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Digital twins for well-being: an overview

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REVIEW

Digital twins for well-being: an overview [version 1; peer review: 1 approved with reservations]

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Abstract

Digital twin (DT) has gained success in various industries, and it is now getting attention in the healthcare industry in the form of well-being digital twin (WDT). In this paper, we present an overview of WDT to understand its potential scope, architecture and impact. We then discuss the definition and the benefits of WDT. After that, we present the evolution of DT frameworks. Subsequently we discuss the challenges, the different types, the drawbacks, and potential application areas of WDT. Finally we present the requirements for a WDT framework extracted from the literature.

Keywords

Digital Twin, Internet of Things, CPS, Healthcare, AI, Machine Learning, Well-being

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Introduction

Digital twins enable the monitoring, understanding, and optimization of all functioning of humans, and provide constant health insight to improve quality of life and well-being¹. The key benefit of the DT system is that DT utilizes artificial intelligence (AI) to remove the barriers of interoperability between heterogeneous data². In addition, the machine learning (ML) aspect of AI enables prediction or decision making from heterogeneous digital data³. Therefore, DT can be advantageous to preventive, cost-effective, and guided healthcare. Furthermore, it can benefit early identification of health issues before they develop.

Digital twins have been growing rapidly as a field of academic research for over a decade. To look at the trend of research in this domain, we surveyed published articles related to digital twin. The graph in Figure 1 illustrates the growth of DT for well-being as a field of academic research compared to the growth of DT for other sectors like the production and manufacturing industry. Overall, it can be observed from this graph that the academic contribution on DT experienced a fluctuation from 2002–2016. After 2016, the curve experienced an increasing trend till 2019. From 2019–2020 there was a drop in overall DT academic research. The academic research on DT in other sectors, excluding health and well-being, experienced fluctuation throughout the period, and after a rise from 2019–2020, it dropped slightly in 2021.

In contrast, publications discussing DT in the health and well-being field experienced a gradual increase from 2017–2019. Then till 2021 this trend experienced a visible surge. Interestingly, in 2021 the research on DT for health and well-being reached almost the same level as the other sectors. Comparing this trend to the overall sector, it is evident that recently DT is being studied much more for health and well-being.

There are several surveys in the literature in the field of DT; however, most surveys are generic and have focused on the manufacturing industry. So far, there has been little work done to survey DT for well-being, which is the key focus of this paper. As DT in healthcare is still at its early stage of adoption and demands a general understanding on the definition, consideration, challenges, and success to establish it for the betterment of healthcare, Knowledge of these factors will provide the requirements to design a well-being digital twin (WDT) framework.

The rest of the paper is organized as follows. In the next section, we present the definition of WDT. Then, we present the benefits of WDT. After that, we discuss the trend of digital twin frameworks. In the subsequent section, we discuss the technologies for WDT. Then we discuss the special considerations for WDT. After that, we present the key challenges and discuss WDT in the industry. In the subsequent section, we provide an overview of various types of WDT in literature. We provide the drawbacks and the potential application areas. Finally, in the last section, we conclude the study by providing the requirements we found through our study.

Definition of well-being digital twin

This section presents definitions of DT in health and well-being. The goal of this section is to pick the most used definition from the literature for WDT model. From 2019–2021 researchers have increasingly studied DT in the well-being industries. The authors in these publications have described DT from diverse perspectives to fit well-being. Based on these studies, we discuss four definitions of DT in the context of well-being in Table 1.

It can be observed from the above table that data visualization and monitoring are common as well as innate features

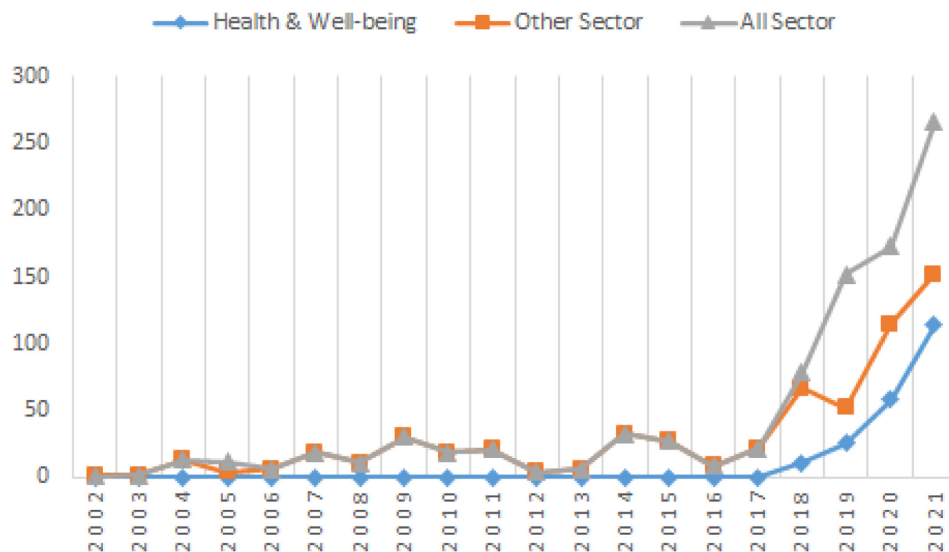


Figure 1. The number of digital twin publications in different fields based on surveyed papers between 2002 and 2021.

Table 1. Definition of digital twin (DT) in the context of well-being (paraphrased from the literature).

