The Promise of Mobile Technologies for the Health Care System in the Developing World: A Systematic Review

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***Abstract*—Evolution of mobile technologies and their rapid penetration to people's daily lives, especially in the developing countries, have highlighted mobile health, or m-health, as a promising solution to improve health outcomes. Several studies have been conducted that characterize the impact of m-health solutions in resource-limited settings and assess their potential to improve health care. The aim of the present paper is twofold: i) present an overview of the background and significance of m-health, and ii) summarize and discuss the existing evidence for the effectiveness of m-health in the developing world. A systematic search in the literature was performed in Pubmed, Scopus, as well as reference lists, and a broad sample of 98 relevant articles was identified which were then categorized into five wider m-health categories. Although statistically significant conclusions cannot be drawn since the majority of studies relied on small scale trials and limited assessment of long term effects, this paper provides a systematic and extensive analysis of the advantages, disadvantages, and challenges of m-health in developing countries in an attempt to determine future research directions of m-health interventions.**

***Index Terms*—mobile technologies, mobile health, m-health, developing countries, health care system, developing world, low-resource settings, low- and middle- income countries.**

I. Introduction

The performance of a country's healthcare system is affected both by its economic growth and the invested resources. Limited national financial resources entails inadequate investment on health, resulting in underdeveloped health infrastructure and information systems, shortage on health personnel, limited availability of medical equipment and drug products [1]-[3]. In turn, proper function of the health care system has positive effects on a nation's economy, given that healthy mental and physical conditions enhance productivity, with a resulting reduction in spending on medical services [4]. Financially strained groups have generally poor access to health services and they tend to be more prone to health-risky behaviors due to reduced educational opportunities and insufficient health related knowledge [3], [5]. Such circumstances mainly occur in countries of the developing world, where limited resources have a direct impact on the healthcare systems. Therefore, the introduction of novel approaches to deliver healthcare in these countries is an urgent need, which could significantly contribute toward a vastly improved overall quality of the healthcare system and, consequently, citizens' health.

Mobile health, or m-health, is a term used to indicate the application of mobile technologies to the health sector and it has shown promise for improving the healthcare system in the developing world. The number of people having access to mobile phones is increasing rapidly, especially in the developing world [6], [7] while the dramatic evolution of mobile technologies and wireless communications are expected to render mobile devices increasingly more accessible. The ubiquity of mobile phones along with the increased interest in m-health applications, has led to an effort to employ such devices in order to support healthcare in financially vulnerable populations [8].

Mobile devices have been utilized to provide educational opportunities at a large-scale and promote healthy behaviors, enhance disease surveillance, improve the efficiency of logistic procedures, monitor patients, as well as train and educate unprofessional health workers [9]. Apart from short messaging services and calls, recent enhanced functionalities of mobile devices facilitated the introduction of various supporting software applications (e.g. decision support systems, electronic health records, internet browsing) [10]. Moreover, through the use of novel sensor systems, low cost and miniaturized medical devices providing point of care diagnostics and patient monitoring have become a reality [11].

Although the widespread use and the evolution of mobile and medical technologies are encouraging signs towards facilitating the expansion of m-health sector, there are several other parameters that need to be taken into account in order to draw conclusions on its benefits in the developing world. For example, cultural variations among different populations, socioeconomic barriers in vulnerable groups, organizational and functionality issues of the healthcare system in very low resource settings, as well as the readiness of citizens and health workers to integrate such practices into their daily lives, are some factors that can significantly influence the effectiveness of these methods.

Thus, a controversy has arisen as to whether m-health is indeed the most effective solution to break the link between economic status and the performance of the healthcare system.

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To this end, several studies have been conducted that implement m-health interventions in low-resource settings in order to evaluate their potential to enhance the performance of health services and improve health outcomes.

The aim of the present review paper is twofold: i) to present an overview of m-health as a means to support the healthcare system, and ii) to identify a broad sample of studies incorporating m-health interventions in the developing world and summarize their findings, in order to assess the promise shown by utilizing m-health in developing countries. Section II provides the background and the evolution of m-health, as well as the rationale behind its deployment. Section III presents the literature search strategy and the inclusion criteria, as well as the m-health categories employed in this study, namely i) citizen education and behavior change communication, ii) remote data collection and data management, iii) sensor systems and point of care diagnostics, iv) electronic decision support, v) health worker education, consultation and work planning. In Section IV, the findings of the included studies in each one of the aforementioned categories are summarized and the advantages, disadvantages, challenges and ways forward involving the various m-health practices are evaluated. Finally, the overall role of m-health in the healthcare system of developing countries and related important challenges are discussed.

II. M-HEALTH OVERVIEW

A. Electronic health

Electronic health, or e-health, which refers to the use of information and communication technology (ICT) for health, has shown great promise as a cost-effective practice to enhance the efficiency of the healthcare system and improve health outcomes by using technologies such as computers, internet, satellite communications and mobile devices. E-health strategies initially relied primarily on the widespread use of the Internet in order to organize and support access to health related information. The applications of interest involved health information systems and knowledge management, electronic health records, open access to medical articles and eLearning for health workers [12]. Rapid advances in ICTs, the incremental rate of their adoption and their declining costs (Fig. 1) further supported the role of e-health as a key component in enhancing the healthcare system. As a result, e-health drew significant commercial and research interest, and several projects and initiatives have been established aiming at integrating ICT in the health sector [12], [13].

In order to support the development of e-health strategies and maximize their effectiveness, the World Health Organization (WHO) founded the Global Observatory for e-health (GOe) in 2005, committed to study e-health implementations and provide appropriate information and guidance regarding such initiatives [14]. As its first action towards organizing such knowledge, the GOe conducted a world-wide survey during the period of 2005-2006 to collect initial data on existing e-health activities and draw its first conclusions. Though this survey made clear the importance of a worldwide implementation of e-health solutions, these were at a very early stage in developing countries and there was a significant gap with the developed world. This could be attributed in part to the lack of infrastructure (e.g. fixed line communication technologies, computers) and national policies involving ICTs and information management in resource limited settings [12], [15], [16]. However, a desire to deploy e-health in developing countries was observed and global funding trends encouraged the awarding of grants in support of it.

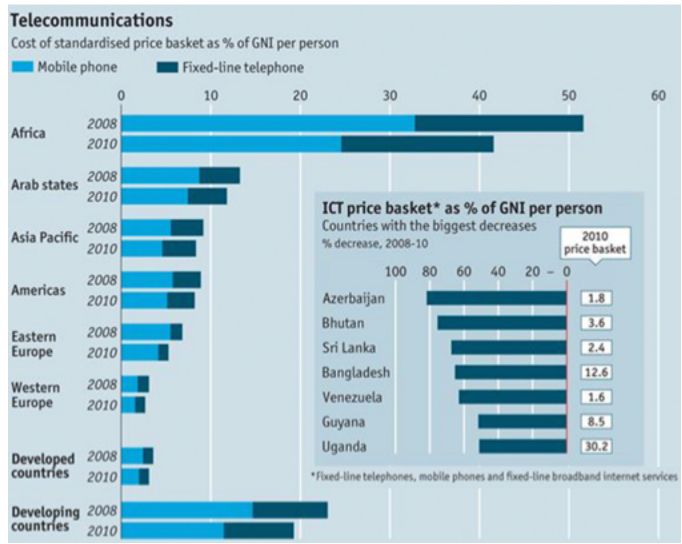

Fig. 1: Decline in costs of mobile and fixed line telephones in the period between 2008 and 2010, (as percentage of Gross National Income - GNI), presented by the International Telecommunication Union [17].

B. Expansion of the m-health sector

The employment of ICTs to improve a country's healthcare system was complemented by the dramatic evolution and penetration of mobile technologies and wireless communications. Wireless systems provided a new opportunity enabling the development and expansion of existing e-health strategies while bypassing fixed line technologies, while holding the potential to reduce technological gaps among countries with different economic status [12]. This opportunity, called mobile health or m-health, is an emerging and quite significant component of e-health, and is defined by the WHO [18] as the practice of medicine and public health through the use of mobile devices such as mobile phones, tablets, PDAs, wireless patient monitoring systems and diagnostic tools.

A key factor supporting the development of m-health strategies as a means to improve the healthcare system and health outcomes is the dramatic penetration of mobile phones into society, especially in the developing world, where the rate of mobile phone subscribers in 2013 was almost 90% [6], [7]. According to the World Bank, in 2015, mobile cellular subscriptions per 100,000 people were 98,329 worldwide and 93,388 in low and middle income countries, representing an increase of 21,815 and 23,344 subscriptions per 100,000 people since 2010, respectively [19]. Among low and middle income countries, subscriptions per 100,000 people increased from 82,048 in 2010 to 102,375 in 2015 in Middle East and North Africa; from 95,506 to 109,845 in Latin America and

Caribbean; from 69,924 to 101,421 in East Asia and Pacific; and from 44,410 to 76,066 in sub-Saharan Africa [19].

The concept of m-health is further supplemented given the declining costs of mobile technologies. During the period between 2013 and 2017, the average selling price of smartphones dropped from USD 305.8 to USD 245.1, corresponding to a decrease of 19.8%, and is expected to further decline to USD 214.7 by 2019 [20]. Middle East and Africa have experienced a rapid decline in smartphone average price, from USD 339 in 2013 to USD 230 in 2017 (decrease of 32.1%). The costs of mobile networks are also continuously declining. According to the International Telecommunication Union (ITU), the drop of mobile broadband prices as a percentage of gross national income (GNI) per capita for the period 2013-2016 was 4% worldwide and almost unchanged (0.3%) for the developed countries, while the corresponding drop in the developing countries was equal to 5.6% (Fig. 2) [21]. In 2016, the cost of mobile communication was lower than fixed broadband in most developing countries [21].

