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DIGITAL TWIN OF PATIENT IN CLINICAL WORKFLOW

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ABSTRACT: The concept of a digital twin being made use of in healthcare is an emerging research area. Digital twins in healthcare have the potential to enable more precise and personalised care, especially for patients experiencing chronic conditions. Previous work has identified digital twins as mathematical models. Digital twins have been classified as grey box, surrogate and black box models. Based on this classification, the black box models can handle data intensive and sophisticated problems. This makes black box models a candidate for constructing digital twins of patients. Such digital twins can then assist clinicians in clinical decision making. This has the potential to reduce cognitive burden on clinicians, to increase precision and personalisation of care through enhanced use of data, and to improve patient outcomes and cost implications. However, introducing such digital twins to healthcare would be a significant intervention that would alter traditional clinical workflows. As such, we present in this paper one of the first attempts of conceptual mapping of altered next generation primary care clinical workflows that would allow the incorporation of digital twins of patients in managing chronic conditions.

Keywords: artificial intelligence, chronic health conditions, clinical workflow, digital twin, machine learning, personalised care, precision medicine, primary care

BACKGROUND

A digital twin can be defined as a digital replica of a whole or a partial aspect of a physical-world entity (Barricelli et al. 2019). The twin can connect with the physical entity through some form of data transfer, and thereby simulate the physical entity's characteristics (Barricelli et al. 2019). This concept has over time been revolutionising many industries, including product design and smart manufacturing (Tao et al. 2018). Emerging from the aerospace and aviation sectors, more recently the concept is being applied to healthcare fields as well (e.g. genomics (Björnsson et al. 2020), aged care (Liu et al. 2019), cancer care (Wickramasinghe et al. 2021)). The key features that make digital twins attractive are that digital twins enable easy visualisation, reasoning, experimenting and forecasting of certain aspects of a physical world entity, in a way that is efficient and cost effective (Singh et al. 2021).

Realising how such features become beneficial in healthcare, we present in this paper one of the first attempts of conceptualising the introduction of digital twins to healthcare. Specifically, we are considering the construction and the use of digital twins of patients. Just as in a typical scenario like product design and failure forecasting in the manufacturing sector, we see potential in the construction and use of digital twins of patients in healthcare. The benefits lie especially in managing chronic conditions. Some work related to cancer (Wickramasinghe et al. 2021) and dementia (Wickramasinghe et al. 2022: p.ooac072; Wickramasinghe et al. 2022: p.e066336) have already begun. The objective is to enable data-driven decision support to clinicians, and thereby enhance precision and personalisation of diagnosis and care — a pressing issue and an aspiration in modern healthcare (World Alzheimer Report 2018).

While constructing and implementing the usage of digital twins is a complex synergy between artificial intelligence and digital health, another facet that must not be missed is the clinical workflow. Our earlier works (Wickramasinghe et al. 2021, 2022: p.ooac072; Wickramasinghe et al. 2022: p.e066336) indicate that the introduction of digital twins will almost certainly cause significant alterations to existing clinical workflows. This aspect must be paid serious attention and must be managed through intelligent change management considering not only data, technique and technology issues, but also people and process issues. In that interest, we present in this paper one of the first attempts to conceptualise and map out how primary care workflows might alter at the introduction of digital twins. We keep our conceptualisation agnostic of a health condition; however, we focus on managing chronic conditions that would require multiple clinical visits and long-term engagement. Such a conceptualisation becomes important as that would help us to foresee numerous implementation challenges that might have to be addressed including the pain points, specific technology requirements, any specific clinical training or education components required, and also to foresee points for value creation. Hence, the overarching research question under consideration is: 'How can we design and develop digital twins to support clinical decision making for various healthcare contexts?'

DIGITAL TWIN INCORPORATED PRIMARY CARE CLINICAL WORKFLOWS

The digital-twin-incorporated primary care clinical workflows are discussed in this section in three generations: Generation 0, Generation 1 and Generation 2. Generation 0 is the present-day practice with no digital twins, but with electronic record keeping. We use a recent cross-case comparative analysis study (Davis et al. 2019) from the United States to identify the basic components of modern clinical workflows. This study summarises four phases of the clinical workflow: (1) Identifying (the problem); (2) Engaging/transitioning; (3) Providing treatment; and (4) Monitoring/adjusting care. We agree with this listing and thus draw foundation from here to our analysis. We thus present an analysis of Generation 0 detailing current practice, without digital twins. Then we extend to discuss Generation 1 clinical workflows. Generation 1 is the phase where digital twins of patients will be constructed with data, over time. This will be a learning phase in artificial intelligence sense. We discuss how and where the traditional workflow (i.e. Generation 0) will have to alter to facilitate this new generation. Then, we discuss Generation 2, which is the workflow in which digital twins are available for use to support clinical decision making.