Reference	Definition	Features
1	Digital twins enable the monitoring, understanding, and optimization of all functioning of humans, and provide constant health insight to improve quality of life and well-being.	Data visualization Prediction, Intelligence, Analysis, Decision making, Feedback loop
4	Personal digital twins are data-driven solution that depicts individuals' health status based on regularly collected health parameters.	Data visualization, Data monitoring
2	DT is a digital representation of a human in a computer or a server on the cloud.	Data monitoring, Data visualization
5	A digital twin is a simulation technology that delivers digital health insights while also allowing prediction and recommendation within a feedback loop.	Data visualization Prediction, Simulation, Analysis, Recommendation, Feedback loop

of DTs^{1,3}. In addition, predictive well-being and personalized well-being are the two fields of well-being that can be aided by DT. Interestingly, both fields require intelligence to satisfy the goals of edge applications⁶. The authors in 1 addressed the importance of this fact and attributed DT with intelligence.

The integration of intelligence in DT has become crucial to support the needs of current well-being applications. In our opinion, since AI acts as the brain of the DT, it is highly required that health twins have proper intelligence to support the decision-making of its application.

The prediction process in DT applications is often supported by data science and machine learning algorithms (MLA). However, the more specific explanation would make the decision-making process of DT trustworthy and meaningful^{7,8}. For instance, if a health twin is used to monitor diabetes risk factors from activity history (e.g., exercise, steps, beats per minute(bpm), etc.), it should also be able to show the contribution of potential risk factors for an individual. This could be an option to embed explainable intelligence health twin.

It can be observed from Table 1, that the definition by El Saddik¹ covers diverse features so that WDT fits various applications of healthcare.

Benefits of WDT

In recent years, growing research has welcomed digital twin in the well-being sector. This section presents the benefits behind the increasing demand for studying DT for health and well-being.

1. WDT can support coronavirus disease 2019 (COVID-19) response applications for virtual health checkups².
2. WDT can save time and money when testing treatments⁴.
3. WDT allows understanding hidden pattern of health insights⁹.

4. Continuous data visualization¹⁰ and test simulation is offered by DT technology.
5. Treatment plans can be evaluated without involving or harming real patients⁷.
6. "What if analysis" feature of DT could be beneficial for planning treatments¹.
7. Early and emergency prediction facility could be enjoyed anytime⁹.
8. Personalized (patient centric), and preventive well-being digitalization could be supported broadly with WDT¹.

It can be observed from the above points that due to the outbreak of COVID-19, early and emergency prediction of disease has become an important consideration for the well-being of individuals. Due to the predicting capabilities of DT through ML, digital twin has gained popularity for designing various frameworks for well-being.

Digital twin frameworks

In this section we discuss components and features of significant DT frameworks till 2021 to find out which framework suits best in the context of WDT. The goal of this section is to find a suitable type of DT framework that fits WDT.

Based on our review, the revolution of DT architecture has been illustrated in Figure 2. It can be observed that the DT architecture has experienced a rapid transformation from 2014 to 2021 and this is still continuing. The four types of DT frameworks are the following:

1. 3-Dimensional DT¹¹
2. Cloud cyber-physical system (Cloud CPS) based DT¹²
3. Intelligent DT³
4. Industry 4.0 DT¹³

4 Significant Digital Twin Framework Evolution

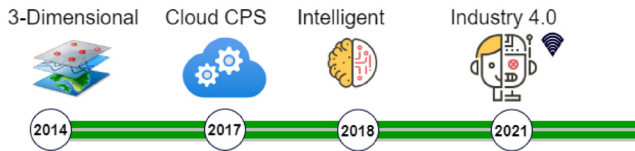


Figure 2. Evolution of digital twin framework. CPS=cyber-physical system.

Grieves first introduced the standard three-dimension DT architecture in his product lifecycle management (PLM) course at the University of Michigan in 2003. This can be regarded as the pioneer DT. The conceptual framework by Grieves proposed three basic components¹¹:

1. Physical space – consists of aircraft, radar, related real infrastructures, and assisting functionalities.
2. Connection – represents the physical data virtually and provides information for controlling the physical space.
3. Virtual space – presents the virtual counterpart of the original mission-related infrastructures.

The basic 3-layer DT frameworks are comprised of three major processes¹²- calibration, control, and augmentation. In detail, the AR/VR system in the frameworks collects data from the virtual part and intelligently presents it to the user after the calibration procedure. However, these three-dimensional frameworks could not handle open and user-oriented broader applications such as agriculture, well-being, and medicine for real-time decision-making¹⁴. The reason behind this is that Greive's architecture did not consider the application of the software as a service (SASS) category¹³. The SAAS applications are cloud-based software systems that provide services over the Internet. In this era of IoT, most of the applications have shifted to SAAS to deal with big data. Dropbox, G suites, and Amazon web services are some common examples of SAAS applications¹⁵.

A digital twin is perhaps a subset of the cyber-physical system (CPS), and both lead to the smart manufacturing idea. There is indeed a strong distinction between the two technologies: the CPS is tied to science, while DTs are intricately linked to technological advances. Both contribute to smart manufacturing¹⁶. The CPS-based DT framework has been widely proposed by researchers. CPS-based architectures have opened a door to establish a bridge between IoT and DT¹². Therefore, DT is no longer only tied to the manufacturing industry and has gained potential to advance other industries including farming and well-being.