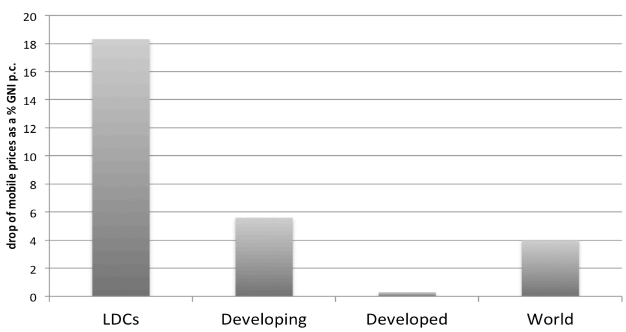

Fig. 2: Drop of prices of mobile broadband as a percentage of GNI per capita worldwide, in developed countries, in developing countries and in least developed countries (LDCs) for the period 2013-2016.

Moreover, mobile networks are becoming increasingly widespread. Since 2012, mobile broadband subscriptions have increased more than 20% worldwide and more than 30% in the developing world (Fig. 3). Currently, the number of mobile broadband subscribers in developed countries is about twice that of developing countries, and the rates of growth indicate positive signs towards bridging this gap [21]. Fixed broadband subscriptions are increasing at a lower rate (Fig. 3) (9% increase worldwide and lower than 15% in developing countries since 2012) and there is a large gap between developed and developing countries (31 fixed broadband subscriptions per 100 inhabitants in developed countries versus 9 in developing countries) [21].

C. *Initiatives of the m-health domain*

M-health evoked wide interest and several organizations started developing m-health projects in order to improve healthcare in the developing world. According to a report published by United Nations Foundation and Vodafone Foundation in 2009, 51 m-health projects aiming at supporting health education and awareness, remote data collection, remote monitoring, communication and training for healthcare workers, disease and epidemic outbreak tracking, diagnostic and treatment support, were operating in 26 developing countries, with the most of activity taking place in India, Rwanda, South Africa, Peru and Uganda [22]. As the utilization of mobile devices for health purposes had shown such promise, the GOe conducted a second global survey in 2009 including a section particularly on m-health in order to gather information and determine strategies to implement and evaluate m-health activities [18].

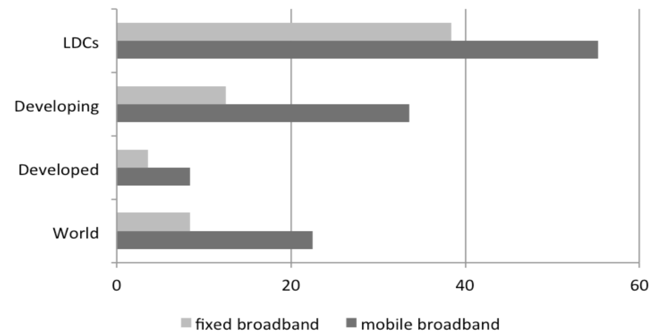

Fig.3: Percentage increase of mobile broadband and fixed line broadband subscriptions from 2012 to 2017 worldwide, in developed countries, in developing countries and in least developed countries (LDCs).

The survey produced encouraging results regarding the expansion of m-health. Of the 112 nations that participated in the survey, 83% reported at least one m-health initiative, while a small gap was observed between high and low income countries (87% and 77% of the high and low income countries, respectively, stated to have at least one m-health initiative). Analysis by the type of m-health initiatives demonstrated variable adoption with respect to the income level of participating countries. For example, health surveys and surveillance were prevalent among low income countries, while the adoption of m-health enabled patient records was very high in the high income but insignificant in other groups. Fig. 4 demonstrates the adoption of m-health initiatives by income level and type of m-health initiative, for the 14 types of m-health determined by the WHO.

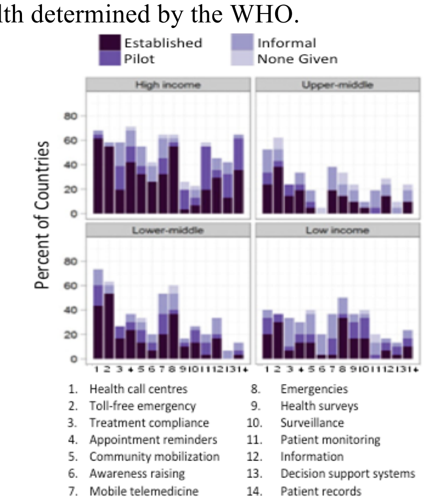

Fig 4: Stage of adoption of m-health initiatives by m-health type and national income based on the GOe's second global survey in 2009 [18].

A disparity was identified involving the strategies of evaluating m-health activities according to a country's economic growth. The proportion of countries that conducted evaluation of m-health programs were 23%, 14%, 7% and 7% in high-, upper- middle-, lower-middle- and low- income countries, respectively and 12% in general [18]. This can be attributed to the fact that stronger economies have more advanced and mature m-health programs that are more capable of incorporating evaluation methods.

In 2015, the GOe conducted the third global survey and found that m-health continued to spread significantly [23]. Among the 125 participants, 87% stated to have at least one m-health program operating in their country, while the gap between high- and low income countries remained low, with 91% and 80% of them reporting at least one m-health program, respectively. WHO investigated the same 14 types of m-health initiative as in the 2009 survey along with a new type (mLearning) and indicated a significant increase in m-health adoption in almost all categories (Fig. 5), apart from awareness raising (not included in the figure) where a decrease of 25% was observed. The most widespread types of m-health delivery were emergency toll-free telephone services and health call centers, with 75% and 72% of the participating countries reporting the existence of such programs, respectively [23]. Such emergency response programs are expected to be widely adopted, given that mobile phones are becoming the leading means of communication, especially in remote areas. Furthermore, there has been a dramatic increase in the adoption of programs aiming at providing information and guidance to healthcare workers, such as decision support systems and access to health related information, which increased by 29% and 39% respectively since 2010. Patient monitoring and surveillance initiatives also received more attention, with a growth in adoption by 29% since 2010.

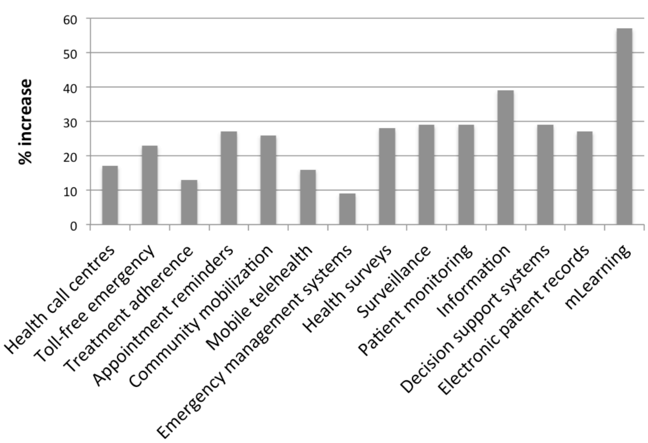

Fig. 5: Increase of percentage of countries reporting m-health programs by m-health type in 2010 and 2015.

Though m-health has become more widespread, the development of strategies to provide evaluation of the quality and safety of such initiatives has proven to be rather difficult both for governments and industry [23]. The rate of participating countries conducting evaluation of m-health programs remained low (14% in 2015 compared to 12% in 2010), and there is still a significant gap between high- and low- income countries. It is therefore desirable to focus on providing feedback on m-health and determine the impact of its various applications, in order to determine specific needs and take proper future actions.

D. Related m-health technologies

The functionality of mobile devices underwent a significant change; in fact, they can be a substitute for the majority of e-health applications requiring fixed line technologies, while being integrated in existing e-health strategies [12]. A basic technology of m-health, SMS messaging, has been widely employed due to its simplicity, low cost and scalability in low resource settings. SMS messages have been utilized in several m-health applications such as appointment and medication reminders, dissemination of massive health related information and health promotion, notification of test results, maternal and infant health applications, disease surveillance, health worker training and consultation, as well as patient data collection and monitoring [22], [24].

TABLE I
TYPICAL IMPLEMENTATIONS OF MEDICAL MONITORING DEVICES

Type of Devices	Examples
Wearable Devices [11], [30]	Smart watches for heart rate monitoring
	Watch-type blood pressure device
	Ring-type device for heart rate and temperature measurement
	Photoplethysmographic (PPG) ring
	Ear-worn PPG sensors
	Glove and hat based PPG sensors
	Electrocardiogram (ECG) necklace
	Eyeglasses-based device for heart rate
	Textile wearable devices
Implantable Devices [32], [33]	Pacemakers
	Retina Stimulators
	Cochlear Implants
	Glucose Monitors
	CardioVascular Pressure Monitors
	Intracranial Pressure Monitors
	Deep-Brain Neurosensors
Injectable Devices [33]	Neurostimulators
	Oxygen Sensing Sensors
	Peripheral Artery Disease monitors
Ingestible Devices [33]	Medication Adherence
	Drug delivery capsule
	Gastric stimulators
	Imaging of the digestive system

Mobile apps constitute a very important advancement in mobile technologies. The m-health app market has undergone dramatic changes. According to a report released by the Quintiles IMS institute for healthcare informatics, 23,682 iOS apps were identified that were genuinely related with health [25]. In 2015, the number of iOS health related apps increased by more than 100%, with 65% of the apps involving wellness management (e.g. fitness, dietary habits, stress) and 24% disease and treatment management (e.g. maternal health, medication reminders, health information, assistance for health workers, disease specific application) [26]. Such apps have started to be deployed in the developing world and have provided several opportunities for the development of their healthcare system, which could not have been supported by using standard mobile device functionalities such as SMS texting or mobile phone calls. An example is the implementation of decision support systems and media enriched interactive guidelines running on mobile phones of front-line community health workers [27]. M-health mobile apps usually support wireless communication with other devices or connection to the Internet, which in combination

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with the evolution and widespread use of mobile networks is quite beneficial for efficient data collection and management [26].

