajdan, A.; et al. The 'Digital Twin' to enable the vision of precision cardiology. *Eur. Heart J.* **2020**, *41*, 4556–4564. [CrossRef]
- 90. Zhang, J.; Li, L.; Lin, G.; Fang, D.; Tai, Y.; Huang, J. Cyber resilience in healthcare digital twin on lung cancer. *IEEE Access* **2020**, 8, 201900–201913. [CrossRef]
- 91. Zhang, J.; Tai, Y. Secure medical digital twin via human-centric interaction and cyber vulnerability resilience. *Connect. Sci.* **2021**, 34, 895–910. [CrossRef]
- 92. Mao, R.Q.; Lan, L.; Kay, J.; Lohre, R.; Ayeni, O.R.; Goel, D.P. Immersive virtual reality for surgical training: A systematic review. *J. Surg. Res.* **2021**, *268*, 40–58. [CrossRef] [PubMed]
- 93. Bjelland, Q.; Rasheed, B.; Schaathun, H.G.; Pedersen, M.D.; Steinert, M.; Hellevik, A.I.; Bye, R.T. Towards a Digital Twin for Arthroscopic Knee Surgery: A Systematic Review. *IEEE Access* **2022**, *10*, 45029–45052. [CrossRef]
- 94. Laaki, H.; Miche, Y.; Tammi, K. Prototyping a digital twin for real time remote control over mobile networks: Application of remote surgery. *IEEE Access* **2019**, *7*, 20325–20336. [CrossRef]
- 95. Zinchenko, K.; Song, K.T. Autonomous Endoscope Robot Positioning Using Instrument Segmentation with Virtual Reality Visualization. *IEEE Access* **2021**, *9*, 72614–72623. [CrossRef]
- 96. Karakra, A.; Fontanili, F.; Lamine, E.; Lamothe, J. HospiT'Win: A predictive simulation-based digital twin for patients pathways in hospital. In Proceedings of the 2019 IEEE EMBS international conference on biomedical health informatics (BHI), Chicago, IL, USA, 19–22 May 2019; IEEE: Piscataway, NJ, USA, 2019; pp. 1–4.
- 97. Lu, Q.; Xie, X.; FANG, Z.; Chen, L.; Ye, Z.; Pitt, M. An inter-hospital digital twin for response to COVID-19 pandemic based on blockchain–A proof of concept. *Sustain. Cities Soc.* **2021**, *in press*.
- 98. Peng, Y.; Zhang, M.; Yu, F.; Xu, J.; Gao, S. Digital Twin Hospital Buildings: An Exemplary Case Study through Continuous Lifecycle Integration. *Adv. Civ. Eng.* **2020**, 2020, 8846667. [CrossRef]
- 99. Farsi, M.; Daneshkhah, A.; Hosseinian-Far, A.; Jahankhani, H. (Eds.) *Digital Twin Technologies and Smart Cities*; Springer: Berlin/Heidelberg, Germany, 2020.
- 100. Shahat, E.; Hyun, C.T.; Yeom, C. City digital twin potentials: A review and research agenda. *Sustainability* **2021**, *13*, 3386. [CrossRef]
- 101. Boje, C.; Guerriero, A.; Kubicki, S.; Rezgui, Y. Towards a semantic Construction Digital Twin: Directions for future research. *Autom. Constr.* **2020**, *114*, 103179. [CrossRef]
- 102. Sacks, R.; Brilakis, I.; Pikas, E.; Xie, H.S.; Girolami, M. Construction with digital twin information systems. *Data-Centric Eng.* **2020**, 1, e14. [CrossRef]
- 103. Lee, D.; Lee, S.H.; Masoud, N.; Krishnan, M.S.; Li, V.C. Integrated digital twin and blockchain framework to support accountable information sharing in construction projects. *Autom. Constr.* **2021**, *127*, 103688. [CrossRef]
- 104. Hu, X.; Cao, H.; Shi, J.; Dai, Y.; Dai, W. Study of hospital emergency resource scheduling based on digital twin technology. In Proceedings of the 2021 IEEE 2nd International Conference on Information Technology, Big Data and Artificial Intelligence (ICIBA), Chongqing, China, 17–19 December 2021; IEEE: Piscataway, NJ, USA, 2021; Volume 2, pp. 1059–1063.
- 105. Song, Y.; Li, Y. Digital Twin Aided Healthcare Facility Management: A Case Study of Shanghai Tongji Hospital. In *Construction Research Congress* 2022; American Society of Civil Engineers (ASCE): Reston, VA, USA, 2022; pp. 1145–1155.