Nowadays, well-being applications have a diverse range of goals due to the increasing number of connected things. This

scenario has raised the demand for intelligent frameworks. In an intelligent framework the AI interference engine and data mining techniques are used to capture qualitative and quantitative information to provide real-time tracking, forecasting, and collective decision making. The WDT applications often require to collect and process heterogeneous data to forecast health issues. Therefore, the intelligent DT architectures are more suitable for WDT¹. In addition, the industry 4.0 framework also provides similar features like the intelligent framework. However, the core concept of Industry 4.0 frameworks can be explored through hybrid Cloud CPS and AI DT architectures. The authors in 1, proposed an ecosystem (Figure 3) that includes a communication model for the interaction between a real twin and digital twin. This communication model includes three major parts:

1. Sensing/actuating,
2. Intelligence, and
3. Representation of the twins connected through a tactile internet.

The authors compared digital twin sensors, for instance, IoT, haptics, etc. to the five human senses of a real twin. The human brain is compared with the machine intelligence of the digital twin. An example of the ML based DT framework can be a DT having the capability of predicting the risk of diabetes from a person's activity history and provide recommendations (e.g., have a walk). Therefore, we believe that the intelligent DT framework is most suitable for WDT systems. In addition, the AI inference engine is the prime focus to design a WDT framework.

Technologies for WDT framework

This section discusses the underlying technologies for a WDT framework. The purpose of this discussion is to understand the required technologies and capabilities for a WDT framework.

DT could be used to enjoy the full potential of AI-enabled healthcare. Although AI is related to IoT and CPS, we have focused on the basic technologies to develop a full-fledged WDT. Let us understand this by an example. Suppose that we want to create a DT of mental well-being with a goal of personalized stress prediction and monitoring. To implement this, we will need the following stepsL

1. Initially, we will need smartwatch exercise data (daily activities), social media histories, phone logs, etc.¹⁷ Here we will need IoT.
2. Then, to use these sources to get data we may need computation algorithms, which can be done using CPS¹⁸.
3. After that, we will need to prepare the heterogeneous data from diverse sources that we have collected for predicting stress. Pre-processing is done to fit data to the prediction algorithm. Data Mining is employed for this purpose⁵.

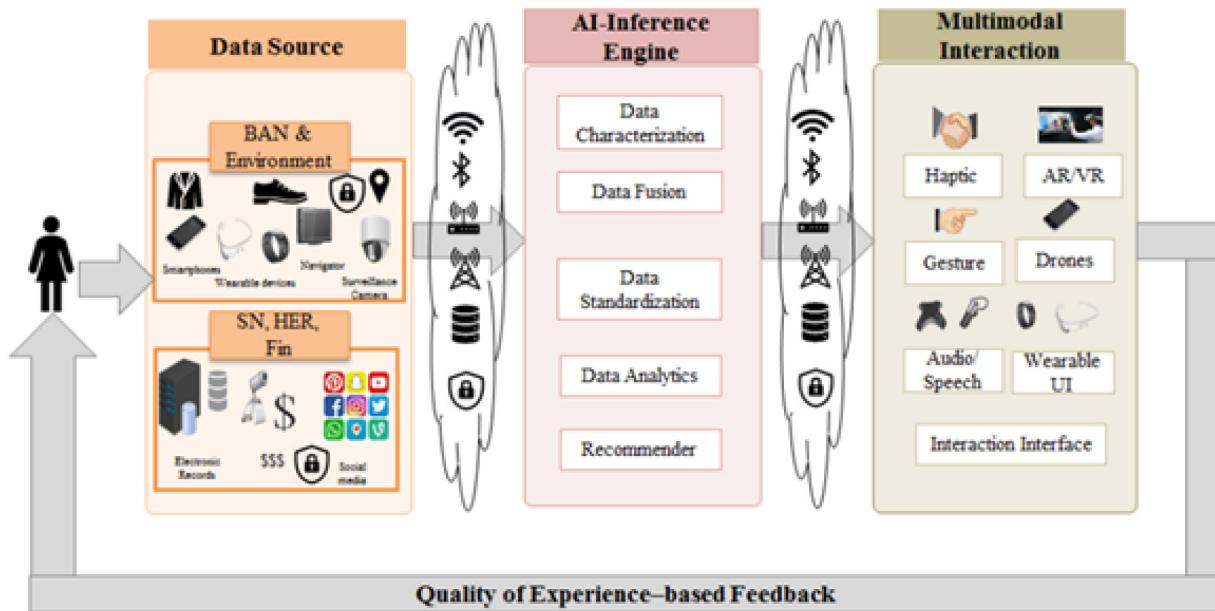


Figure 3. Ecosystem of the digital twin for health and well-being adapted from 1 BAN=body area network; AI=artificial intelligence; AR/VR=augmented reality/virtual reality; UI=user interface.

4. Then with the preprocessed data, classifiers will be built by training classification algorithms (support vector machine, decision tree, random forests, Bayesian nets, etc.). This is supported by ML technology⁹.
5. The DM and ML will be combined to build Artificial Intelligence in the WDT¹.
6. Finally, the desired mental health twin will be prepared with the capabilities of stress management.

From this example, we can observe how the emerging key technologies represent mental well-being to predict a health issue (stress). The WDT from the above process will provide a way to visualize numerous data views of stress and predict whether an individual is stressed. However, to control the risk factors (e.g., physical activities, social activities, bio-sensor readings), the WDT needs to support multiple diagnoses. Because the risk of disease varies from person to person, the same individual can suffer from multiple problems. Therefore, a DT framework for health and well-being needs to consider heterogeneous data and employ multiple disease/disease risk prediction mechanisms using a dynamic ML process.

Special considerations for WDT

We have compared the well-being digital twin (WDT) with product digital twin (PDT) and discovered the distinct subjects between these two types of DTs. The comparison was conducted to understand special considerations for WDT.

In an earlier period, the key research concern was how PDT can be constructed¹⁵. Health domain applications usually involve patient monitoring, health monitoring, disease prediction, and other well-being applications. As soon as DT was considered to aid the health domain, the research focus was moved to address how the digital replica of a human can be created?². The key differences between product DT and WDT are tabulated in Table 2.