Generation 0: A mapping of the conventional primary care clinical workflow

Conventional clinical workflow is studied first. This helps to understand how the digital twin incorporation enhances, yet builds on, conventional clinical practice. The discussed conventional workflow is based on the hypothetico-deductive approach of clinical decision making of Banning (2008), Barrows & Tamblyn (1980) and Edwards et al. (2004) and the clinical workflow analysis of Davis et al. (2019).

The conventional workflow is depicted in Figures 1 and 2. Depicted in Figure 1 is how a patient progresses over time through multiple clinical encounters. The workflow within a clinical encounter is depicted in Figure 2.

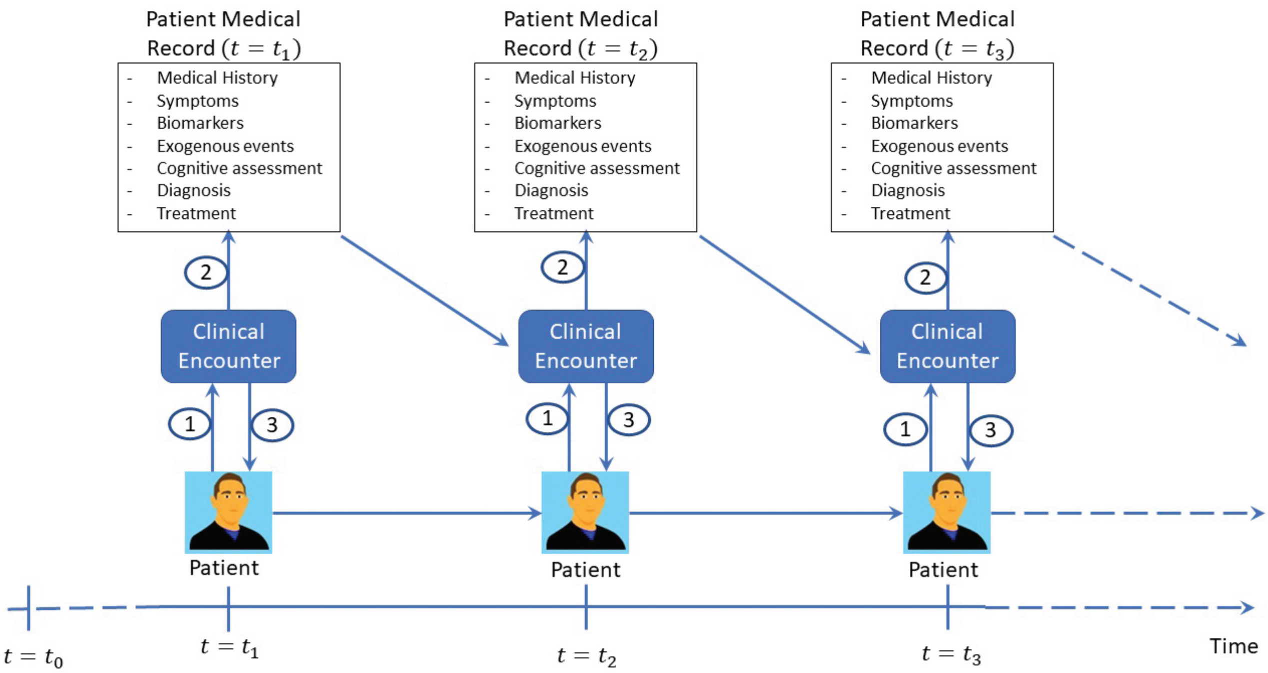

Figure 1: Mapping of a conventional primary clinical workflow (Generation 0) along time prior to incorporating digital twins. The circled numbers imply the following steps: (1) The patient consults the clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) The clinician communicates the diagnosis and treatment plan.