- 106. Zhao, J.; Feng, H.; Chen, Q.; de Soto, B.G. Developing a conceptual framework for the application of digital twin technologies to revamp building operation and maintenance processes. *J. Build. Eng.* **2022**, *49*, 104028. [CrossRef]
- 107. Burlacu, A.; Iftene, A.; Jugrin, D.; Popa, I.V.; Lupu, P.M.; Vlad, C.; Covic, A. Using Artificial Intelligence Resources in Dialysis and Kidney Transplant Patients: A Literature Review. *Biomed. Res. Int.* **2020**, 2020, 1–14. [CrossRef]
- 108. Wingfield, L.R.; Ceresa, C.; Thorogood, S.; Fleuriot, J.; Knight, S. Using Artificial Intelligence for Predicting Survival of Individual Grafts in Liver Transplantation: A Systematic Review. *Liver Transplant.* **2020**, *26*, 922–934. [CrossRef]
- 109. Briceno, J.; Calleja, R.; Hervás, C. Artificial intelligence and liver transplantation: Looking for the best donor-recipient pairing. *Hepatobiliary Pancreat. Dis. Int.* **2022**, 21, 347–353. [CrossRef] [PubMed]
- 110. Martínez-Gutiérrez, A.; Díez-González, J.; Ferrero-Guillén, R.; Verde, P.; Álvarez, R.; Perez, H. Digital Twin for Automatic Transportation in Industry 4.0. *Sensors* **2021**, 21, 3344. [CrossRef] [PubMed]
- 111. Gao, Y.; Qian, S.; Li, Z.; Wang, P.; Wang, F.; He, Q. Digital Twin and Its Application in Transportation Infrastructure. In Proceedings of the 2021 IEEE 1st International Conference on Digital Twins and Parallel Intelligence (DTPI), Beijing, China, 15 July–15 August 2021; IEEE: Piscataway, NJ, USA, 2021; pp. 298–301.
- 112. Wright, N. Death and the Internet: The implications of the digital afterlife. First Monday 2014, 19. [CrossRef]
- 113. Moreman, C.M.; Lewis, A.D. (Eds.) Digital Death: Mortality and beyond in the Online Age: Mortality and beyond in the Online Age; ABC-CLIO: Santa Barbara, CA, USA, 2014.
- 114. Stokes, P. Deletion as second death: The moral status of digital remains. Ethics Inf. Technol. 2015, 17, 237–248. [CrossRef]

- 115. Javaid, S.; Zeadally, S.; Fahim, H.; He, B. Medical Sensors and Their Integration in Wireless Body Area Networks for Pervasive Healthcare Delivery: A Review. *IEEE Sens. J.* **2022**, 22, 3860–3877. [CrossRef]
- 116. Patrone, C.; Lattuada, M.; Galli, G.; Revetria, R. The role of Internet of Things and digital twin in healthcare digitalization process. In *The World Congress on Engineering and Computer Science*; Springer: Singapore, 2018; pp. 30–37.
- 117. Wu, Q.; Liu, J.; Wang, X.; Feng, L.; Wu, J.; Zhu, X.; Wen, W.; Gong, X. Organon-a-chip: Recent breakthroughs and future prospects. Biomed. Eng. Online 2020, 19, 9. [CrossRef]
- 118. Baillargeon, B.; Rebelo, N.; Fox, D.D.; Taylor, R.L.; Kuhl, E. The Living Heart Project: A robust and integrative simulator for human heart function. *Eur. J. Mech. A/Solids* **2014**, *48*, 38–47. [CrossRef] [PubMed]
- 119. Martinez-Velazquez, R.; Gamez, R.; El Saddik, A. Cardio Twin: A Digital Twin of the human heart running on the edge. In Proceedings of the 2019 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Istanbul, Turkey, 26–28 June 2019; IEEE: Piscataway, NJ, USA, 2019; pp. 1–6.
- 120. Subramanian, K. Digital Twin for Drug Discovery and Development—The Virtual Liver. *J. Indian Inst. Sci.* **2020**, *100*, 653–662. [CrossRef]
- 121. Coorey, G.; Figtree, G.A.; Fletcher, D.F.; Redfern, J. The health digital twin: Advancing precision cardiovascular medicine. *Nat. Rev. Cardiol.* **2021**, *18*, 803–804. [CrossRef] [PubMed]
- 122. Barnabas, J.; Raj, P. The human body: A digital twin of the cyber physical systems. In *Advances in Computers*; Elsevier: Amsterdam, The Netherlands, 2020; Volume 117, pp. 219–246.
- 123. Shengli, W. Is human digital twin possible? Comput. Methods Programs Biomed. Update 2021, 1, 100014. [CrossRef]
- 124. Lamb, K.; Barrett, M.; Pilosof, N.; Fenby-Taylor, H.; Walters, A. *Digital Twin Journeys: The Journey to the Smart Hospital of the Future*; Centre for Digital Built Britain: Cambridge, UK, 2021.
- 125. Hassani, H.; Huang, X.; Silva, E. Digitalisation and Big Data Mining in Banking. Big Data Cogn. Comput. 2018, 2, 18. [CrossRef]
- 126. Hassani, H.; Huang, X.; Silva, E. Big data and climate change. Big Data Cogn. Comput. 2019, 3, 12. [CrossRef]
- 127. Hassani, H.; Yeganegi, M.R.; Beneki, C.; Unger, S.; Moradghaffari, M. Big data and energy poverty alleviation. *Big Data Cogn. Comput.* **2019**, *3*, 50. [CrossRef]
- 128. Hassani, H.; Huang, X.; MacFeely, S.; Entezarian, M.R. Big data and the united nations sustainable development goals (UN SDGs) at a glance. *Big Data Cogn. Comput.* **2021**, *5*, 28. [CrossRef]
- 129. Comito, C.; Forestiero, A.; Zumpano, E. (Eds.) *Integrating Artificial Intelligence and IoT for Advanced Health Informatics: AI in the Healthcare Sector*; Springer Nature: Berlin/Heidelberg, Germany, 2022.
- 130. Comito, C.; Falcone, D.; Forestiero, A. AI-Driven Clinical Decision Support: Enhancing Disease Diagnosis Exploiting Patients Similarity. *IEEE Access* **2022**, *10*, 6878–6888. [CrossRef]