Based on the differences presented in Table 2, there exists a couple of challenges, for example, the Fitbit can collect and represent the beats per minute (bpm), step count, etc. using the accelerator, gyroscope, and pressure sensor. However, various physical states are extremely complex to capture. For instance, Skin rubbing count as irritation, and Count of food intake as polyphagia are two important health insights to predict diabetes risk¹⁹. Specially designed biosensors would be required to retrieve this information. Some biosensors may not be viable to implement or may require complex and time-consuming development²⁰.

Another notable difference between PDT and WDT is social media. In this digital era of connectivity, humans have an additional life affecting their mental as well as physical state - the social media life. If a person is disturbed by Facebook posts, comments, or messages, physical data alone will not be enough to predict their stress level⁴.

Several researchers have suggested data mining as a vital technology to mitigate health data mapping complexity²¹.

Table 2. Differences between product digital twin and health digital twin.

Subject	Product Digital Twin (PDT)	Health Digital Twin (WDT)
Mental State	Product does not have mental state correlated with all other factors.	Health risk factor can be governed by human mental state.
Nature of Rules	The rules of product physics are almost similar and fixed for same category.	Rules for human physics may vary from person to person, even day to day.
Social Media	Product life cycle cannot be affected by social media.	DT has strong correlation with social media.
Mapping Complexity	Mapping product status digitally is less complex than health status.	Mapping health status digitally is more complex than product status.
Data	Capturing product data needs less preprocessing.	Health data are more heterogeneous and unstructured.
Data Preprocessing	Less rigorous than Health Twin	Rigorous data preprocessing is required.
Ethical Consideration	Product DT is free of complex ethical consideration.	Human life is precious and systems for human health require to consider several ethical concerns.

In one of our works²², we proposed a knowledge-driven epidemiology library to identify and predict associated risk factors of disease as well as the recommendations. Precisely, some missing data can be mapped using ML and AI²³. The key idea here is predicting the values of an attribute based on other correlated attributes. However, here comes the new challenge - heterogeneity of data⁵. To avail the benefit of ML or AI for mapping health insights, we need to handle heterogeneous data from diverse sources. For instance, electronic health records (EHR), historical health data, continuous health status, social media activity, and raw sensor data are some notable sources of health data⁴.

Finally, human-related systems have to deal with several challenges, especially when it is an autonomous system. Comparatively, the degree of challenges in WDT is more complex than the PDT. These challenges are discussed in more details below.

Key challenges

In this section, we present various challenges to designing a WDT framework for predictive well-being applications.

- **Technical issues:** The seamless feature and capability of handling heterogeneous data with an interoperability standard proposed in 17, has made DT a four-in-one technology to represent digital health²⁴. DT could be used to enjoy the full potential of AI-enabled smart well-being. Although AI is connected to IoT and CPS, here we have focused on the basic technologies to develop a full-fledged WDT. Let us take the following scenario to explain the WDT.
- **Data bias:** The prediction by WDT can suffer from racial or other biases and cause inequalities in health care²⁵. A model trained with wrongly-labelled data is threatening to the WDT applications. For instance, if a

classifier is trained with available sensor data and ignores notable features of diabetes prediction because those were not measurable by the sensor, the result of prediction will lose reliability²⁶.

- **Level of autonomy:** To what extent patients can access autonomy is another ethical concern. Autonomous clinical decision support systems (CDSS) are very risky in some cases. If the classifier makes an irrational prediction and associated recommendation and the patient starts to follow those recommendations it may harm their health. For example, if 8–10 hours of sleep is wrongly identified as insomnia and the system recommends increasing sleep hours as a precaution, it can put the individual's health at risk. Which level of autonomy can be offered to the patient is one of the key ethical concerns²⁵.
- **Trust in intelligence:** AI is still in the process of establishing²⁵. The context of product and well-being is far different from each other²⁷. If the accuracy of a system is 76%²⁸ it refers to the fact that 24% is incorrect. In the case of well-being, it may be proven fatal. For example, the classifier may predict that a person has a lower risk of diabetes, while they actually have a higher risk. *How medical trust can be assured?*, is a big ethical question. In other words, transparency in machine learning-based prediction is required^{26,29}.
- **Data visualization issue:** Rigorous data pre-processing may provide better accuracy, but this may bring another ethical issue which may hide visualization of real health issues.
- **Consent of human:** In general, the human is the key input source for WDT. The WDT system may need data sharing and collection using third-party applications or

labeling by human intervention. Taking patient’s consent and allowing them to modify consent should be implemented.

WDT in industry

Digital twins are utilized in a variety of certain other industries to monitor, maintain, and simulate probable consequences if any problems emerge while the apparatus is in use. Since well-being costs are rising globally, and the world’s population is growing, it is the right time to adopt digital twins to improve the system and provide a more efficient solution for both well-being professionals and patients without causing harm to either.

According to reports, digital twins might bring a 900% cost savings in hospitals and a 61% reduction in blue code hospital incidents, which includes emergencies in adult well-being³⁰. Many prominent names are competing to be a part of the development of the first fully-fledged digital twin. Some remarkable names including Siemens, Phillips, and IBM are all leading runners. These leading companies are utilizing their massive databases and financial muscle. Other companies, on the other hand, are beginning to experiment and push the boundaries further for the growth of digital twins. In Table 3, we have provided information about the industrial progress of DT in well-being.

After reviewing the current industrial advances, we found that digital twinning of equipment, wards, medical information, and critical patients. However, the digital twin for early risk prediction of disease is still less explored.

Types of WDT

This section present an overview of various types of DTs proposed in the well-being domain. Initially we discuss existing work on various DT for health and well-being. Then, we present a summary of the existing work.

