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Mobile Health Technologies for Diabetes Mellitus: Current State and Future Challenges

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ABSTRACT The prevalence of diabetes is rising globally. Diabetes patients need continuous monitoring, and to achieve this objective, they have to be engaged in their healthcare management process. Mobile health (MH) is an information and communications technology trend to empower chronically ill patients in a smart environment. Discussing the current state of MH technologies is required in order to address their limitations. Existing review articles have evaluated the MH literature based on applicability and level of adoption by patients and healthcare providers. Most of these reviews asserted that MH apps and research have not reached a stable level yet. To the best of our knowledge, there is no clear description of solutions to these problems. In addition, no one has investigated and analyzed MH in its contextual environment in a detailed way. We conducted a comprehensive survey of MH research on diabetes management articles published between 2011 and September 27, 2017. In this survey, we discuss current challenges in MH, along with research gaps, opportunities, and trends. Our literature review searched three academic databases (ScienceDirect, IEEE Xplore, and SpringerLink). A total of 60 articles were analyzed, with 30% from ScienceDirect, 38% from IEEE Xplore, and 32% from SpringerLink. MH was analyzed in the context of the electronic health record (EHR) ecosystem. We consider dimensions such as clinical decision support systems, EHRs, cloud computing, semantic interoperability, wireless body area networks, and big data analytics. We propose specific metrics to analyze and evaluate MH from each of these dimensions. A comprehensive analysis of the literature from this viewpoint is valuable for both theoretical and developmental progress. This paper provides a critical analysis of challenges that have not been fully met and highlights directions for future research that could improve MH applicability.

INDEX TERMS Mobile health, diabetes mellitus, electronic health record, cloud computing, clinical decision support system, big data analytics, wireless body area network, medical informatics.

I. INTRODUCTION

A. RATIONALE OF THE STUDY

The number of elderly people with chronic diseases and disabilities is increasing drastically [191]. Chronic diseases cause 70% of deaths and account for 78% of healthcare expenses in the United States [103]. About half of Americans have one chronic disease, and one-quarter have two or more. Diabetes mellitus (DM) is a chronic disease associated with greater rates of cardiovascular conditions, kidney disease, vision problems, and non-traumatic amputations [6]. DM is a leading cause of morbidity and mortality worldwide. About 9% of the US population has some form of diabetes, and the number is expected to increase [18], [19]. DM can lead to a decrease in quality of life, an increase in medication costs, and high mortality rates. Patients with

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diabetes, especially type 2 DM, are often elderly. In addition, physicians are often overloaded with patients and their data. DM is a silent disease; a patient can have diabetes for a long time without knowing it. This can cause many complications. In 2014, there were 29.1 million Americans with DM, including 8.1 million who were undiagnosed [76]. Continuous monitoring of some vital signs is a critical step because it can prevent the occurrence of DM. However, it is often difficult for people with diabetes to adhere to complex self-management regimens. For example, many people do not test their blood glucose level, or do not inject insulin as frequently as required [4]. One survey [5] showed that only 50% to 70% of Americans with diabetes received the recommended eye examinations to prevent vision loss. The management of chronic diseases requires involvement by the patient in self-monitoring, self-control, and self-management of conditions during the day [18].

DM cannot be cured, but it can be prevented, detected, and managed [162]. *DM prevention* through continuous lifestyle monitoring can delay the development of diabetes and save money. *DM detection* can be achieved by using risk assessment tools to delay or prevent the development of DM, even from the pre-diabetes state [91]. *DM management* is long, costly, and requires continuous adherence to medical care (e.g., taking medicines, following a diet, and engaging in exercise and education). In addition, it requires ongoing self-management and monitoring to mitigate the potential risks [191]. The regular and daily decisions made by patients with diabetes (e.g., eating healthy, tracking physical activity, administering insulin and other medications, monitoring blood glucose, undergoing foot and eye care, participating in laboratory studies, making regular clinic visits, maintaining education) are very important for DM management [92]. Poor adherence to these activities can lead to significant mortality and morbidity, as well as poor quality of life [3], [18].

As a solution, information and communications technologies (ICT) can assist both patients and physicians to improve adherence by introducing them to electronic health (e-Health) [6], [61]. According to the World Health Organization (WHO), mobile health (MH) is a component of e-Health. By using mobile phones and smart devices, MH provides promising opportunities to improve diabetes prevention, detection, and self-management with continuous measurements of a patient's bio-signs [162]. Of all medical conditions, diabetes is the condition most targeted by current commercial mobile apps, followed by depression and asthma [22]. With MH, blood glucose data can automatically be collected, transmitted, and aggregated with other physiological data. These data can be analyzed, stored, and presented as actionable information. MH removes geographic barriers and engages patients in their health management by creating a smart environment. It can decrease costs and improve outcomes. In other words, MH supports the transition from clinic-centric to patient-centric healthcare where each agent (hospital, patient, physician, and service) is seamlessly connected to the others [151]. MH can serve patients with diabetes in several ways including (1) in-hospital professional decision support; (2) continuous and real-time monitoring of medication dosages, meals, lifestyle changes, vital signs, and provision of timely recommendations; (3) management of patients' primary care clinical schemes; (4) personalized care for acute diabetes conditions; and (5) support for active and continuous self-monitoring and self-management.

Many of the current MH interventions for DM (74%) focus on medication adherence and healthy lifestyle choices, and another 33% of the apps address DM prevention [23]. The majority of the required data by these apps are entered manually [77], [153]. In 2014, more than 382 million people around the globe suffered from diabetes. Most of these people were between ages 40 and 59, where requiring a lot of data from them is not an acceptable situation [162], [191]. In addition, physicians are often overloaded with patients, so mobile apps must not add to the burden by requiring a lot of data entry. By early 2016, over 1,500 different apps related to DM management existed on the market [12], [21], [78]–[84] and were available from Apple's App Store and Google Play. Apps fall into different categories, such as logbooks and diaries (e.g., Glucose Buddy and MyNetDiary); electronic health records (EHRs) and connectivity platforms (e.g., Glooko, Diasend, mySugr Scanner, and Tidepool); fitness and food regimens (e.g., Fitbit, myFitnessPal, Figwee, and GoMeals); and lifestyle monitoring (e.g., WellDoc, Omada, Withings, and iHealth). In addition, many different devices are available for tracking health factors (e.g., body weight and body mass index [BMI], dietary intake, physical activity, blood pressure, blood glucose). Even with a large number of apps, their real effect is still not seen. On the other hand, MH can result in major advances in expanding healthcare coverage, improving decision-making, monitoring chronic conditions, and helping in emergencies [28]. All of these improvements can be achieved for DM.

As a medical problem, DM needs personalized detection procedures, self-monitoring, and treatment [162]. This personalization process requires the complete history of the patient, not just a set of parameters entered in real time. Villarreal *et al.* [198] asserted that most of the current mobile apps for patient monitoring through mobile devices were not developed by considering the personal characteristics of each patient. They were developed based on the general behavior of the disease. Many apps depend on a set of unified questions asked for all patients in the same way. Based on their answers, the same set of information is used to derive conclusions. For example, the American Diabetes Association (ADA) provides a calculator with only seven parameters to diagnose diabetes, which is not sufficient; WellDoc [63] is a diabetes-monitoring app requiring manual entry of food and glucose parameters; METABO [64] is a monitoring app for recording and interpreting the patient context. These applications provide general monitoring, regardless of patients' individual peculiarities. This kind of monitoring is helpful for both patient and physician. To prescribe a suitable drug, a mobile app needs to have the patient's medical history, current medical conditions, vital signs, symptoms, and a diagnosis, as well as drug contraindications, side effects, and allergies. These factors are often compounded by uncertainty and semantic complexity. Manual entry of these data causes the application to create incorrect results that hamper physician decisions regarding patients. As a result, we need to look at MH technologies and applications in the context of global healthcare systems or the EHR ecosystem [56]. These technologies must be integrated or plugged as components in the existing medical systems. In addition, the development of MH applications has to include four aspects [30]: (1) a mobile client with medical sensors, (2) a wireless network medium, (3) a distributed cloud service, and (4) an EHR backend system.

B. OBJECTIVE OF THE STUDY

The primary aim of this paper is to provide a comprehensive review of the recent peer-reviewed literature on MH interventions for DM. In this survey, we study MH technologies in the context of the EHR ecosystem. In addition, we try to answer two questions: Can we consider MH applications as a component of an EHR system? Can MH applications be plugged into the EHR environment? To address these questions, we must check the interoperability between applications and distributed EHR systems, and check the clinical decision support system (CDSS) capabilities provided by MH apps (if any) and the compatibility with EHR decision support standards. We should determine the roles for Internet of Things (IoT) wearables and wireless body area networks (WBANs) to facilitate data aggregation and knowledge provision. We should determine the role of big data analytics to improve the intelligence from MH decisions. To the best of our knowledge, no studies have discussed these issues.

The remainder of this paper is organized as follows. Section II provides a definition of MH technology. Section III covers related work for MH in the DM domain. Section IV explains the methodology used to conduct this study. Section V presents the results and a discussion. Section VI looks at current challenges and future directions, and Section VII is the paper conclusion and future work.

II. MOBILE HEALTH

According to the Pew Research Center [8], 81% of households with an annual income above $75,000 a year and 47% of households with an income below $30,000 a year had smartphones. For example, 90% of Americans used mobile phones in 2014, and 64% used smartphones [13]. About five billion individuals had mobile phones worldwide [18], and about 500 million used mobile apps for sport, diet, and chronic disease management in 2015 [20], [152]. Szydło and Konieczny [191] pegged the availability of mobile phones at 100% in developed countries. Therefore, the opportunities for real-time health data tracking and individualized feedback are enhanced due to the widespread uptake of smartphones, wearable devices, and mobile apps [6]. The WHO defines e-Health as "*the use of ICT for health,*" and according to Pawar *et al.* [61], MH is "*the application of mobile computing, wireless communications, and network technologies to deliver or enhance diverse healthcare services and functions in which the patient has a freedom to be mobile, perhaps within a limited area.*"

MH receives a lot of attention from patients, healthcare professionals, application developers, network service providers, and researchers [1]. According to a Pew 2013 Research Center report, 69% of US adults tracked at least one health indicator, such as weight, diet, or exercise level, highlighting the potential impact of mobile apps for self-monitoring [9]. The tools used in MH include text messaging, video messaging, web sites, and mobile phone applications. These tools can provide immediate access to healthcare resources and patient records, and can transmit clinical data or communicate with healthcare providers. According to one WHO survey [2], these tools are not costly, and provide service around the clock, which makes them a potentially viable option in a wide variety of settings. MH can extend the reach of healthcare services to places where little or no healthcare is available, such as rural areas. It can provide faster emergency services, improve CDSS capabilities, and enhance the detection, prevention, and management of chronic diseases. However, MH is more than just some applications on a mobile phone. It includes numerous sophisticated applications that involve sensors, WBANs, and mobile devices to provide numerous healthcare services, plus healthcare professionals, intelligent CDSSs, EHR backend systems, social media, cloud computing, and big data analytics tools [28].

Regarding diabetes detection, many mobile apps can take input from a patient in the form of a questionnaire and return a risk score for developing diabetes or one of its complications. These are known as risk calculators. The most popular, official, and widely used risk calculators include one from the ADA[1] (with seven questions) and the Canadian diabetes risk questionnaire (CANRISK)[2] with 13 questions. Most of these risk factor calculators are naïve. They depend on a short list of patient factors and process them in a shallow manner [153]. *Regarding DM management*, physical activity, healthy eating, medication adherence (e.g., insulin dosing), monitoring (e.g., blood glucose and weight tracking), education, and problem solving are the six essential behaviors for improving DM self-management [10]. Many mobile apps offer options to support these behaviors [11]. In 2009, the number of apps was 60; in 2011, it was 260; and in 2015, there were more than 1100 publicly available apps. However, no robust studies evaluated the impact of apps on DM self-management [12]. Szydło and Konieczny [191] asserted that most of the offered solutions in MH are of the closed variety, and there are few differences between the offered solutions. No applications provided customized

[1] *http://www.diabetes.org/are-you-at-risk/diabetes-risk-test/*
[2] *http://www.diabetestest.ca/*

and personalized services, and their results were not accurate [152]. *Regarding blood glucose tracking*, the majority of apps require manual data entry, while others receive transmitted data from external devices, such as glucometers, via USB connection or low-energy Bluetooth. Some apps support data upload features, which enhances direct sharing of data. *Regarding data sharing*, most apps are designed only for the patient's perspective. In addition, some apps enable the sharing of data between physician and patient via email. Most of the education apps (95%) provide general and non-evidence–based information about the disease. In addition, the information is not tailored to every specific patient [6].

III. RELATED WORK

In recent years, we have seen great advancements in medical information technology [162]. Yang *et al.* [62] summarized these technologies in health sensing, big data analytics, and cloud computing. MH is one of the technologies that benefit from these advancements. It has gained increasing attention from researchers due to its practical relevance to patients, healthcare service providers, developers, and others. Concentrating on DM, there are many existing surveys of its research and applications, which differ according to the embedded components in the proposed systems [78]–[84]. Embedded features in current proposals include delivering a short message service (SMS), providing a CDSS, connecting to an EHR, providing big data analytics, connecting to a cloud environment, and using sensing devices and WBANs. For DM, the majority of the studies published used SMS technology in disease prevention or management [75]. Generally, researchers encourage the use of diabetes apps to track blood glucose and improve diabetes management and self-monitoring systems [89]. However, the current state of diabetes apps may not reach this goal [90]. Fu *et al.* [90] asserted that current apps have limited functionality and interaction. For example, the clinical effectiveness measured by reductions in glycated hemoglobin (HbA1c) only ranges from 0.15% to 1.9%.

Most of the existing surveys on MH discuss commercial mobile applications' effects on patient health. They concentrated on the benefits of mobile applications for enhancing patient monitoring and disease prevention [1], [6], [7], [12], [16]. The reviewed topics fell into categories that include the following: app descriptions (number of available apps, cost, user ratings, language, security, social networking, and audience [such as patient or physician]), usability analysis, and app content (self-monitoring, education). Some surveys asserted that we cannot measure an application's success [18]. Other studies asserted that we have not yet reached the needed level of utilization [24]. They discussed the functionalities provided and the ratings of these applications. The majority of the current MH apps for diabetes prevention and management are standalone, depending on the data collected from the patient in real time.

