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# Healthcare 4.0: A review of frontiers in digital health

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**Abstract**

Healthcare 4.0 is a term that has emerged recently and derived from Industry 4.0. Today, the health care sector is more digital than in past decades; for example, spreading from x-rays and magnetic resonance imaging to computed tomography and ultrasound scans to electric medical records. With the wide spectrum of digital technologies underpinning Healthcare 4.0 to deliver more effective and efficient health care services, in this article, we use the *wisdom pyramid methodology* to conduct a systematic review of current digital frontiers in Healthcare 4.0.

This article is categorized under:

Technologies > Computer Architectures for Data Mining
Application Areas > Health Care
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Fundamental Concepts of Data and Knowledge > Knowledge Representation

**KEYWORDS**

artificial intelligence, digital health, Healthcare 4.0, Internet of things (IoT), ontology, social network

## 1 | INTRODUCTION

Health care systems face major challenges with spending accounting to 10% of gross domestic product for the European Union and Australia while 18% for the United States (Kaiser Family Foundation, 2018), increasing demand for provision of care in aging societies and better health and well-being management. Recent examples show that digital health technologies have the potential to mitigate or even eliminate these challenges. Emerging digital health care services is expected to reduce costs, improve user experience and increase the quality of care (Siemens, 2018).

Today, the health care sector is digital that is, from x-rays and magnetic resonance imaging (MRI) to computed tomography (CT) and ultrasound scans to electronic medical records (EMRs; Mestres, 2017). For example, a recent survey (Frost and Sullivan, 2018) estimates that medical imagining data could soon reach the petabytes range forcing big data tools and technologies for capturing, analyzing, managing, and viewing data. This data will be coupled with emerging digital data sources such as the Internet of things (IoT) including sensors and wearables, smart mobile devices, and social media. This trend enables the development of novel Healthcare 4.0 services that can help both of health-care providers (e.g., health practitioners, hospitals, and clinics) and users to move toward demanding and researching personalized, proactive, and predictive health-care models.

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Healthcare 4.0 is a term that has emerged recently and derived from the Industry 4.0. Inspired by the fourth paradigm—data-intensive scientific discovery (Hey, Tansley, Tolle, 2009), Healthcare 4.0 is a collective term for data-driven digital health technologies such as smart health, mHealth (mobile health), wireless health, eHealth, online health, medical IT, telehealth/telemedicine, digital medicine, health informatics, pervasive health, and health information system. It describes the digital frontiers and disruptive innovation in the health care sector that is driving new business models and value networks (Herrmann et al., 2018). Advancements and adoptions of Healthcare 4.0 are occurring across many developed countries in the world with the digital health market expected to grow to $223.7 billion by 2023 (Prescient, & Strategic Intelligence, Sept, 2018).

In this article, we use the *wisdom pyramid* (Wikipedia, 2018) as presented in Figure 1 to conduct a systematic review of frontiers in digital health. We break the digital underpinning of Healthcare 4.0 into a hierarchy of *digital data foundations*, *digital knowledge representation*, and *digital knowledge learning and prediction*. The *wisdom pyramid* provides a systematic approach to review data/information and digital knowledge representation and learning that provide the ability to capture, store, and interpret existing knowledge as well as translate it into wisdom to empower decision-making underpinned by machine learning (ML) and artificial intelligence (AI). The word *wisdom* is associated with deep expertise in different health care related areas driving decision-making.

The data/information stem from multiple cutting-edge digital technologies such as IoT including wearables, mobile smartphones, social networks (e.g., Facebook and Twitter), and the traditional EMRs that include medical imaging data. The knowledge available within the health care areas is generally represented using *ontologies* such as geneontology, pubmed, and semantic sensor networks (SSNs). The advance in AI techniques (e.g., ML, pattern recognition, natural language processing (NLP), deep learning, semantic reasoning, image processing, and computer vision) provides the capability to learn the deep expertise required to facilitate the decision-making process. The amalgamation of *digital data foundations*, *digital knowledge representation*, and *digital knowledge learning and prediction* paves way to the development of novel Healthcare 4.0 application such as remote health care, diseases monitoring, detection/prediction, captology, assisted living, epidemic monitoring, automated clinical decision support, elderly care, mental health, health education, and many more leading toward efficient personal/community care solutions and improved patient experience.

Figure 2 provides an illustration on how the wisdom pyramid methodology can be applied in developing a taxonomy of the digital technologies underpinning Healthcare 4.0. As illustrated, the digital data foundation layer comprises multitude of digital data sources from IoT to social media that provide valuable data essential for digital health care. The knowledge representation and learning layers fuse together existing domain knowledge from ontologies and semantic data stores such as PubMed (PuMmed, 2018) and use AI techniques for learning and prediction and extract wisdom, an essential requirement in aiding decision-making.

Based on the aforementioned wisdom pyramid methodology, in this article, we present a review of advancements in the digital data foundation, knowledge representation, and learning that focus on the development of novel Healthcare 4.0 services and applications. We conclude the article with a comprehensive analysis of some open challenges that need to be addressed for widespread adoption of Healthcare 4.0.

The article is organized as follows. Section 2 describes digital data sources relevant to Healthcare 4.0. Section 3 contains an overview of how knowledge is represented digitally in Healthcare 4.0. Section 4 describes the contributions of AI in Healthcare 4.0 and Section 5 discusses emerging application areas. Section 6 concludes the article with an overview of open issues and challenges.

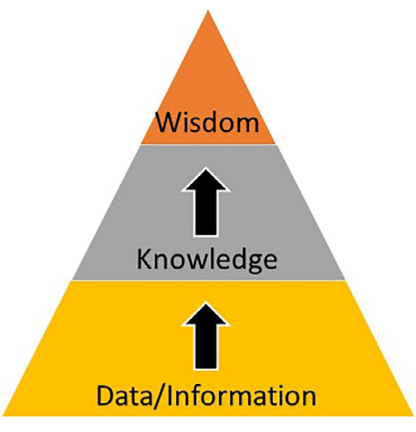


**FIGURE 1** Wisdom pyramid

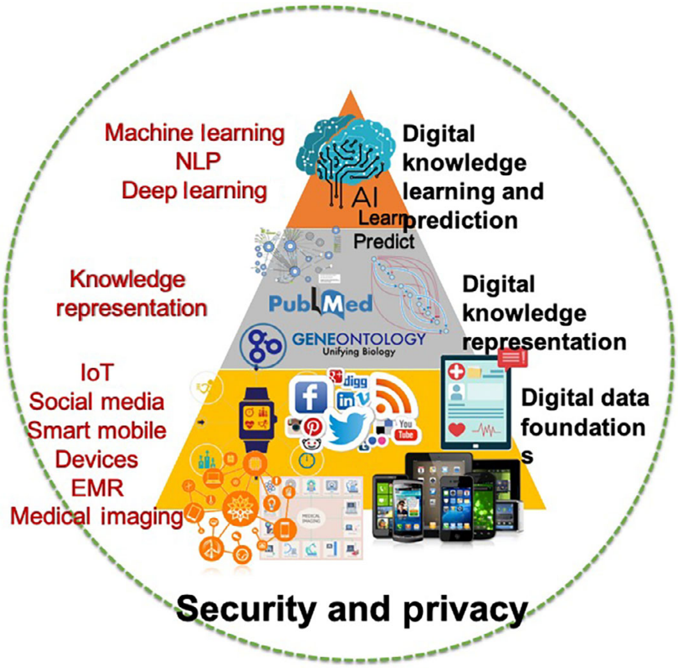


**FIGURE 2** Healthcare 4.0: Taxonomy of digital technologies, services, and applications

## 2 | HEALTHCARE 4.0: DIGITAL DATA FOUNDATIONS

In this section, we describe the current emerging technologies, refering to them as *digital data foundations*, that underpin the development of Healthcare 4.0 applications and services. In particular, we provide a detailed review of technologies such as the IoT including mobile smartphones and wearables, social networks, and EMRs.

### 2.1 | Internet of things

IoT is the one of the fastest adopted technology pushing the frontiers of Healthcare 4.0 (Georgakopoulos & Jayaraman, 2016). It is estimated that the IoT health care market will be worth $158 billion by 2022 (MarketsandMarkets™, 2018). IoT bring several key capabilities to Healthcare 4.0 that brings about effectiveness in applications such as remote monitoring of patients with chronic conditions, elderly people and those requiring constant supervision (A. R. M. Forkan & Khalil, 2017). IoT in digital health target highly personalized, affordable, accessible, and on-time Healthcare 4.0 services for everyone.

#### 2.1.1 | Wearable IoT

Wearable IoT is defined as an electronic, mobile, context-sensitive device that can be incorporated into items worn by the user (such as on the body or cloth) and can be operated and accessed without or with very little hindrance to user activities (Perera, Liu, & Jayawardena, 2015). Wearable IoT devices are capable of delivering personalized, immediate, and goal-oriented feedback based on specific tracking of health data obtained via various embedded sensors (e.g., accelerometer, gyroscope, temperature sensor, moisture, location, heart rate sensor, and blood pressure monitor) (Hiremath, Yang, & Mankodiya, 2014). Low cost wearable IoT devices can provide long lasting functionality without requiring continual recharging. The flexible size makes them easier to wear and use continuously.