Moreover, m-health has been significantly supplemented by advances in microsystems and microelectronics, which have enabled the fabrication of novel sensor systems with wireless communication capabilities (Fig.6a) [28]. Such technologies permit the development of low cost diagnostic tests (e.g. malaria tests (Fig.6d) [29], electrocardiogram (ECG) recording (Fig.6b) [30], ultrasound scan (Fig.6c) [31]) and medical monitoring devices (e.g. wearable (Fig.6e-Fig.6f), implantable, injectable and ingestible sensors [11], [32], [33]) that also support real time transmission of patient data, presenting great advantages in point-of-care diagnostics and patient management [34]. Typical implementations of medical monitoring devices are presented in Table I. The deployment of the various mobile device functionalities and their effectiveness are analyzed in section IV.

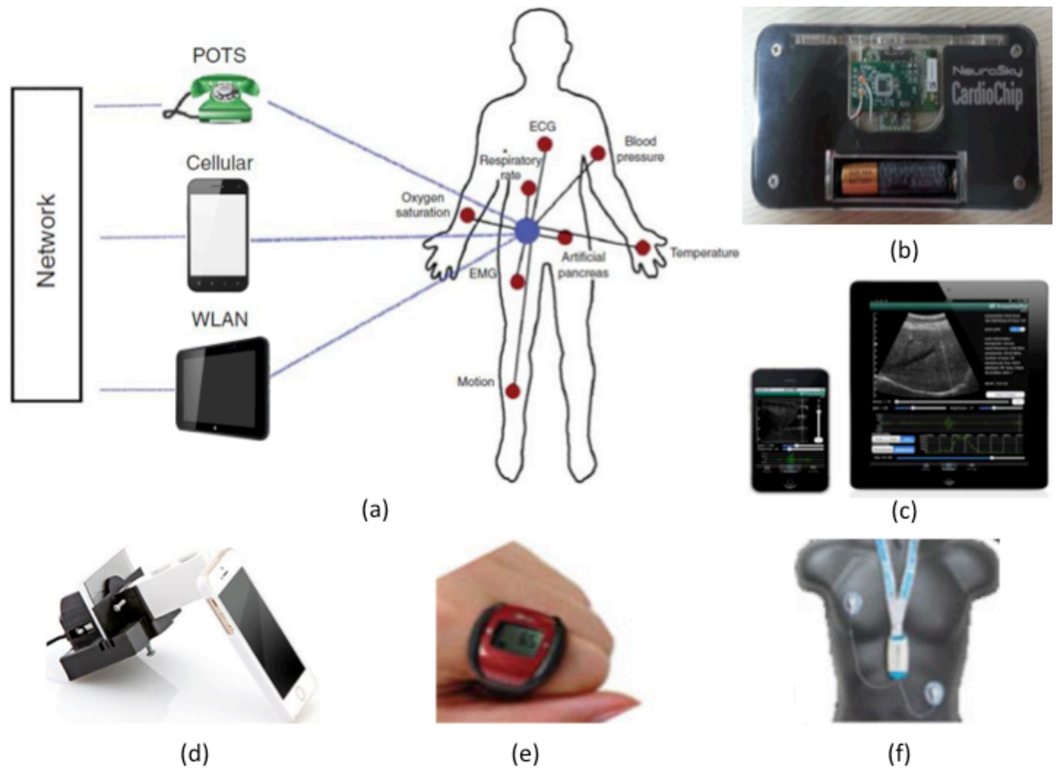

Fig. 6: Examples of novel m-health technologies: (a) Concept of interconnected body sensor networks, where on-body and in-body medical devices perform measurements of physiological signals and transmit them to a remotely located receiving device (blue node) placed onto patient's body. Such a node may retransmit data on data network, either through Plain Old Telephone Services (POTS) or wireless systems, such as cellular phones and devices with wireless local area network (WLAN) capabilities [35]. (b) Mobile device for ECG recording [30]. (c) Tablet and smartphone based ultrasound scan [31]. (d) Mobile microscope for Malaria diagnosis [29], [36]. (e)-(f) examples of wearable devices [11]: (e) ring-type device for pulse rate and (f) wireless ECG necklace.

III. Methods

A. Literature Search and Inclusion Criteria

A systematic literature search was conducted in the beginnings of December 2017 using the online databases Pubmed and Scopus. By combining appropriate keywords with Boolean operators, the following expression was formed: ((mhealth OR m-health OR mobile health OR mobile phone OR mobile device OR cell phone OR mobile intervention) AND (developing world OR developing countries OR low-resource settings OR resource limited settings OR low-income country OR middle-income country)).

Fig. 7 shows the number of articles retrieved per year. Since the present review study focuses primarily on recent advances in m-health technologies, and both databases demonstrated a rapid increase in search results from 2010, the search was limited to include articles published between 2010 and 2017.

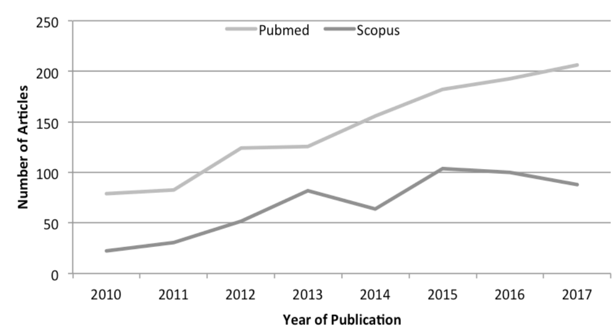

Fig. 7: Articles retrieved from Pubmed and Scopus, with respect to the year of publication from the beginning of 2010 until beginnings of December 2017.

The search produced 1,149 and 543 results in Pubmed and Scopus, respectively. Moreover, 27 articles were identified through reference lists. After removing duplicates using Endnote software, 1,619 articles remained, 1,122 of which were excluded based on title, following the strategy proposed in [7], [37]. A total of 497 abstracts were screened, resulting in 134 full text views, of which 98 were included in this review. The search strategy is illustrated in Fig. 8.

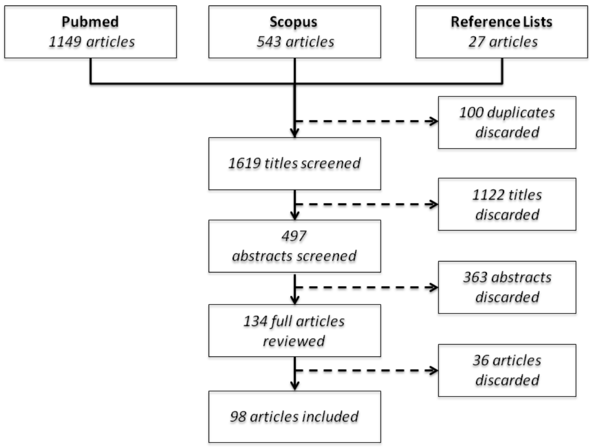

Fig. 8: Search strategy.

In order for an article to be included, it should satisfy the following criteria:
1. It should be written in English language.
2. It should include a trial evaluating an m-Health intervention as defined by World Health Organization [18].
3. The trial should be performed in a developing country as classified by the International Monetary Fund [38].

B. M-health intervention categories

Based on the type and the purpose of intervention, the following categories have been proposed as a framework for studying m-health applications [39]:

1. Citizen Education and Behavior Change Communication
2. Data collection and reporting
3. Sensors and point of care diagnostics
4. Electronic decision support
5. Electronic health records
6. Provider-to-Provider Communication: User Groups, Consultation
7. Provider Training and Education
8. Provider Work Planning and Scheduling
9. Supply chain management
10. Registries and Vital Events Tracking
11. Human Resource Management
12. Financial Transactions and Incentives

In the present paper, after completion of the literature search, the aforementioned classifications were modified in order to generate five wider m-health categories. Due to identified overlaps among m-health applications falling in “Provider Training and Education”, “Provider Work Planning and Scheduling” and “Provider-to-Provider Communication: User Groups, Consultation”, those categories were merged into “Health Worker Education, Consultation and Work Planning”. For similar reasons, “Supply Chain Management”, “Electronic Health Records”, “Registries and Vital Events Tracking” and “Data collection and reporting” formed the category “Remote Data Collection and Management”. Moreover, given that no articles related to “Human Resource Management” and “Financial Transactions and Incentives” were identified, those two categories were eliminated. Thus, the m-health categorization employed in this study is as follows:

A. Citizen Education and Behavior Change Communication
B. Remote Data Collection and Data Management
C. Sensor Systems and Point of Care Diagnostics
D. Electronic Decision Support
E. Health Worker Education, Consultation and Work Planning

All categories are explained at the beginning of their corresponding subsections in Section IV (subsections IV-A to IV-E). It is noted that some studies evaluate m-health deployment that matches more than one of the aforementioned classifications. In such cases, the study is included in the category that fits best in our judgment.

IV. Results

In this section, an analysis based on the reviewed studies is presented for each m-health category. Fig. 9 depicts the number of studies retrieved per m-health category. The category “Citizen Education and Behavior Change Communication” represents the most reported type of m-health applications.
The studies by category and country conducted are summarized in Table II. Due to the robustness of randomized control trial (RCT) as a study design we chose to summarize the methods and primary outcomes of RCTs in Tables III-IX. It is noted that the abbreviations IG and CG denote the participants in the Intervention Group and the Control Group as described by the RCTs, respectively. When an RCT uses more than one intervention groups, an index with the corresponding number is used to differentiate among the interventions (e.g. IG1, IG2,…,IGn). Moreover, in column 4 (“intervention description”), when the action involving the CG is not described, it means that CG participants followed usual care and traditional methods with no further action taken (e.g. absence of the intervention receiving the IG).

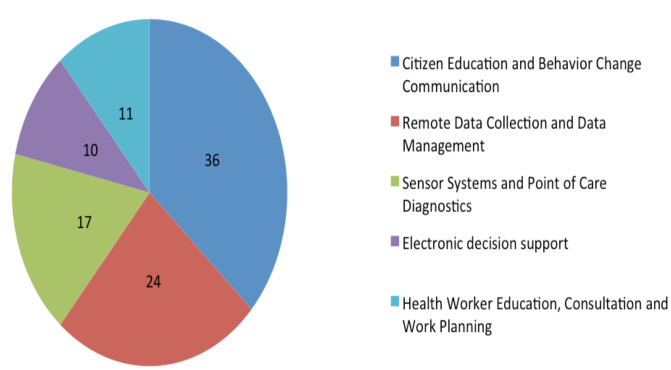

Fig. 9: Distribution of articles based on the m-health categorization.