Rehman *et al.* [1] surveyed some of the mobile applications related to DM, physical activity, and smoking. This survey mentioned that apps mainly depended on the provision of SMS messages to patients with diabetes. SMSs tended to be used for medication adherence, appointment reminders, and to deliver motivational messaging [7]. This is not adequate, because a patient needs personalized and specific guidance for effectiveness. This requires connections with the EHR, a CDSS, a WBAN, the cloud, big data analytics, and clinical practice guidelines (CPGs) [48], [49], which were not discussed. Hartz *et al.* [6] reviewed DM prevention and management technologies and identified less explored areas where MH tools showed promise; they asserted that wearable activity trackers and mobile apps were the most prominent MH technologies for type 2 DM. In addition, they asserted that non-invasive and invasive wearable devices, blood glucose tracking, diabetes education, and data sharing could improve DM management. However, their paper did not discuss the technical advances or limitations of the technologies.

Brzan *et al.* [56] evaluated 65 apps for diabetes management (21 from Google Play, 31 from the App Store, and 13 from the Windows Phone Store). They stated that 56 of these apps (86.15%) did not meet even minimal requirements, or did not work properly. In addition, they concluded that only nine of the 65 reviewed apps (13.85%—five from Google Play, three from the App Store, and one from the Windows Phone Store) could be versatile and useful enough for diabetes self-management. Fijacko *et al.* [91] surveyed type 2 DM risk-assessment mobile apps; they asserted that nine out of 31 reviewed mobile apps disclosed the name of a risk calculator, but no upgrade was done to this information. Diabetes risk assessment is not only about calculators; the whole of the patient EHR profile must be taken into consideration, and decision rules must be imported from standard CPGs and updated regularly. Garabedian *et al.* [12] found only 20 peer-reviewed articles published since 2010 with robust evidence of the effectiveness of MH interventions for diabetes, such as HbA1c enhancement. Gray *et al.* [16] surveyed type 2 DM risk calculators based on smartphones. Miah *et al.* [66] reviewed MH from an information systems–design point of view; they identified the design themes of MH apps. Georga *et al.* [77] presented the state of the art in wearable medical devices for monitoring and controlling blood glucose levels (e.g., OneTouch Verio Sync, Guardian REAL Time, Freestyle Navigator II, iPro Evaluation, GlucoDock, iBGStar, Dario, and GlucoDay S). In addition, they surveyed mobile diabetes self-management interventions. Lee [93] reviewed the limitations of type 2 DM apps, concluding that MH has great potential to improve DM management, but expressed concern over connections with EHR ecosystems, provision of CDSS capabilities, and security and privacy enhancement. In addition, the International Diabetes Federation surveyed the role of MH in improving DM management [94]. They concluded that integration with existing healthcare systems, privacy, and interoperability issues must be handled to improve acceptance levels and service effectiveness. Olla and Shimskey [97] proposed a taxonomy of MH applications. Khansa *et al.* [88] tried to identify the gaps in mobile apps by monitoring 31 patients with diabetes. Khansa *et al.* [88] and Olla and Shimskey [97] concluded the following: (1) there is a lack of interaction between patients and healthcare providers, (2) there are challenges in managing the complex care of diabetes, and (3) there is a lack of standards. This means that mobile apps were not connected to the healthcare organizations' EHR systems. In addition, the apps did not model and handle problems correctly. Most of the previous reviews concentrated on the medical limitations of MH studies and applications. They all highlighted the problems, but they did not provide direct causes of the problems, and did not offer applicable and clear solutions to them. They all declared that DM prevention and self-management apps were not fully useful; in addition, we can see the increased percentage of patients with diabetes, and the increased number of DM complications.

In this study, we try to analyze the causes of the current limitations in MH, and we suggest some applicable solutions to enhance the capabilities of these critical applications. We evaluate MH in its global context, where MH has to be treated as a pluggable component in the EHR ecosystem. To achieve these goals, the current literature was surveyed to study the importance of MH technology as a whole, and its importance for diabetes prevention and management. A total of 60 studies from the diabetes literature were extensively reviewed to highlight the current limitations of diabetes MH research.

IV. METHODS

This study conducts a review of the literature on diabetes mobile health, which was carried out in the following steps.

A. INFORMATION SOURCES AND SEARCH STRATEGY

In this study, we depend on three academic databases (DBs): ScienceDirect[3] (SD), SpringerLink[4] (SL), and IEEE Xplore[5] (IX). MH research for diabetes mellitus was not popular before 2011. As a result, these databases were used to collect the journal conference research papers published from 2011 to 27 September 2017, inclusive. For the search strategy, we used "$" AND "#" where "$" represented keywords like *mobile health*, *MH*, *mobile application*, and *mobile computing* and "#" represented other groups of keywords, including [*EHR* OR *electronic health record* OR *medical record*], [*CDSS* OR *DSS* OR *decision support* OR *expert system*], [*interoperability* OR *integration*], [*diabetes mellitus*], [*big data* AND *medical*], and [*cloud computing* AND *medical*]. Other searched keyword groups include [*Internet of Things* AND *diabetes mellitus*], and [*wearable* AND *diabetes mellitus*]. The last group of keywords was [*diabetes mellitus* AND (*WBAN* OR *BAN* OR (*wireless*) *body area network* OR *sensor area network*)].

[3] *http://www.sciencedirect.com/*
[4] *https://link.springer.com/*
[5] *http://ieeexplore.ieee.org/Xplore/home.jsp*

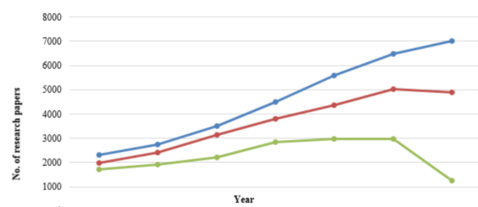
We acknowledge that many other areas are highly important and should be included, such as security, privacy, (wireless) networking, global positioning systems (GPSs), and sensors, among others. Due to length restrictions, we had to limit the scope of the review, and it is our sincere hope that others will cover omitted topics.

B. ELIGIBILITY CRITERIA

First, we collected the current literature for each combination of keywords from the three databases, and we then selected from each category a set of representative papers to study deeply and analyze. All the studied papers are in English. To examine the importance of MH research, we first surveyed the literature for each group of keywords, and then concentrated on diabetes for deeper study. The exclusion criteria were non-medical studies, security and privacy, GPSs and geographic information systems, electronics, non-English studies, studies where the searched keywords are not in both the title and the abstract, and studies that focused on multiple diseases. If the full text of the paper was not available, it was excluded.

C. STUDY SELECTION

We collected the relevant articles for our topic from the three databases, as shown in Fig. 1. The SD database has the largest number of papers in the MH domain, followed by SL and IX databases. In addition, we noticed that the number of research papers increased from 2011 to 2016. For example, the SD database held 7.2% of all papers from 2011 to 2017. However, in 2016, that database held 20.19% of the total, a difference of 12.99% over 2011. In the same way, the SL database held 7.69% of all papers from 2011 to 2017, but in 2016, it was 19.67%, a difference of 11.98%. The IX database held 10.76% of all papers from 2011 to 2017, and in 2016, it was 18.67%, an additional 7.91%. This means that the topic got much more attention in this period.



	2011	2012	2013	2014	2015	2016	2017
ScienceDirect	2314	2730	3492	4496	5602	6486	7010
Springer.Link	1970	2408	3148	3791	4357	5040	4904
IEEE Xplore	1709	1917	2216	2852	2965	2965	1258

FIGURE 1. The total number of papers for each year.

By concentrating on DM, Fig. 2 illustrates the number of research papers from all databases in each year. As can be seen, diabetes research papers were increasing each year except 2012. This shows that the MH topic garnered more interest as a method to improve diabetes detection, prevention, monitoring, and management.

Fig. 3 shows the total number of articles in the diabetes mellitus domain, grouped by keywords. These statistics were

FIGURE 2. The total number of papers for diabetes mellitus from all databases.

collected from all three academic databases. For *mobile health*, DM was in 12.36% of the literature; and for the abbreviation *MH*, DM was in 14.09%. Similarly, for the term *mobile computing*, DM was in 2.08% of the literature; for the term *mobile application*, DM was in 4.91%.

We can see that mobile health technologies and research received a great deal of attention in the period under study. Fig. 3 shows that WBAN technology was of great interest. However, the percentage of patients with diabetes still increased, and diabetes still produced complications and severe comorbidities. This means that diabetes mobile apps did not have the intended effect. To solve this issue and to propose suitable solutions, we have to criticize the current state of the literature according to specific guidelines.

For each of the surveyed topics including the relationships between MH and EHRs, big data, CDSSs, cloud computing, the IoT, and WBANs], we concentrated on diabetes mellitus mobile health advancements. Our strategy included the following steps, which are detailed in the next section.

1. We include the original articles in the analysis.
2. We discuss the criticality or importance of each topic to the success of mobile health.
3. We give examples from the literature in general.
4. We put specific focus on DM to measure the advancements in each topic, to define gaps and challenges, and to suggest guidelines for possible future research directions.

V. RESULTS AND DISCUSSION

To derive the dimensions of this study, we performed a comprehensive literature survey of MH. We classify the MH challenges into the following five categories: (1) connectivity between MH and EHR systems and their semantic interoperability, (2) MH's CDSS capabilities, (3) big data analytics features, (4) connectivity with cloud computing environments, and (5) connectivity with WBANs and the IoT. For every category, we conducted a literature review of the current research status; then, we identified several research challenges that need to be addressed. These challenges may provide a platform and directions for future research in the MH domain and can affect how MH applications will be designed, developed, evaluated, and adopted. We decided that security and privacy issues are outside the scope of this study.

We agree that MH cannot solve all healthcare problems. In addition, MH may not completely automate the delivery of healthcare services because of the potential damage and injuries to the patient's health. However, MH applications must add real and advanced value to all parties (e.g. patients and healthcare professionals). These values can be achieved only by working with a complete picture of these integrated and complementary technologies (mobile devices, the IoT, WBANs, CDSSs, EHRs, big data, and the cloud).

A. RECORD SELECTION AND ARTICLE TYPE

For each category, we selected the most suitable and original set of articles based on the article title and abstract. We independently reviewed the titles and abstracts of potentially relevant articles based on the inclusion criteria; studies that violated the inclusion criteria were excluded. Selected studies were retrieved for full-text review. These articles were extensively reviewed by all the authors of the study, and data were extracted from each article. The extracted data depended on the category of the article. For instance, for diabetes/mobile CDSS papers, the collected data include the decision support mechanisms used, connections to WBANs, execution of continuous machine learning, interactions with EHRs, handling of uncertainty, etc. Conducting an analysis of these articles enables us to get an extensive overview of the current state of research in MH, and uncovers future research challenges.

Our review was done with the following steps based on the PRISMA[6] methodology. Fig. 4 is a flow diagram that identifies the sequence of steps taken to identify the most relevant list of articles. In the *identification phase*, a total of 3540 articles were identified and collected based on searches of the three databases. In the *screening phase*, we excluded duplicates (n = 2404), and we screened the titles, abstracts, and keywords of the remaining articles (n = 1136) based on the defined inclusion criteria. A total of 880 articles were removed as not relevant, based on title, abstract, and keywords. In the *eligibility phase*, the full text of each remaining article matching the inclusion criteria (n = 256) was reviewed, and 196 articles were additionally excluded as not relevant based on the exclusion criteria. Finally, for the *inclusion phase*, 60 articles complying with our eligibility criteria were chosen for this study.

B. CATEGORIZATION OF MH RESEARCH

In this section, a general analysis of each category is provided to determine the state of the art. Next, we concentrated on diabetes research to compare it with the current state of the art in each category.

1) MH AND EHR SEMANTIC INTEROPERABILITY

An EHR contains comprehensive patient medical and administrative data. Connecting MH apps to this repository is critical, because it allows the combination of all patient historical

[6] *http://www.prisma-statement.org/*

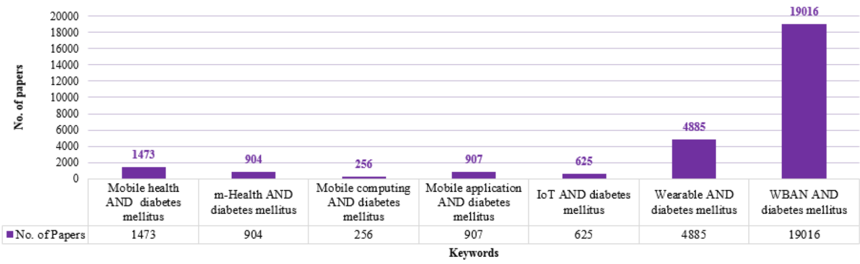


FIGURE 3. The total number of papers for diabetes mellitus grouped according to keywords.

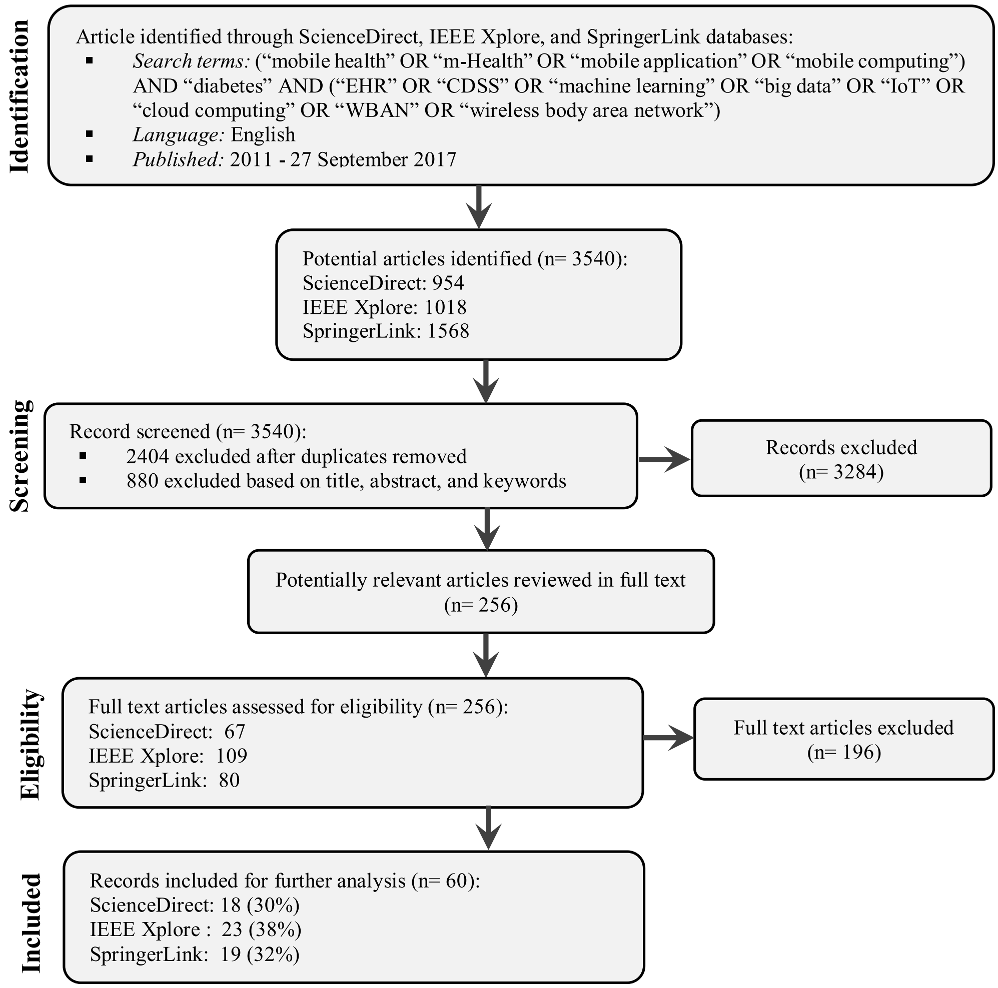


FIGURE 4. PRISMA flow diagram for our study selection process.

and real-time data, whereas mobile devices have less memory and less storage capacity [56]. This connection provides end-to-end comprehensive care, and supports sharing of real-time data between healthcare provider, physician, and patient. Iwaya *et al.* [65] asserted that an MH application has to connect with an EHR system and provide decision support capabilities. The collected data can subsequently be supervised and studied by physicians. In addition, these data can be integrated with other patient data and used by machine learning tools to discover advanced information. Moreover, the apps can automatically get more data about the patient, so they have more information and can provide accurate real-time decisions [102].