Health twins

A recent study¹⁰, has investigated digital twin studies in the health domain from the perspectives of patient monitoring, the pharmaceutical sector, hospitals, and wearable technologies. They anticipated that AI would play a pivotal role in accelerating DT in the well-being industry. In this study, the authors discussed various use cases of using DT such as clinical decision support system (CDSS), surgery planning, and medicine prediction. The authors emphasized that various remedial forecasts can be produced if the ML and AI approaches are employed in digital twins. The predictions can optimize processes and information usage. However, they did not elaborate on how ML and AI could advance WDTs.

On the contrary, the authors in 1, narrated that the AI-interference engine has treated data characterization, standardization, analysis, prediction, and recommendation together as the enabler of ML and AI in WDT. Similarly, in 7, the authors considered data mining as a powerful tool for enabling simulation in cloud WDT.

In 4, the authors considered the heterogeneous data collection issues and proposed a standardized ISO/IEEE 11073 DT framework architecture for health and well-being. This model provides the process of collecting data from personal health devices, processing that data, and providing feedback to the user in a closed feedback loop. The ISO/IEEE 11073 enabled AI well-being systems can subdue the data interoperability issues in well-being. However, data mining not only supports obtaining powerful input datasets to feed simulation models but also supports efficient processing to understand simulation outputs. In general, the process is obtaining a balanced dataset for decision support⁵.

In 25, the authors recommended DTs as a breakthrough tool for care management of persons with multiple sclerosis (pwMS) to cope with the complexities of this chronic, multidimensional

Table 3. Industrial progress on digital twin (DT) well-being.

Company	Product/Service
Siemens ³¹	3D Digital Heart Twin, that facilitates doctors to simulate surgical procedure and to verify tests on patients causing severe injury. One of the first full-fledged ward management twins.
GE well-being ³²	Simulation to assist in sensualizing data from multiple sources in order to generate a Digital Twin of the hospital for testing alternatives. Plethora of hypothetical scenarios to be examined, all at a low risk.
IBM ³³	Efficient and personalized patient centered treatment using digital twin of patient.
Dassault Systèmes ³⁴	3-D models of a live heart, on which artificial silico models can be run and cardio research can be conducted
NHS ³⁵	A testbed for testing whether low-cost 5G connectivity aids technologically deprived people by offering consistent access to digital community and personal solutions.
Digitwins ³⁶	a comprehensive modelling system that would allow numerous treatment simulations to be done without causing harm to the patient.
Phillips ³⁷	AI-enabled cardiac models that can, convert 2D ultrasound images into data that doctors may use to identify issues or automatically analyze scans to help surgeons plan procedures.

condition at the individual level. They highlighted that AI-enabled analysis could be employed to develop DT of patient characteristics. More specifically, the potentiality of AI on various disease parameters such as clinical and para-clinical outcomes, multi-omics, biomarkers, and patient-related data was discussed for handling the heterogeneous and vast amount of patient-related data. The authors in 4, also emphasized the fact that DT can handle a diverse set of health parameters for decision making.

The authors in 38 proposed CloudDTH to address the issue of real-time supervision and the accuracy of crisis warnings for the elderly in well-being services. Similar to 6,39 the model in 38 adopted³. Although classifier interpretation like⁴⁰, could contribute to this framework, the authors preferred the monitoring process as a black-box prediction. The what-if analysis could not be supported fully with the framework.

Healthcare center management twin

In 27, the authors present the concept of agent-based WDT by merging the DT notion with agents in a modeling and simulation framework based on mirror worlds. The key idea of this work was designed for trauma management. In simple words, their DT symbolizes the operative phase of trauma rehabilitation, which begins when the trauma is classified as severe in the preceding phase. It can be observed clearly that prediction and the use of intelligence are required to support this predictive software agent. To implement the semantic reasoning capability of the software the author sought to employ semantic web technology. However, one of the key challenges to implementing semantic web is a heterogeneous representation of evolving ontologies, which is obvious in the health domain. Furthermore, the ethical implication of WDT requires a trustworthy and authorized source of knowledge 'as it's related to humans^{26,29}.

In 41, the authors proposed a HospiT^W framework that can forecast unforeseen events earlier to determine the impact on the hospital and feasible strategies to mitigate the harm. Furthermore, they proposed a method to connect the HospiT^W with a real hospital to enable the tracking, monitoring, and validating that the hospital functionality is going in the proper direction and at the correct time. The authors realized that IoT AI, BAN will be the core technology to implement their idea. Precisely, they employed artificial intelligence interventions to decide the suitable scenario to practice in a real hospital, incorporating numerous parameters regarding risks, finances, and so on. This part of the study was proposed to activate validation.

Organ condition twin

In 39, the authors presented the cardio twin architecture for detecting ischemic heart disease (IHD). They used a convolutional neural network (CNN) to classify non-myocardial and myocardial diseases. The authors classified features from electrocardiograms and completed the assignment with 85.77% accuracy. In cardio twin, the authors employed CNN-based classification to apply intelligence for meaningful Data visualization.

Similar to 39, machine learning was considered as the key enabler of DT coaching in 6. Likewise³⁹, authors designed a DT coach system based on the DT ecosystem in 3. These two works evaluated the universal DT well-being ecosystem in a specific application context. Inevitably, the authors in 6,39 obtained better accuracy to prove the implementation of DT.

The goal of 40 is resembling⁶, that aimed at indulging DT as an alternate of human-in-the-loop in data noise reduction. Likewise⁶, the authors also worked on a smart fitness management system to monitor athletes and recommend preventive measures for better fitness. The authors preferred K Nearest Neighbour(KNN) algorithm for data noise reduction and classifier interpretation to analyze individual health parameters. Precisely, based on the user's activity history the fitness management system can recommend which behavior needs to be changed. For instance, increase carbohydrate in 3 units. To retrieve the suggestions using ML, the authors employed a counterfactual classifier explanation algorithm^{42,43}. The key idea of this algorithm is to provide values of different attributes for a particular class prediction.