TABLE II
STUDIES INCLUDED FOR ANALYSIS BY COUNTRY AND CATEGORY

	Citizen education and behavior change communication	Remote data collection and management	Sensor systems and point of care diagnostics	Electronic decision support	Health worker education, consultation and work planning
Kenya	[41] [42] [55] [70] [71]	[82] [84] [89] [95]	[106] [109]		[126] [128]
Lesotho	[45]				
India	[44] [62] [68]	[91] [98]	[115]	[27] [118] [120]	[136]
Cameroon	[46] [51]				
Pakistan	[47] [63]	[92]		[124]	
South Africa	[48] [58] [54] [57] [66]	[91]	[101] [108]	[117]	
Cambodia	[64]				
Democratic Republic of the Kongo	[64]				
Brazil	[40]			[123] [125]	
Mozambique	[49]		[100]		
Uganda	[50] [53] [56]	[86] [99]	[110]		
Swaziland	[52]	[96]			
Guatemala	[59] [69]	[79] [80]	[105]		
Argentina	[59]				
Peru	[59]				[127]
Honduras	[60]				
Mexico	[60]				
Philippines	[61] [64] [72]				
Bolivia	[65]				
Nigeria	[67] [43]				
Ecuador	[73]				
Zanzibar	[74] [75]				
Vietnam		[76]			[129]
Nepal		[90] [77]	[116]		
Ghana		[78]	[104]	[122]	
Malawi		[78]			[135]
Sri Lanka		[81]			
Ethiopia		[83]			
Mali		[85]			
Madagascar		[87]	[113] [114]		
Rwanda		[88]			
Paraguay		[94]			
Zambia		[97]			
Zimbabwe			[101]		
Bangladesh		[93]	[103]		
Egypt			[111] [112]		
Haiti			[107]		
China				[27]	
Colombia				[119]	
Tanzania			[102]	[121]	[133]
Botswana					[130] [131]
Thailand					[134]
Indonesia					[132]

A. *Citizen Education and Behavior Change Communication*

Within this category fall applications that exploit mobile communications to deliver informative or motivational text messages, phone calls, audio or multimedia messages, aiming to disseminate health information to the citizens and promote healthy behaviors such as healthy dietary habits, preventive measures against infections, uptake of proper health services and medication adherence. This was the most reported category, including 36 articles.

1) *Communicable Diseases*

M-health has been investigated as a means to induce appropriate behavior changes among HIV and/or tuberculosis patients. In Brazil [40], Kenya [41], [42], Nigeria [43], India [44] and Lesotho [45] Short Message Service (SMS) medication reminders have proven to be successful in improving adherence of HIV infected people to antiretroviral therapy (ART), as well as suppressing their viral loads. Contradictive results however have been indicated by two studies undertaken in Cameroon [46] and Pakistan [47], where delivery of SMS reminders did not influence adherence outcomes among HIV and Tuberculosis patients, respectively, suggesting that the impact of such interventions might vary with respect to the implementation site, the experience and familiarity of patients with receiving treatment, as well as cultural variations in behavior towards medical practice [46], [47]. The importance of the content and timing of delivering message reminders has also been highlighted for motivating proper uptake of medication [41]. Interactive voice response (IVR) calls have been evaluated as an alternative to enhance treatment adherence and have proven to be quite effective, as well as more acceptable than text messages [44].

TABLE III
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR THE MANAGEMENT OF HIV AND TB (CATEGORY A: CITIZEN EDUCATION AND BEHAVIOR CHANGE COMMUNICATION). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
T. M. Da Costa et al, 2012 [40]. Brazil.	Text messages for improving medication adherence of HIV patients.	**n=21** HIV positive women; IG: n=8; CG: n=13. Duration: 4 months.	IG received an SMS message 30' before the planned time of the last antiretroviral dose on Sundays, Saturdays and alternate working days.	Self-reported medication adherence > 95%: 100% in the IG and 84.62% in the CG. Adherence according to pill counting method: 50% in the IG and 38.46% in the CG. Adherence according to MEMS medication monitors: 75% in the IG and 46.15% in the CG.
C. Pop-Eleches, 2011 [41]. Kenya.	Text messages for improving medication adherence of HIV patients.	**n=428** HIV patients; IG1: n=70; IG2: n=72; IG3: n=73; IG4: 74; CG: n=139. Duration: 48 weeks.	IG1 and IG2 received daily short and long text reminders, respectively; IG3 and IG4 received weekly short and long text reminders, respectively.	Rate of patients with medication adherence >= 90% according to MEMS medication monitors: 40%, 42%, 53%, 53% and 40% in IG1, IG2, IG3, IG4 and CG, respectively.
RT Lester et al, 2010 [42]. Kenya.	Text messages for improving HIV management and medication adherence of HIV patients.	**n=538** HIV patients; IG: n=273; CG: n=265. Duration: 12 months.	IG received weekly SMS providing HIV related information and asking them to report on their health status within 48 h;	Rate of patients with self-reported medication adherence >95% : 62% in the IG and 50% in the CG. Patients with undetectable viral load: 57% in the IG and 48% in the CG.
O. Maduka et al, 2013 [43]. Nigeria.	Text messages combined with counseling sessions for improving medication adherence of HIV patients.	**n=104** HIV patients; IG: n=52; CG: n=52. Duration: 4 months.	IG received SMS medication reminders twice a week and attended monthly counseling sessions with resident doctors.	Rate of patients with self-reported medication adherence > 95%: 76.9% in the IG and 55.8% in the CG. Changes in median CD4+ cell count: Increase of 382 cells/ml in the IG and 230.5 cells/ml in the CG.
L. Mbuagbaw, 2012 [46]. Cameroon.	Text messages for improving medication adherence of HIV patients.	**n=200** HIV patients; IG: n=101; CG: n=99; Duration: 6 months.	IG received weekly SMS medication reminders that also included a phone number for the patients to call and seek for advice.	Rate of patients with no missed doses according to self-reporting: 81.2% in the IG and 83.8% in the CG at 3 months; 79.2% in the IG and 79% in the CG at 6 months. Rate of patients with medication adherence >95% according to Visual Analogue Scale: 51.5% in the IG and 66.7% in the CG at 3 months; 71.3% in the IG and 66.7% in the CG at 6 months. Mean number of pharmacy refills: 2.3 in the IG and 2.2 in the CG at 3 months; 3.8 in the IG and 3.7 in the CG at 6 months. (see [46] for more information on adherence measurement methods)
S. Mohammed et al, 2016 [47]. Pakistan.	Text messages for improving medication adherence of TB patients.	**n=2,207** TB patients; IG: n =1,110; CG: n=1,097. Duration: Period between Mar 18, 2011 and Feb 25, 2014.	IG received daily SMS medication reminders, requiring their response after receiving their doses.	Rate of patients who were successfully treated: 83% in the IG and 83% in the CG.
JJR Bigna et al, 2014 [51]. Cameroon.	Phone calls and text messages for improving appointment adherence of children exposed to or infected with HIV .	**n=242** carers of children exposed to or infected with HIV; IG1: n=61; IG2 n=60; IG3: n=60; CG: n=61. Duration: Period between Jan. 28-May 24, 2013.	IG1 received a text message and a phone call 3 and 2 days before the appointment; IG2 received a phone call and IG3 a text message 2 days before an appointment.	Appointment attendance rates: 89%, 85%, 75% and 51% in the IG1, IG2, IG3 and CG, respectively. Difference in efficiency between intervention methods (considering communication costs - staff working time): 1.2, 1.5 and 0.4 for the IG2 against IG1, IG3 against IG1 and IG2 against IG3, respectively.
K. de Tolly et al, 2012 [54]. South Africa.	Text messages for promoting HIV Counseling - Testing (HCT) services.	**n=2,533** citizens; IG1: n=438; IG2: n=438; IG3: n=438; IG4: n=438; CG: n=801. Duration: 3 weeks (IG1-IG3); 1 month (IG2, IG4).	IG1 received 3 and IG2 10 motivational SMSs; IG3 received 3 and IG4 received 10 informational SMSs.	Rates of individuals who received HIV testing: 49%, 69%, 55%, 58% and 57% in the IG1, IG2, IG3, IG4 and CG, respectively.

Simpill solution, a system that uses a device with wireless communication capabilities attached to a pill package to monitor pill uptake and send SMS alerts when a patient delays in taking his/her doses, has been implemented and shown promise in improving treatment compliance of Tuberculosis patients [48]. Evaluation of this system in South Africa indicated improved health state as a consequence of Simpill, while an analysis on the return of investment for employing this system demonstrated reduced overall costs to the healthcare system. Positive stance towards medication reminders further support the role of m-health in improving patients' adherence to treatment [40], [44], [45] and the inexpensiveness of SMSs enhances the feasibility of implementing and sustaining such interventions [42]. Private-public partnerships can further improve the cost efficiency of employing text messaging for health purposes [42]. Concerns involving such interventions have been reported due to differences in availability of mobile phones, as well as confidentiality issues, given that in some settings more than one person shares the same cell phone [41], [42], [46].