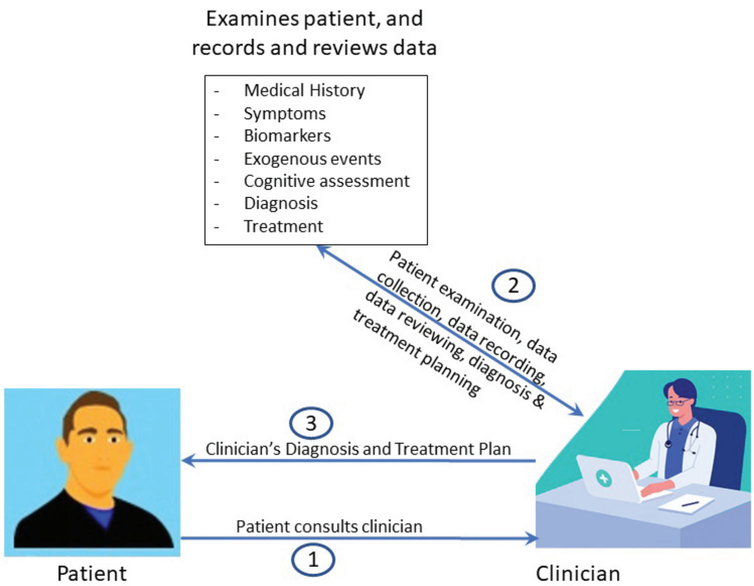

Figure 2: Mapping of the detailed workflow (Generation 0) within the 'Clinical Encounter' block in Figure 1. The circled numbers imply the following steps: (1) The patient consults the clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) The clinician communicates the diagnosis and treatment plan.

Two outputs result from each clinical encounter (i.e. as per Figure 1): (1) A diagnosis and a treatment plan for the patient; (2) A medical record of the patient. The content of the medical record is subject to the health condition under investigation. The previous medical records provide input to subsequent clinical encounters as indicated in Figure 1.

Prior to digital record keeping and clinical decision support systems being used in healthcare, patient medical records were kept entirely on paper. The use of paper-based records is still not uncommon (Skyttberg et al. 2016). The shortcomings of paper-based records and their incompatibility with electronic Clinical Decision Support Systems (CDSSs) are well known. Such limitations with paper records over the years have led to the adoption of electronic record keeping and modern CDSSs (Alpert 2016; Hersh 1995). The strengths of going electronic include reduction of medical errors and improving efficiency of clinical workflows (Alpert 2016; Hersh 1995). In addition, making use of big data capabilities for clinical research is a modern desire (Alpert 2016). With the availability of genomic data, there is enormous potential for data-driven knowledge discovery and enabling precise and personalised care (Alpert 2016; Björnsson et al. 2020). Bridging the gap between patient data and enabling data-driven decision support for precise and personalised care, is where digital twins of patients come to play (Björnsson et al. 2020). The remainder of this paper elaborates on this potential. A way in which digital twins can be introduced to enhance conventional clinical workflows is discussed.

Generation 1: Clinical workflow augmentation to enable the construction of digital twins

Machine learning plays an essential role in 'big data' clinical research (Reiz et al. 2019; Solenov et al. 2018). Data and machine learning are essential to realise digital twins as well in our contexts. As such, one of the first requirements to realise digital twins will be good quality data (Reiz et al. 2019; Solenov et al. 2018). However, the existing banks of medical data, although quite rich, do suffer from lack of accessibility and interoperability (Adler-Milstein 2017; Shaw et al. 2019; Ulapane & Wickramasinghe 2021). This leads to a 'cold start' problem in the machine learning sense (Pliakos et al. 2019). It is reasonable to assume that there is likely to be a 'cold start' challenge in many clinical applications when one tries to introduce machine learning solutions. Therefore, Generation 1 of the augmented clinical workflow is aimed at alleviating the 'cold start' problem by systematically collecting relevant clinical data in a structured form that is easy to be used for machine learning purposes. The proposed approach for systematic data collection extends by enhancing the 'Patient Medical Record' block in Figure 1. This is achieved by introducing a digital twin generation, update and data retrieval mechanism as depicted in Figure 4. Thus, shown in Figures 3 and 4 is the Generation 1 of the augmented clinical workflow that incorporates digital twins.