By integrating MH apps and the hospital EHR repositories, the fast and automatic collection of high-quality data helps to improve usability, especially for the elderly.

However, an EHR system is always distributed with heterogeneous components, each with different standard data models (e.g., Health Level 7 [HL7] v2, Reference Information Model [RIM] v3, Fast Health Interoperability Resources [FHIR], Clinical Document Architecture [CDA], OpenEHR, ISO/IEEE 11073, CEN EN13606, and Digital Imaging and Communications in Medicine [DICOM]). Each has different encoding terminologies (e.g., Systematized Nomenclature of Medicine Clinical Terms [SNOMED CT, or SCT], Logical Observation Identifiers Names and Codes [LOINC], Unified Medical Language System [UMLS], RxNorm, International Classification of Diseases [ICD], Medical Subject Headings [MeSH]), different datatypes, different schemas, different vendors, different formats, etc. [102], [106]. Linking EHRs with MH apps requires solving the problem of semantic integration and interoperability, because there is no universal standard or terminology [25]. Ahmadian *et al.* [114] revealed that the diversified terminologies adopted by EHRs and CDSSs result in problems of semantic interoperability. Many organizations help in defining global standards, including the International Organization for Standardization (ISO), HL7, WHO, and the International Medical Informatics Association (IMIA).

There are many standards for data transfer, including binary, Extensible Markup Language (XML), JavaScript Object Notation (JSON), Comma Separated Variable (CSV), and so on. However, the data may be represented in the same format but with different semantics. Medical data must be fetched via the standards of the EHR to preserve semantics and consistency.

In addition, the collected data from IoT devices must be standardized, compatible, and semantically consistent with the patient's EHR data to preserve the meaning of the integrated data. MH and sensor-collected data can be added to the EHR, or a gateway can be used with a standard interface (e.g., HL7 CDA) to communicate different types of data [98]. Khan *et al.* [175] proposed Adapter Interoperability Engine (ARIEN) as a middleware gateway among EHRs to provide semantic mapping between different standards using the *Mediation Bridge Ontology* (MBO); this centralized middleware has many limitations, and it was improved with distributed middleware by Lomotey and Deters [176]. Up to the time of writing this article, there were no unified standards for data storage and communications. The EN13606 standard tried to harmonize them with HL7 v3's RIM and CDA, and openEHR archetypes. Other studies [102] depended on EN13606 as a reference framework to build an interoperable EHR. This study implemented the iCabiNET system's access standard EHR from mobile apps.

Interoperability between healthcare systems must be handled. The world's biggest professional services company recognized that interoperability is a key enabler of scalable MH.

It includes syntactic interoperability (e.g., patient age and date of birth), and semantic interoperability (e.g., liver disease is a hepatopathy, and choledochocele is a type of liver disease). Syntax interoperability can be achieved by using a unified standard, such as HL7 RIM or OpenEHR, which unify the structure (i.e., data model) of the data. In addition, in case of heterogeneous standards, the mappings between standards using a semantic ontology can solve the problem. For semantic interoperability, Berges *et al.* [87] asserted that EHR semantic interoperability has not been achieved yet. The Joint Initiative for Global Standards Harmonization[7] defined semantic interoperability as "*the ability for data shared by systems to be understood at the level of fully defined domain concepts*." It is the ability of many computer systems to exchange data, where the receiving system accurately and automatically interprets the meaning of that data as defined by the sender. HL7 defines semantic interoperability as "*the ability to import utterances from another computer without prior negotiation, and have your decision support, data queries, and business rules continue to work reliably against these utterances*." Interoperability can be seen from different perspectives as *technical* (i.e., the exchange of messages between systems via XML, service-oriented architecture [SOA], and web services), *semantic* (i.e., using common information models, like HL7 RIM, and common terminologies like ICD) and *procedural* (i.e., the interoperability of people interacting with technology) [106].

Semantic interoperability must exist among different EHR systems. In addition, it must be maintained between EHRs and CDSSs; between different CDSSs, EHRs, and mobile apps; and between EHRs and sensing devices [48], [49], [87], [88]. A full study of semantic interoperability issues, and solutions was compiled by Pileggi and Fernandez-Llatas [74]. Park *et al.* [71] asserted that the current mobile apps for disease management have issues with reliability, interoperability, and scalability. In the e-Health domain, where data are clinical and biomedical, SemanticHealthNet[8] is a chronic heart failure project that ended in May 2015. It focused on semantic interoperability of biomedical knowledge. It developed an ontological framework that is compliant with SCT, HL7 CDA, ISO/EN13606, and OpenEHR. This facilitated seamless exchange of EHR data. HL7 developed CDA to semantically exchange messages between heterogeneous EHR systems; Haque *et al.* [98] used this format to propose a framework where mobile apps send and receive secure CDA messages to/from EHRs.

Recently, HL7 developed FHIR. It can accurately support storing, exchanging, and using health information in a mobile environment; it overcomes the limitations of HL7 V2 and CDA. However, in the MH domain, there are heterogeneous data that need to be considered. These data are from different resources with heterogeneous formats, such as IoT sensor data. Web Ontology Language 2 (OWL2) extensions should be incorporated to solve the problem of heterogeneous medical ontologies, terminologies, and standards. Mouttham *et al.* [106] proposed an interoperability ontology for collaborative care delivery. Based on this ontology, they

[7] *http://www.skmtglossary.org*
[8] *http://www.semantichealthnet.eu/*

proposed a generic EHR architecture to support interoperability between different parties including MH. Xu *et al.* [42] handled the heterogeneity problem of medical data formats in IoT platforms by using a semantic data model.

Antón-Rodríguez *et al.* [101] proposed an EHR system (EHRmobile) accessible from mobile devices, based on HL7-CDA R2 and DICOM standards and a MySQL database, for patients with mental disabilities. Parashar *et al.* [25] built the mOpereffa Android-based mobile app. They designed the mobile user interface based on standard OpenEHR archetypes to ease subsequent integration with the EHR backend. However, the demo was very abstract. It has not been applied to, or tested for, any medical problem, and its performance was not tested. A mobile application for a standard EHR called Healthsurance was proposed by Jain *et al.* [99], which is based on mOpereffa. Its main idea is to generate a dynamic GUI based on openEHR archetypes. The authors first created archetypes using Archetype Definition Language (ADL); the archetypes are then parsed by an ADL parser and wrapped into Java classes; then these classes are used to build dynamic GUI forms, and the data are stored in a MySQL relational database based on Hibernate technology and a generic schema, i.e. entity attribute value (EAV).

Archetypes have attracted interest when building interoperable systems, because approximately 100 archetypes are enough to build an interoperable primary care EHR [100]. Microsoft adopted OpenEHR in its Connected Health Framework v.2 [26]. However, there are many global standards that use different mechanisms other than archetypes. In addition, many studies did not discuss the problem of unstructured sensor and real-time data. The majority of the studies physically store the mobile data in a database at specific intervals. The contents of these databases are synchronized with EHR data. Utilizing gateways with standard interfaces can connect the complete EHR in a hospital with mobile personal health records (mPHRs) stored on smart devices or in the cloud [104], [105]. PHR message formats have some XML-based standards, including the ATSM E2369-05 Continuity of Care Record (CCR) [107] and the HL7 Continuity of Care Document (CCD) [108].

According to the National Alliance for Health Information Technology [71] "*a PHR is an individual's electronic record of health-related information that conforms to nationally recognized interoperability standards that can be drawn from multiple sources while being managed, shared, and controlled by the individual*." Zapata *et al.* [105] evaluated 24 mobile PHR applications. The results showed that all PHR studies are not suitably structured and have many limitations. Lomotey and Deters [104] tried to solve the problem of data synchronization between an EHR and a mobile PHR database by proposing a distributed mobile architecture based on distributed cloud-hosted middleware. Hsieh *et al.* [40] proposed a mobile EHR system based on the HL7 standard to help nursing staff administer medications. The system was based on the HL7 exchange standards (i.e., CDA) to communicate data between end users and distributed heterogeneous databases. However, the system could not handle semantic interoperability as required, simply because it was based on a single standard (i.e., HL7). Park *et al.* [71] proposed the Self-Management mobile Personal Health Record (SmPHR). It offers chronic disease management in an Android 4.0.3–based mobile app. The system implemented standard protocols that try to provide interoperability between various health devices and EHRs. The sensor data were collected in a SQLite database through ISO/IEEE 11073, and for transmission to the EHR, these data were converted to EHR's HL7 V2.6 standard.

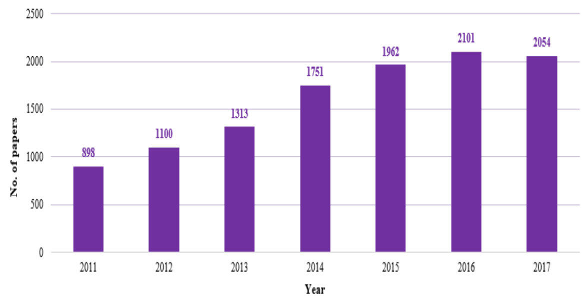


FIGURE 5. **Progress in the literature on EHRs and semantic interoperability for the MH domain.**

From the three databases, we surveyed the existing studies that connect MH to EHRs with interoperability and integration. The number of papers increased each year, as shown in Fig. 5, which means this topic attracted interest. However, this problem is still a hot point of research. Ontologies and their formal description logics can provide intelligent solutions for the problem. Ontologies are superior to relational databases and taxonomies in terms of expressiveness [109]. They support knowledge sharing, reuse, and inference. Yilmaz *et al.* [109] proposed an architecture for developing intelligent EHR systems. It stores data using OWL ontologies and supports sharing of data between different hospitals. However, they built a local ontology, and there will be a problem integrating standards-based systems. The optimum solution for this kind of problem is the harmonization of OWL ontologies, medical terminologies, and EHR standards to implement the whole interoperability stack. For example, Noran and Panetto [110] argued that the healthcare interoperability approach defined by ISO 14258 should be based on predefined shared ontologies. To the best of our knowledge, there are no such studies in the MH domain.

After studying the literature regarding the relationship between mobile health, EHRs, and semantic interoperability, we concentrated on the diabetes domain. We measured the current research status in diabetes regarding these technologies. As shown in Table 1, the evaluation is based on a set of important metrics, including the following.

1. *Data format*: determines the format of the collected data in an EHR or a PHR as either a relational database or a NoSQL database.

TABLE 1. Diabetes-related EHR studies.

Study, year	Data format	Destination	Syntax interoperability	Diabetes type	Semantic interoperability?	Platform	Connection with WBAN?	Handles unstructured big data?	Citations
SmPHR [71], 2016	SQLite relational database	Personal mobile device	HL7 V2.6, CCR, CCD, ISO/IEEE 11073	T1, T2	No	Android (PHR)	Yes	No	86
Jung et al. [152], 2014	Relational database	Local PHR server	HTTP XML	T1, T2	No	Android (PHR)	No	No	30
Yoo and Chung [177], 2017	Relational database	Local PHR server	HTTP and HL7	T1, T2	No	Android (PHR)	No	No	11
Sujansky and Kunz [178], 2015	Microsoft HealthVault	PHR in the cloud	ISO/IEEE 11073, HL7 v2.x, DIRECT	T1, T2	SCT	Cloud (PHR)	Yes	Yes	15
Zhang et al. [179], 2017	Relational database	Local EHR server	HL7 vMR	T2	SCT	Local server (EHR)	No	No	1

2. *Destination*: determines if the data are collected in a private mobile device, in the cloud, or on local servers.
3. *Syntax interoperability*: determines the open standards data model used to handle syntax interoperability between different data models.
4. *Diabetes type*: determines the covered diabetes type. The codes used are T1 for type 1 DM, T2 for type 2 DM, and G for gestational DM, but not all studies defined a specific type.
5. *Semantic interoperability?*: indicates how interoperability between different encoding and terminology systems is handled.
6. *Platform*: determines the physical location of the storage and whether it is a full EHR or a PHR.
7. *Connection with a WBAN?*: indicates if the study supports the collection of IoT sensor data in an EHR database.
8. *Handles unstructured big data?*: indicates if semi-structured and unstructured data, such as social media data and freely entered data, are handled within the collected data.

In general, the number of quality studies on mobile health for diabetes based on the EHR is not high. Table 1 lists the most relevant papers studied. As seen in Table 1, all the studies have many limitations that need to be addressed. Due to space restrictions, we use the table's comparisons only to highlight the limitations in the literature. Although T1 and T2 diabetes are treated differently, the majority of the studies did not differentiate between them. Many studies still depend on relational databases for EHR and PHR storage. Although the current open source technologies of NoSQL databases are still not suitable for storing sensitive medical data, a relational database cannot deal with current medical big data.

Syntax and semantic interoperability are critical for building distributed environments with diverse data formats, terminologies, data models, and sources. In addition, handling (collecting, storing, processing, and analyzing) big data collected from a WBAN has not been properly handled in the literature.

FIGURE 6. Progress in the literature on the CDSS and MH.