Mobile phone interventions have also been utilized to prompt patients to maintain their drug pickup or follow-up visits. SMS and/or mobile phone call reminders in Mozambique [49] and Uganda [50] have hinted at improvements in pill-refill appointment adherence of HIV and/or tuberculosis patients, thus also implying positive changes in medication compliance. Both means of communication have presented high acceptability, with the calls receiving more positive feedback [50]. Similar effects have also been reported by a study undertaken in Cameroon [51], where either just mobile phone call reminders, or combined with SMSs were more successful than just SMSs in motivating carers of children exposed to or infected with HIV to attend their follow-up appointments. However, a trade-off between effectiveness and cost efficiency arose, given that phone calls were more expensive than SMSs. Financial support from mobile communication companies has been presented as a solution for rendering such interventions more affordable [51]. A no-cost alternative has been introduced in [52], where missed call notifications (buzzing) were used as appointment reminders to HIV patients. However, a trial of this method conducted in Swaziland presented no impact on appointment adherence. The absence of positive outcomes might be associated with several factors, such as age, cultural differences, as well as the distance that the patients need to travel in order to attend their appointments [52]. In agreement with the case of medication reminders analyzed in the previous paragraph, confidentiality and privacy matters were considered as challenges involving such interventions [49] [50].

The role of m-health in promoting HIV/AIDS counseling and testing (HCT) services in developing countries has been investigated. A survey conducted in Uganda which distributed educative SMSs among mobile phone subscribers promoting HCT exhibited high acceptability and increased significantly the uptake of HIV tests [53]. This success was attributed in part to radio advertisements informing citizens on the survey prior to its implementation, as well as the fact that HIV tests were free of cost, thus eliminating financial barriers. The number and content of text messages delivered to the citizens have proven to significantly affect their willingness to be tested for HIV, as reported from a study undertaken in South Africa [54].

Text messaging has also been introduced as a means to disseminate HIV/AIDS information to the public and support the adoption of safe sexual practice. In Kenya, implementation of a program to increase contraceptive knowledge through educative SMS messages was well accepted, exhibiting the potential of such a cost efficient method to encourage safe behaviors [55]. On the contrary, another m-health intervention tested in Uganda, which delivered SMS-based Quizzes including HIV/AIDS related questions, had very limited impact [56]. Analysis on the answers provided to the Quizzes revealed that people who already possessed relative knowledge responded correctly, while lesser educated groups were discouraged from completing the quiz, and thus less likely to benefit from this intervention. Those results suggest that it is important to take into consideration the characteristics of various vulnerable groups in cases of applications aiming to provide massive education [56]. Table III summarizes the RCTs performed for the management of HIV through mobile interventions.

2) Non-Communicable Diseases

Several non-communicable conditions such as hypertension, diabetes and cancer require healthy lifestyle and proper self-management in order to prevent the prognosis. The results obtained from related RCTs performed for the management of diabetes are presented in Table IV.

Distribution of behavior change SMSs either alone [57], [58], or combined with phone calls [59] have exhibited the potential to prompt hypertensive patients to adopt healthy dietary habits in developing countries such as South Africa, Guatemala, Argentina and Peru. In [59], however, apart from nutrition, no effects on uptake of physical exercise and systolic blood pressure were observed, suggesting that some aspects of a person's lifestyle might be more difficult to modify according to his/her background, and that m-health strategies might need to be supplemented with components other than just text messages and calls (e.g. direct communication with physicians) in order to induce more drastic behavioral changes. Moreover, in [57], although patients were encouraged to consume healthy food, no increase in hypertension knowledge was noticed as a result of the messages' educational content, concluding that it is more meaningful to deliver SMSs as reminders aiming to motivate changes, rather than aiming to deliver generic health-related information. Instead, in [58], the SMS-campaign with information on hypertension and tips on healthy living was implemented with South African deaf. The obtained results showed that SMSs are an effective and acceptable way of improving deaf population's health knowledge. Another m-health approach has been trialed in Honduras and Mexico, according to which hypertension patients were provided a blood pressure monitor and received weekly automated calls [60].

TABLE IV
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR THE MANAGEMENT OF DIABETES AND HYPERTENSION (CATEGORY A: CITIZEN EDUCATION AND BEHAVIOR CHANGE COMMUNICATION). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
A. Rubinstein et al, 2016 [59]. Guatemala, Argentina, Peru.	Phone calls and text messages for improving hypertension management.	**n=637** patients with prehypertension; IG: n=316; CG: n=321. Duration: 12 months.	IG received weekly text messages and monthly counseling calls promoting healthy diet and physical exercise.	Changes in BP: 0.01 relative increase of diastolic blood pressure (DBP) and 0.37 relative decrease of SBP in the IG compared to the CG.
J.D. Piette et al, 2012 [60]. Honduras, Mexico.	Home based blood pressure (BP) and monitoring phone calls for improving hypertension management.	**n=200** patients with high systolic blood pressure (SBP); IG: n=99; CG: n=101. Duration: 6 weeks	IG were provided an electronic home BP monitor and received weekly monitoring and behavior change automated calls.	Overall changes in BP: 4.2 mm Hg relative decrease of SBP in the IG compared to the CG. Changes in BP in the subgroup of low literate participants: 8.8 mm Hg relative decrease of SBP in the IG compared to the CG.
C. Tamban et al, 2014 [61]. Philippines.	Text messages for improving diabetes management.	**n=104** patients with Diabetes Mellitus; IG: n=52; CG n=52. Duration: 6 months	IG received SMS messages motivating medication adherence and healthy lifestyle 3 times a week.	HbA1c levels at 3 months: 7.13 in the IG and 7.53 in the CG. HbA1c levels at 6 months: 6.99 in the IG and 7.34 in the CG. Uptake of physical exercise at 6 months: 37.4 mins/exercise in the IG and 31.44 mins/exercise in the CG. Dietary compliance at 6 months: 2.61 meals/day in the IG and 2.29 meals/day in the CG.
A. Pfammater et al, 2016 [62]. India.	Text messages for improving diabetes management.	**n= 1,925** diabetic patients; IG: n=982; CG: n=943. Duration: 6 months.	IG received in total 56 behavior change text messages.	Dietary changes: Increased vegetables and fruits, and less fat consumption in the IG compared to CG. Physical exercise: No difference in uptake of physical exercise was observed between the IG and CG. (See [62] for information on healthy behavior score scale).
M. Shahid et al, 2015 [63]. Pakistan.	Phone calls for improving diabetes management.	n=440 patients with Diabetes Mellitus; IG: n=220; CG: n=220. Duration: 4 months.	Both IG and CG were provided a blood glucose monitoring form to monitor their blood glucose. IG received monitoring phone calls every 15 days from physicians.	HbA1c levels: decrease of 1.46 in the IG and 0.48 in the CG. Dietary compliance: Increase of 26.3% in the IG and 2.3% in the CG. Uptake of physical exercise: Increase of 28.1% in the IG and 2.3% in the CG.
J. Van Olmen et al., 2017 [64]. Cambodia, Philippines, Democratic Republic of the Kongo.	Text messages for promoting self-management support during the routine care of subjects with diabetes	**n=781** patients with diabetes; IG: n=401; CG: n=380. Duration: 2 years	IG received multiple weekly self-management text messages, depending on the country involved (5 in DR Kongo, 6 in Cambodia, 2 in Philippines).	Primary outcome: HbA1c levels was lowered in 33.9% of subjects in the IG and 31.1% in the CG (not statistically significant). Secondary outcome regarding development of HbA1C over 2 years: more than half of the participants remained at the same HbA1c category after 2 years
JD Piette et al, 2016 [65]. Bolivia.	Phone calls for improving diabetes and hypertension management.	**n=72** hypertensive patients; IG: n=27; CG n=45. Duration: 4 months.	IG received weekly monitoring and self-management IVR calls through which they could also provide feedback for their informal caregivers. CG received weekly standard IVR calls without the opportunity to provide feedback.	IVR call completion rate: 62% in the IG and 44.9% in the CG. Health state: Increased probability of reporting healthy state and reduced probability of reporting illness in the IG, with an adjusted odds ratio (AOR) of 2.6 and 0.42, respectively.
M. Sharma et al. 2017 [68]. India.	Phone calls and text messages for improving physical activity and healthy diet	**n=382** participants; IG: n=190; CG n=192. Duration: 8 months.	IG received monthly a 20-minutes phone call and weekly text messages, reiterating the importance of modification of behavioural risk factors.	Increased consuming of adequate diet and increased physical activity in the IG compared to CG. Significant changes of the Body Mass Index, the systolic blood pressure, the fasting blood glucose and HDL cholesterol level in the IG group.

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Very positive results such as reduced systolic blood pressure, depression symptoms and problems with medication were reported by employing this method, suggesting that enabling self-monitoring might be a key component in improving the effectiveness of interventions to inspire behavioral change [60]. High acceptability towards those methods has been reported, supporting their potential to achieve healthy lifestyle changes in the developing world [57], [60]. SMS interventions have also proven to be effective on improving eating habits of diabetic patients in the Philippines and India, as well as reducing their HbA1c levels; however, controversial results involving physical activity were observed indicating that, as in the case of hypertensive patients, more drastic practices might be needed to accomplish specific behavioral changes [61], [62]. Further, in agreement with the case of hypertension [60], self-monitoring (e.g. self-blood glucose monitoring form) combined with mobile phone calls can be highly effective as reported by a trial undertaken in Pakistan, where utilization of this method was successful in reducing HbA1c levels, as well as improve dietary compliance and physical exercise among diabetic patients [63]. A factor that contributed to the success of this strategy was the fact that a physician called directly the patients, which, in contrast to simple SMS texting, enabled more meaningful physician-patient communication [63]. However, a study conducted in three countries (Democratic Republic of Kongo, Cambodia and Philippines), aiming to test the same m-health SMSs intervention, led to inconclusive results for the reduction of HbA1c levels [64]. Although a greater drop of HbA1c levels was observed in the intervention group compared to the control group, the difference was not statistically significant. In general, there were no significant effects of the intervention on intermediate outcomes or other outcomes [64]. A novel approach towards improving diabetes and hypertension management is presented in [65], where interactive voice response calls delivered to Bolivian diabetic and hypertensive patients in order to monitor their condition, were enhanced by offering them the choice to provide feedback on their caregivers. This addition resulted in a higher response rate to the calls and improved health condition, providing the opportunity of making citizens feel that their opinion matters, in order to motivate proper self-management [65]. Communication and peer support may sometimes motivate patients better manage their condition. To this end, a mobile phone application connecting women with diabetes mellitus to pairs, allowing them to exchange text messages and support each other's healthy lifestyle has been implemented and evaluated in South Africa [66]. Although this application was acceptable among users and helped them cope better with their condition, no improvements were observed in blood glucose levels, body mass index and healthy habits.