The key difference between Figure 3 in contrast to Figure 1 is that the Patient Medical Record in Figure 1 which would traditionally be recorded in paper form, or in some way similar to an Electronic Medical Record (EMR),

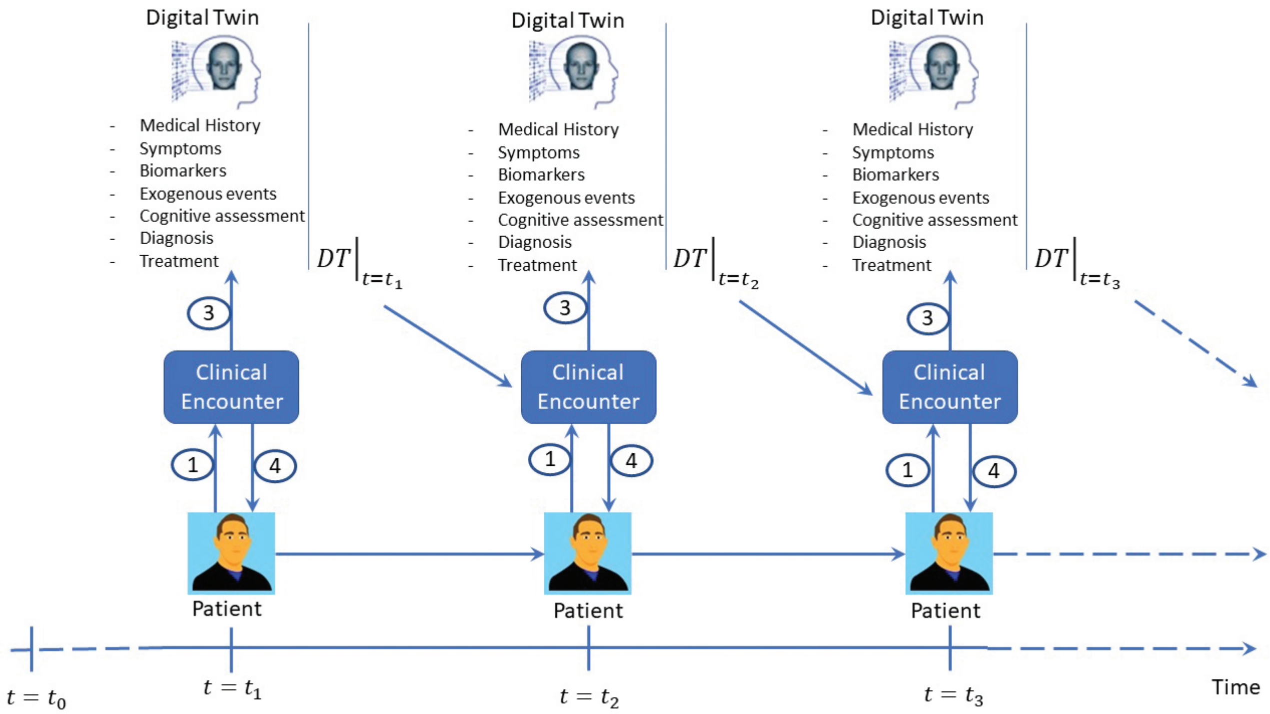

Figure 3: Mapping of digital twin incorporated proposed primary care clinical workflow (Generation 1) along time. The circled numbers imply the following steps: (1) The patient consults clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) If a digital twin doesn't exist, a digital twin is automatically created from data recorded in (2), if a digital twin exists, it will automatically get updated from data recorded in (2) and the existing data will be retrieved and displayed to the clinician; (4) The clinician communicates the diagnosis and treatment plan.

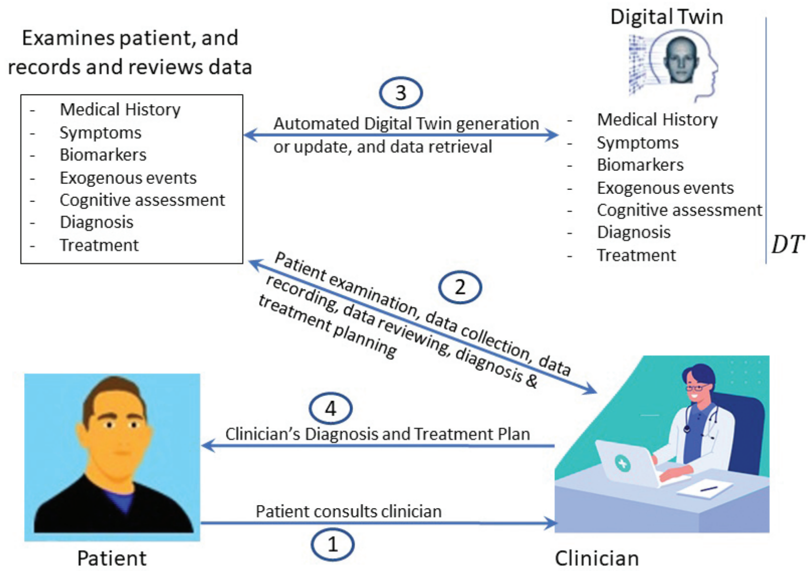

Figure 4: Mapping of the detailed workflow (Generation 1) within the 'Clinical Encounter' block in Figure 3. The circled numbers imply the following steps: (1) The patient consults clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) If a digital twin doesn't exist, a digital twin is automatically created from data recorded in (2), if a digital twin exists, it will automatically get updated from data recorded in (2) and the existing data will be retrieved and displayed to the clinician; (4) The clinician communicates the diagnosis and treatment plan.