Millions of wearable IoT devices are being employed in various Healthcare 4.0 applications. Some examples are shown in Figure 3. The popular categories include smart watches (e.g., Pebble, Samsung gear, Apple watch), wristband sensors (e.g., fitbit, metawear, Garmin vivosmart), smart glasses (e.g., Microsoft HoloLens, Google glass), e-textile and health monitors (e.g., heart rate, electrocardiogram [ECG], blood pressure monitors). Such wearable IoT devices allow continual data acquisition of various physiological condition of human body such as ECG (Yang, Zhou, Lei, Zheng, & Xiang, 2016), heart rate (Venkatraman & Yuen, 2016), blood pressure, reparation rate, blood oxygen saturation, body temperature, blood glucose, electromyogram (EMG), photoplethysmogram (PPG), and electroencephalogram (EEG).

## 2.2 | Fabric and flexible sensors

Another new product category that is fast emerging as a common Healthcare 4.0 wearable technology is low-cost disposable patches that are worn continuously for days at a time and then discarded (Lee et al., 2018). A few examples of such patches are presented in Figure 4. One of the most exciting potential developments in wearable patches is Sano Intelligence's continuous blood chemistry monitoring patches. It has been demonstrated to measure blood glucose and potassium levels, and aims to measure a full metabolic panel, including kidney function and electrolyte balance (Sano Intellignece, 2012). A promising concept pioneered by mc10 is stretchable digital tattoos named BioStamp for the continuous monitoring of vital signs with flexible electronics patches (USA Today, 2018). These stretchable electronics track and wirelessly transmit information such as heart rate, brain activity, body temperature, and hydration level, and may be available to athletes. The Zio Patch from iRhythm (2-week use) can be worn to monitor cardiac rhythm and warn of arrhythmias (iRhythm, 2018). Another interesting example of new patch technology is a continuous blood pressure monitoring patch from Sense A/S (SenseA/S, 2018). Instead of the cumbersome pressure cuff, there is a small arm patch with electrodes that sense the changing impedance of tissue around a vessel and convert it into a blood pressure reading via a waistband sensor. One of the classic use cases for wearable patches is the continuous glucose monitor (CGM) worn by diabetics and other self-trackers. New developments mean that the current state-of-the-art technology is available in several CGM solutions where an under-the-skin CGM uses a sensor and transmits glucose readings every 1–5 min to an external receiver or insulin pump.

Australian Centre for NanoMedicine (ACN) at UNSW has developed a new wearable sensor that informs exposure to ultraviolet rays (Greg, 2018). This can change color in the sun and could provide an affordable tool to help prevent deadly skin cancers. The stick-on patches can be tuned to suit individual skin types. L'Oréal-owned skincare brand La Roche-Posay, ultra voilet sense (UV Sense) is a battery-free IoT wearable sensor that can measure your UV exposure and store up to 3 months worth of data (L'Oréal, 2018).

### 2.2.1 | Ambient IoT

Nonwearable (i.e., ambient) IoT devices containing sensors such as motion, door, pressure, video, object contact, and sound sensors are widely used in several Healthcare 4.0 applications (Plantevin, Bouzouane, Bouchard, & Gaboury, 2018) such as remote patient monitoring, fall detection, anomaly detection in daily behavior (A. R. M. Forkan, Branch, Jayaraman, & Ferretto, 2019) and elderly care (A. Forkan, Khalil, & Tari, 2014). Such IoT sensors (Figure 5) have proven to be very successful and useful in elderly care as elderly people generally dislike being obliged to wear a monitoring devices or if they are suffering from mild dementia and may not remember to wear them. Moreover, wearable IoT sensors are difficult to install on the body and require professional adjustments. Although the data collection process using wearable IoT is usually easier than using ambient sensors, restrictions regarding wearing the sensors on body could discourage people from adopting them. Wearable devices also can generate an uncomfortable feeling during


**FIGURE 3** Popular wearable Internet of things devices in Healthcare 4.0


**FIGURE 4** Flexible disposable patch sensors that can be attached to skin

long-term skin attachment and so external or ambient sensors are highly accepted in application where users do not prefer the use of wearable devices. Ambient IoT devices gather real-time data continuously and therefore can rapidly detect any changes in pattern by analyzing historical data. A proper data analytics over the captured data from sensors can provide a better view of daily behavior in real-world scenario.

## 2.3 | Mobile smartphones

Mobile smartphones play an important part in our daily activities and have revolutionized Healthcare 4.0. The mobile smartphone-based health application market (mHealth apps) was valued at \$4.19 billion in 2016 and is estimated to increase by 44.2% by 2025 (Grand View Research, 2018). Mobile smartphones are no longer used only as a communication device but the plethora of sensors and the corresponding data they produce have opened immense opportunities for personalized medical treatment, track behaviors, and movement (Aledavood et al., 2019) and, providing personalized plan for a balanced lifestyle (Ernsting et al., 2017). A recent report (Statista, 2019) shows that a total of 44,384 iOS health care apps were released in apple store and 41,377 in google play store between 2015 to 2019. According to another survey, 58.23% of smart users have downloaded and used health-related applications on their mobile smartphones attributed these devices as a major contributor of health data. (Krebs & Duncan, 2015).

Digital health technology has made it possible to manage self-health providing brief real-time snapshots which were only seen in hospitals and clinics before. mHealth apps allow health-care providers to effectively streamline communications between patients, providers, and their caregivers. Also, these apps enable for 24/7 management of a patient's condition along with the ability to personalize health care per patient. For example, Apple created the “Apps for Healthcare Professionals” section within the medical category of the iTunes Appstore, a unique feature among mobile app marketplaces. In 2013, this section was further divided into subcategories including: reference, medical education, EMR and patient monitoring, nursing, imaging, patient education, and personal care. Google similarly launched a “Google Play” shop that provides a wide variety of health care apps, including some for health professional, for mobile devices that use the Android operating system (Cheng, Fang, Hong, & Yang, 2017).

## 2.4 | Social media

Social media refers to a group of Internet-based applications that build on the multifaceted and technological foundations of Web 2.0 and allow the creation and exchange of user-generated contents (Kaplan & Haenlein, 2010). In 2017, there are about 2.46 billion users on social networks and this number is rapidly growing (Statista, 2018).

There are many different social media sites available today such as Facebook, Twitter, Reddit, and Instagram (Aichner & Jacob, 2015). These sites can be classified into 13 categories: social networks, video sharing, blogs, microblogs, forums, business networks, collaborative projects, enterprise social networks, photo sharing, products and services review, social bookmarking, social gaming, and virtual worlds (Statista, 2018).

Twitter is one of the most widely used social media providing microblogging services. Twitter has currently about 335 million monthly active users (Statista, 2018). In recent years, Twitter has been widely used as a platform to disseminate and share health-related information. Patients with chronic diseases are more actively using online social media to express their feelings and symptoms, share their experiences, and provide mutual support (Chou, Hunt, Folkers, & Augustson, 2011).

Twitter's Application Programming Interface (API) platform facilitates collecting recent and historical tweets using free and paid access options. Aggregation and analysis of large volumes of tweets can provide valuable insights and


**FIGURE 5** Ambient Internet of things sensors for unobtrusive monitoring

perception into the health and health care system of a given population/community. From the perspective of digital health, analysis of social media data can lead to the following benefits: (a) monitoring and surveillance of pandemic diseases (e.g., influenza (M. J. Paul & Dredze, 2011)), (b) gaining better knowledge about public health and health care needs (Griffiths et al., 2012), (c) monitoring quality of health care delivery and detecting poor clinical care (Greaves, Ramirez-Cano, Millett, Darzi, & Donaldson, 2013)), (d) sharing psychological support among certain patients such as in the cancer community (Sugawara et al., 2012), (e) investigating risk factors of chronic diseases (Delir Haghighi, Kang, Buchbinder, Burstein, & Whittle, 2017), (f) pharmacovigilance studies including understanding public perceptions toward drug therapies (Sarker et al., 2015), and (g) understanding sentiments of clinical practitioners toward various policies, medications, rural health, and so on.

### 2.5 | Electronic medical records

EMRs or electronic health record (EHR) is a digital version of a patient's medical history that includes the key administrative clinical data relevant to that person's care under a particular health-care provider. EMR data can include demographics, progress notes, description of health problems, medications, vital signs, past medical history, clinical data generated during the diagnostic process, coded billing data, immunizations, admission and discharge summaries, progress notes, pathology or radiology test results, x-ray images, and many more technical reports (Figure 6). Moreover, clinicians are now using voice recognition, captured images using mobile device camera, and documentation templates that are directly recorded as information feeding into the EMR. Eighty percent of data in global EMR database are unstructured text or images (Wong, Murray Horwitz, Zhou, & Toh, 2018). EMR are built to share information with other health-care providers and organizations—such as pathological laboratories, general practitioners, specialists, medical imaging facilities, pharmacies, emergency facilities, school, and workplace clinics—so they contain information from all clinicians involved in a patient's care.

EMR has made it possible to easily access health data and make grouping of patients into the medical care, status, and outcomes from a diverse patient population. EMR also has the ability to support care-related activities directly or indirectly through evidence-based decision support, quality management, and outcomes reporting. Extracting and discovering useful clinical information from these EMR data pose a challenge as it is difficult to define rules for such unstructured data and manual review is not feasible on a large scale (Wong et al., 2018). EMR also provides the foundations for several longitudinal studies.

## 3 | DIGITAL KNOWLEDGE REPRESENTATION

As presented in the Figure 1, data or information obtained from the technologies described in Section 2 are transcribed and represented as digital knowledge. The digital knowledge underpins the rich domain knowledge that is pivotal to several Healthcare 4.0 applications and services. In this section, we describe some of the technologies that provide the ability to represent knowledge to support the development of Healthcare 4.0.

### 3.1 | Ontologies

Ontology is a formal specification of entities or objects and their relationships in a domain. Being machine interpretable, ontologies can be used for automated processing of tasks to support decision-making. Further, ontologies contain domain information and hence can provide rich contextual knowledge for data analysis.