The authors in 40, used greedy algorithms to optimize the top 5 attributes contributing to the classifier's outcome. The works presented in this paper showed an interesting way to embed intelligence in DT predictive system. However, the counterfactual algorithm cannot show any range or threshold to understand how different parameters contribute to a decision. Moreover, the suggestions need to be defined by involving the rule provider (human). In addition, the counterfactual algorithm suffers from the Rashomon effect^{42,43} that causes multiple explanations for each instance. This poses another level of complexity to analyze which explanation to pick.

By contrast, in 28 the authors recommended explainable AI (XAI) based DT as a solution to retrieve classifier prediction for the clinical decision support system. They conducted an empirical analysis on a liver disease prediction using an SVM classifier. They utilized the Lime XAI algorithm^{43,44} to interpret classifier prediction. The benefits of using local interpretable model-agnostic explanations (LIME)^{45,46} are that it is easy to implement, and supports heterogeneous types of datasets (e.g., clinical data, local health records) in diverse format image (mixed, nominal, binary, etc). In addition, multiple classification algorithms like decision trees, random forest, and Bayesian networks are supported by LIME. Another notable feature of LIME is that it can be handled dynamically or in default mode. Therefore, if any CDSS demands using all features it can be supported. Furthermore, if the system requires selective or optimal features it can be supported. In the context of well-being, it's one of the key requirements, that data diversity is handled best. The key difference between the counterfactual algorithm and the XAI algorithm is the way of interpreting the classifier.

The counterfactual algorithm directly shows a value of attributes while the XAI algorithm shows association and comparative relations with a threshold. For example, if the risk

class is 1 then how many attributes are contributing at the side of 1 and how many are contributing to 0 is demonstrated. The XAI opens a prospective door for WDT to mitigate the lack of accountability of prediction issues. There exists another algorithm Shapely⁴⁶ for implementing XAI, which has modified LIME. However, the output of LIME is more convenient to visualize. Unlike counterfactual algorithms, it requires less rigorous development for selecting explanations⁴³.

Cardiovascular twin

In another work, the authors used neural networks to predict abdominal aortic aneurysm (AAA) and its severity employing the inverse analysis methodology of the DT in 47. This study also achieved an acceptable level of accuracy of 97.79%. A deep neural model was employed to capture the bi-directional context links between dangerous code phrases in 18. The authors aimed at confirming cyber resilience on well-being big data on lung cancer. Their Bidirectional Long Short-Term Memory (Bi-LTSM) model performed with better accuracy than other classification based DTs.

The IoT context-aware DT in 48, predicted cardiovascular conditions from electrocardiogram (ECG) data with various machine learning algorithms above 90% accuracy for each. The proposed ECG heart rhythm classification also performs with the highest accuracy³⁹. However, how this proposed ML-based prediction is different from regular ML prediction is not clear from the study. Furthermore, how trust can be added to the prediction was not addressed.

The studies discussed above are mainly of two categories. Some of the studies have been conducted to present the state-of-the-art of DT, other have been conducted to address several health issues as well as to satisfy diverse range of goals. In Table 4, we summarize the application-specific literature in terms of the type of well-being domain, application goal key features, fundamental technologies addressed by the contemporary WDT researchers. In addition, we tabulate the proposed twins and associated threats in the studies.

In summary, we highlight the following points presented in Table 4:

1. WDT has been widely proposed for P4-medicine: personalized, pPredictive, preventive, and participatory. The real-time monitoring, prediction, intelligence and simulation features of WDT has made it possible to support multiple domains of well-being.
2. Either health twins or organ twins have been proposed in literature. Some authors have proposed treatment organization management^{27,41}.
3. CDSS, precision medicine and regulatory monitoring are common application goals of WDTs. Since DT can offer the best of four trendy technologies (IoT, CPS, DM, ML), it has been warmly accepted for the decision-making and data visualization in well-being.

4. IoT and different ML algorithms have been utilized to construct several types of WDTs.
5. Handling multiple sources and black-box prediction are two common threats in the current studies. The nature of the applications often requires explanation for the prediction.
6. Counterfactual algorithm and XAI algorithm are two solutions that have been proposed in the literature for retrieving explanation of prediction.
7. Some recent studies have taken the ethical challenges of DT into account⁴⁹.

In the next section we discuss the ethical consideration of DT.

Drawbacks of WDT

Although DT has gained success in the production industry, it is at the early stage of adoption in the health and well-being sector. From the difference between digital twins of product and health, we found that WDT needs some extra considerations due to handling human health. Some of the drawbacks of WDT are:

- **Inadequate or missing data:** To represent a human health conditions data of various features are required. However, the sensing technology still has limitations to capture various data like eat count, drink count, irritation, etc. The scarcity of this data and information may lead to inaccurate models and suggestions. For an example, for predicting diabetes risk, polyphagia is a mandatory feature, which can be learned from the number of time an individual eats. Such data can be captured through user input via specific apps.
- **Ethical overheads:** The accessibility, duration of data access, consent, and ethical conditions should all be specified. Due to dealing with human health WDT faces ethical overheads.
- **Trust in AI:** AI models like deep learning or neural networks might be good for accuracy but not explainable enough. For WDT applications this is another extra concern.
- **Necessity of domain knowledge:** Iterative development of the connected healthcare services commonly require practitioners and caregiver's engagement for data validation, and data labelling.