is being recorded as a digital twin as shown in Figure 3. The step of digital twin generation and/or update and/or data retrieval occurring within a clinical encounter is illustrated in Figure 4.

It is important to note that the digital twin is automatically generated and/or updated while the clinician enters relevant data into a structured interface of some computerised or mobile information system. A special feature of the digital twin is that it is saved in a structured numeric form. Hence, there will be an automated translation process which translates clinical data into a structured numeric form that can be easily used for machine learning tasks.

Furthermore, the clinician can retrieve data from an existing digital twin as well. In the retrieval process, an automated inverse transformation occurs from numeric form to plain language for the clinician to comprehend. Apart from the novelty of digital twin incorporation in Figure 4, the clinician's decision-making process is identical to that of the conventional workflow (i.e. the one in Figure 2). The clinician may have more convenience in retrieving existing data and visualising them; however, in this generation of the workflow the clinician is not able to have the assistance of a machine learning solution, supposedly because a 'cold start' problem persists.

The digital twins generated and updated over time in this generation though, will be securely saved over time. This is a point where the latest updates of blockchain technology and implications to health data (Attaran 2022) might become useful in terms of data integrity and security. These digital twins saved over time will form a dataset that potentially enables machine-learning-based decision support to clinicians in the subsequent generation of clinical workflow augmentation. The further augmented workflow with the assistance of machine learning constitutes Generation 2 of the workflow augmentation.

Generation 2: Clinical workflow augmentation to enable the construction, updating and the use of digital twins to ensue simultaneously

By the time Generation 2 of the clinical workflow can be implemented, there will be a bank of previous digital twins collected from Generation 1. These previous data can be used to train machine-learning models to assist clinical decision making. The workflow augmentation by way of incorporating machine-learning models is illustrated in Figures 5 and 6.