**FIGURE 6** Examples of electronic medical records

Figure 7 shows the two types of ontologies that are widely employed in Healthcare 4.0. One is called *medical domain ontologies* that describe specific domain concepts and terminologies used in health care. The other set of ontologies, named *device ontologies*, describe the data sensed from technologies described under digital data foundation in particular the IoT. Some well-known and mostly cited medical domain ontologies are described as follows:

- *Systematized Nomenclature of Medicine – Clinical Terms (SNOMED-CT)* ontology, created over the years by health community, is considered as the main ontology for presentation of clinical concepts, terms, and relationships. It covers areas used in medical practice such as clinical findings, symptoms, diagnoses, pharmaceuticals, body structures, medical devices, and social contexts. Each concept is assigned a unique *ConceptID* and a *Fully Specified Name (FSD)*, which can be interpreted as being a unique human–readable description of that concept. SNOMED-CT provides a consistent way for indexing, storing, retrieving, and aggregating clinical data that can enhance the interoperability between different health information systems (Schulz, Suntisrivaraporn, Baader, & Boeker, 2009).
- *Logical Observation Identifiers Names and Codes (LOINCS)* provide a universal code system for laboratory test results and other clinical observations. For each observation, such as arterial blood gases, homo-gram or serum potassium, the database includes a code, a short name, a long formal name, and synonyms. The aim of LOINCS is to provide common codes and terminologies, so that when hospitals, pharmaceutical manufacturers, researchers, and public health departments receive messages from multiple sources, they can easily or automatically file in the right slots of their medical records, research, and public health systems (Forrey et al., 1996).
- *MedDRA (Medical Dictionary for Regulatory Activities)* ( MedDRA, 2004) is a rich and highly specific and standardized terminology to facilitate sharing of regulatory information internationally for medical products used by humans (MedRa, 2015). Products covered by the scope of MedDRA include pharmaceuticals, biological, vaccines, and drug-device combination products. MedDRA is available to all for use in the registration, documentation, and safety monitoring of medical products both before and after a product has been authorized for sale. Products covered by the scope of MedDRA include pharmaceuticals, biological, vaccines, and drug-device combination products.
- *Common Terminology Criteria for Adverse Events (CTCAE)* are a coding for adverse events that occur in the course of cancer therapy. Adverse events are considered any unintended or unfavorable symptom, sign, or disease temporarily associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure (Program, 2003).
- *Foundation Model of Anatomy* (Rosse & Mejino Jr, 2003) is an ontology developed and used to describe human anatomy. It contains approximately 75,000 classes and over 200,000 terms. Hundreds of relationships are used to semantically describe human anatomical structures, from microscopic parts such as macromolecules, cells and their parts, and portions of tissues, to macroscopic anatomical structures such as body parts and the whole organism itself. The FMA is available in Web Ontology Language (OWL) format and its subparts are used for specific anatomy or application ontologies such as Semi-automated (SEMIA) ontology, Medical Ontology (Medico), and others.
- *ICD-10 (International Classification of Diseases Tenth Revision)* was issued by the World Health Organization (WHO) as a classification system for diseases and other related aspects in medical practice, including symptoms, abnormal findings, causes of diseases, death certificates, and health records (World Health Organization, 1993). The ICD is used by member states of WHO for compilation of national mortality and morbidity statistics, for epidemiological research and for assessment of trends in public health and illnesses. However, ICD-10 is not an ontology in the strict sense, but is usually kept as thesaurus and used for classification. There are no relationships defined between the

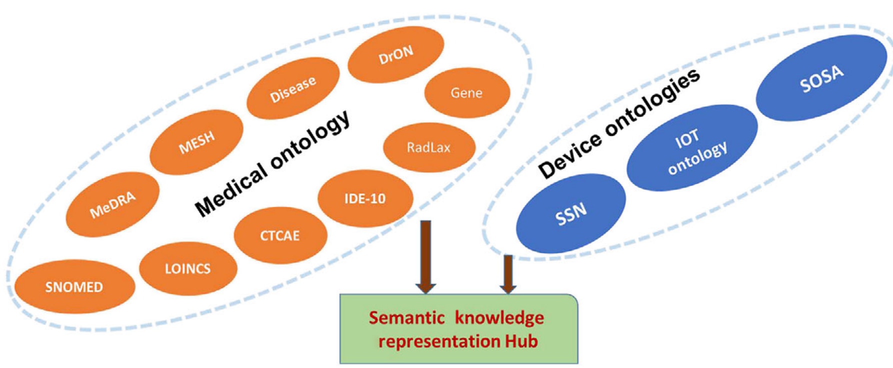


**FIGURE 7** Overview of ontologies employed in Healthcare 4.0

terms, as does not provide distinctions between terms on an ontological level. In recent years, an OWL version of ICD-10 is developed to provide better and more formal way to describe the terms and their relationships at ontological level. In addition, the next version of ICD is under construction and it is expected to overcome some existing limitations.

- *RadLex (Radiology Lexicon)* (Mejino Jr, Rubin, & Brinkley, 2008) is a comprehensive lexicon that aims to provide a unified language for standardized indexing and retrieval of radiological information resources. RadLex includes many complex domains that are necessary for radiologists, such as image quality, treatment, anatomic location, and uncertainty. RadLex although provides a unified lexicon for radiologist, it is not an ontological framework. It has the potential to evolve to an ontology, but further steps are required.
- *Gene ontology (GO)* project provides ontologies to describe attributes of gene products in three nonoverlapping domains of molecular biology. Within each ontology, terms have free text definitions and stable unique identifiers. The vocabularies are structured in a classification that supports "is-a" and "part-of" relationships. GO molecular function terms represent activities rather than the entities (molecules or complexes) that perform the actions, and do not specify where, when, or in what context the action takes place. Examples of individual molecular function terms are the broad concept of "kinase activity" and the more specifically "6-phosphofructokinase activity" (a subtype of kinase activity).
- *Disease ontology (DO)* represents a comprehensive knowledge base of 8,043 inherited, developmental, and acquired human diseases (Disease Ontology, 2018).
- *DrOn* is an ontology of drug products, their ingredients, and their biological activity. It allows semantic reasoning and help to understand the meaning to drug properties. Classes derived from each source are serialized in separate modules. For example, the classes in DrOn that are programmatically derived from RxNorm are stored in a separate module and subsumed by classes in a manually curated, realist, upper-level module of DrOn with terms such as "clinical drug role," "tablet," "capsule," and so on (Hanna, Joseph, Brochhausen, & Hogan, 2013).

In addition, below we describe ontologies that have been used to describe digital data foundation in particular the IoT sensors in order to provide a unified representation of such sensing data sources and enable them to be fused with respective domain ontologies. p