2) MH AND THE CDSS

There are many mobile apps to help users with chronic diseases. A CDSS is a computer program that provides personalized decision support based on a knowledge base and a patient database. Fig. 6 illustrates the importance of CDSS studies, and shows the increases in CDSS usage every year. However, the CDSS impact on patient outcomes is marginal [160]. Without decision support capabilities integrated with the EHR system, the EHR is only a repository of a huge volume of raw data that cannot be utilized to provide real assistance for patients and physicians. Integration of the two facilitates self-monitoring, delivers customized and actionable knowledge, elicits positive behavior changes, and supports effective self-management of DM. It is essential at three different levels of complexity. *The first level* is implemented on the patient's mobile device, and this system is for lightweight and extremely time-sensitive decisions that do not require much processing, do not need much data, preserve battery lifetime, and at the same time, need to be fast (even with a lost internet connection). *The second level* is implemented in the cloud, and it depends on the EHR level exported to the cloud and the amount of metrics collected from the patient via WBAN. The CDSS offers decisions that are more complex, that require processing power and analysis of a large set of data. *The third level* is in the healthcare backend system, which is the most complex level. It depends on the whole EHR system. This type can be used in public health strategic decisions and for decisions that depend on deep analysis of the medical temporal data.

A mobile CDSS must be smart enough to make the correct decision in real time [77]. Farmer *et al.* [85] proposed a system to collect patient data and send it to a domain expert for decision making.

This is not suitable for DM; MH CDSS applications are critical for chronic disease management because they can make decisions in critical situations where the patient cannot contact a physician, e.g., a diabetes patient goes into a coma at night [47]. To do that, the CDSS must be built with a formal, standard, and up-to-date knowledge base. In addition, it must make customized decisions based on specific (i.e., current and historical) patient profile data. The CDSS can reduce the patient's visiting times and improve quality of life by providing suitable guidance anytime, anywhere. As asserted by the HL7 standard, the CDSS must be scalable, intelligent, interoperable, and accurate. Many incorrect decisions occur due to lack of correct and complete data [28], [44], [47]. The incorrectness can come from manual interaction of the patient with the CDSS when entering data. The CDSS must be able to access the complete patient history in addition to current-state data. Sensing devices and WBANs can improve this process because they provide continuous monitoring of the patient's vital signs, and automatically transfer these data to a mobile device. For patients with diabetes, this real-time monitoring can avoid many adverse events. Generally, many of the current DM CDSS tools are utilized to provide treatment adjustments, but only for research purposes [77], [86].

Healthcare professionals must consider symptoms, medical history, lab results, and diagnostic tests (among other things) in reaching medical decisions. A mobile CDSS must have the ability to access the medical history of the patient stored in distributed and heterogeneous EHR environments to make sophisticated, individualized, and customized decisions [48]. Moreover, the CDSS has to be active by extracting the most recent information from every suitable resource, such as recent CPGs inferred knowledge from machine learning techniques, social media, and domain experts [47]. This capability can be achieved by building a CDSS based on a standard interface (e.g., the HL7 GELLO common expression language and the vMR data model) and a sharable and standard knowledge base (e.g., HL7 Arden Syntax, Guideline Interchange Format [GLIF], Sharable Active Guideline Environment [SAGE[9]], PROforma, Prescribing Rationally with Decision-Support in General-Practice Study [PRODIGY], Asbru, and Global Uniform Interoperable Data Exchange [GUIDE]). Zhang *et al.* [113] proposed a CDSS based on a sharable knowledge base where each knowledge module is semantically well defined based on standard information model, medical terminology, and representation formalism. Service-oriented architectures can provide some solutions to this issue [113], [148]. Loya *et al.* [148] surveyed CDSSs and provided some future directions. Currently, in mobile computing and MH domains, there are many systems for specific needs, but they are independent, isolated, and incompatible with surrounding environments [46]. These systems are not usable because they quickly become out of date. The current EHR environments have significant limitations in allowing pluggable CDSS services within complex workflows [49].

Integration of the EHR and CDSS, and interoperability between heterogeneous CDSSs require the handling of semantic interoperability challenges [44], [48], [147], [160]. Zhang *et al.* [160] asserted that a CDSS must be based on CPG information represented in a standard format and integrated into the EHR with encoded and standard content. Interoperability is based on terminologies, definitions of concepts, and reference models. Standards like HL7's CDA, RIM, Arden Syntax, and vMR can play a critical role in this issue, where patient data and decision knowledge are mapped to/from standard data model formats [47], [113]. Terminology can be based on standard medical terminologies, such as SCT and UMLS, and/or OWL2 ontologies (e.g., gene ontology [GO], the Foundational Model of Anatomy [FMA], Disease Ontology [DO], Diabetes Mellitus Treatment Ontology [DMTO], Diabetes Diagnosis Ontology [DDO], etc.)[10] [36], [72]. Definitions of concepts can be based on archetypes, as in openEHR, using Archetype Definition Language. Many standardization organizations have proposed reference models, such as RIM under HL7. Zhang *et al.* [160] proposed a solution for CDSS semantic interoperability that is based on a representation of CDSS knowledge and data using an OWL ontology and HL7's RIM. Sáez *et al.* [44] proposed semantic interoperability of a rule-based CDSS and an EHR focusing on standardized input and output documents conforming to an HL7 CDA wrapper However, there are no such studies into mobile environments. A small number of studies in the literature handled these issues, and nearly no existing apps have implemented these capabilities. Torre-Díez *et al.* [50] reviewed CDSSs in ophthalmology, and concentrated on mobile apps available from the Google Play virtual store[11] for Android devices and the App Store[12] for Apple's iOS. They concentrated on whether the CDSS is connected to an EHR, the cloud, and data mining algorithms. They asserted that existing CDSSs are hardly ever applied in a practical way, and they are far from reaching potential optimization in healthcare systems. This can explain why the number of patients with diabetes keeps increasing, despite the huge number of diabetes mobile apps. Castaneda *et al.* [147] tried to answer such questions, and asserted that current CDSSs provide weak features because they have to be integrated with EHR systems via standards.

[9] *http://sage.wherever.org/*

[10] *http://bioportal.bioontology.org/*

[11] *https://play.google.com*

[12] *http://store.apple.com*

TABLE 2. Some smart CDSS studies evaluated according to a set of measures.

Study, year	Used techniques	Has application?	Handles uncertainty?	Managed disease	Semantic interoperability?	Data sources	Data encoding	Uses semantic ontology?	Citations
Miller and Mansingh [27], 2017	CBR + AHP	No	No	NA	No	Custom patient + drug databases	NDF-RT	No	3
Verma et al. [39], 2017	C4.5, KNN	No	No	Waterborne	No	User-centric	No	No	1
Vedanthana et al. [115], 2015	NA	Yes	No	HIV, Hypertension	No	EHR	No	No	13
Bourouis et al. [116], 2014	ANN	Yes	No	Retinal disease	No	Images from microscopic lens	No	No	43
Forkan and Khalil [117], 2017	Rule-based	No	No	Vital sign anomalies	No	Wireless sensors	No	No	5

Other barriers against mobile CDSSs include the unstructured, varying, and uncertain (i.e., vague) nature of medical data, which are difficult for computer systems to process. One possible solution is the encoding of CDSS information and EHR data with unified and standard medical ontologies, such as RxNorm, ICD, etc. Using ontologies and semantic reasoners in combination with the CDSS reasoning mechanisms enables the creation of more intelligent apps capable of discovering new information and inferring facts from the available information [111]. Bobed *et al.* [111] asserted that the popular and currently available description logic (DL) reasoners (e.g., CB, ELK, HermiT, jcel, JFact, Pellet, and TrOWL) could be used on Android-based devices. In addition, there are new mobile DL reasoners (e.g., mTableau, Pocket KRHyper, Delta, and Mini-ME) developed for mobile devices [111]. However, there has not been widespread adoption of these efforts in the medical domain. Pappachan *et al.* [112] used a semantic reasoner in a mobile device to infer possible diseases for rural patients, given their symptoms and context, where connectivity is usually nonexistent. Uncertainty can be handled by fuzzy logic and statistics.

A fuzzy ontology extends fuzzy semantics. However, there is no support for any fuzzy ontology reasoners, such as fuzzyDL, on mobile devices yet [111].

In the literature for MH, there are some studies that tried to handle part of these requirements [27], [39], [45], [47], as shown in Table 2. Miller and Mansingh [27] proposed the design and implementation of a distributed, intelligent, mobile agent–based CDSS called OptiPres for drug prescriptions. The authors asserted that the mobile system must be integrated with an EHR system and with artificial intelligence techniques, such as case-based reasoning (CBR) or rule-based reasoning (RBR). Vedanthana *et al.* [115] proposed Decision-Support and Integrated Record-keeping (DESIRE), a tablet-based nursing CDSS tool to assist rural clinicians taking care of hypertension and HIV patients in Kenya. This app supports the retrieval of patient data from an EHR using cellular networks. However, as seen in Table 2, this app has many limitations. For example, they tried to integrate the EHR with a CDSS but did not rely on any standards. In addition, the reasoning mechanism was not discussed. Bourouis *et al.* [116] proposed an Android-based intelligent system integrated with a microscopic lens that supports patients' regular eye examinations after a diagnosis of retinal disease. The authors used artificial neural networks (ANNs) to analyze the retinal images to identify retinal disease conditions.

Another dimension that improves the efficiency of a CDSS and enhances its inference capabilities is the integration of a CDSS knowledge base with a real-time machine-learning (ML) engine to keep the CDSS up to date [40], [54], [117], [149]. These CDSSs, classified as Type Four CDSSs according to the Australian National Electronic Taskforce Report 2000 [45], can update their information dynamically, incorporating new predictive models or employing incremental learning methods. The ML engine can continually mine the collected big data to infer new information, which can be used in reactive and preventive monitoring of patients. The learning approaches can be divided into data-driven approaches, knowledge base approaches, and hybrid approaches [141].

Data-driven approaches are classified as supervised, semi-supervised, or unsupervised algorithms. Supervised learning approaches (with completely labeled training data) are artificial neural networks, Bayes networks (BNs), decision trees (DTs), support vector machines (SVMs), k-nearest neighbor (KNN), etc.

For instance, Gyllensten and Bonomi [142] proposed a feed-forward neural network with five-fold cross validation to train the data of free-living subjects in daily life from a single accelerator. Unsupervised learning methods (without any labeled training data) include K-means clustering and the Gaussian mixture model [143]. Semi-supervised techniques fall in between unsupervised learning and supervised learning [200].

Knowledge-based approaches represent and extract knowledge from a domain expert to build a CDSS. These approaches consist of syntax-based, logic-based and ontology-based approaches. The syntax-based approach uses grammar, which defines the structure based on language modeling. It follows a hierarchical structure for two layers of hidden Markov models (HMMs) and BNs on the bottom, with context-free grammar on top. A logic-based method (e.g., description logic) describes concepts, and uses logical rules for high-level reasoning. The ontology is flexible and used in the IoT-enabled healthcare field due to its reusability, computational completeness, decidability, and practical reasoning algorithms.

Hybrid approaches combine both data-driven and knowledge-based approaches. Qi *et al.* [141] collected a set of machine learning studies that are based on WBAN data. Ahmed and Abdullah [51] and InSook *et al.* [52] discussed the potential importance of data mining applied to a CDSS. Big data mining, semantic data mining, and temporal data-mining algorithms are the important techniques for discovering knowledge from the patient's historical and real-time data [62]. Verma *et al.* [39] proposed a cloud-based IoT framework to monitor students for waterborne diseases. After collecting sensor data and storing them in the cloud, temporal classification algorithms (i.e., a decision tree by C4.5 and k-nearest neighbor) were used to mine information from these data; then, the information was used to build a CDSS to alert various parties.

Forkan and Khalil [117] developed a real-time, multi-label classification algorithm to forecast vital-sign values and their related abnormalities. The framework depends on a set of wireless sensors that collect a patient's vital signs and send them to the cloud; these data are classified using machine learning techniques to predict the patient's upcoming anomalies. This study only depended on the collection of some vital signs to provide the prognosis of a patient. This is not enough, because to diagnose a disease, all of the patient's medical history must be considered.

Regarding diabetes, there are many CDSS studies. Georga *et al.* [77] discussed mobile self-management support interventions in diabetes care. They asserted that most systems are educational, and the data are entered manually. Donsa *et al.* [14] studied how CDSSs and machine learning can improve the individualization of patients' diabetes treatments. Hanauer *et al.* [15] proposed a computerized reminder system for blood glucose monitoring, and argued that using cellphone text messaging provided a portable, acceptable, and inexpensive method for managing diabetes. The evaluation of these CDSSs is based on the following metrics.

1. *Knowledge base format*: determines the format of the CDSS knowledge base and the utilized standard, such as HL7 Arden Syntax, Asbru, EON, GLIF3, GUIDE, and PROforma.
2. *Has application?*: indicates if the proposed study implemented an application or not.
3. *Handles uncertainty?*: indicates if the system handles the vague nature of diabetes by using some fuzzy technologies, such as fuzzy inference engines or fuzzy ontologies.
4. *Cloud-based?*: indicates if the application is connected to a cloud environment to process the large amounts of patient data, and if it has access to machine learning modules.
5. *Semantic interoperability?*: indicates the semantic interoperability techniques between CDSS and EHR systems, such as HL7 vMR.
6. *Has temporal dimension?*: indicates if the proposal handles the temporal nature of chronic disease.
7. *Diabetes type*: indicates the covered diabetes type. The codes used are T1 for type 1 DM, T2 for type 2 DM, and G for gestational DM.
8. *Data sources*: indicates the sources of data used to make personalized decisions (i.e., connection with an EHR, social media, and IoT sensors) to define if the CDSS depends on the patient's whole profile or depends on real-time input.
9. *Attached machine learning module?*: indicates if the CDSS includes machine learning capabilities that continuously infer knowledge from collected big data to keep the knowledge base up to date.
10. *Knowledge based on CPGs?*: indicates if the CDSS knowledge base relies on CPGs, because CDSSs must support evidence-based medicine by building the knowledge base from standard CPGs.
11. *Data encoding*: indicates if the system standardizes the data by encoding them with standard medical terminologies to support integration and interoperability.
12. *Uses semantic (fuzzy) ontology?*: indicates if the study utilized a semantic (fuzzy) ontology in data or knowledge representation and inference.