Mobile phone communications have been presented as a valuable tool for improving cancer care. In Nigeria, oncology patients were provided the mobile phone number of their oncologists and could call them any time to ask for advice [67]. A significant increase in follow-up appointment attendance was observed, with patients feeling satisfied and more confident with the fact that they could receive consultation without having to travel long distance to attend a clinic [67].

Finally, a recent study carried out in India has focused on modifying two risk factors for the primary prevention of non-communicable diseases, namely physical inactivity and unhealthy diet. Results demonstrated that SMSs and phone calls led to statistically significant changes in physical activity, as well as to significant reductions in physiological risk factors [68].

3) Vaccination Coverage

Proper and timely childhood immunization is crucial to decrease disease outbreaks and mortality from preventable diseases. The rapid advancement and adoption of mobile technologies has provided an opportunity to improve immunization coverage by motivating parents to have their children vaccinated. The corresponding RCTs conducted are included in Table V. SMS messages have been used as reminders of vaccination appointments in Guatemala and Kenya, suggesting that an increased number of children were completing immunization series [69], [70]. Improved vaccination compliance was also demonstrated by another intervention, which provided SMS reminders to Kenyan mothers and enabled conditional cash transfers through mobile phones [71]. Several mothers however reported that their husbands did not permit them to participate in this intervention, revealing significant challenges regarding vulnerable groups that should be considered when implementing such applications [71]. Sticker reminders have been suggested as an alternative to SMSs but have shown limited impact [70], while a study in Philippines evaluated whether delivering messages with pictures to parents would increase their motivation to bring their children to vaccination appointments compared to plain text reminders, but presented no difference [72]. However, pictures might be more advantageous in illiterate groups of people [72]. In the majority of studies involving vaccination compliance, parents seemed to have positive stance towards such m-health interventions [69], [70], [72].

4) Maternal and Neonatal Health

M-health has shown great promise in motivating women to uptake proper health services, as well as evoking healthy behaviors, towards improving maternal and infant health. The related RCTs are summarized in Table V. A study in Ecuador assessed the impact of an m-health intervention, offering postpartum women both an education session and the availability to consult a nurse via mobile phone [73]. Positive behavior changes such as breastfeeding, postnatal care visits, proper use of contraception, as well as a reduction in infant illness were observed as a result of this intervention, while the acceptance was high among participating women. Very positive outcomes have also been reported as a result of another mobile phone based intervention consisting of SMS messages encouraging pregnant women to receive proper care and a voucher system enabling them to call their midwives [74], [75]. Implementation of this application in Zanzibar increased the rates of women attending prenatal care visits and having a skilled birth attendant at delivery, while also reducing neonatal mortality rates.

TABLE V
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR THE IMPROVEMENT OF VACCINATION COVERAGE AND MATERNAL AND NEONATAL HEALTH (CATEGORY A: CITIZEN EDUCATION AND BEHAVIOR CHANGE COMMUNICATION). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
Domek et al, 2016 [69]. Guatemala.	Text messages for improving vaccination compliance.	**n=321** children receiving the first dose of primary vaccination series; IG: n=160; CG: n=161. Duration: 6 months.	IG received 3 SMS reminders in the week prior to the 2nd and 3rd dose of the vaccination series.	Completion rate of the 2nd dose: 95% in the IG and 90.1% in the CG. Completion rate of the 3rd dose: 84.4% in the IG and 80.7% in the CG.
A. Haji et al, 2016 [70]. Kenya.	Text messages and Sticker messages to improve vaccination compliance	**n=1,116** children receiving the first dose of pentavalent vaccination series; IG1: n=372; IG2: n=372; CG: n=372. Duration: period between February and October 2014	IG1 received text reminders 2 days before and on the same day of the appointments for the 2nd and 3rd dose of pentavalent vaccines. IG2 received sticker reminders with the same timing.	Rates of withdrawal from the vaccination series: 4% in the IG1, 16% in the IG2 and 17% in the CG.
Maslowsky et al, 2016 [73]. Uganda.	Phone calls to improve maternal and neonatal health.	**n=178** Postpatrum women; IG: n=102; CG: n=76. Duration: 3 months	IG received an education session by a nurse via phone within a 48 h period after hospital discharge and were able to contact a nurse for advice.	Self-reported breast feeding: 86.7% in the IG and 66.7% in the CG. Attendance of newborn check-up: 72% in the IG and 53.3% in the CG. Use of any kind of contraception: 76% in the IG and 68.3% in the CG.
Lund et al, 2012 [75], 2014 [74]. Zanzibar.	Text messages phone calls to improve maternal and neonatal health.	**n=2,550** pregnant women; IG: n=1311; CG: n=1239. Duration: period of 2009-2010	IG received motivational SMSs (varying timing) and were able to call their midwives by using appropriate voucher system.	Perinatal mortality rate: 19 per 1000 births in the IG and 36 per 1000 births in the CG; Reduced in the IG with an odds ratio (OR) of 0.50. Rate of women delivered with skilled attendant: 60% in the IG and 47% in the CG.

B. Remote Data Collection and Data Management

This category includes applications for efficient and reliable data collection and management for various purposes, such as enhancing disease surveillance, enabling collection of patient information in order to monitor them more effectively, improving the efficiency of healthcare logistic processes, and supporting supply chain of medical products. Twenty-four studies were identified falling in this category. Analytical description of the unique RCT included in this category is presented in Table VI.

Effective monitoring is essential for predicting outbreaks, epidemics and pandemics of infectious diseases and limiting their potentially devastating consequences. In low resource settings, surveillance is problematic due to the lack of financial recourses, medical staff and facilities. Advances in mobile technologies and the widespread use of mobile phones have demonstrated promise in enhancing early detection of such diseases. The role of front line community health workers has been highlighted as a key component in supporting surveillance by employing mobile communications. Studies undertaken in Vietnam [76] and Nepal [77] have proven the feasibility of utilizing community health workers to enhance case notification rates of diarrhea, respiratory infections and other influenza related symptoms using mobile phones, thus enabling the healthcare system to track disease trends and better prepare for managing outbreaks. Similar positive outcomes were demonstrated in [78] as a result of an SMS-based reporting system trialed in Ghana and Malawi, aiming at the detection of cases of lymphedema and hydrocele, where the reliability of the SMS reports provided by community health workers was compared with a physician's diagnosis. High diagnostic accuracy was observed in all cases, apart from hydrocele reports in Ghana. Two studies were carried out in Guatemala [79], [80]: the former concerned the surveillance for symptoms of influenza-like illness, while the latter focused on the collection of syndromic data (acute febrile illness and acute gastroenteritis) for the detection of dengue virus. Both studies reported the design of mobile phone app-based participatory surveillance systems, presenting satisfactory levels of simplicity, flexibility and timeliness [79] as well as high rate of agreement between mobile phone parental reporting and nurse home visit reporting [80]. In Sri Lanka, a mobile participatory system for dengue surveillance (Mo-Buzz) was developed, intended for use by both public health inspectors and the general public [81]. It mainly includes health education materials regarding dengue transmission, symptoms, treatment, and prevention, but offers also dynamic mapping in order to inform about potential outbreak regions and, therefore, facilitate preventive measures. However, the system is still in its infancy, presenting a relatively low uptake, revealing the fact that the initial acceptance of such systems may be significantly slow. Finally, high and timely notification rate, but low accuracy was indicated by a trial conducted in Kenya, where community health workers were assigned to report Malaria cases via SMS [82]. Those findings suggest that, although it is feasible to improve the effectiveness of infectious diseases surveillance through mobile phones, the accuracy of data collected vary with respect to the location and the kind of disease. The background and knowledge of the health workers need to be taken into account when implementing such interventions, while appropriate training and supervision is required in order for them to interpret correctly the patients' symptoms and improve the quality of the collected data [76], [78], [79], [82].

The potential use of mobile technology to enhance screening and patient monitoring procedures by collecting patient data and forming electronic records has been investigated. In Ethiopia, the use of mobile phone based electronic forms resulted in improved data accuracy and completeness compared to paper based methods [83]. Moreover, in Kenya, a mobile platform for patient data collection aiming at supporting home based health services provided by community health workers demonstrated advantages in cost efficiency and high acceptance rate by the users [84].

Several benefits have been indicated in childhood care through such interventions. In Mali [85] and Uganda [86], applications running on health workers' mobile phones, enabling them to collect health data, have proven to be an effective way to identify children at risk and link them to the healthcare system in order to initiate appropriate treatments. Positive results have also been reported on the efficiency of logistic procedures of the healthcare system and medication supply management, as well as on the willingness of health workers to cooperate with each other and administer their services [85], [86].

M-health applications for data collection have also found application in improving maternal and prenatal care. Studies in Madagascar [87], Rwanda [88], Kenya [89] and Nepal [90] have demonstrated the feasibility of mobile phones to enable efficient reporting of pregnancies, as well as highly accurate and complete data collection involving the status of pregnant women, resulting in increased follow up, uptake of prenatal care and facility based delivery rates. Positive feedback received both by pregnant women and health workers further enhance the possibility of successfully implementing and adopting such novel methods in developing countries [87], [88]. High acceptability was also reported in [91], where an Android based application for data collection of HIV positive pregnant women was evaluated in South Africa, aiming at limiting the transmission of the infection from the mother to the infant. Even though such applications have the potential to improve maternal and neonatal health, challenges may arise such as poor cellular or network signal, difficulties in mobile phone maintenance due to limited financial resources and lack of electricity in some remote areas [87], [88], [90]. Additionally, a number of challenges are associated to the resources required, the development of quality control procedures and phones' technical issues, such as battery's life and limited internal memory capacity [90].