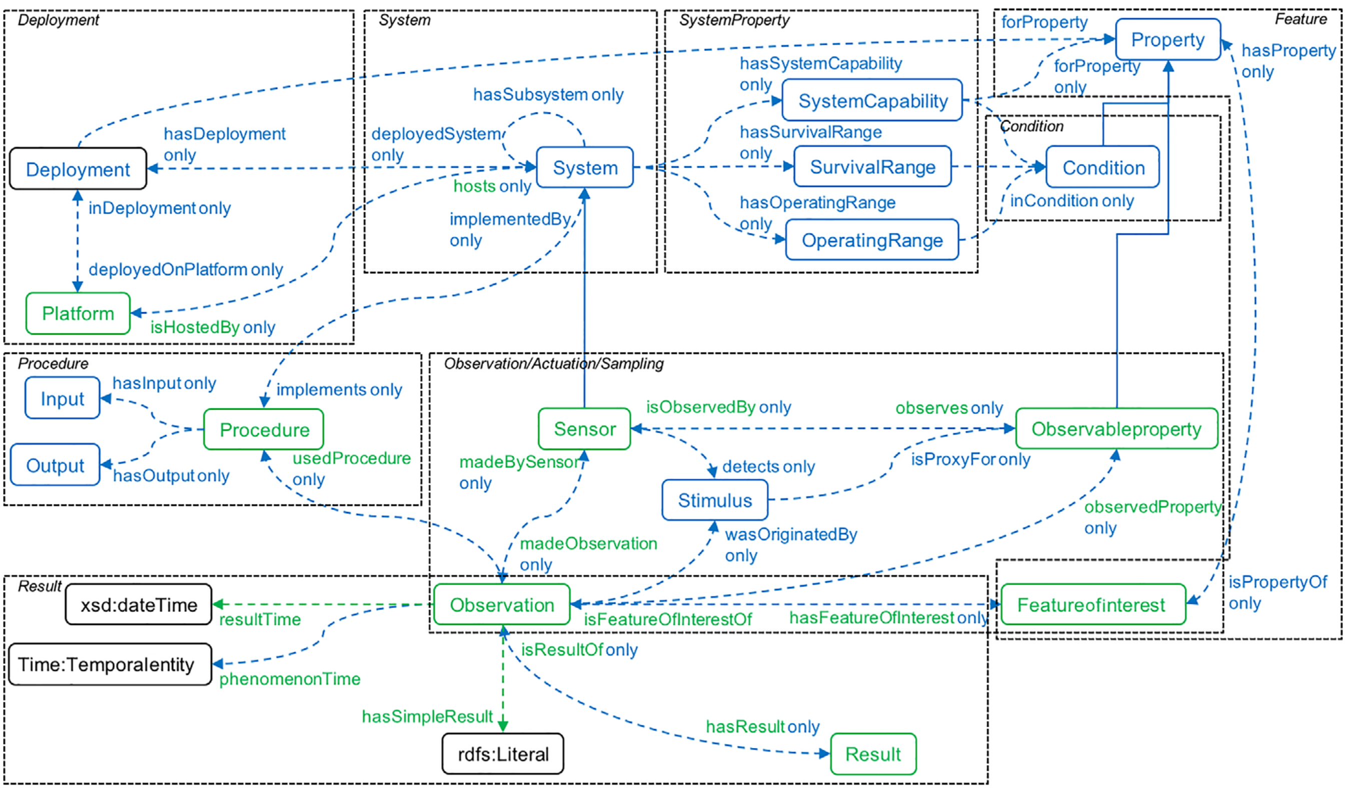


**FIGURE 8** Overview of semantic sensor network ontology

- *Semantic Sensor Network Ontology (SSNO)* is an upper ontology developed by W3C to provide a shared and agreed set of common concepts to enable semantic interoperability across SSN domain. The main aim of SSNO was to begin a formal process for building ontologies that represent semantically capabilities of sensors and sensor networks. The full SSNO contains 41 classes and 39 object properties and extends DOLCE-Ultralite (DUL) upper ontology. Thus, including DUL extension, it is composed of 117 concepts and 142 objects in total (Compton et al., 2012). Figure 8 provide an illustration of the SSNO. Recently, some health-related platforms such as kHealth (Anantharam, Barnaghi, & Sheth, 2013) have been developed using SSNO. The SSNO specifically is used for knowledge modeling that help to discover, access, search, integrate, and interpret data (and extract information). It is also used on modeling data (representation of observations) from various sensors data sources such as mobile smartphone, temperature, humidity, video cameras, and so on. These observation are provided a standardized representation by the SSNO.
- *Federated Interoperable Semantic IoT/cloud Testbeds and Applications (FIESTA-IoT)* ontology is build from the existing leverage a number of core concepts from various mainstream ontologies and taxonomies, such as SSN, M3-lite (a lite version of M3 and also an outcome of this study), WGS84, IoT-lite, Time, and DUL (Agarwal et al., 2016).
- *IoT-lite ontology* is a lightweight ontology to represent IoT resources, entities, and services. IoT-lite is based on the SSN ontology. The loT-lite can present IoT platform without consuming excessive processing time. However, it is also a meta-ontology that can be extended in order to represent IoT concepts in a more detailed way in different domains. In addition, it is used for knowledge discovery, finding the pattern and unified the information from the heterogeneous IoT platforms (Bermudez-Edo, Elsaleh, Barnaghi, & Taylor, 2015).

## 3.2 | Knowledge bases

A knowledge base is a machine readable technology which stores structured and unstructured information (Auer et al., 2007). It provides real-world facts and associated information. A well-organized and rich knowledge base can provide insightful information to the end users. More specifically, knowledge base is not a static collection of resources but dynamic resources that may have self-capability to learn by using the AI. For example, PubMed (as depicted in Figure 9 is a knowledge base that stores bibliographic information of biomedical and life science. This bibliographic knowledge base stores 5.1 million of articles including molecular biology databases. The skeleton of huge amount of bibliographic

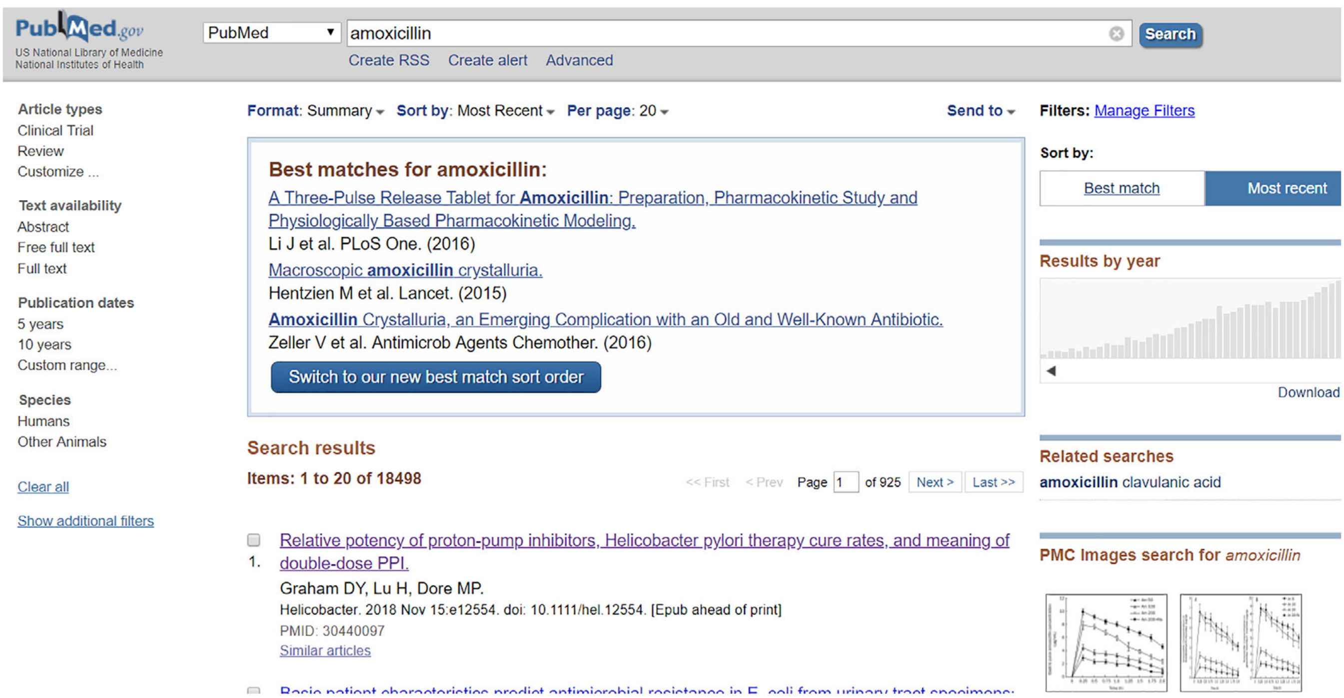


**FIGURE 9** An example of medical bibliographic knowledge base

information is based on the MESH terminologies, and GOs. Using these ontologies, PubMed search functionality provides right articles to the end users by filtering unnecessary articles from the database (Doms & Schroeder, 2005).

PubMed is maintained and updated by the National Library of Medicine on a weekly basis. It also provides links to other knowledge base such as DbPedia (Auer et al., 2007) and PharmGKB (Hewett et al., 2002). Moreover, self-learned devices can be learned from the knowledge base and provide the right answers when someone ask or search queries. Such devices are Google home and Amazon Echo.

## 4 | THE RISE OF AI IN HEALTHCARE 4.0: TOWARD DIGITAL KNOWLEDGE LEARNING AND PREDICTION

A key aspect of the wisdom pyramid presented in Figures 1 and 2 is the ability to generate wisdom from data/information and knowledge. From the perspective of Healthcare 4.0, wisdom provides applications the ability to make decision and/or assist users to make informed decisions. AI is a branch of computer science that develops machines capable of functioning as an intelligent human in reasoning, discovering meaning, and learning and generalizing past experience. Powered by AI, these days, AI techniques are being used by many industries especially in digital health domains due to their unprecedented improvement and learning/reasoning capabilities.

Nowadays, AI has rapidly advanced and been actively leveraged in a wider range of Healthcare 4.0 areas that include disease detection (or diagnostics), personalized health care service provision, and drug discovery. AI facilitates the development of several Healthcare 4.0 applications and services enabling the move from prescriptive to predictive medicine. This advancement mainly comes from (a) the rapid increase in the computational power of computers, (b) increased availability of large amounts of digital health care data described in Section 2 including the developments in wearable IoT devices, intelligent sensors, needed to develop and test advanced and sophisticated AI techniques, and (c) significant improvements in AI algorithms (e.g., deep learning based on neural networks).

One of the important features of current AI technologies is to intelligently handle increasing volume of structured, unstructured, and heterogeneous (e.g., text vs. image vs. sensor data) health data. The goal of AI in Healthcare 4.0 is to assist health-care professional in making accurate clinical decisions, provide users/patients more efficient personalized services, and overall improve the efficiency of the health care system by reducing costs, making it accessible and reduce medical errors. In this section, we provide a review of relevant branches of AI that have been repeatedly discussed in recent years in the literature to facilitate the development of Healthcare 4.0 applications.

### 4.1 | Machine learning

ML plays a vital role in discovering valuable insights and patterns as well as deriving complicated rules and trends from health care data. ML has been defined as a "program that learns to perform a task or make a decision automatically from the data, rather than having the behaviour explicitly programmed" (AL & IS, 2018). In the health care sector, ML has been effectively used to build data analytical models that are able to explore useful features from the enormous amount of medical data as well as learn insightful patterns and knowledge from the data. Broadly, the data can be divided into two parts (F. Jiang et al., 2017): (1) patients' traits and (2) their medical outcomes. The former commonly include demographic data (e.g., demographic information, disease history, and disease-specific data (e.g., diagnostic imaging, gene expressions, physical examination results, clinical symptoms). The latter often collected in clinical research (e.g., disease indicators, patients' survival times and quantitative disease levels—e.g., tumor sizes).