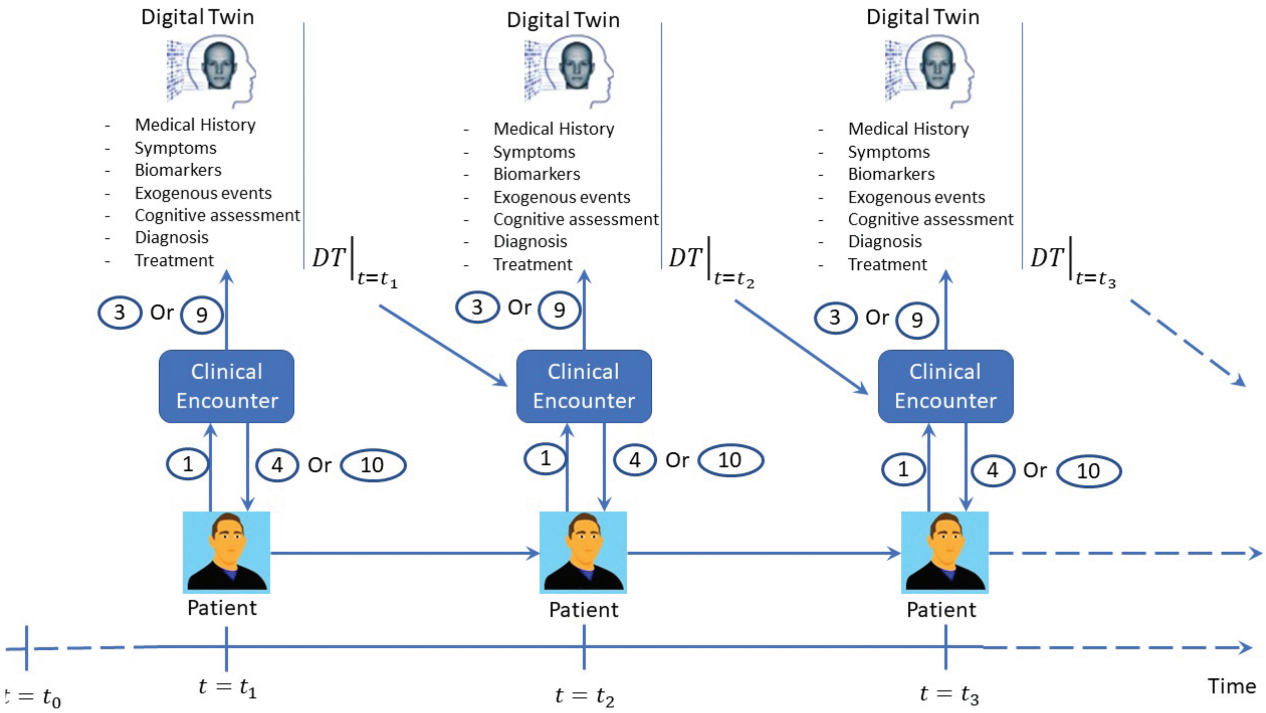

Figure 5: Mapping of the digital twin incorporated proposed primary care clinical workflow (Generation 2) along time. The circled numbers imply the following steps: (1) The patient consults clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) If a digital twin doesn't exist, a digital twin is automatically created from data recorded in (2); if a digital twin exists, it will automatically get updated from the data recorded in (2) and the existing data will be retrieved to display to the clinician; (4) The clinician communicates their diagnosis and treatment plan if the present assessment is sufficient; (5) If further assessment is required, the clinician sends a query to a machine-learning model learned from the digital twins of past patients; (6) The machine-learning model acquires current patient's data from the digital twin, performs inference, and records the inference in the digital twin; (7) The machine-learning model communicates the inferred diagnosis and treatment plan to the clinician; (8) The clinician makes an augmented decision on diagnosis and treatment plan and records it; (9) The digital twin is automatically updated according to data recorded in (8); (10) The clinician communicates their augmented diagnosis and treatment plan.