Potential application area

Based on the analysis of WDT discussed so far in this review, we summarize the following potential application areas (Figure 4):

- **Collecting and managing vast healthcare data:** Several applications like activity monitoring apps and

Table 4. Summary of work related to WDT. Here, AI = artificial intelligence, CDSS = clinical decision support system, CNN= convolutional neural network, DM = data mining, IoT = internet of things, KNN = K nearest neighbour, ML = machine learning, MLP = multilayer perceptron, SVM = support vector machine, Bi-LSTM = bidirectional long short-term memory.

Reference	Published in	Well-being Domain	Application	Key Features	Enabling Technologies	Threats
38	2019	Personalized, Preventive	Elderly Health Monitoring	Regular monitoring	IoT, AI	Integration of AI
10	2019	Participatory, Personalized, Predictive, Preventive	Smart well-being	CDSS, Drug Discovery	DM, ML, AI	Data Heterogeneity, Integration of AI
28	2019	Participatory, Personalized, Predictive, Preventive	detection of Liver disease	CDSS	ML, XAI: Lime	Lower accuracy in prediction
39	2019	Preventive, Predictive, Participatory	Ischemic Heart Disease Detection	CDSS, Regular Monitoring	ML: CNN	Recommendation extraction
41	2019	Preventive, Predictive	Hospital's Anomaly Prediction	Abnormal event Prediction	ML	Handling data heterogeneity
17	2020	Personalized, Participatory	Smart well-being	Regular Monitoring	DM, ISO/IEEE 11073 Standard,	Big Data handling
50	2020	Participatory, Personalized, Predictive, Preventive	Fitness Management	Regular Monitoring, Recommendation	ML: KNN, SVM Counterfactual algorithm	Recommend extraction
51	2020	Participatory, Personalized, Predictive	Personalized Medicine	Drug discovery	ML AI	Integration of AI Handling multiple health parameters
6	2020	Participatory, Personalized, Predictive	Coaching Athletes	Regular Monitoring	ML: CNN	Prediction result is not explainable
27	2020	Participatory, Personalized, Predictive	Trauma Management	Monitoring Trauma Center	AI Robotics	Integration of AI Handling multiple health parameters
25	2021	Participatory, Personalized, Predictive, Preventive	Health Monitoring of Multiple sclerosis	CDSS	ML DM	Handling multiple health parameters
48	2021	Participatory, Personalized, Predictive, Preventive	Heart Condition Classification	CDSS, Regular Monitoring	ML DM	Handling multiple health parameters
47	2021	Participatory, Personalized, Predictive	Blood circulation Analysis	Regular Monitoring	LTSM, ML: MLP	Prediction is not explainable

heart rate monitoring systems usually require to collect and process real-time data which is usually vast in quantity. WDT can facilitate such applications with the capabilities of IoT and CPS.

- **Meaningful data visualization:** To visualize meaningful data and to analyze and identify critical/hidden

conditions, the ML and DM capabilities of WDT can be beneficial.

- **To facilitate predictive healthcare:** Predictive healthcare applications for early-stage risk prediction of disease, specialist check-up recommendations, and patient-specific recommendation systems are still less

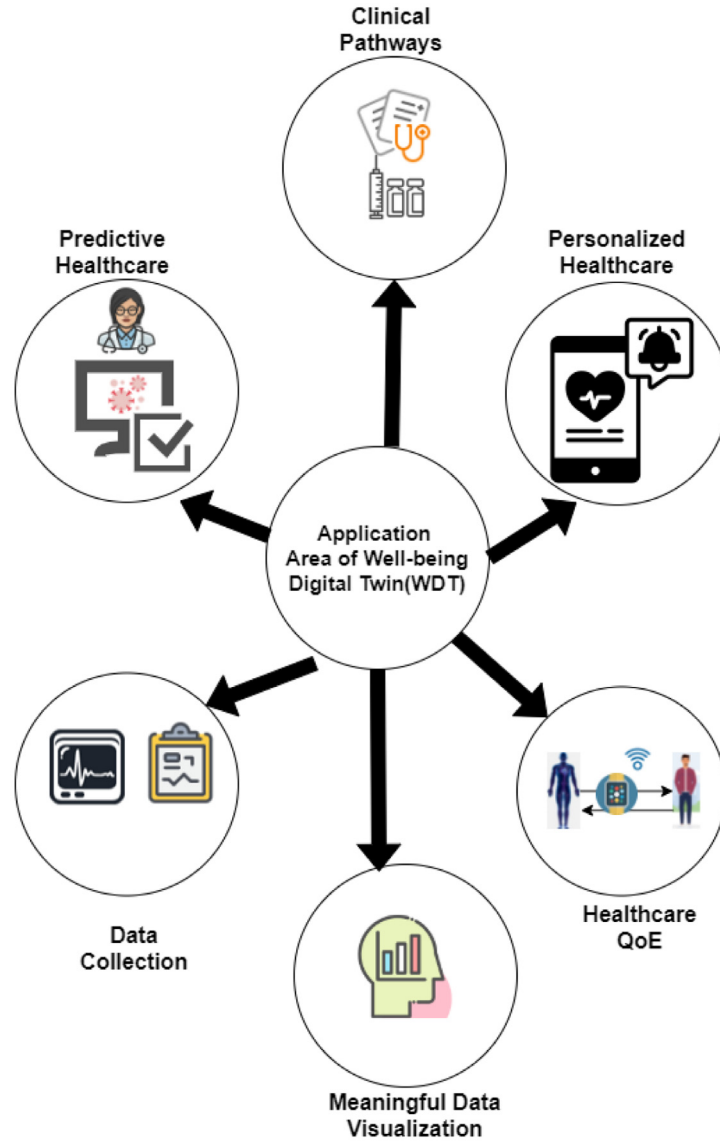


Figure 4. Potential application areas of well-being digital twin (WDT). QoE=quality of experience.

explored through DT than other healthcare applications. Early stage or patient-specific predictive healthcare can be explored through WDT. The AI inference engine of WDT can advance this application area.