Often used as synonym for AI, ML is a branch of AI that focuses on the development of algorithms to learn from data and can be classified broadly into (1) supervised learning and (2) unsupervised learning. In the health care areas, supervised learning focuses often on learning importance patterns or information from the data mentioned above as well as predicting the best treatment processes with their probabilities closer the ideal treatment processes or other outputs under considerations. For example, the outcome can be formed as the probability of getting epidemic diseases in a particular future time, and the level of their critical factors, and so on. Today, supervised learning is considered more clinical relevant, thus health care AI applications often use supervised learning. Examples of relevant techniques include classification algorithms such as logistic regression algorithms, support vector machines, random forest, eXtreme Gradient Boosting (XGBoost) (Shi et al., 2019), and neural network-based algorithms. Recently, XGBoost has been known as a dominating algorithm in Kaggle competitions for structured or tabular data. XGBoost is an implementation of gradient boosted decision trees designed for speed and performance (Hatton et al., 2019). Also, the logistic regression algorithms have been proven to be useful for predictive analysis. Logistic regression is used to describe data and to explain the relationship between features of the data and the prediction outcomes. Logistic regression can also be seen as a simpler deep learning algorithm.

Unsupervised learning (Y. Kwon, Kang, & Bae, 2014; Miotto, Li, & Dudley, 2016) is often used to understand distribution of features from data. Clustering is a representative example in this learning. For example, clustering can group patients with similar traits together into different clusters, maximizing and minimizing the similarity of the patients within and between the clusters. K-mean, Gaussian mixture, and principal component analysis (PCA) have been widely used for unsupervised learning. Especially, PCA is powerful for identifying the main components (or traits) and their directions of subjects data without a loss of the original subject information.

Supervised learning requires well-annotated data that provides an accurate description of the reality (often referred to as ground truth). Unsupervised learning algorithms use an exploratory approach to find patterns in data while semisupervised uses a combination of unsupervised and supervised learning.

## 4.2 | Deep learning

Today millions of digital medical images such as MRIs and CT scans are stored in hospital database to capture thinner slices of the body and three-dimensional (3D) and Four-dimensional (4D) medical images using advanced diagnostic devices become the norm. Image processing is very important part of the AI. AI methods can tackle the huge amount of data from images and signals (e.g., audio). Images and biosignals are analyzed by the deep learning algorithms such as artificial neural networks (ANNs) (J. Jiang, Trundle, & Ren, 2010). ANNs are computing systems based on the networks that comprise animal brains.

Recent experiments have demonstrated cases where AI-driven algorithms using deep learning have outperformed human doctors with regard to diagnosis of some medical conditions. Now deep learning-based approaches are used in heart disease classification (Karthikeyan & Kanimozhi, 2017), diabetes detection (Tharani & Yamini, 2016), predictive medicine based on patient history (Pham, Tran, Phung, & Venkatesh, 2016), and clinical management using EHRs (Razavian, Marcus, & Sontag, 2016). Deep learning technology can also contribute significantly toward image processing and interpretation of the medical images (e.g., X-days).

Recently, deep learning algorithms have been increasingly popular for analyzing and understanding diagnostic image data and other prediction tasks. These algorithms have been quietly often used for supervised learning. These algorithms can be seen as complex extensions of the logistic regression (see above) in general. The logistic regression contains an input layer and an output layer, where the input layer has a node for each predictor variable (feature) and all input nodes are connected to the output node where each connection has its own weight. The output node calculates the sum of the weights of the input nodes and the logistic function finally measures the relevance degree of the sum as the final output. Deep learning algorithms are commonly based on an idea of using neural networks. Neural networks in a deep learning model expand on the structure of the logistic regression model by adding multiple hidden layers between the input and output layers. The nodes in the hidden layers can make the model complex and nonlinear relationships between the predictor variables and the outcome. By adding multiple hidden layers, where each layer can contain multiple nodes, neural networks allow deep learning models to model complex relationships and interactions in between features as well as between the input data and the outcomes.

In the medical areas, convolutional neural network (CNN), recurrent neural network (RNN), and deep belief network (DBN) have been often used. More descriptions of the use of these models in the medical areas can be found in F. Jiang et al. (2017).

## 4.3 | Natural language processing

NLP is an integral part of AI that connects between human languages and technologies. Using advanced AI algorithms, it is possible to crack down the semantic meaning from unstructured text. Specific tasks for NLP systems include summarizing large blocks of narrative text such as a clinical note, mapping data elements present in unstructured text to structured data in an EMR, converting data in the other machine-readable formats for reporting purposes, using of optical character recognition tool to read text from scanned documents, utilizing speech recognition to allow users to convert clinical notes, or other information that can then be turned into text.

NLP uses automatic text classification that helps to automatically identify the text from the large collection and classify the contents according to the predefined classes. NLP is therefore very important for Healthcare 4.0, and it has many AI-in-health care usages such as patient risk prediction by extracting free text data and vital sign data from clinical texts in EMR, cohort building by capturing important information from medical documents, concept identification for disease normalization, and extract information from biomedical literature to support clinicians.

NLP is built by a combination of rule-based and ML algorithms (e.g., support vector machines and conditional random fields) (Heintzelman et al., 2012). Topic modeling is one of the most popular NLP techniques that can automatically discover topics from a collection of clinical documents. It supports different algorithms such as latent Dirichlet allocation (LDA) and Latent semantic indexing (LSI). LDA is a generative statistical model that is widely used for topic identification based on Bayesian topic models (Blei, Ng, & Jordan, 2003). Maximum entropy (MaxNet) modeling, another NLP approach, is used to recognize and categorize medications mentioned in the unrestricted text of clinical documents generated in clinical practice. IBM Watson is the most famous example of NLP usage in health care. Alchemy API in Watson service can quickly and easily extract and analyze metadata from unstructured text.

## 4.4 | Social data analytics

Social data analytics is fast emerging as a connection between data, data science, and empowering communities that harness the power of digitization and automation. Sentiment analysis and topic modeling are the most common methods used for social media content analysis. Sentiment analysis mainly includes lexicon-based and learning-based methods (Younis, 2015). The lexicon-based method uses a lexicon of opinion words including positive, negative, and neutral words to assign a polarity score to each unigram that will then be added up to compute the polarity score of the entire text. The learning-based methods train sentiment classifiers using features such as unigrams or bigrams. Compared to lexicon-based methods, ML-based approach can produce higher accuracy but requires manual labeling and training data (Zhang, Ghosh, Dekhil, Hsu, & Liu, 2011). On the other hand, Lexicon-based methods are more efficient, but they can result in low recall.

Thematic analysis is a technique for identifying, detecting, and analyzing hidden thematic structure in large textual datasets (Braun, Clarke, & Terry, 2014). Thematic analysis can be achieved by performing topic modeling or graph analysis and community detection. Topic modeling can be considered as an unsupervised text classification that is used to cluster text into categories and detect the common themes within the documents of a corpus (Alghamdi & Alfalqi, 2015). Graph analysis is a different approach for thematic analysis that represents each term as a node in a network and uses the edges that connect these nodes to show the relationships between the terms (Tighe, Goldsmith, Gravenstein, Bernard, & Fillingim, 2015). Using graph analysis, community detection can be performed to identify communities (clusters of related terms) in a large network.

## 4.5 | Semantic reasoning

Semantic web, linked data (i.e., resource description framework), and ontology are subsumed under AI. All of them enable computer to understand the information by its own. One of the approaches is semantic modeling. This approach is based on explicit, human interpreted concepts, relationship, and rules that contain the desired knowledge of domain (Berners-Lee, 1998). This knowledge can be presented in a simple way, called knowledge base or knowledge graph. The knowledge graph or knowledge base is also kind of linked data that combined the different ontologies. To retrieve appropriate information from the knowledge base, reasoner can be used that can dynamically combine the knowledge to answer of the given questions. A reasoner is a software program that infers logical effects from a set of explicit asserted real-world facts or axiom that help for reasoning tasks such as classification, debugging, and querying. In addition, reasoner rules can be integrated into the ML algorithms to predict information relevant to a given context. Some of popular reasoners are developed in the recent years such Jena (McBride, 2001) inference system, Pellet, RACER, FACT++, Snorocket, Hermit, CEL, ELK, SWRL-IQ, FuzzyDL, Clipper, and so on. These reasoners have different characteristics such as inference ML algorithms, supporting logic, degree of completeness of reasoning, and others.

## 5 | HEALTHCARE 4.0: EMERGING APPLICATION AREAS

In Sections 2, 3, and 4, we provide a review of the current state of the art in Healthcare 4.0 using the proposed wisdom pyramid methodology described in Figure 1. In this section, we provide a review of current emerging application areas under the Healthcare 4.0 paradigm. These applications areas encompass one or more Healthcare 4.0 applications/services.

### 5.1 | IoT wearable remote health care monitoring

IoT wearable monitoring is an emerging area in Healthcare 4.0 and it is changing the way we capture and process our biological data. The application domain includes remote patient monitoring services, smart home (Alaa, Zaidan, Zaidan, Talal, & Kiah, 2017), hospital patient monitoring, rehabilitation (Bisio, Delfino, Lavagetto, & Sciarrone, 2017), self-tracking, performance sports (Camomilla, Bergamini, Fantozzi, & Vannozzi, 2018), and children, youths and elderly care (Misra, Mukherjee, & Roy, 2018). IoT wearable devices supported by AI-driven intelligent data processing techniques have great potential for early detection of physiological and behavioral changes and identify clinical episodes of several chronic diseases (A. R. M. Forkan, Khalil, Tari, Foufou, & Bouras, 2015). A key goal is to identify abnormalities at the earliest possible stage. The data processing for such IoT applications can be made more cost-effective using Fog-based computational model (Battula, Garg, Naha, Thulasiraman, & Thulasiram, 2019) (Liu, Chang, Guo, Mao, & Ristaniemi, 2018).