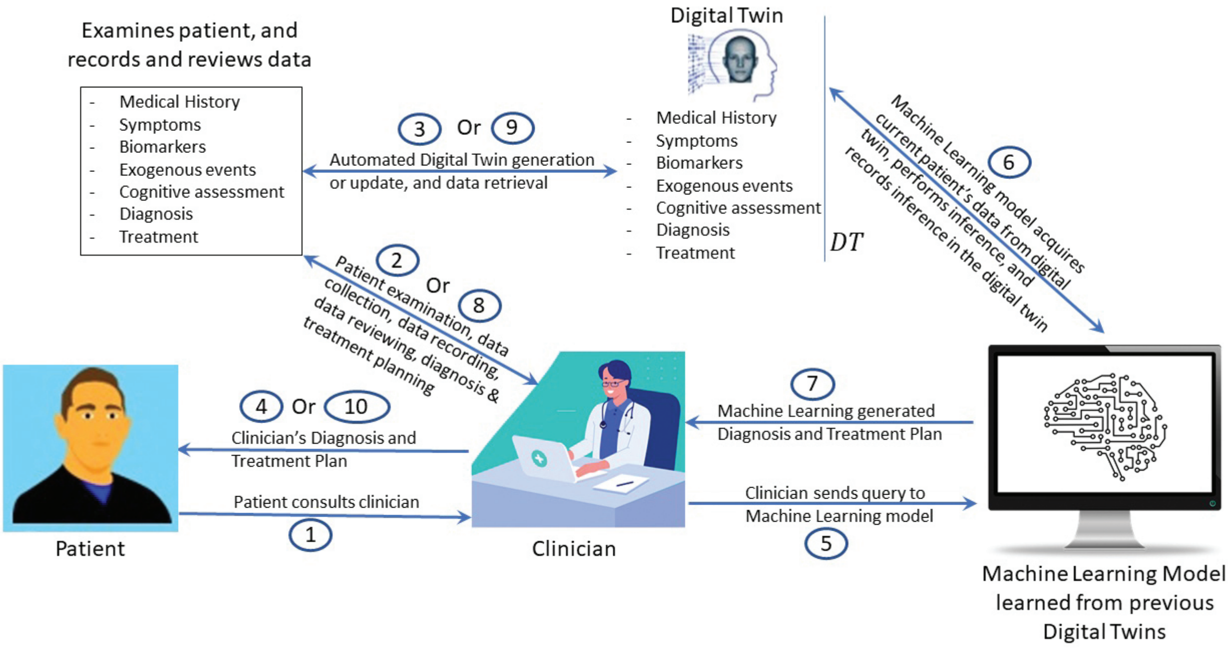

Figure 6: Mapping of the detailed workflow (Generation 2) within the 'Clinical Encounter' block in Figure 5. The circled numbers imply the following steps: (1) The patient consults clinician; (2) The clinician collects patient data, records patient data, reviews patient data (if already available), examines patient, and decides on diagnosis and treatment plan; (3) If a digital twin doesn't exist, a digital twin is automatically created from data recorded in (2); if a digital twin exists, it will automatically get updated from the data recorded in (2) and the existing data will be retrieved to display to the clinician; (4) The clinician communicates their diagnosis and treatment plan if the present assessment is sufficient; (5) If further assessment is required, the clinician sends a query to a machine-learning model learned from the digital twins of past patients; (6) The machine-learning model acquires current patient's data from the digital twin, performs inference, and records the inference in the digital twin; (7) The machine-learning model communicates the inferred diagnosis and treatment plan to the clinician; (8) The clinician makes an augmented decision on diagnosis and treatment plan and records it; (9) The digital twin is automatically updated according to data recorded in (8); (10) The clinician communicates their augmented diagnosis and treatment plan.

In this workflow, the clinician in a clinical encounter, after meeting the patient, examines the patient, collects and reviews the data, and records them via the clinician's interface, and the digital twin of the current patient is either automatically created or updated in the same manner as in the Generation 1 workflow. However, in the Generation 2 workflow, the clinician will have two opportunities to decide on a diagnosis and a treatment plan before communicating them.

The clinician can decide on a diagnosis and a treatment plan and communicate them at the stage of initial collection and/or reviewal of data — this decision pathway is indicated by numbers '2' and '4' in Figure 6. The '2' and '4' combined pathway indicates the first opportunity for the clinician to decide and communicate. In case the situation requires further assessment and decision making, the clinician has the facility via their interface to send a query to a machine-learning model that is learned from previous digital twins. This machine-learning model acquires the data of the current patient in the form of a digital twin, and thereby provides two types of outputs: (1) A likely diagnosis; and (2) an inferred best treatment plan.

The clinician then receives in plain language the outputs produced by the machine-learning model. The clinician at this point can take into account the machine-learning model's output, and combine that with the clinician's expertise and judgement, and make an augmented decision about the diagnosis and treatment plan — thereby making clinical decisions in an Augmented Intelligence (Long & Ehrenfeld 2020) paradigm. This latter decision pathway is indicated by the combination of steps '5', '6', '7', '8', '9' and '10'. This latter pathway is the second opportunity the clinician gets to decide and communicate, supported by the augmented intelligence paradigm.

A salient feature about the digital twins being updated following the augmented intelligence paradigm, is that the outputs of the machine-learning model, and any intermediate and final decisions made by the clinician, will be recorded within the twins. This information will be useful for future iterations to update or improve the machine-learning models, as well as to guide evidence-based clinical practice — thereby facilitating knowledge discovery (Holzinger 2014). Moreover, recording of such data may provide expanded source data for clinical trials as well.

DISCUSSION AND FOCUS FOR FUTURE WORK

The present state of clinical care practice has numerous limitations and challenges — e.g. medical errors (Garrouste-Orgeas et al. 2012); lack of precision and personalisation in treatment (Wickramasinghe et al. 2022: p.ooac072); clinical trials failing to deliver promises (Smith et al. 2019); gaps in systematic capturing of evidence (Wickramasinghe et al. 2021); suboptimal use of available data (Prada-Ramallal et al. 2019); cognitive burden on clinical staff and workload (Dalal et al. 2019); suboptimal patient outcomes (Tronstad et al. 2021); adverse cost implications (Chandra et al. 2021), and so on. These are serious concerns in a growing and increasingly complex healthcare service sector that is also stretched by an aging population and a population at large that is impacted by modern lifestyles and other environmental factors (World Alzheimer Report 2018). These challenges also are a catalyst for increasing the prevalence of chronic diseases — the specific focus of this paper. Addressing these new and emerging challenges demands more robust and sophisticated in-silico data capture and simulation facilities that include techniques like using the concept of digital twins in healthcare (Smith et al. 2019).

Seeking to fill this gap, this paper presents conceptual mapping of digital- twin incorporated clinical workflows that enable augmented intelligence-based decision making by clinicians. The contribution is made in theory building — an important first step for facilitating technology development to enhance healthcare, prior to implementation (Morrison 2015). The workflow maps presented in this paper can be used to foresee numerous implementation challenges that might ensue and will require addressing. These include any potential pain points, specific technology requirements, any specific clinical training or education components required, and any opportunities for value creation. The conceptual maps of clinical workflows presented in this paper are generic, and thus carry the ability to be altered for specific health conditions.