Table 3 presents a summary of the evaluation of the most relevant and suitable studies. These 12 metrics are interrelated and must be handled together to build an intelligent and interoperable CDSS. However, it is clear from Table 3 that there is no complete study that adequately handles all of the evaluation metrics. As a result, all of these systems need improvement to achieve the required level of intelligence, applicability, interoperability, accuracy, and acceptability by the community. Moreover, these results confirm the results of the other surveys of DM mobile apps in the most famous stores, including Google Play, the App Store, and the Windows Phone Store. For example, Brzan *et al.* [56] asserted that only nine out of 65 reviewed apps (13.8%) could be versatile and useful enough for successful self-management of diabetes. In addition, most applications provide naïve support for both patient and healthcare provider [163].

Different types of diabetes require different ways of managing them; as a result, the majority of people with diabetes still use paper-based methods for tracking their blood glucose level [65]. Regarding ML capabilities, only four out of 20 CDSS studies (20%) have attached ML capabilities. Wang *et al.*[166] proposed an antihyperglycemic medication recommendation system based on a shared decision-making (SDM) process for type 2 DM. They employed a multi-label classification model that uses class-imbalanced EHR data.

TABLE 3. Some diabetes mobile CDSS studies evaluated according to a set of measures.

Study, year	Knowledge base format	Has application?	Handles uncertainty?	Cloud-based?	Semantic interoperability	Has temporal dimension?	Diabetes type	Data sources	Attached ML module	Knowledge based on CPGs?	Data encoding	Uses semantic (fuzzy) ontology?	Citations
Hussain et al. [47], 2013	Standardized HL7 Arden Syntax rules	No	No	Yes	HL7 vMR, CDA	No	T1, T2	Sensor, EHR, social media, user	No	No	SCT	OWL	30
Jung et al. [152], 2014	No standardized set of rules	Android	No	No	No	No	T1, T2	EHR, user questionnaires	No	No	No	No	30
Ali et al. [153], 2017	No standardized SWRL rules	No	Yes	No	No	No	T1, T2	Wearable sensors	No	No	No	Yes	1
MobiGuide [154], 2017	Standardized rules in Asbru	No	No	No	HL7 vMR	Yes	G	Sensors, EHR	No	Yes	SCT	Yes	4
Jung & Chung [155], 2016	No standardized set of rules	Android	No	No	HL7	No	T1, T2	User, EHR	No	Yes	No	No	8
METABO [156], 2015	No standardized set of rules	Android	No	No	No	No	T1, T2	User	No	No	No	No	15
Lim et al. [157], 2016	No standardized set of rules	No	No	No	No	No	T2	Sensors, EHR	No	Yes	No	No	19
PDTF [158], 2015	SPARQL queries	Android	No	No	HL7 CDA	Yes	T1, T2	User	No	Yes	No	Yes	0
UHMS-HDC [159], 2017	SQL queries	Android	Yes	No	No	No	T1, T2	User	No	No	No	No	0
Zhang et al. [160], 2016	Standardized SPARQL & SWRL rules	No	No	No	HL7 RIM, OWL 2	No	T2	EHR	No	Yes	Yes	Yes	19
PICARD [161], 2016	Standardized rules in Asbru	No	No	Yes	SOA	Yes	All	Sensors, EHR	No	Yes	SCT	No	11
EMPOWER [162], 2016	Standardized rules in GLIF	Android	No	No	ISO 13606, Open-EHR	No	T2	User, EHR	No	Yes	No	No	13
Wang et al. [166], 2016	No standardized set of rules	Android	No	No	No	No	T2	EHR	Yes	Yes	No	No	3
Brown et al. [167], 2013	No standardized CBR	No	No	No	No	No	T1	User	No	No	No	No	4
Zhang et al. [168], 2016	No standardized set of rules	NA	No	Yes	No	No	T2	Sensors, WeChat	No	Yes	No	No	3
FoodForCare [169], 2016	No standardized set of rules	Android	No	Yes	No	No	All	User	No	Yes	No	No	0
ImHS [170], 2016	No standardized set of rules	Android	Yes	Yes	No	No	T1, T2	User	No	Yes	No	No	7
Inside Me [171], 2016	No standardized set of rules	iOS	Yes	No	No	No	All	Sensors, user	Yes	No	No	No	0
CBIHCS [172], 2014	No standardized set of rules	No	No	Yes	No	No	All	Sensors	Yes	No	No	No	74
SMIE [173], 2015	No standardized CBR	Android	No	Yes	HL7 vMR	No	All	Social media, trajectory, email	Yes	Yes	SCT	Yes	6

The system aims to provide a recommended list of available antihyperglycemic medications. They utilized 2542 cases, each with 77 features and eight output labels. They achieved 0.0941% for hamming loss, 0.7611% for accuracy, 0.9664% for recall, and 0.8269% for F1 score. Busssadee *et al.* [171] used both logistic regression and random forest ML techniques based on the Pima Indian Diabetes Dataset for diabetes risk assessment. Kaur and Chana [172] performed real-time monitoring of user health data for diabetes diagnosis. They utilized principal component analysis (PCA), a k-nearest neighbor classifier, and a naive Bayes classifier to prepare and classify the data. They achieved a classification accuracy of 92.59%. Fatima *et al.* [173] proposed a system to monitor health conditions, emotions, and patients' interests from their tweets, their trajectories, and email analysis using natural language processing techniques, an ontology, and ML algorithms.

3) MH AND BIG DATA

Medical data are a mixture of structured and unstructured data, which are difficult for computer systems to process [27]. The EHR collects the patients' complete historical data; in addition, connecting MH apps with the IoT and a WBAN causes continuous sensing and capture of readings from wireless sensors for many of the patient's vital signs [151].

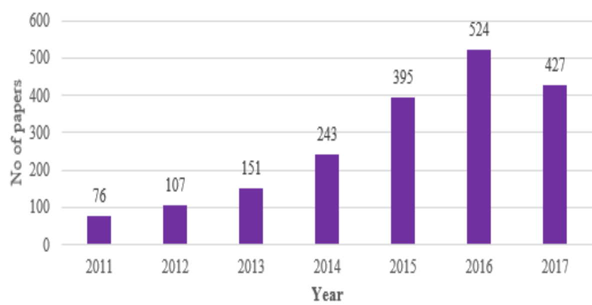


FIGURE 7. Progress of the literature in big data MH research.

Moreover, other sources, such as social media, have to be considered. This issue is referred to as big data. Fig. 7 is the progress of big data research in the MH domain. As illustrated, this problem gained the attention of research in the literature because of its critical role in the EHR ecosystem.

The flood of big data from a large collection of patients can be described with the Five V's: volume (i.e., measured in petabytes, exabytes, zettabytes, and yottabytes), velocity (i.e., speed in creating, capturing, extracting, processing, and storing data); variety (e.g., types include text, image, genomic, transcriptomic, proteomic, metabolomic, social media, medical record, and sensor readings), veracity (i.e., uncertainty, incompleteness, and imprecision of data), and value [120]. Rodríguez-Mazahua *et al.* [121] reviewed big data tools, challenges, and trends. Big data cannot be processed, analyzed, or stored by mobile devices with limited storage, memory, processing power, and battery power. Social media and social networks like Facebook have great potential to enhance healthcare [119]; these data can be analyzed implicitly by running data science algorithms (machine learning, predictive analytics, descriptive techniques, etc.) on the aggregated data to discover hidden patterns; or users could be explicitly asked to collect specific data [122].

The volume of worldwide healthcare data was equal to 500 petabytes in 2012, and it is expected to be 25,000 petabytes in 2020 [199]. These data are collected from different sources in the form of structured, semi-structured, and unstructured formats. In addition, these data must be kept for a long time in the patient's EHR historical records in order to perform complex analyses. The question that many physicians ask is, "What am I going to do with all that data?" [149]. Big data analytics technologies have to be integrated with MH applications to continuously discover hidden information. Cloud computing provides a convenient, cost-effective, real-time, and scalable computing environment for storing, (pre)processing, and analyzing big data [67], [151]. After handling security and privacy issues, cloud computing can provide three layers of service. *At the fist level*, infrastructure as a service (IaaS), such as Amazon's Elastic Compute Cloud (EC2) and Simple Storage Service (S3), as well as Google Cloud Storage, makes it easy to store big data in the cloud. Many other providers, such as AT&T, IBM, Microsoft, Qubole, VMWare, salesforce.com, and Rackspace, provide this infrastructure. *At the second level*, platform as a service (PaaS) offers a combination of storage and computing services, including Microsoft Azure, Google's Compute Engine, Google Fusion, Google App Engine, and Google Cloud Dataflow, and VMWare's Cloud Foundry. *At the third level*, software as a service (SaaS) provides analytical applications to deal with big data. The providers at this level of service include salesforce.com, AppDynamics, BloomReach, and Rocket Fuel.

Cloud computing provides real-time big data sharing, access, and analytics for MH apps from anywhere and at any time. Relational databases are not capable of handling volumes of data that are too big, too fast, and too diverse [120]. Relational databases require predefined schemas; they are based on the atomicity, consistency, isolation, and durability (ACID) transaction-management attributes, which are too strict for many apps. As a result, big data storage based on NoSQL databases, Hadoop computing, and cloud-computing models seem to provide an alternative solution for enhanced insight and decision-making [31]. NoSQL and NewSQL data stores provide high throughput for voluminous and heterogeneous data in a distributed environment because they are schema-less and based on basic availability, soft state, and eventual consistency (BASE) transaction management [32], [121]. Open source NoSQL database formats include document-based (e.g., MongoDB[13] and CouchDB),[14] column-based (e.g., Google Bigtable, Cassandra, SimpleDB, DynamoDB, and Hbase),[15] key value–based (e.g., Memcached,[16] Redis,[17] Riak,[18] and Voldemort),[19] and graph-based (e.g., Neo4J[20] and HyperGraphDB). Grolinger *et al.* [123] surveyed the existing NoSQL databases and concentrated on the data models, querying, scalability, partitioning, replication, consistency, concurrency control, and security issues. However, data are not useful in and of themselves. Big data discovery enables scientists to uncover hidden patterns and correlations from the analysis of a large volume of diverse data. MapReduce is the standard big data processing framework [164]. The Hadoop[21] project is an open source realization of MapReduce. Wang *et al.* [33] discussed some big data applications in healthcare, including large datasets for EHRs, CDSSs, and WBANs. Unfortunately, there are no perfect data management solutions using the cloud to manage big data [70].

Big data solutions are based on heterogeneous data sources [164]. Zillner and Neururer [127] proposed a road map for developing big data healthcare apps, and they asserted the critical roles of semantic enrichment, sharing, and integration of data. Improving the quality and interoperability (i.e., technical, syntactic, and semantic) in a big data environment can be achieved by data coding and standardization using standard data models, XML, and ontologies [124], [127]. Sánchez-de-Madariaga *et al.* [126] compared relational and NoSQL database approaches to store, recover, query, and maintain a standardized EHR based on the ISO/EN 13606 standard; they asserted that document-based NoSQL databases perform better than relational ones when database size is extremely high. Ontologies can bridge the semantic gap between different data sources, and provide a unified interface over all of these heterogeneous data. In addition, ontology rules and DL reasoners semantically analyze these data and discover hidden and complex information. Big data analytics tools (e.g., Apache Spark, Apache Mahout, and Storm) and techniques (e.g., data mining, machine learning, and statistics) can very much benefit from this unified, consistent, and integrated big data. Marcheschi [125] evaluated the existing e-Health standards (i.e., DICOM, HL7 vMR, and HL7 FHIR) for big data interoperability, and asserted that the success of big data analytics is tightly connected with handling interoperability between heterogeneous data sources. Rathore *et al.*[128] proposed a real-time CDSS for emergency response. The system is based on a WBAN with connected wireless sensors on

[13] *http://www.mongodb.org/*
[14] *http://couchdb.apache.org/*
[15] *http://hbase.apache.org/*
[16] *http://memcached.org/*
[17] *http://redis.io/*
[18] *http://basho.com/riak/*
[19] *http://www.project-voldemort.com/voldemort/*
[20] *http://neo4j.com/*
[21] *http://hadoop.apache.org/*

TABLE 4. Some diabetes big data studies.

Study, year	Storage location	Storage format	Diabetes type	Sources	Interoperability with EHR	Analytics capabilities	Analytics tool	Citations
Abbas et al. [181], 2016	SaaS in the Ubuntu cloud	NA	T1, T2	WordNet database, Twitter	No	Semantic analysis of social networks (Twitter), collaborative filtering	twitteR package of R	9
CDF [182], 2014	Facebook cloud	Facebook database	All	Facebook, vital-sign sensors	No	Social network analysis (Facebook)	None	7
Kumar et al. [183], 2015	NA	Data warehouse	T1, T2	EHR, PHR, external sources	Health Information Exchange	NA	NA	27
Shah et al. [124], 2015	NA	Heterogeneous formats	All	Heterogeneous data sources	OWL ontology with SNOMED CT	Ontology semantics, SWRL rules	Protégé	19
SMIE [173], 2015	NA	NA	All	EHR, Twitter, email, trajectory	HL7 vMR, SNOMED CT	Smart CDSS by rough sets and CBR	Social media adapter, Alchemy API	6
Mezghani et al. [139], 2015	NA	NoSQL databases	All	EHR, social media, sensors	OWL ontology	Semantic reasoning based on WH_Ontology	Semantic MediaWiki	20

patients' bodies. The heterogeneous sensor data from all the patients are collected, stored in the cloud, and processed in a Hadoop ecosystem. The authors concentrated only on the format and structure of the collected data from the sensors, and did not consider integration with the rest of the patient profile in an EHR. As a result, CDSS decisions may be affected.

Having access to well-curated and high-quality data has the great benefit of improving the efficiency and effectiveness of a CDSS in personalization of predictions, earlier diagnoses, and better treatments [118]. A report from the McKinsey Global Institute [122] estimated that if the United States used big data creatively and effectively in healthcare, then the potential value from that data could be more than US$300 billion every year, two-thirds of which would come from reducing expenditures by about 8%. Big data analytics decisions can outperform the domain experts [120]; smart devices can make as accurate, or more accurate, decisions than medical experts. As a result, the McKinsey report stated, "*In the hospital of the future, big data is one of your doctors*"; however, there remain challenges to overcome [121].

Regarding the relationship between DM and mobile big data, some studies did not handle the complete picture of big data. Hence, we tried to compare these studies under the following set of metrics.

1. *Storage location:* determines where big data are stored, either in a local server or in the cloud.
2. *Storage format:* determines the format of the data, either relational or NoSQL format.
3. *Diabetes type:* determines the types of diabetes the study handled (T1, T2, or G).
4. *Sources:* determines the sources of big data, such as social media, Semantic Web Rule Language (SWRL) sensors, etc.
5. *Interoperability with EHR:* determines how the study solves the interoperability challenge between big data sources and EHR systems.
6. *Analytics capability:* determines the capabilities of the study, including machine learning, predictive modeling, data mining, statistics, etc.
7. *Analytics tools:* determines the tools used to perform data analysis tasks.