An example of IoT wearable devices is shown in Figure 10. IoT wearables are used in tracking of numerous chronic diseases. Several commercially available wristband IoT wearables devices can track heart rate, steps, blood pressure, calories, and sleep quality (Bunn, Navalta, Fountaine, & Reece, 2018). These biological parameters can be used to detect health abnormalities and disease progression. Various high-level user activities can be inferred by analyzing long-term captured data from wearable devices that can be used to provide different health-related services (Mukhopadhyay, 2015). Body-worn ECG sensors are used to detect different arrhythmias, myocardial infarction, and heart failure (Azariadi, Tsoutsouras, Xydis, & Soudris, 2016; Lee et al., 2018; Yang et al., 2016). An AI-driven intelligent data processing algorithm detects cardiac abnormalities based on real-time ECG data from ECG sensors. Similarly IoT wearable devices are used in detecting epilepsy (Beniczky, Polster, Kjaer, & Hjalgrim, 2013) from convulsive seizures through electrodermal activity and accelerometery. This is a useful improvement over lab-based EEG method in modern health as the device can be worn continuously. Wearable solutions provide pain-free glucose monitoring to maintain daily habits for diabetes patients

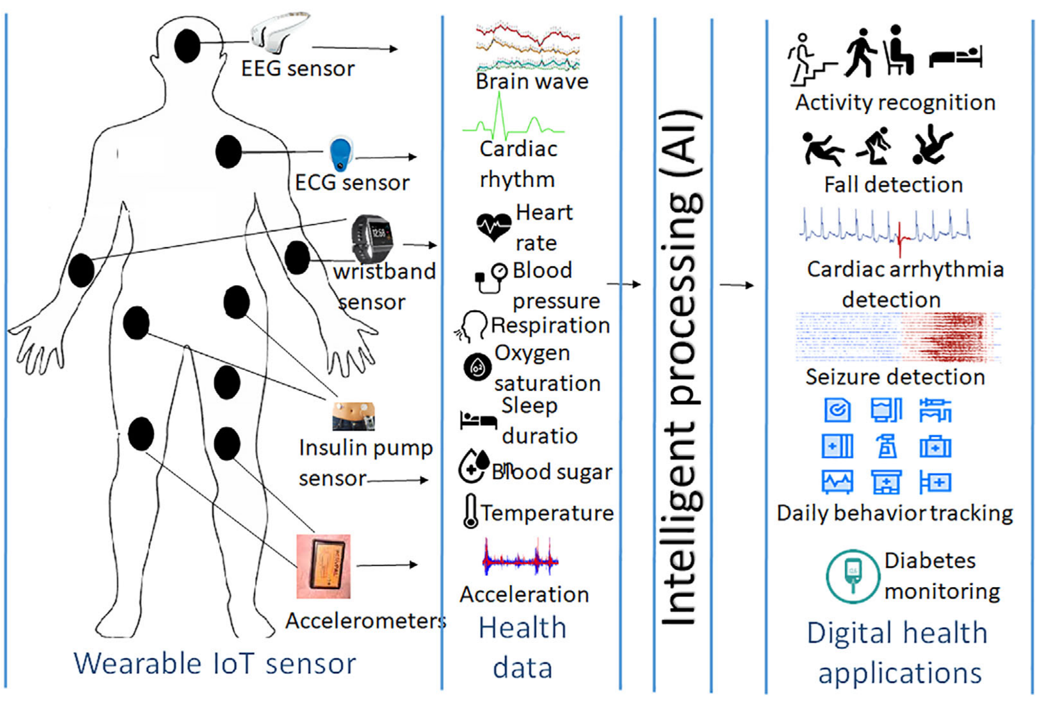


**FIGURE 10** Wearable Internet of things devices and their applications in Healthcare 4.0

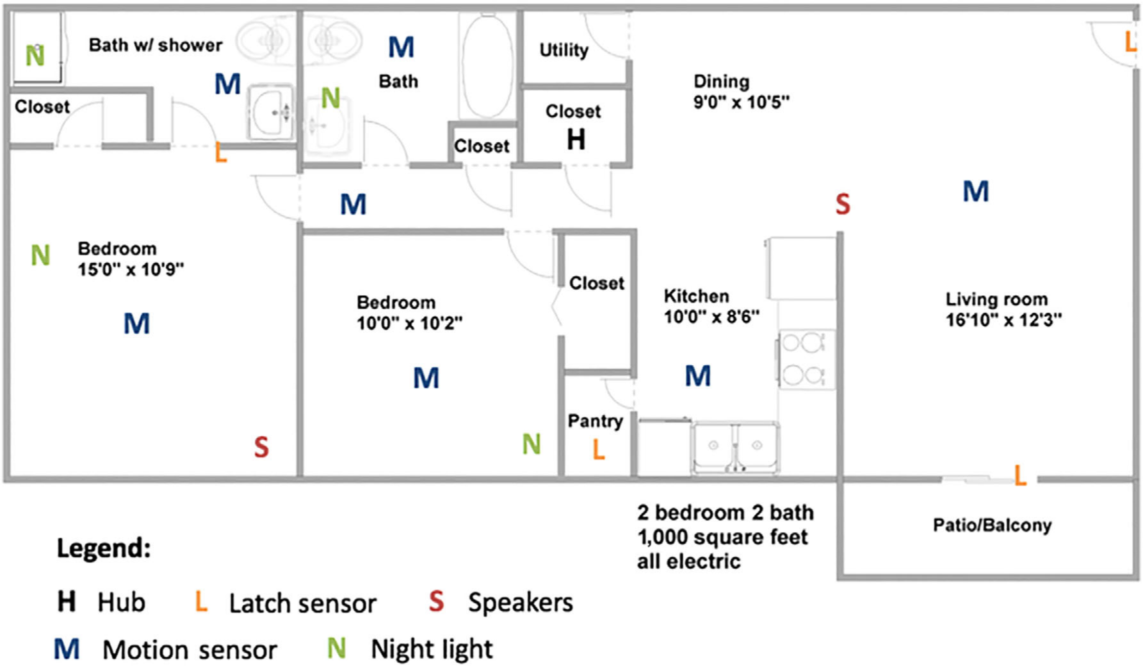


**FIGURE 11** An illustration of ambient assisted living

(Siddiqui, Zhang, Lloret, Song, & Obradovic, 2018). Levels of mental attention can be monitored with a small number of nongelled EEG electrodes.

## 5.2 | Ambient-assisted living

Ambient IoT devices can be easily placed in different location of a home to monitor human behavior and their health status. IoT sensors (e.g., motion sensors) installed in a home allow observation of daily behavior of individuals in the home via a nonintrusive approach. Several IoT devices provide the effective infrastructure to continuously monitor daily behavior of older adults in an unobtrusive way (Suryadevara, Mukhopadhyay, Wang, & Rayudu, 2013).

We have developed such unobtrusive system for detecting anomalous situations in assisted living environment named HalleyAssist (A. R. M. Forkan et al., 2019) using real-world data collected from different nonwearable IoT sensors. Figure 11 presents an example deployment scenario where different motion and latch sensors along with speaker and bulb are placed in different location in a house. A central hub gathers information from all IoT sensors. Magnetic switch and latch sensor are easily installable and used to detect the opening and closing of doors and windows. This data is then used to generate events and detect pattern such as number of toilet visits. Temperature sensor provides continuous data to detect the temperature of the ambient environment. Such sensors can detect the presence of users in rooms by utilizing the changes in temperature. Pressure sensors detect the presence on chairs or in bed. They can be used to detect *sit-to-stand* transfers and *stand-to-sit* transfers. Floor sensors detect situations such as falls and report immediately to an emergency response team. Water flow sensor continuously measures the flow of water in taps or showers and can be used to determine the hydration requirements of the user/person. Sensors such as microphones are utilized to detect different events such as daily activities, for example, the sound that is generated while handling dishes, when a person falls on the ground, or detecting Parkinson's disease (Kan, Kawamura, Hasegawa, Mochizuki, & Nakamura, 2002). More advanced ambient IoT bed sensors can detect vital signs such as heart rate and respiration (Kortelainen, Mendez, Bianchi, Matteucci, & Cerutti, 2010). All such ambient sensors do not raise privacy issues for in-home monitoring and avoids the inconvenience of wearable devices.

Ambient IoT sensors are also shaping Healthcare 4.0 structure in hospitals. For hospitals, preventing infection is imperative and given that thousands of sick and infected patients walk-in every day, hospital should strictly maintain hygiene. Hand hygiene monitoring systems help in setting and detecting a degree of cleanliness among health care and medical staff. The simplest function of hand hygiene IoT devices is to beep whenever medical staff comes in close proximity of a patient bed without washing their hands (Mieronkoski et al., 2017).

Ambinet IoT device such as Sensordrone contains a selection of sensors, including gas, humidity, light, and pressure and provide information about environment. It is now possible to use such environmental sensors to measure a range of concerns including air quality, barometric pressure, carbon monoxide, capacitance, color, gas leaks, humidity, hydrogen sulphide, temperature, and light. Other new home and environmental sensing solutions include the air quality.

## 5.3 | Mobile smartphone applications

A growing number of health and wellness monitoring mobile smartphone applications (mHealth apps) have appeared in recent past and are helping change people's perception toward digital technologies and how they manage and assess their health. Various mHealth apps also now available in marketplace such as Apple and Google Play store to assist health professionals with many important tasks, such as: information and time management, health record maintenance and access, communications and consulting, reference and information gathering, patient management and monitoring, clinical decision-making, and medical education and training. Some of these mHealth apps have been studied critically by medical professionals for their potential diagnostic capabilities, such as detecting acute coronary syndrome (Rathi, Kalantri, Kalantri, & Rathi, 2016), arrhythmias, or blood pressure. The ability to download medical apps on smart mobile devices has made a wealth of mobile clinical resources available to health practitioners. Different medical apps for many purposes are available, including ones for electronic prescribing (Haffey, Brady, & Maxwell, 2014), diagnosis and treatment (O'neill & Brady, 2012), practice management, coding and billing, CME or e-learning, and so on.