Accelerating advances in machine learning and deep learning (Reiz et al. 2019; Solenov et al. 2018), the Internet of Things, mass data storage, fast computing, and mobile computing (Wickramasinghe et al. 2021) are all enablers for the proposed further development and application of digital twins in healthcare. Incorporating these advances is essential to facilitate fast and adequate computation requirements for machine-learning model training and use with the available modalities of modern health data that include the likes of imaging data, and genomics. The accessibility of cloud computing and supercomputer platforms have advanced over the decades and are promising to cater for the computing needs required for this space (Aggarwal & Madhukar 2017).

Lack of quality in existing data to enable producing reasonably performing machine-learning models (i.e., the ‘cold start’ problem) (Smith et al. 2019), cyber security concerns, susceptibility for data breach, and surveillance capitalism (Wickramasinghe et al. 2021), and the lack of openness and interoperability of health information systems and platforms (Adler-Milstein 2017), are some factors that can be identified as potential barriers for implementing digital twins. The approach to solve the ‘cold start’ problem is to first enable enhanced data capture in electronic form to ensure quality datasets continue to build over time (Smith et al. 2019). Meanwhile, related technologies such as blockchain in healthcare (Attaran 2022) may hold keys to address some of the data security and management issues, and in improving interoperability via secure data sharing across different health information platforms. Improving the interoperability of health information platforms (Adler-Milstein 2017) continues to stand as a vital enabler to realise the full potential of digital twins.

Two acute and specific risks can be foreseen to associate with extended storage and use of data coupled with machine-learning models and concepts like digital twins. Addressing such risks would be vital and are great focus areas for future research.

The first risk is the possibility of theft of compromising health and medical data. Data theft has been an ongoing issue and an increasingly common one especially in Australia (Cross et al. 2021). One way of addressing this issue is by making systems immune to cyber-attacks by design. This can be done by keeping the systems disconnected from the internet and making them function through intranets. If, for example, a system is designing for just one hospital, the hospital can have its servers located within the hospital premises and the system can be made accessible via a local network from within the hospital. Remote access, if needed, can be granted through virtual private networks owned and managed by the hospital. If such systems are to be expanded, say if a system must be expanded across multiple hospitals, then too, a dedicated and unique server network can be implemented. When that happens though, there will be a possibility for third parties to monitor network activity and perhaps even tap into some data that is being transferred. This vulnerability can be addressed to a good extent through data encryption, but there will be no way of guaranteeing 100% security. Once it is known that the systems are by design quite immune to cyber-attacks, it can be conceded that any threat would more likely come from the inside. This means the vulnerability then lies in data breaches happening from authorised stakeholders who are using the network. Again, there is no 100% guarantee of preventing breaches happening with the aid of authorised stakeholders; however, since it is known that a threat lies from the inside, architectures such as blockchain could be made use of for tracing the stakeholders that could have been responsible for a data breach. This would at least enable some form of accountability, although some damages caused by such breaches may not be accountable by repercussion imposed on the responsible parties.

The second risk would lie in the authority and accountability about the clinical decisions made when using Artificial Intelligence (AI) for decision support. Simply put, who makes the decision here? Is it the AI model, or is it the clinician? The accuracy of AI models is subject to the data they are being trained with. Then, the accuracy of a clinician is subject to human error. Thus, if considered in isolation, both AI models and clinicians have their own weaknesses. Therefore, a golden question to be answered is to what extent the weaknesses in present clinical decision making can be addressed by a fusion between AI models and clinicians, and how best the AI models can be used within clinical workflows to achieve substantial improvements in clinical decision making. Answering this question would require longitudinal research over time involving incremental introduction of AI models to healthcare and learning over time through the evidence of patient outcomes and clinician satisfaction.

This paper has served to answer the posed research question: 'How can we design and develop digital twins to support clinical decision making for various healthcare contexts?' The proposed use of digital twins not only offers the potential to enhance clinical care, but also serves as a means for data and evidence capture over time. This is, for instance, identified as a key action area by the World Health Organization especially in spaces like dementia (Global Action Plan 2017). This becomes an enabler for knowledge discovery (Holzinger 2014) and may overcome some limiting attributes of clinical trials (Smith et al. 2019).

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Conflict of interest
The authors declare no conflicts of interest.

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