- **Personalized healthcare system:** There are several individual-specific applications for well-being—for instance, digital coaching, elderly healthcare, immune system care etc. The ML capabilities of DT can support such predictive applications.
- **To understand clinical pathways:** For planning treatment, surgery and medication, DT has been used commonly. Testing treatment on a digital replica of human health subdues the risk of hampering human health. Moreover, since the procedure is done on the DT instead of the human, it can be done several times.

- **To improve healthcare quality of experience (QoE):** The bi-directional communication between a human and their digital twin can improve the healthcare QoE. The multimodal interaction through a wearable device or smart device may contribute to improving the healthcare QoE.

Requirements

Based on the different WDT research discussed so far in this section, we summarize the following requirements for future development of WDT:

1. **Heterogeneous data source:** A WDT framework connecting multiple health data sources, including EHR, social media, wearable sensors, etc., will be able to support multiple diagnoses. For example, various non-communicable diseases (NCDs) like diabetes,

stroke, and heart attack can be diagnosed from the same model. Hence, intelligent data (sensory) fusion mechanisms are needed.

2. **Algorithm selection:** Different algorithms are good at handling datasets with different properties⁵². Therefore the framework will require selecting suitable machine learning algorithms dynamically.
3. **Prediction from EHR:** Creating a vast knowledge base is complex, costly, and time-consuming. EHRs like prescriptions, diagnosis records, etc., include medical practitioner's identification by default. Therefore, using EHRs to train the classifiers and extract rules and ground truth can reduce the cost and time for manual data preprocessing and data labelling. In addition, it includes the status of the patient's signs, symptoms, risk factors, and numerous patterns.
4. **Explainable prediction:** The works discussed in this study could provide more explanation to the users. More specifically, rationale of why an instance is categorized as normal or abnormal could provide a user-friendly DT. The XAI will act as a powerful tool to explain the classifier and bring trust to the intelligence.

Conclusions

Overall, we found that DT in the health domain is much more than data collection and visualization, and demands embedding as much intelligence as possible into DT. The WDT works discussed in this review could provide more explanation to the users on their assessments and recommendations. On one hand the WDTs need to provide consistent, continuous health status. On the other hand, the health care industry must deal with multiple challenges. Furthermore, there are considerable hazards in collecting, transferring, and storing data including personal information, which can be difficult to gather and manage ethically. Industrial companies appear to be more focused on digital anatomy or digitizing smaller features such as heart rate and tailored fitness, among other things. Certainly, all goals are equally crucial in moving digital well-being forward.

Data availability

No data are associated with this article.

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This paper presents a survey about Digital Twin Technology in the domain of well-being. The paper offers a great source of information for researchers who are interested in the domain by citing a really good and recent number of works that have been done in this domain. My comments about the paper are the following:

- The sentence *"As DT in healthcare is still at its early stage of adoption and demands a general understanding on the definition, consideration, challenges, and success to establish it for the betterment of healthcare, Knowledge of these factors will provide the requirements to design a well-being digital twin (WDT) framework."* needs rephrasing.
- In the paragraph *"the rest of the paper... our study"* contains frequent repetitions of *"Then"*, *"After that"*, and *"In the subsequent"*. I suggesting using terms like First, Second, Third etc.
- In the paragraph *"For instance, if a health twin is used to monitor diabetes risk factors from activity history (e.g., exercise, steps, beats per minute(bpm), etc.), it should also be able to show the contribution of potential risk factors for an individual. This could be an option to embed explainable intelligence health twin"*, I do not quite understand the option of embedding explainable intelligence health twin. Do you mean here that embedding a twin that can intelligently explain the contribution of health risk factors to the user is possible?
- In the section *"Benefits of WDT"*, the sentence *"This section presents the benefits behind the increasing demand for studying DT for health and well-being."* should be rephrased. Are you trying to tell the benefits that result from the increase in the number of studies of DT for health and well-being, or you would like to summarize the benefits of using DT in the domain of health care and well-being?
- The sentence *"In this section we discuss components and features of significant DT frameworks till 2021 to find out which framework suits best in the context of WDT"* should be rephrased. I would recommend something like *"In this section, we discuss the components and features*

of the significant DT frameworks that were proposed recently to find out the framework that may best fit the context of WDT”.

- In the sentence “*rapid transformation from 2014 to 2021 and this is still continuing*”, I would remove the phrase “*and this is still continuing*”.
- The phrase “*The conceptual framework by Grieves proposed three basic components:*” should be rephrased to “Grieves’ conceptual framework proposes three basic components”.
- In the paper, you refer to a real twin. Is a real twin the real user? I would add a bracket to say what a real twin is since the survey is not necessarily read by domain experts.
- Remove the L from “*we will need the following stepsL*”. In addition, please keep the present tense when mentioning the needed steps. For example, “we need” or “we may need” and not “we will need”.
- In table 3, the Product/Service description for Siemens seems confusing and needs to be rephrased.
- In the sentence “*After reviewing the current industrial advances, we found that digital twinning of equipment, wards, medical information, and critical patients.*”. Are you trying to say “After reviewing the current industrial advances, we found that digital twinning of equipment, wards, medical information, and critical patients have been explored”?
- The authors have given numerous DWT design challenges; however, I believe the paper should also address societal challenges, such as the public acceptance of the technology and the acceptance of health care workers in adopting such technology.

Overall, the paper is well organized but it needs to be well revised. There are many grammatical mistakes and a misuse of punctuations.

Is the topic of the review discussed comprehensively in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Internet of things, Artificial Intelligence, and Embedded Systems

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