The majority of diabetes studies concentrated on big data analysis in isolation from an EHR environment. For example, Chennamsetty *et al.* [184] proposed a big data predictive analytics technique for EHR data based on Hadoop and Hive. Medical data were collected from different resources into a Hive data warehouse, and Hadoop MapReduce analyzed these collected data. Moreira *et al.* [180] proposed RBFNetwork, which was an ANN-based study to predict gestational DM. This study concentrated only on the analytical side. These studies utilized regular data sets used in mining a regular database. Table 4 shows the most suitable studies.

No studies proposed solutions for critical big data challenges, such as semantic interoperability with EHR systems, the role of big data in improving CDSS knowledge bases, the exact relationship between big data collected from different resources (such as social media and sensors), and the professional medical data inside healthcare organizations. In addition, as shown in Table 4, many studies are abstract and have limited details. As a result, the big data research related to DM mobile health applications is still in its infancy.

4) MH AND CLOUD COMPUTING

Mobile cloud computing (MCC) is becoming the heart of healthcare systems [134]. Fig. 8 shows the increasing importance of MCC research in the MH domain. Wearable and

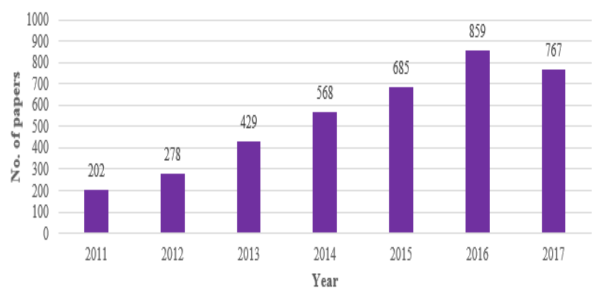


FIGURE 8. Progress in the literature for cloud computing research in MH.

mobile devices that automatically collect sensor data, data entered manually by users, social media data, and EHR data generate a huge amount of information (i.e., big data). Mobile devices have little memory and processing power. Therefore, MH backend systems (EHRs, CDSSs, social media functions, and sensor processes) can migrate into the cloud environment [39]. Ahnn and Potkonjak [30] proposed an optimization model for cloud-based health monitoring to optimize energy savings and to minimize execution time through computation offloading. Makam *et al.* [53] asserted that a CDSS in the cloud is feasible and a very reasonable way to achieve better support in making clinical decisions. They tried to optimize the cost of communications and computations. This environment can provide a huge storage capacity to collect historical and real-time sensing data, and can provide efficient computing, CDSS capabilities, EHR hosting, and big data analytics capabilities.

Cloud computing (CC) is defined by the National Institute of Standards and Technology (NIST) as "*a model for enabling ubiquitous, cost-effective, scalable, convenient, distributed, on-demand access to a shared pool of configurable computing resources (e.g., networks, servers, storage, applications and services) that can rapidly be provisioned and released with minimal management effort or service provider interaction*" [55]. The MCC Forum defined MCC as "*an infrastructure where both the data storage and the data processing happen outside of the mobile device*" [135]. CC supplies the main ingredients of computing resources, such as CPUs, storage, network bandwidth, virtual networks, and virtual machines, as commodities at a low unit cost. The cloud environment has many advantages, including availability, information sharing, accessibility, scalability, measured services, multi-tenancy, interoperability, rapid elasticity, fault tolerance, and load balancing; however, security and privacy issues are big barriers [31], [54].

Regarding accessibility, MCC can provide nationwide health information sharing and exchange by providing global connectivity between different parties [134]. Patients and physicians can access EHRs and CDSS capabilities from anywhere and at any time with just mobile devices. Doukas *et al.* [34] designed a simple user interface on the Android OS for patients to upload their medical data to the cloud. Henian *et al.* [129] proposed a cloud-based real-time electrocardiogram (ECG) monitoring and analysis system, where patients are allowed to upload and access their ECG records. Many public health management systems, such as Microsoft Health Vault, Google Health, Dossia, and Mphrx, are based on MCC.

Yao *et al.* [59] also proposed a cloud-based medical service delivery framework to facilitate the exchange of resources between a large general hospital and its associated smaller healthcare institutions. Kyriazakos *et al.* [136] proposed eWALL, a cloud-based MH platform for creating a home care environment.

The system depends on a gateway to integrate data from different sensors, and another gateway integrates collected data with the cloud environment based on MongoDB; data transmission between gateways is in JSON format.

Regarding information sharing, the sharing of medical information is based on the selected cloud deployment model. Cloud providers have four deployment models: public, private, hybrid, and community. In addition, inter-cloud connectivity can be implemented to improve information sharing [55].

Interoperability is required among different systems within the same healthcare provider, among different healthcare providers, among an mPHR and cloud providers, and among different cloud providers [134]. The integration of the collected heterogeneous data from distributed EHRs, hospital information systems, wireless sensors, and social media requires handling the challenge of semantic interoperability [46]. Semantic ontologies and standards provide full interoperability, where new systems, databases, devices, and other components can smoothly plug into the ecosystem; however, few of the existing works, to our knowledge, concentrate on this point. Interoperability can only be ensured if homogeneous technologies are used by different healthcare providers across their legacy systems at the syntactic and semantic levels, and this is very unlikely. Bahga and Madisetti [131] discussed the key role of interoperability in cloud-based EHR systems.

Rodrigues *et al.* [60] studied the risks of hosting EHRs on cloud servers, but they concentrated on the security and privacy issues. Lupse *et al.* [57] and Vida *et al.* [58] described the environment of two Romanian hospital departments with two different clinical subsystems that are capable of exchanging data based on HL7 CDA. Sachdeva and Bhalla [132] improved the interoperability between EHRs by using the openEHR standard. Liu and Park [130] proposed an inter-cloud connection gateway for information sharing between two clouds. Doukas and Maglogiannis [133] proposed a gateway for smooth information sharing between healthcare organizations. Inspired by the interoperability between peripheral devices and operating systems, Abdulnabi *et al.* [134] proposed a solution to the interoperability problem based on the mPHR by providing interfaces (drivers in peripheral devices) between mPHRs and providers' EHR systems.

In the cloud, different healthcare providers' EHRs and patients' mobile mPHRs are registered, where a provider can connect with the mPHR only if it provides interface software that can understand the format of the incoming data from the patient's mPHR and translate it into the format used by the provider's internal EHR. This interface was based on the HL7 CDA. As a result, many patients could interact with many providers, and vice versa.

Regarding service availability, cloud services can be categorized into three models: SaaS, PaaS, and IaaS. Computing is provided as a utility, much like electricity, water, gas, etc., where you pay for what you use. Each mode provides a set of services. Botta *et al.* [67] surveyed the integration possibilities between the IoT and cloud computing; they asserted that

IoT and cloud computing are two complementary technologies, as shown in Table 5.

TABLE 5. Complementary aspects of the IoT and CC [67].

Property	IoT	Cloud computing
Displacement	Pervasive	Centralized
Reachability	Limited	Ubiquitous
Components	Real-world things	Virtual resources
Computational capabilities	Limited	Virtually unlimited
Storage	Limited or none	Virtually unlimited
Role of the internet	Point of convergence	Means for delivering services
Big data	Source	Means to manage

Integration of the cloud and the IoT supports the delivery of other *X*aaSs, such as sensing as a service (*SaaS*), sensing and actuation as a service (*SAaaS*), sensor as a service (*SenaaS*), database as a service (*DBaaS*), or data as a service (*DaaS*), among other services [68]–[70]. SenaaS [164] is a model to encapsulate both physical and virtual sensors into services according to the SOA approach; it focuses on providing sensor management as a service, rather than providing sensor data as a service. In addition, Sensor-Cloud [164] is an infrastructure for managing physical sensors by connecting them to the cloud; it bundles the physical sensors into virtual sensors where users can combine them to achieve advanced results.

MCC can also provide predictive analytics for the patient's collected data. Sareen *et al.* [137] proposed an MH framework based on the WBAN and MCC to diagnose and monitor the Ebola virus; the collected data from sensors were used in a J48 decision tree algorithm to evaluate the level of infection in patients.

Regarding DM and MH applications, very little research is carried out in this field. Although MCC offers many advantages to manage complex diseases, proposed studies did not fully utilize the advantages of MCC. For example, Baskaran *et al.* [185] proposed an MCC-based tool to manage type 1 DM. This study collects data from wearable devices along with EHR medical data, but it did not look at how to integrate all these types of data, or how the CDSS components can benefit from these different collected data. We evaluated available studies under the following metrics.

1. *Service type:* determines the type of service: IaaS, PaaS, or SaaS.
2. *Data format:* determines the supported data format in the cloud: sensor, social media, image, or medical data.
3. *Implemented components in the cloud:* determines the supported modules for the whole EHR ecosystem in the cloud (EHR database, PHR, CDSS, big data analytics, and big data collection).
4. *Diabetes types:* determines the type of diabetes (T1, T2, or G).
5. *Handles interoperability?:* indicates if the cloud environment manages interoperability between implemented components. For example, if the system collects EHR medical data, social media data, and sensor data, then how can it integrate all of these types of data?
6. *Mobile-to-cloud interface:* how the mobile device interfaces with the cloud, e.g., using representational state transfer (REST) or JSON.
7. *Cloud type:* determines if it is private, community, public, hybrid, or virtual.

Table 6 provides a summary of the evaluation process in the available studies. All of the evaluated research supports access to MCC by smart devices like mobile phones. As seen in the table, the research into diabetes MH in a cloud environment remains in the early stages. For example, all of the studies concentrate on the CDSS component, not the whole EHR ecosystem. As a result, no study has focused on the interoperability problem among EHR medical data, mobile collected data from sensors, and social media. The following conclusion was reached by Griebel *et al.* [54]: "*Few successful implementations yet exist and many papers just use the term cloud synonymously for using virtual machines or web-based with no described benefit of the cloud paradigm.*"

5) MH AND THE WBAN

The IoT comprises uniquely identifiable and interoperable things/sensors connected to a network wirelessly and automatically via smart sensors based on standards and interoperable communications protocols [151]. Li *et al.* [140] reviewed the definitions, architecture, technologies, standards, and applications of the IoT. The WBAN is a health-monitoring paradigm that consists of a collection of (inter) communicating devices including (sensors, actuators, communications, and processing facilities) connected via wireless sensor network (WSN) and worn on the body, providing an integrated set of personalized services to the patient [138]. Fig. 9 illustrates the popularity of WBAN research in the MH domain. A sensor is responsible for the data acquisition process by converting physical phenomena to an electrical signal, which is then amplified, conditioned, digitized, and communicated within the WBAN.

FIGURE 9. WBAN research popularity in the MH domain.

Advanced ICT includes smartphone devices; SMS, General Packet Radio Service (GPRS), and WiFi/Asymmetric Digital Subscriber Line (ADSL) data transfer technologies; 3G, 4G, and 5G wireless technologies; lowering of technology costs; miniaturization of low-power electronics

TABLE 6. Some diabetes cloud computing studies.

Study, year	Service type	Data format	Implemented components in the cloud	Diabetes type	Handles interoperability?	Mobile-to-cloud interface	Cloud type	Citations
Baskaran et al. [185], 2015	SaaS	EHR relational data, sensor data file	CDSS, EHR database	T1	No	NA	Public	4
Verma et al. [39], 2017	IaaS	Sensor temporal data file	CDSS	All	No	NA	Public (Amazon EC2)	1
CBIHCS [172], 2014	SaaS	Sensor data file	CDSS	All	No	Web Service Resource Framework	Public (Amazon EC2)	74
MoPSS [187], 2017	SaaS	Physiological relational database	CDSS	All	No	NA	Public (Windows Azure)	2
Pai et al. [188], 2017	SaaS	JSON files	CDSS	All	No	MQTT protocols, TLS	Private (Meghamala[23])	0
DLSMS [189], 2015	NA	Relational database	CDSS	T2	No	NA	NA	3

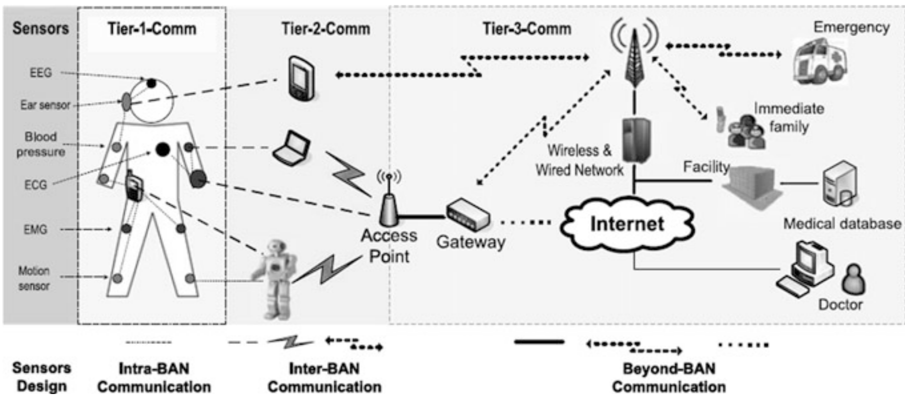


FIGURE 10. Generic mobile patient monitoring architecture [190].

(e.g., sensors); and it increases the emergence of MH technology [28], [138]. This includes the use of location tracking, intelligent devices, and body sensors to collect and transmit fully detailed and accurate vital sign measurements about the human condition, such as body temperature, blood pressure, heart rate, and motion, in order to process them in real time and/or store them in dedicated data repositories. These data are used for continuous patient monitoring, real-time diagnosis of chronic diseases, and to provide continuous elder healthcare [39]. Catarinucci *et al.* [41] surveyed the advances in IoT-based healthcare technologies including architectures, platforms, applications, and trends.

The IoT enables not only human-to-human but also machine-to-machine (M2M) communications from anywhere, at any time, and for anyone [151]. Goudos *et al.* [95] reviewed all of the recent IoT technologies. Universal wireless access and accurate collection of high-quality and voluminous data increase accessibility for healthcare providers and improve communications reliability among medical devices, patients, and healthcare professionals. Many IoT benefits in the healthcare domain were identified by Farahani *et al.* [151].

Hayajneh *et al.* [138] surveyed the state of the art in wireless technologies, protocols, and standards in the WBAN, such as Bluetooth (IEEE 802.15.1), ZigBee (IEEE 802.15.4), IEEE 802.15.6, and WiFi (IEEE 802.11). The authors proposed a general framework for the WBAN, and asserted that the WBAN deserves special consideration.