A broad choice of mHealth apps that assist with answering clinical practice and other questions at the point of care exist, such as: drug reference guides, medical calculators, clinical guidelines and other decision support aids, textbooks, and literature search portals (Mosa, Yoo, & Sheets, 2012). There are even mHealth apps that simulate surgical procedures or that can conduct simple medical exams, such as hearing or vision tests. Many mHealth apps are not intended to replace desktop applications but are meant to complement them in order to provide a resource that has the potential to improve outcomes at the point of care. mHealth apps are also having impact on the home health care market, enabling patients to leave the hospital for home sooner. A home health-care worker can use Health Insurance Portability and Accountability Act (HIPAA)-compliant secure messaging to communicate with colleagues. They can even retrieve a patient's EHRs securely using their smartphone or a tablet. The more a home health-care worker can do from the field, the more time they get to spend with patients (Ventola, 2014).

Another emerging mHealth application area is Medication adherence. Medication adherence is an expensive and damaging problem for patients and health-care providers. Patients adhere to only 50% of drugs prescribed for chronic diseases in developed nations. Digital health has paved the way for innovative mHealth app solutions to tackle this challenge. There are more than 97,000 mHealth applications/platforms available from different providers (Ahmed et al., 2018) that assist patients to adhere to medication and monitor their medication intakes. It is evident from the

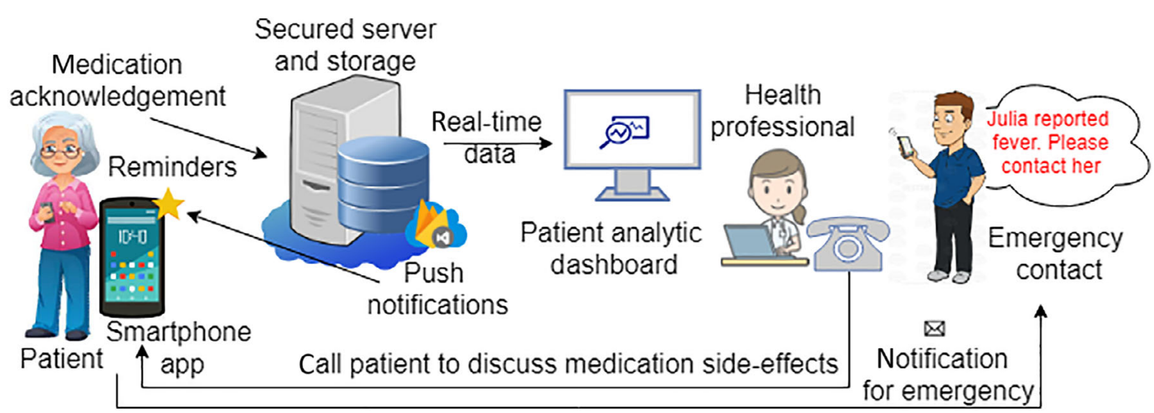


**FIGURE 12** mHealth medication adherence application

literature that there has been a highly positive impact of using mHealth apps for medication adherence. One such highly ranked app is medisafe (Santo et al., 2016). A total of 5,881 medication adherence apps are studied in Ahmed et al. (2018) and concluded that the adoption of effective adherence mHealth apps can improve patient welfare in the process. Figure 12 illustrates a mHealth medication adherence application.

## 5.4 | Clinical health care management

Continuous collection of digital health care data about patients can help identify potential anomalies early on and provide proactive prescription to prevent potential risks (Watters, 2015). Given the enormous amounts of the data, AI-driven Healthcare 4.0 can digest the data, detect patterns, analyze, and predict about future outcomes. These include services for diagnosing potential diseases and helping health carers to make decisions about treatments. It is noted that diagnostic errors happen to around 10% of patient deaths and between 6 and 17% of all hospital complications. Thus, identifying the presence and absence of diseases or metastatic of diseases for pathologist is considered to be very important, and ML can greatly help as an automated diagnostic tool. Electronic heath record (EHR) can also help identify infection patterns and provide patients with risk information before they show symptoms. AI and ML algorithms can help to enhance the prediction and accuracy of the emergence of infection faster as well as provide more accurate alert services to health-care professionals. Several Healthcare 4.0 applications have been used to assist the diagnosis of cancer and cardiology (F. Jiang et al., 2017). For example, it shows that IBM Watson for Oncology can be useful in assisting cancer diagnosis through NLP techniques and ML from large amounts of unstructured data. Also, deep CNNs have the potential in identifying different types of skin cancers. The CNNs were trained on more than 120 k clinical images consisting of more than 2,000 different diseases, demonstrating highly achievable capabilities in classifying skin cancers (Esteva et al., 2017).

According to S. Paul and Wetstone (2018), more than 17 million people died from cardiovascular diseases in 2015 corresponding to 31% of all global deaths. In this area, cardiac image data (e.g., ultrasound, CT) have been mainly used that can assess heart anatomy and function as well as detect heart-related pathologies. The study in S. Paul and Wetstone (2018) shows that deep learning techniques (i.e., CNNs) can be used to analyze these images automatically and thus reducing manual work of radiologist (which is in shortage) and improving diagnostic efficiency.

For example, Wong et al. (2018) shows that ML can be used to model complex diagnostic decision-making process from clinical inputs to identify individual with health outcomes. Also, it proposes that ML can be useful for extracting and structuring diagnostic information, largely stored in free texts (e.g., clinical notes) and images. Modern ML (e.g., deep learning) has the potential in automatically or semiautomatically extracting and leveraging useful clinical information via the ability to understand and analyze human language models and powerfully learn the features of images for image recognition.

## 5.5 | Virtual assistants and chatbots

Virtual personal assistance tools, such as Siri, Google Assistant, or Amazon Alexa, have limited capabilities in terms of their intelligence (i.e., able to answer basic questions), but in the future they will have more robust knowledge and intelligence of individuals' dietary behaviors, exercises, and medications from their daily routine (Watters, 2015 Apr).

Personalized health assessment tools are currently being used for individual persons. For example, Ada Health Companion has equipped with the AI chatbot app (Medical News Bulletin, 2017) that attempts to interactively communicate with an individual about his/her symptoms, provide an answer to what could be wrong using medical knowledge base, and suggest what could be done next (e.g., visiting a doctor, pharmacist, or seeking emergency care). Another examples is the IBM chatbot that provides information and advice to people living with arthritis (IBM Press Release, 2017) in which the machine is able to learn about patients through interactions (questions and answers) and provide personalized information in a form that feels like a natural conversation.

Chatbots are also able to connect patients with clinicians for diagnosis or treatment (Figure 13). Conversation agents such as Ada and IBM chatbot will emerge to be more prevalent. These tools will be able to provide day-to-day advice through conversations on keeping more balanced and healthy lifestyle, offer guidance on whether an individual needs to

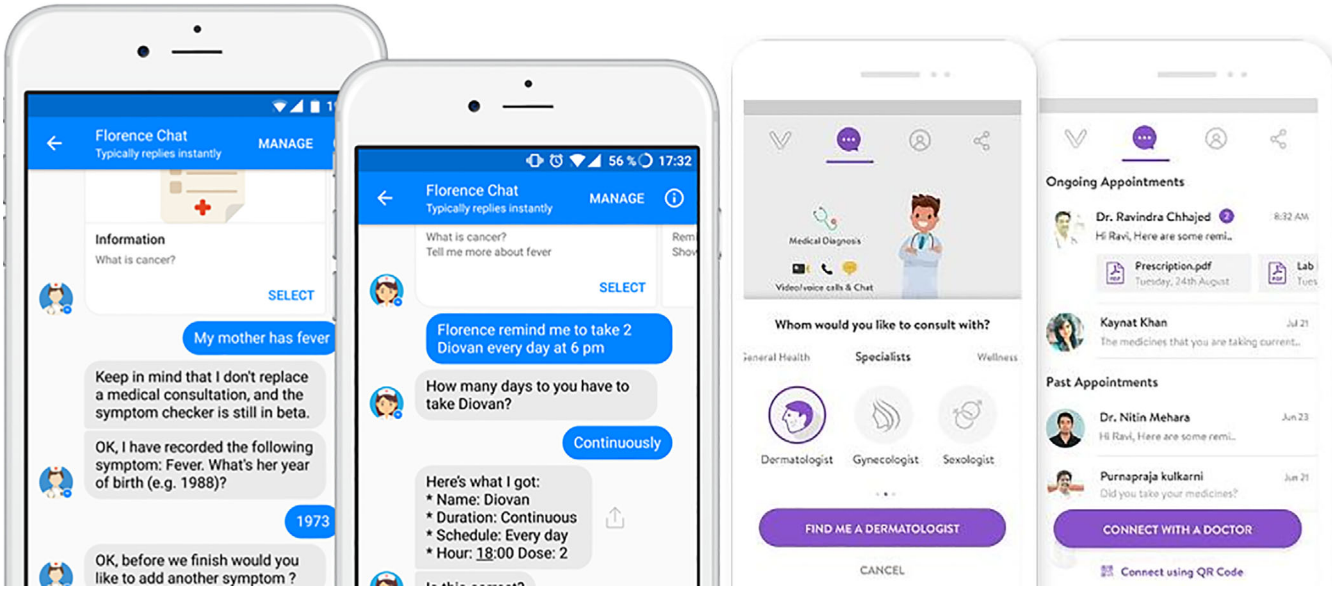


**FIGURE 13** Health care chatbot

meet a health-care professional for his/her medical concern, and also assist with tasks such as medical reminders (Watters, 2015).