TABLE VI
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR HOME BASED MONITORING (CATEGORY B: REMOTE DATA COLLECTION AND MANAGEMENT). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
D. Simonyan et al, 2013 [85]. Bamako, Mali.	Evaluation of the Djantoli (formerly Pesinet) program, aiming to provide home based monitoring through a mobile phone application for data collection, health education and financial support for children.	**n=180** childen; IG: n=91; CG: n=89. Duration: Period between Nov2010 and Apr 2011	IG received home visits by properly trained weighing agents, who collected and sent their health data to a general practitioner (GP) for analysis. The WAs performed a follow-up visit every two weeks. The follow-up period was 16 weeks for each child.	Incidents of disease: 206 in the IG and 168 in the CG. Number of children received consultation: 85 in the IG and 28 in the CG.

Electronic registries and mobile information technology (IT) platforms accessible via mobile phone web browsers or SMSs for remote data collection and processing have been developed, aiming at supporting administrative procedures involving bone marrow transplantation, blood transfusion, or other surgical operations [92], [93], [94]. Studies have pointed to the feasibility and positive outcomes of implementing such systems in developing countries [92], [93]. Deployment of a blood information management system in Bangladesh reduced the time needed for blood transfusion in cases of emergency during women's perinatal period [93], while an information technology (IT) platform employed in Pakistan and India facilitated proper management of patients in need of bone marrow transplant, achieving very encouraging rates of successful operations at a fraction of the cost over a 5-year period [92].

Such technologies have also shown promise in clinical research as reported in [95], where employment of an open-source platform for clinical research data collection in Kenya reduced the data errors and the time needed for the study's completion, while facilitating efficient control and review of the data. Although mobile IT platforms have demonstrated benefits, several factors must be considered, depending on the implementation site, such as the health facility's existing organization and resources, as well as the capability and willingness of health personnel to replace traditional paper based methods with novel technological tools [94], [95].

Furthermore, m-health has improved the performance of laboratory examinations. In fact, in rural areas, medical laboratories are usually distant from the facility attended by the patient and, therefore, there is a significant delay (turn-around time) to send patient samples to the laboratory and receive back the examination results. In Swaziland [96] and Zambia [97], SMS messages have been trialed as a means to deliver HIV test results from the laboratory to the remote health facility, resulting in significant reduction of turn-around time and rate of missed reports [97] compared to paper based methods. However, further research is required in order to determine the cost benefits, the reliability of the transmitted data and positive effects in the long term [96], [97].

Another significant issue of the healthcare system in developing countries is the lack of a highly functional supply chain of drugs, vaccines and other medical products. In India, a mobile IT platform has been implemented aiming at enhancing vaccine inventory monitoring and management [98]. The use of this system has been widely adopted and has had several benefits such as increase of vaccine availability, limited time intervals for stock replenishment and low error rates, while the performance of the supply chain stabilized 13 months after implementation. Moreover, a mobile application for palliative medication data management has been utilized in Uganda, resulting in significantly improved time efficiency of pharmaceutical data collection and processing, as well as limited stock expiration rates [99]. M-health has shown the potential to substantially support supply chain management in the developing world. Further investigation on the users' behavior and the resources of implementation sites would be necessary prior to scaling-up such applications [98], [99].

C. *Sensor Systems and Point of Care Diagnostics*

Novel tools utilizing sensor systems and/or images, enabling remote diagnostic procedures, alleviate the burden on citizens in remote areas to travel long distance in order to attend a health facility. This m-health domain was represented by 17 articles. The outcomes of the two RCTs included in this category are provided in Table VII.

The Xpert MTB/RIF assay, an automated molecular test capable of diagnosing tuberculosis (TB), has demonstrated the potential to improve tuberculosis care. GxAlert, a tool for uploading test results generated by the Xpert platform was successfully installed at health centers in Mozambique, enabling real time monitoring and processing of patient data, while also generating SMS alerts to inform patients on their situation [100]. However, Internet connectivity and organizational issues of the healthcare system were some challenges that needed to be addressed in order to exploit the full potential of this system [100]. Another scheme trialed in South Africa and Zimbabwe, where mobile vans were equipped with the Xpert system to provide tuberculosis tests, increased the rates of TB patients initiating proper and timely treatment [101]. Though this approach seemed quite beneficial in improving TB management, an analysis on its cost efficiency would be required due to the high price of the Xpert platform [101].

In another study conducted in Tanzania, an electronic patient management algorithm, named e-POCT, has been implemented relying on the latest evidence of pediatric fever management based on studies from both low- and high-income settings [102]. e-POCT is built into an application, which guides the clinician through the entire consultation and recommends management based on a few clinical elements as well as point-of-care tests. The proposed algorithm was found not to be inferior than a well-established current disease management tool, the Integrated Management of Childhood Illness algorithm (ALMANACH), achieving a significant reduction in the proportion of both clinical failures and severe adverse events [102]. However, there are rising costs associated to additional components required for the e-POCT algorithm. Expansion of the study to different geographical settings and populations with higher HIV and malnutrition rates should be also considered to confirm the study's outcomes.

A mobile platform, namely portable health clinic (PHC), incorporating various types of monitoring tools such as blood pressure, blood sugar, temperature, weighting scale and other non-electrical devices, as well as a wireless communication system to transmit the measured physiological parameters to a central database, has been developed [103]. This system was successfully deployed in Bangladesh as a means to provide routine health check-up, showing promise in improving the healthcare system by offering vulnerable populations access to a variety of standard diagnostic tests.

Sensors systems have demonstrated the potential to enhance task shifting to lesser trained health workers. In Ghana, community health workers were assigned to report on the state of pregnant women via mobile phone. When a woman was unable to attend antenatal care, a technician visited her place and used a portable ultrasound system to perform scans and transmit them for evaluation by a health professional. This practice led to an increase in the rate of women attending a clinic during delivery [104]. Moreover, a mobile phone based system incorporating sensing capabilities including doppler scanning, aiming at supporting the assessment of pregnant women has been implemented and has received positive feedback by Guatemalan health workers [105]. In Kenya, a project has focused on training midwives to perform basic ultrasound using a tablet platform to identify high-risk pregnancies [106]. After scanning the patients, an interim report was generated by the midwives and sent electronically, together with all images, to the main hospital for validation. Encouraging outcomes of the study include short transmission times, no degradation of image quality and excellent correlation between final outcomes of the pregnancies and diagnoses on the basis of reports generated by the midwives. Towards the same direction a feasibility study has been conducted in Haiti, to investigate whether high quality ultrasound images could be transmitted in real-time and interpreted remotely by a tele-intensivist using commercially available video-chat software [107]. The ultrasound acquisitions have been performed by nine non-physicians health workers who had previously followed a short training session. The tele-intensivist found that a high ratio (90%) of the acquired images were of high quality, enabling the remote decision-making process. Additionally, he/she reported no technical problems, without founding difficulties in receiving images or providing instructions to the health workers. However, the limited number of participants (midwives, health workers) involved in both studies constitutes a severe limitation [106], [107]. A study in South Africa demonstrated the feasibility and high acceptance by community health workers to perform hearing screening tests during home visits using a smartphone application (hearScreenTM), showing promise in alleviating the high burden of hearing loss in developing countries [108]. The importance of cultural and economic variations among different locations, as well as the abilities of health workers has been highlighted in order for such interventions to be effective [104], [105], [108].

Risk of stroke is rapidly increasing in Africa and, due to limited access to health services, risk factors such as cardiac arrhythmia remain undiagnosed. To this end, a mobile electrocardiogram recording platform was implemented and tested at a Kenyan hospital [109]. Through the use of this system, patients with cardiac arrhythmias, who were previously undiagnosed, were identified. The acceptance expressed by the hospital's health workers and the successful implementation support the vision of a wide spread network of mobile ECG devices throughout health facilities in low resource settings, thus enabling detection of atrial fibrillation and enhancing prevention of stroke incidence [109]. However, some of the hospital staff expressed uncertainty as to whether they were capable of interpreting ECGs correctly, meaning that users would be required to receive proper training.

Smartphone photos have been investigated as a means to enable diagnosis in rural areas by remote health professionals. The feasibility of implementing tele-dermatology services in low resource settings has been supported in Uganda [110] and Egypt [111], [112], where patients sent pictures of their dermatological conditions to remote dermatologists for analysis. A satisfying rate of accurate diagnoses was achieved in both studies, while in [110] acceptance among local health workers was observed. In Madagascar, transmission of smartphone photos of women's cervix demonstrated the feasibility to enable remote screening for cervical cancer, since the achieved images were judged by physicians to be of good quality and therefore capable of guiding them throughout the decision-making process [113], [114]. A mobile microscope for oral cancer screening that uses a tablet to capture magnified images has been proposed as part of a telemedicine screening system in India [115]. The obtained digital images were found to be an excellent substitute for glass slides, as they were interpreted accurately remotely and showed excellent cellular details for cytology diagnosis. Finally, a study conducted in Nepal has focused on the early detection of blindness and visual impairment and proposed the screening of visual fields through a tablet application [116]. Different group of participants (control group, patients with evidence of diabetic retinopathy, patients with glaucoma) have been evaluated and the achieved classification results are quite encouraging regarding the potential to develop a reliable tablet-based solution for visual field screening. The use of such methods is still in early stage and their evaluation is limited to feasibility studies. Larger trials would be required to determine their contributions to the healthcare system [110], [111]. Limitations might arise from smartphone availability, as well as the available resources in very low resource settings to support such services [111].