The sensors' lower-level data are collected in middleware (i.e. a patient information sink), such as a smartphone, laptop, or tablet [104]. Next, these data are sent to the healthcare provider to be integrated with other data sources for further analysis based on the type of connection, as seen in Fig. 10 [190]. Currently, Continua Alliance[23] is an interesting standardization initiative to improve interoperability between these remote patient-monitoring devices [191]. Integrating WBANs with local and global MCC has numerous advantages, and provides effective solutions to the challenges of large amounts of processed data, mobility of monitored users, and the network coverage area. They are almost 20 times faster, and 10 times more energy efficient [145]. On the other hand, several unresolved issues may hinder a successful marriage between these technologies [146]; some of these issues are related to the communications standards in WBANs, the integration between WBANs and hybrid clouds, and the authorization of social networks. Almashaqbeh *et al.* [145] proposed a cloud-based distributed real-time remote health monitoring system for tracking the

[23] *http://www.continuaalliance.org*

health status of non-hospitalized patients using a WBAN and private and public clouds.

The WBAN and wearable devices connected with smartphones and EHR systems improves the usability and accuracy of MH apps and supports the development of highly sophisticated solutions to critical medical problems.

However, every IoT domain and vendor produces its own IoT platform; and new platforms, which must cooperate with existing ones, are continuously added to the domain [35]. Seamless integration and effective harnessing of these components in a smart environment raises many research issues [141]. There are many underlying communications protocols, data formats, and technologies for sensor data (e.g., accelerometers, gyroscopes, altimeters) [67]. Due to a lack of worldwide acceptable standards, interoperability techniques remain limited. There is a clear necessity for standard protocols, architectures, and application programming interfaces (APIs) to facilitate the connections among heterogeneous smart objects. In addition, wearable sensor detection accuracy needs further improvement [29]. Pawar *et al.* [61] proposed a wireless communications generic architecture for mobile patient monitoring systems based on a set of body area networks (BANs) and a backend system.

IoT interoperability has been studied by researchers on many levels, such as devices,[24] middleware,[25,26] and services.[27] However, the semantic and linked data layers have received less consideration [67]. The data layer of the IoT protocol stack uses the compressed extensible markup language (XML) format, the Efficient XML Interchange (EXI) protocol, and World Wide Web Consortium (W3C) standards. EXI encodes XML documents in a binary data format, which makes them general, minimal, efficient, flexible, and interoperable [95].

However, in medical applications, XML portability and interoperability are not sufficient. Semantic interoperability between these devices and between these technologies and the medical standards is gaining momentum worldwide.

Qi *et al.* [141] cited the challenges that face the implementation of personalized healthcare systems based on IoT technology, including (1) the shortage of cost-effective and accurate smart medical sensors, (2) unstandardized IoT system architectures, (3) heterogeneity of connected wearable devices, (4) multi-dimensionality of data generated, and (5) interoperability. The authors divided IoT research into three related layers (sensors, data processing, and applications), each with specific challenges. As stated by Farahani *et al.* [151], IoT interoperability occurs at different abstraction layers, such as the following.

1. *Network layer:* IoT networks are scattered among various low-power networking protocols, such as Bluetooth Low Energy (BLE) and ZigBee, and conventional networking protocols, such as WiFi.
2. *Messaging layer:* a variety of application-level protocols exist, including message queuing telemetry transport (MQTT), constrained application protocol (CoAP), and extensible messaging and presence protocol (XMPP). Each of them has a unique protocol for processing messages.
3. *Data annotation layer:* different standards exist for integration, exchange, and retrieval of EHRs, such as HL7 and OpenEHR.

Mezghani *et al.* [139] asserted that the diversity, variety, distribution, and volume of wearable-device data make medical data processing and analytics more difficult; they extended the basic NIST cloud and big data reference architectures with knowledge as a service (*KaaS*) mechanisms based on an ontology to give meaning to heterogeneous data. They proposed the Wearable Healthcare Ontology (*WH_Ontology*), which facilitates heterogeneous data aggregation from wearables in order to make better decisions. However, the lack of standards in the IoT decreases the comprehensiveness of IoT products. Li *et al.* [140] reviewed the IoT standards and standardization organizations and asserted that it is the role of a service-oriented architecture to achieve interoperability among the heterogeneous devices on four layers. Data are represented in a semantic web environment in layers that include XML, the Resource Description Framework (RDF), ontologies (e.g., OWL), and logic. There are many research papers on semantic technologies and the IoT, which is called the semantic web of things (SWoT) [95]. Ruta *et al.* [96] proposed a general framework for the SWoT.

The collected data from sensors must have the same semantics and be understood correctly by every participating system, such as the CDSS and the EHR [35]. In January 2016, the European Commission funded seven projects to deal with various aspects of interoperability in the IoT. Interoperability can be handled at each layer of the software stack; however, semantic interoperability at the highest level using shared and standard ontologies can solve the problem. Maia *et al.* [43] presented EcoHealth, a web middleware platform to connect physicians and patients using a WBAN. EcoHealth integrates data from heterogeneous sensors; those data are utilized for monitoring patients' conditions. The IEEE 11073 personal health device working group (PHD WG) provides standardization for transmitting the measured data from different devices to monitoring systems [73].

An ontology allows the exchange of information such that meaning is automatically interpreted by the receiver in the way intended by the sender. In addition, it supports the interrelation of heterogeneous data to be used and analyzed in unified ways. Goudos *et al.* [95] asserted that the semantic web is a key enabler for IoT technologies. Jabbar *et al.* [144] proposed the IoT-based semantic interoperability model (IoT-SIM); they semantically annotated a patient's data using RDF semantics with Simple Protocol and RDF Query Language (SPARQL) to retrieve patient records. Bendadouche *et al.* [37] studied the integration of IoT data with semantic modeling and linked data. However, semantic

[24] *http://www.onem2m.org/*
[25] *https://www.fiware.org/*
[26] *http://www.gambas-ict.eu/*
[27] *http://ict-iotest.eu/iot-est/*

TABLE 7. Some diabetes WBAN studies.

Study, year	Sensors	Gateway	Research question	Diabetes type	Wireless protocol	Networking technology	Category	Connection with EHR?	Connected to cloud?	Semantic interoperability?	Citations
CGMS [193], 2017	Body-connected sensors for blood glucose, body temp., and environment temp.	Android	Continuous glucose monitoring	All	nRF	WiFi, GPRS, 3G	Single patient	No	Yes	No	3
MoPSS [187], 2017	Smart-shirt connected sensors for temp., ECG, blood glucose, pressure, heart rate, and oximetry	Android	Continuous monitoring and CDSS	All	Bluetooth	WiFi	Multi-patient	No	Yes	No	2
Movital [194], 2011	Body-connected sensors for blood glucose	NA	Diabetes therapy management	All	6LoWPAN	NA	Single patient	Remote DB	No	No	200
Huzooree et al. [195], 2017	Body-connected sensors for blood glucose, temp., and blood pressure	Android	Diagnosis and continuous monitoring	All	Bluetooth, ZigBee	IEEE 802.11/ WiFi/ GPRS	Single patient	Remote DB	No	No	1
Mezghani et al. [139], 2015	Body-connected sensors for blood glucose, blood pressure, heart rate	NA	Continuous monitoring and CDSS	All	NA	NA	Multi-patient	Yes	Yes	Yes	20
Chen et al. [196], 2016	Smart-clothing sensors for pulse rate, temp., ECG, myocardio, blood oxygen, EEG	Smart-phone	Continuous monitoring	All	BLE, low-power WiFi	4G, WiFi	Single patient	No	Yes	No	74
Al-Taee et al. [197], 2015	Body-connected sensors for blood glucose, blood pressure, pulse rate, and weigh scale	Android	Self-management and CDSS	T1	Bluetooth	3G/LT, WiFi	Single patient	Remote DB	No	No	15

interoperability can be handled by an ontology based on formal description logic, such as $\mathcal{SROIQ}$ ($\mathcal{D}$), $\mathcal{ALC}$, $\mathcal{SHOIN}$ ($\mathcal{D}$), etc.; or written in formal language like OWL 2 and RDF; and automatically inferred by reasoners, such as Pellet, Racer Pro, Hermit, Fact++, etc.

Many of the existing ontologies for the IoT domain were developed for specific research projects, so they are prototypes and often incomplete. The W3C Semantic Sensor Network (SSN) ontology was developed as a joint project of several organizations. It is considered the standard ontology for semantic sensor networks and is based on the Descriptive Ontology for Linguistic and Cognitive Engineering (DOLCE) UltraLite (DUL) ontology. The OpenIoT ontology is a recent one based on the W3C SSN.[28] However, these ontologies are generic, which require extensions. The Wireless Semantic Sensor Network (WSSN) ontology [37], the Sensor Cloud Ontology (SCO) [38], IoT-lite and the oneM2M base ontology are some important extensions. Any WBAN application that requires handling of interoperability must first start with the W3C SSN ontology; then, it should be extended by adding sensor-level semantics (concepts, properties, etc.), or extended to represent concepts that formalize information concerning application areas of interest. For example, for medical domains, the SSN ontology can be extended with medical ontologies[29] such as SNOMED CT, LOINC, ICD, and DMTO [36]. Regarding DM, Table 7 presents a comparison among a set of WBAN studies in the DM domain. The comparison is done according to the following metrics.

1. *Used sensor types:* determines the number and types of sensors that measure biological variables.
2. *Gateway:* determines the types of gateway (nodes) that collect data from all sensors.
3. *Research question:* determines the medical purpose of the study (i.e., DM diagnosis, treatment, self-monitoring, or lifestyle, etc.)
4. *Wireless protocol*: determines the wireless communications protocol used, such as Bluetooth, ZigBee, WiFi, or IEEE 802.15.6.
5. *Networking technology*: determines the networking technology between the mobile device and cloud or healthcare servers.
6. *Category*: indicates whether the system demonstrates multi-patient or single-patient monitoring.
7. *Connection with EHR?:* indicates if the WBAN data are integrated with a healthcare backend system (i.e., an EHR system).
8. *Connected to the cloud?:* indicates if the study utilizes the cloud to collect sensed data for further integration and analysis.
9. *Semantic interoperability?:* indicates if the research handles semantic interoperability between real-time sensed data and other historical medical data.

Table 7 illustrates that wirelessly collected data are treated separately from the patient's EHR data. It is clear from Table 7 that semantic interoperability between sensed data and EHR medical data has not been studied, which is an important measure. Hence, this is not acceptable on the medical side, and causes the resulting apps to produce shallow, and possibly wrong, assistance because they depend on real values from not fully accurate devices, and they ignore the complete patient history. These challenges should be handled in future research to reach the ultimate goals from WBANs.

VI. CHALLENGES AND FUTURE DIRECTIONS

In this section, we present the current challenges and the possible future research directions for developing MH systems. Proper handling of these challenges can improve the output of MH applications, improve their capabilities and intelligence, and enhance patient trust level and acceptance. Syaifuddin and Anbananthen [165] asserted that the majority of DM apps are standalone and mainly focus on glucose levels. Chomutare *et al.* [163] suggested that DM mobile apps should support insulin and medication management, diet, physical activity, complications, weight, blood pressure,

[28] *https://www.w3.org/2005/Incubator/ssn/ssnx/ssn*
[29] *http://bioportal.bioontology.org/*

education, social media, alerts, communications, and patient monitoring. This section is divided into different categories of interrelated challenges regarding EHRs, CDSSs, CC, big data, and WBANs. We believe issues related to security and privacy, sensor and (wireless) network physical characteristics, and protocols are outside the scope of this paper.

A. MH AND EHR CHALLENGES AND FUTURE DIRECTIONS

Chronic diseases like diabetes cannot be managed without the patient's complete medical profile and history. All required data are in the EHR repositories. As MH supports patient-centric medicine, the EHR plays a critical role in this new paradigm. Following are some inferred challenges and future directions from the survey.

1. The EHR ecosystem has many different interconnected and distributed components, including EHR data sources, CDSSs, laboratory information systems, radiology information systems, pharmacy information systems, etc. These systems must work as a single unit. Using standards can handle this issue, but there is no unified standard [25]. Each component may have unique standards and terminology, with different characteristics and formats [202]. Syntax interoperability among different standards (e.g., OpenEHR, CEN/ISO EN13606, ISO/IEEE 11073, HL7, CCD, ASTM, etc.) is a big challenge. In addition, semantic interoperability among different medical terminologies and encoding systems (e.g., SCT, LOINC, UMLS, ICDx, ATC, ICF, and CPT 4) is a big challenge as well 201]. Centralized middleware [175] and distributed middleware [176] can be used as gateways among heterogeneous systems, but these solutions have limitations.
2. The ability to predict the long-term future of the patient based on some machine-learning and data-mining algorithms is a challenge. For example, the Australian type 2 diabetes risk assessment tool (AUSDRISK)[30] assesses the risk of developing type 2 DM over the subsequent five years. In addition, the QDiabetes risk model by Hippisley-Cox *et al.* [17] estimates the 10-year risk of contracting type 2 DM.
3. MH adds another level of complexity by adding unstructured big data from WBAN sensors and social media data. The new challenge for semantic interoperability is among distributed CDSSs, EHRs, IoT sensors, and social media 202], [205]. This objective would provide great advantages for the outcome of each component in an EHR ecosystem. Hence, there is a great need for standards, ontologies, and medical terminologies [201].
4. A PHR can be built for each patient in order to store collected data. These systems can be stored on a smart device or in the cloud to collect the patient's real-time sensed or manually entered data. A phone-based PHR can provide basic functionality when there is no internet connection. The content of the PHR can be mapped directly to known EHR data items, such as vital signs, or can be unknown by the EHR. Synchronization, sharing, integration, and interoperability between this small database and the hospital global EHR, or between the PHR and CDSSs are challenges 71], [205].
5. Standards are required to unify the representation of patient-generated data in a PHR in order to be compatible with the EHR format of the healthcare provider; the provider must be able to distinguish the clinically generated data in the EHR from the PHR data; and the provider must be able to control the flow of PHR data into the EHR.
6. If PHR data need to be shared with multiple providers with heterogeneous standards, mapping between all of these standards will be required. In addition, if PHR data are not standardized, then a standardized mechanism is required to access and retrieve PHR data.
7. Semantic technologies, including (fuzzy) OWL ontologies, (fuzzy) SWRL rules, and medical terminologies, must unify the meaning of data with different formats, different sources, and different targets [203], [204].