Recently, mHealth chatbot apps have emerged providing personalized health care treatment (Watters, 2015) on smartphones. For example, Your.Md is able to guide personal healthy life, find safe health information, and check medical symptoms. Also, Sonde is a voice-based technology that has been designed to transform the way we monitor and diagnose mental and physical health, working on mobile smartphones. It uses tones in voice to detect symptoms or indicators for physical or mental illness. Safedrugbot offers assistant-like support to health professionals, doctors who need appropriate data about the use of drugs during breastfeeding. Babylon Health uses patient's reported symptom and checks them against a database of diseases using speech recognition, and then offers appropriate service (e.g., connect with doctor in a live video consultation) (Babylon, 2018).

## 5.6 | Society 4.0: Toward empowering communities in Healthcare 4.0 using social data

The popularity of social media analysis in health and medical research has led to exploring and introducing more powerful and sophisticated approaches. For example, by combining sentiment and thematic analysis, researchers could gain an in-depth understanding of the public perception toward different health-related topics. (Christaki, 2016) presents techniques combining different disease sources such as regional and global infectious disease surveillance, health-based web search engines, and communication patterns in social media to predict and prevent future public health threats. (Tighe et al., 2015) applied both sentiment analysis and community detection to study the patterns of communications about pain-related medical events from social media data. They also analyzed the networks of retweets and compared the connectivity patterns with other retweet networks.

The study presented in Delir Haghighi et al. (2017) investigated the subjective experience of patients with Fibromyalgia and any association with coincident environmental factors. They first examined the association between negative sentiment scores (indicative of more severe symptom density) and weather variables. The relationship between the environmental variables and negative sentiment scores was tested to deduce that there was no significant correlation. In this study, the date and time of posting of each tweet along with their location were collected, and this allowed them to collect the climate data for each tweet from the public web APIs. In the second series of tests, the authors used graph analysis to identify the most frequently occurring terms. Weather related terms were identified using community detection.

In the study conducted by Bian et al. (2017) tweets related to Lynch syndrome were collected and analyzed to understand the impact of promotional health information on laypeople's discussions. They first used a combination of

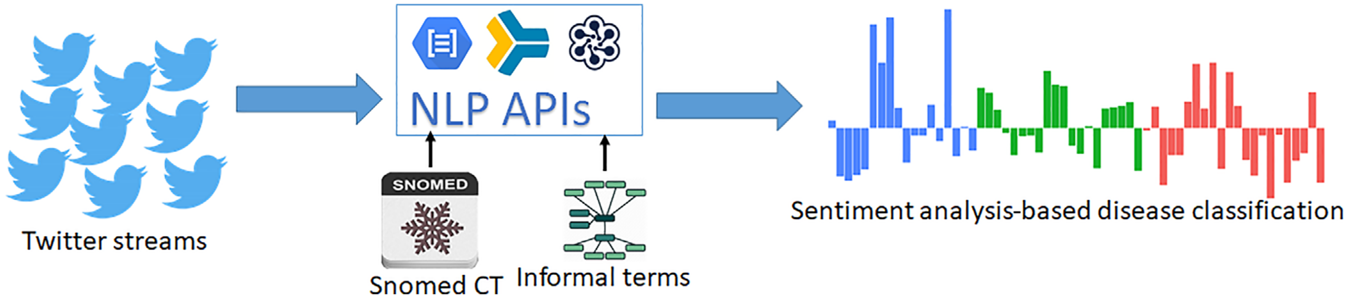


**FIGURE 14** Example of using social media data (Twitter) in Healthcare 4.0

AI techniques including LDA model and CNN. They used the analysis results to examine the correlation between promotional Lynch syndrome-related information and laypeople's discussions. An example scenario of sentiment analysis using NLP tools is demonstrated in Figure 14.

Instagram, a photo and video-sharing social networking platform that has gained a great deal of popularity in recent years for developing AI-driven Healthcare 4.0 application and services. Instagram provides users with creative ways to filter and edit photos so they can express their personal styles. This aspect of Instagram has been utilized in a few studies for investigating and predicting personality traits (Ferwerda, Schedl, & Tkalcic, 2015). The study (Ferwerda et al., 2015) found a significant correlation between personality traits and Instagram picture features applied by users and based on these features they explored personality prediction. In a similar way, authors in Lay and Ferwerda (2018) used "Liked" images on Instagram to predict user personality.

Online health forums as a different category of social media offer a safe and reliable platform where patients and their families can seek information or share their experiences. Three online forums of Reddit, Mumsnet, and Patient have been used for better understanding of health conditions (Cole, Watkins, & Kleine, 2016) including diabetes, chickenpox, and human immunodeficiency virus (HIV), and chronic cough. While online health forums could provide very relevant and useful data, however, accessing and extracting data programmatically from online forums can be difficult due to the lack of supporting APIs compared to Twitter. A recent study introduced a framework to model, rank, and semantically analyze emerging topics across Twitter and Reddit that provides a wider view and better understanding of emerging topics and trends (Pokharel, Delir Haghighi, Jayaraman, & Georgakopoulos, 2018).

Popularity of social media analysis under Healthcare 4.0 will keep increasing because it provides an ideal and low-cost setting for the rapid and dynamic longitudinal collection of very large volume of data worldwide, compared to traditional data collection methods. User generated and first-person data are particularly suited to study chronic diseases and conditions where there is little or poor understanding of the determinants of symptom expression in individuals (Delir Haghighi et al., 2017).

## 5.7 | Privacy and security of health data

Healthcare 4.0 application has enormous potential to produce improved health outcomes and patient experience (J. Kwon & Johnson, 2013). However, the resolution of privacy and security issues remains an ongoing and important challenge. Health care data has become a popular target for hackers. The digital and connected (via Internet) nature of Healthcare 4.0 make them a vulnerable target. Significant measures are required to ensure security and privacy of data collected by IoT devices. Ensuing security using traditional privacy preserving techniques is a major challenge (Susilo & Win, 2007). Health IoT devices can be connected to Internet through a wide range of wireless communication links which made traditional wired security technique unusable and open the door to develop new security protocols. Low-powered IoT devices are not capable of performing computationally expensive operation such as homomorphic encryption (Jayaraman, Yang, Yavari, Georgakopoulos, & Yi, 2017). Therefore, device-based authentication scheme such as PMSec (Yanambaka, Mohanty, Kougianos, & Puthal, 2019) can be effectively used to solve security concern in low-powered IoT medical devices. Many mHealth apps are not reliable enough and even well-known health care institutions often cooperate with third-party developers for app development adding further complexity in the attempt to adhere to relevant safeguards, regulations, and policies. Ensuring the security and privacy of electronic health data stored in the cloud brings with it a new dimension of complication and challenges. Some recently proposed models in information flow for smart health data to the cloud such as Lattice model (Puthal, 2018) can be explored to resolve such challenges. The use of social media platforms is a great way to manage personal health but the implementation of its security compliance is a big challenge.

## 6 | CONCLUSION

A thorough understanding of current digital frontiers in Healthcare 4.0 is expected to be useful for various stakeholders including health-care professionals, patients, and researchers interested in further research and development. This article provided a systematic review of selected number of digital enablers underpinning developments in Healthcare 4.0 and how they are transforming the health care sector. Healthcare 4.0 is envisioned to deliver innovative and qualitative services using advanced technologies (e.g., ML, IoT sensors and devices, social media) that are easily accessible, and simple to personalize, bridge the gap between capturing health information and changing behavior, and drive the adoption of healthy and active lifestyle and behaviors across the life which can result in positive health outcomes at every stage of aging. We conclude this review by identifying some key issues and challenges that need to be overcome in order to drive future development and adoption of Healthcare 4.0 application and services.

Healthcare 4.0 to be successful has to provide a multidisciplinary environment that brings together advances in the different fields including computer science, engineering, economical, social science, public health, epidemiology, and others. This will allow the digital underpinning of Healthcare 4.0 to go past technology to address the social and human aspects in providing quality care.

Digital technologies underpinning Healthcare 4.0 lead to an entirely new data-driven health care applications and systems. As discussed in this article, these data can be heterogeneous and hence required significant efforts toward curation, verification, and validation. Moreover, expert knowledge is also a very important part of health care research because of limited amount of medical data and their quality issues. For example, publicly available medical encyclopedia, Dbpedia, and PubMed are excellent sources of information that could be analyzed to extract valuable knowledge. A critical challenge is to have a good metadata that describe the data to guide further analysis. Hence, due diligence and policies need to be developed to ensure quality of the data being used in the decision-making process.

### CONFLICT OF INTEREST
The authors have declared no conflicts of interest for this article.

### AUTHOR CONTRIBUTIONS

**Prem Prakash Jayaraman**: Conceptualization; methodology; resources; writing-original draft, review, and editing. **Abdur Rahim Mohammad Forkan**: Conceptualization; Investigation; Methodology; Writing-original draft, review, and editing. **Ahsan Morshed**: Conceptualization; Methodology; Writing-original draft, review, and editing. **Pari Delir Haghighi**: Conceptualization; Methodology; Writing-original draft, review, and editing. **Yong-Bin Kang**: Conceptualization; Methodology; Writing-original draft, review, and editing.

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