[30] *https://www.diabetessa.com.au/type-2/the-australian-type-2-diabetes-risk-assessment-tool.html*

B. MH AND CDSS CHALLENGES AND FUTURE DIRECTIONS

The new distributed, mobile, heterogeneous, and data-intensive healthcare environment creates sophisticated CDSS requirements. CDSSs are overloaded with data and information. They must arrive at real-time decisions based on EHR historical data, PHR real-time data, WBAN-sensed data, and social media data. In addition, their decisions must be based on CPGs, big data analytics, data mining, and domain experts' up-to-date knowledge. Following are some of the challenges that need to be addressed to build semantically intelligent, distributed, EHR-pluggable, and accurate CDSSs. Moreover, these challenges provide clear directions for improvements in MH apps.

1. To support evidence-based medicine, a CDSS knowledge base depends on up-to-date information extracted from standard CPGs, machine learning results, and physicians' opinions.
2. Evidence-based medicine is a new trend for disease diagnosis and management. To support this trend, the CDSS knowledge base's logic has to be based on CPGs represented in a computer-interpretable format. Many standards are available to build sharable and standard information, such as HL7 Arden Syntax, GLIF, PROforma, PRODIGY, Asbru, HL7 GELLO, and GUIDE.
3. The CDSS inference process must depend on a clearly defined methodology, such as rule-based reasoning, case-based reasoning, (fuzzy) ontology semantics, etc. [202]–[204]. Some of these techniques can be combined to produce powerful models.

Semantically intelligent CDSSs can use ontologies to infer hidden information with semantic relations by using description logic axioms, such as drug–drug interactions and comorbidity [36], [201], [202].

4. CDSS must be a pluggable component in the global distributed EHR ecosystem. As a result, its knowledge base must comprise compatible EHR data, big sensed and social media data, and mined or inferred information. The CDSS and/or EHR must have a standardized interface that unifies the communications between different systems. A semantic ontology can support this issue; in addition, it supports the creation of a semantically intelligent CDSS.
5. The SOA-based architecture with pluggable service interfaces and sharable data and information can improve interoperability between heterogeneous system components.
6. CDSSs will provide decisions according to the patient's entered data in addition to automatically sensed data from a WBAN. The user interface needs to be improved, especially for the elderly and disabled. Automatic data entry from sensors enhances the app-patient interaction. A very important direction to improve a user interface is by utilizing human–computer interaction (HCI) and brain–computer interface (BCI) technologies to support the creation of a dynamic user interface and the automatic collection of other hard-to-express data, such as a patient's mood, feelings, symptoms, etc.
7. A CDSS needs to integrate multiple types of information in a standardized manner. Knowledge formulated and extracted from social media, CPGs, domain experts, new research, big data predictive analytics, and EHR mining must be collected in a distributed knowledge base and consulted in every decision-making process. Standard knowledge representation and inference mechanisms are critical to achieving these goals.
8. New methods of service delivery need to be investigated. Systems based on text messages (e.g., SMS) showed fewer benefits [174].
9. A CDSS needs to provide individualized services or decisions. It must tailor a custom decision for the individual patient according to the complete medical profile collected from heterogeneous sources, such as distributed EHRs, WBANs, social media, real-time patient-entered data, and inferred information from an EHR database.
10. The diabetes domain is characterized by uncertainty, vagueness, and timeliness. These issues have to be resolved in future systems. Statistical techniques, fuzzy systems, and temporal data mining, can play a vital role in new solutions to these issues.
11. A CDSS needs to provide tailored services based on specific patient characteristics collected from the complete profile distributed over the EHR, a PHR, and social media.
12. A CDSS has to provide assistance at many levels according to time criticality and the complexity of decisions, such as in the patient's smart device for time-sensitive decisions, in the cloud for data-intensive and analytics-oriented decisions, and in the EHR backend system for long-term decisions that require professional intervention.
13. A CDSS has to provide intelligent methods for integrating data and information about single-disease treatments to handle comorbidities and multi-morbidities that normally exist in patients with diabetes [150]
14. A CDSS has to provide comprehensive treatments, including alerts, recommendations, SMS messages, and plans regarding the patient's medicines, drug interactions, lifestyle (diet and exercise), and education.
15. Connectivity with healthcare systems like EHR systems is necessary [48], [49], [56]; this allows the storage and use of the full patient history from the EHR profile. This can save time and enhance the accuracy of application recommendations. However, current EHR environments are heterogeneous because of different standards, terminologies, providers, etc. As a result, to support integration between mobile apps and distributed EHR environments, the interoperability problem has to be resolved.
16. Different types of diabetes, including T1, T2, and G, are different in diagnosis and treatment. As a result, different CDSSs have to be created for the different types. We can see from the comparison tables that the majority of the studies did not differentiate between these different types.
17. CDSSs must be based on the patient's complete profile to provide personalized and more advanced decisions. Some studies [166]–[172] had high performance, but they were based on a very small set of features. Such types of systems are not acceptable for physicians.

C. MH AND BIG DATA CHALLENGES AND FUTURE DIRECTIONS

Big data related to medicine comes in diverse formats and in huge volumes, and high velocity makes it a big challenge to store, process, transmit, share, integrate, secure, interoperate, encode, standardize, and analyze it all. Both physicians and CDSSs must make accurate decisions at the right time for the right patient based on these heterogeneous (historical and real-time) data. Big data challenges in medicine are similar to other domains. This section summarizes some of these challenges and suggests some future directions.

1. Capturing, cleansing, processing, storing, and real-time analysis of big data related to medicine is a challenge. Therefore, CC provides an efficient environment to handle such challenges. However, network bandwidth is a major bottleneck.
2. Challenges in big data analytics are caused by data complexity (i.e., complex types, structures, patterns, and uncertainties) and computational complexity

(i.e., traditional techniques are not suitable). The data are usually multi-source, huge in volume, redundant, uncertain, incomplete, noisy, and dynamic. As a result, new techniques should be presented to support real-time, semantic, and temporal analysis.

3. Big data analytics delivers five values to healthcare: right living, right care, right provider, right value, and right innovation [164]. Sophisticated, intelligent machine-learning algorithms can provide a CDSS with actionable information and can improve its capabilities. They can convert a CDSS from a reactive role to a proactive and predictive system that can predict the near- and long-term future of patients with diabetes. These systems can reduce losses, prevent complications, and improve quality of life. However, processing and analyzing sensor-collected and EHR data for the whole community over a long period is a challenge, even by using a patch-processing paradigm like the Hadoop ecosystem with all its modules. They include the Hadoop Distributed File System (HDFS), MapReduce, NoSQL databases (e.g., Apache Hbase), processing (e.g., Pig, Chukwa, Oozie), analysis (e.g., Apache Storm, Apache Spark, Apache Drill, SpagoBI, D3, and massive online analysis [MOA]), and integration (e.g., Apache's Sqoop and Flume) [121].
4. IoT, medical, and social data have different characteristics. To uniformly deal with such heterogeneous data types, inclusion of a new semantic layer can play an important role.
5. Semantic interoperability must be treated at different levels, including among different networking layers; among different devices (such as sensors, mobile devices, and servers); and among different data formats, such as structured relational databases, semi-structured data (such as CSV, JSON, and XML), and unstructured data such as social media.
6. A large portion of medical data is unstructured in nature. Semantic enrichment of unstructured data using standard ontologies can improve data representation, integration, interoperability, meaning, and the quality of the applied data mining algorithms [124].
7. The collected big data from multiple resources (e.g., relational databases, NoSQL databases, RDF files, CSV files, images, text files, binary files, XML documents) has valuable hidden information. Besides big data analytics, advanced semantics like big, real-time, spatial and temporal data mining techniques need to be applied to these data to extract information. The results continuously refresh the CDSS knowledge base to keep it up to date. In addition, the data's size, biases, and complexity require more scalable and more efficient algorithms using many optimization techniques, such as parallel processing and partitioning.
8. IoT technologies are not yet properly standardized. In an interconnected and distributed EHR system, a malfunctioning sensor may prove fatal to the patient. This issue requires reducing the complexity of connected systems and standardizing applications.
9. The majority of EHR systems utilize structured data in the form of traditional relational databases. However, most medical data are mainly in an unstructured format. The manipulation of unstructured and semi-structured data as structured data risks losing semantic integrity. In addition, a relational database is considered a one-size-fits-all solution for data persistence and retrieval. In the big data era, this paradigm becomes insufficient. NoSQL and NewSQL database formats and their combined computing models, such as Hadoop and MapReduce, can improve EHR system scalability and integration with other sources, such as social media and sensors. However, the open source NoSQL databases with the BASE transaction management model and open-source Hadoop are not preferred in data-sensitive environments. Relational database management systems and NoSQL DB systems must work together in the same environment. There are many issues in such integration (like data integrity, heterogeneity, and interoperability) that require further analysis and research.
10. Regarding social media, all types of data need to be handled, including text, video, audio, and images. Intelligent analysis of such a huge amount of data can uncover valuable knowledge about the patient's future.

D. MH AND MOBILE CLOUD COMPUTING CHALLENGES AND FUTURE DIRECTIONS

Incorporating MCC technology in mobile health computing has many advantages, such as allowing real-time, remote sharing, and access to data from anywhere at any time. Moreover, the MCC provides processing, storage, and analysis of dynamic and large-volume data at reduced costs and with minimum risk. MCC also improves diabetes self-management, and facilitates communications between healthcare providers and patients. However, there is a lack of research into the adoption of MCC for the treatment of diabetes [185]. Following are some related challenges for MCC in the MH environment, which provide directions for future improvements.

1. Creating a cloud-based health informatics platform (i.e., an EHR ecosystem) is a big challenge, especially for comprehensive diabetes management, because diabetes is a complex disease and has many comorbidities and complications. Such an EHR system will have many advanced interrelated medical and nonmedical components. Therefore, issues related to portability, interoperability, and reliability need deeper investigation.
2. Integration of sensors with the human body produces massive amounts of data, which cannot be stored and processed by standalone conventional healthcare systems due to limited storage and processing abilities. However, integration of such big data with MCC

for processing, storage, preprocessing, summarizing, combination, and inference require more efficient techniques to filter and decrease the size of all of such sensed data before utilizing them in real intelligent systems.
3. MH systems can be used inside a small clinic, scaled up to a complete hospital, scaled up to a smart city, or scaled up to a whole country with different hospitals for different specialties. Therefore, scalability issues related to the cloud environment need to be handled.
4. Although not covered in detail in this survey, addressing the following issues is critical. First, security and privacy in MH spans the whole lifecycle of system development, from sensors, to (wireless) networks, to smart devices, to the cloud environment, to the healthcare organization's backend systems. Secondly, the legal, social, and regulatory governance issues regarding the physical location of patient data must be discussed. For example, in South Korea, medical data cannot be stored outside hospitals [186].
5. Designing a cloud-based system, or migration from a non-cloud to a cloud-based system, requires an accurate designing and planning methodology to determine the required functionality, the ins and outs of medical data, the suitable cloud services, and the integration of legacy EHRs with new big data infrastructures, among other issues.

E. MH AND WBAN CHALLENGES AND FUTURE DIRECTIONS

The challenges for WBANs in diabetes treatment are similar to those in other domains. Patients with diabetes often need monitoring of several features that form a network of wireless sensors. Following are some challenges in this area.

1. New generations of mobile applications need to support the automatic and wireless transfer of sensed data to the cloud without any intervention from the patient and with complete and accurate meaning [149].
2. Interoperability between sensors, medical devices, and display equipment will be required for the deployment of comprehensive MH solutions. Standards play critical roles in the exchange, integration, sharing, and retrieval of medical data.
3. Different network technologies offer different QoS classifications. Therefore, effective mapping between different networks should be considered.
4. The accuracy of biological sensors is still not satisfactory. Therefore, many research challenges related to bio-physiological signal-processing accuracy are still open issues.
5. Future trends toward using sensors in MH scenarios should be based on energy scavenging systems with ultra-low power consumption.
6. The MH environment is characterized by high mobility. The design of a suitable WSN architecture to be used for a particular mobile patient-monitoring system is a challenge because it must consider mobility of the patient, the data rate, network coverage, power requirements, and whether patients will carry their own information sinks. A *homogeneous WSN* has the advantage of reducing energy consumption, but has limitations with a high density of users connected to one sink. On the other hand, the *heterogeneous WSN* architecture provides an advantage in wide-area coverage, but power consumption is a limitation, because bridge devices are required.
7. Development of an open MH architecture that allows patients to easily integrate heterogeneous service providers with different hardware and software components, as well as heterogeneous sources of data with different formats and standards, is a challenge and needs to be addressed.
8. The M2M communications standards between invasive/non-invasive devices have not reached a stable state yet, and each standard is suitable for specific applications. For example, IEEE 802.15.6 is a standard designed specifically for the WBAN; however, it appears to provide lower performance in some cases, compared with other technologies [192]. Existing standards, such as those for Bluetooth, IEEE 802.15.6, ZigBee, WiFi, radio frequency ID, and ANT, each offer a different QoS regarding reliability, latency, security, and power consumption, but not one of them provides the optimum QoS. In addition, there are many data routing challenges in WBANs [190].
9. Physical layer protocols must be implemented to minimize power consumption without compromising reliability. These protocols must be convenient for interference-agile places.
10. The QoS requirements must be achieved without performance degradation and with complexity improvement. The memory limitations require efficient retransmission, and error detection techniques.
11. The IEEE 802.15.6 protocol did not build up the whole media access control (MAC) protocol, only the fundamental requirements to ensure interoperability among IEEE 802.15.6 devices. Thus, MAC protocols do not provide effective network throughput and lead to performance degradation under varying amounts of network traffic. Hence, WBANs have precise QoS necessities that must be achieved by a MAC proposal.

Finally, for MH technology to reach its objectives, it must be treated as a pluggable component in a comprehensive EHR ecosystem consisting of integrated, dependent, and interacting technologies of distributed EHR data sources, CDSSs, the IoT, cloud computing, (big) data analytics, WBANs, and sensing technologies. This design is anticipated to lead to a dramatic increase in the adaptability, integrity, autonomy, efficiency, interoperability, functionality, reliability, safety, and usability of MH systems in the medical domain.

VII. CONCLUSION

In this paper, we reviewed the current state of the art related to MH technologies in general, and concentrated on the DM domain in particular. The study reviewed MH from various points of view, including relationships between MH and EHRs, semantic interoperability, the CDSS, the WBAN, the IoT, cloud computing, and big data analytics. For each dimension, the study surveyed the current literature and future research topics, especially in the medical domain.

To achieve this objective, we extensively studied 60 papers related to diabetes mellitus. According to the results, MH applications still have plenty of room for improvement in order to take full advantage of unique mobile platform features and to truly fulfill their potential. The study concluded with a set of challenges that could possibly drive future research and define future directions for the scientific and medically important aspects of this domain.

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