TABLE VII
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR POINT OF CARE DIAGNOSTICS (CATEGORY C: SENSORS SYSTEMS AND POINT OF CARE DIAGNOSTICS). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
GL Calligaro, 2017 [101]. South Africa, Zimbabwe.	Utilization of Sputum Xpert-MTB/RIF and the Determine TB LAM urine test to improve TB management.	**n=875** individuals with possible tuberculosis; IG: n=439; CG: n=436. Duration: Period between Oct 18 2013-March 31, 2015	IG received TB tests at a van equipped with the sputum Xpert-MTB/RIF and the Determine TB LAM urine test; CG received routine testing (laboratory smear microscopy);	Rate of TB patients initiating timely treatment (within 60 days): 53% higher in the IG, compared to the CG.
K. Keitel et al, 2017 [102]. Tanzania.	Utilization of the e-POCT electronic patient management algorithm including host biomarker point-of-care tests for the management of febrile illnesses.	**n=3,169** childen with fever for 7 days or less; IG: n=1586; CG: n=1583. Duration: 2 years	Study clinicians used, during the consultation, the e-POCT algorithm in the IG and an alternative validated electronic algorithm (ALMANACH) in the CG to manage the patient.	e-POCT achieved reduction of 43% in the proportion of clinical failures by day 7 and a reduction of 58% in the proportion of severe adverse events compared to ALMANACH. The proportion of antibiotic prescriptions was lowered from 30% to 11%.

D. *Electronic decision support*

This category includes software tools implemented on mobile platforms that analyze patient data and/or provide step-by-step guidance to healthcare workers in order to assist with diagnostic and/or treatment decision making. The least proportion of studies (10 out of 83) was associated with this category. The details of four corresponding RCTs are provided in Table VIII.

Decision support systems (DSS) for cardiovascular risk assessment have proven to be implementable and used by low skilled healthcare providers, presenting several benefits in cardiovascular management and high acceptability [27], [117], [118]. In rural China and India, a program utilizing community health workers and a smart phone based DSS was effective in increasing the use of anti-hypertensive medication among citizens at high cardiovascular risk, as well as reducing their systolic blood pressure [27]. Factors that contributed to the success of this intervention were the simplified guidelines targeting specifically high-risk individuals, as well as its custom design taking into account variations in culture and available resources among different locations, also making feasible its scalability and sustainability. However, counseling provided by the health workers when assessing the patients had no impact on inducing behavioral changes such as smoking cessation and salt intake reduction, suggesting that adoption of a healthy lifestyle can be a difficult and long term procedure, especially in older people [27].

TABLE VIII
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR ELECTRONIC SYSTEMS ORIENTED TOWARDS DECISION SUPPORT (CATEGORY D: ELECTRONIC DECISION SUPPORT). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
M. Tian et al, 2015 [27]. China and India.	Smartphone based decision support system used by CHWs to perform cardiovascular screening.	**n= 2,086** individuals at high cardiovascular risk. IG: n=1,095; CG: n=991. Duration: 1 year.	IG were managed by CHWs using the decision support system.	Rate of patients using anti-hypertensive medication: 25.5 % higher net increase in the IG compared to the CG.
JF Florez-Arango et al, 2011 [119]. Colombia.	mobile phone application, providing interactive clinical guidelines to CHWs	**n=50** community health workers; IG: n=25; CG: n=25. Duration: N.A.	IG assessed 30 simulated medical cases using the mobile phone application; CG assessed the same cases using paper based guidelines.	Error rate in medical assessments: 33% lower in the IG compared to the CG. Protocol compliance: 30% higher in the IG compared to the CG. Mean duration to complete an assessment: 6.28 mins higher in the IG compared to the CG.
M. Gautham, 2015 [120]. India.	Mobile phone based application providing mobile media-rich interactive guidelines (mMRIGs) for assisting health workers.	**n=16** health workers and **n=126** patients; IG: n=8 health workers and n=65 patients; CG: n=8 health workers and n=61 patients; Duration: 2 months.	Both IG and CG received a 2-day training session on guidelines based assessment; IG health workers used the MRIGs application to provide care to IG patients; CG were provided paper guidelines.	Protocol compliance among male health workers: 26.8% higher in the IG compared to the CG. Protocol compliance among female health workers: 11.95% higher in the IG compared to the CG. (See [120] for more information on protocol compliance measurement).
C. Rambaud-Althaus et al, 2017 [121]. Tanzania.	Mobile phone based application providing interactive guidelines for assisting health workers with providing care to children.	**n=67** health workers and **n=504** children; IG1: n=30 health workers and n=167 children; IG2: n=18 health workers and n=171 children; CG: n=19 health workers and n=166 children;	IG1 and IG2 received a 2-day training session on guidelines based assessment; IG1 health workers used the mobile phone guidelines to assess IG1 children; IG2 health workers used paper based guidelines to assess IG2 children;	Rate of children checked for danger signs: 74% in the IG1, 41% in the IG2 and 3% in the CG. Rate of antibiotic prescriptions: 25% in the IG1, 26% in the IG2 and 70% in the CG.

Utilization of another DSS in South Africa limited the time needed to train community health workers in order to perform assessment of cardiovascular disease risk and improved their diagnostic accuracy compared to a paper based method [117], further supplementing the potential of such systems to make cardiovascular screening more accessible in the developing world. However, the effectiveness of such interventions is highly dependent on the availability and skills of health workers, as well as their motivation to participate in such actions [27], [117].

Applications providing mobile media-rich interactive guidelines (mMRIGs) have been developed and utilized to aid lesser trained front line health workers in resource limited settings. Trials of such applications in Colombia and India have demonstrated several positive effects on health workers' clinical assessments, such as high diagnostic accuracy and protocol compliance, while also high user satisfaction has been reported [119], [120]. Significant advantages of those systems were considered due to their capabilities to reduce the complexity of clinical procedures by dividing them into small and simple steps that could be comprehended by various groups of people regardless of their literacy and skills [119], [120]. Though those two studies hinted at several benefits through the use mMRIGs, they had limited statistical power. Larger and more robust trials need to be conducted in order to determine their effectiveness on enhancing the health care system.

Algorithms running on health providers' mobile phones, enabling interactive guidance have also shown promise in improving childhood care. In Tanzania, smartphone based guidelines increased the performance of health workers in providing proper assessment to children, identifying dangerous signs or infections, as well as prescribing appropriate medication, while an increase in case notification rate of childhood conditions was observed [121]. However, it was challenging to identify pneumonia, suggesting that some conditions might be difficult to diagnose by lesser trained health workers. Nevertheless, this method was proven to be quite beneficial in identifying and managing patients, and has indicated potential for scalability due to the limited period and resources needed to train health workers in using this application [121]. Moreover, an application providing step-by-step guidance for supporting childhood pneumonia diagnosis has been developed and trialed in Ghana [122]. Though this tool exhibited feasibility to be used and seemed to be acceptable by Ghanaian health workers, the trial was performed through simulated clinical scenarios, and further research is required to determine its value under realistic conditions.

A decision support system has been implemented at a healthcare facility in Brazil and utilized by health professionals to assess type 2 diabetes patients during their visits [123]. Though positive feedback about this system was received, its adoption was moderately successful, especially among physicians. Moreover, apart from the subgroup of patients at high risk (HbA1c level ≥9%), no overall significant improvements in glycemic control were observed. Those facts pointed to challenges derived from organizational issues of the healthcare system, as well as from reluctance of some health professionals to embrace m-health and integrate it in their work [123].

Mobile phone applications have also shown potential in improving tuberculosis management. In Pakistan, community laypeople were equipped with an interactive algorithm for Tuberculosis diagnosis support running on their mobile phones and assigned to screen community members. This approach proved to be quite effective for detecting tuberculosis, leading to rapid increase of case notification rates [124].

Finally, a research team in Brazil has proposed a system based on a mobile phone application for the diagnosis of malaria [125]. Digital processing image techniques and a learning process based on artificial intelligence algorithms were properly combined for the development of the system. Images from positive and negative malaria samples acquired using mobile devices were used for the computational experiments. The average accuracy value achieved for the diagnosis was quite high, indicating that such tool could be used in health centers without the need for specific expertise and therefore help break the accessibility barriers of low-resource countries.

E. Health Worker Education, Consultation and Work Planning

The use of mobile devices as a means to train and educate health workers offers them guidance and consultation from other healthcare providers as well as helps them plan their work in order to increase the efficiency of the offered health services. Eleven studies were classified in this category, while only two RCTs were identified, presented in Table IX.

Studies in Peru and Kenya have demonstrated the effectiveness of m-health interventions such as instructive text messages, interactive mobile phone applications simulating clinical cases or instructional videos to educate and improve the skills of health workers and students [126], [127], [128]. In Vietnam though, SMS quizzes delivered to mobile phones of community health workers were not successful in improving medical related knowledge, and attributed this to the fact that SMS can provide little information due to a limitation in the number of characters [129]. A solution would be to provide links to learning materials in the text message in order to motivate health workers to study and acquire relevant knowledge. Text messaging in [126], aiming to provide instructions on malaria management was a success, probably because the messages acted as reminders to health workers and emphasized the importance of completing the tasks described in the text. The positive feedback received by the users [126], [127], [129] encourages further utilization of mobile devices to provide health worker education.

M-health has also provided the opportunity to offer access to medical literature and other sources of information to health workers in developing countries. In Botswana, resident physicians were assigned to undertake simulated clinical cases and answer to medical questions, using an application to retrieve abstracts on Pubmed (PubMed4Hh) or other mobile phone based applications providing information on medical and drug reference [130]. Outcomes suggested that the intervention influenced positively the physicians' performance, with each application presenting superior performance in different types of medical assessment. Thus, it would be essential to conduct further research on specifying information needs and adjusting applications accordingly, in order to augment their effectiveness [130]. However, according to another study in Botswana, mobile health services enabling health workers to send health related queries and receive abstract summaries from Pubmed via SMS along with clinical guidelines, was characterized by limited acceptance and their adoption failed [131]. Those outcomes highlighted the need of optimizing the interface of such applications and make retrieval of the desired information easier in order to enhance its usage by health workers [131]. Furthermore, the role of mobile phones in improving the performance of healthcare providers in developing countries was supported in [132], where the use of Indonesian midwives' mobile phones presented positive correlation with their access to institutional and peer-network information, which in turn was associated with their health-related knowledge.

In our analysis of various m-health interventions, it has been clear that the role of lightly trained front line health workers is of major importance to enhance the healthcare system in developing countries. It is therefore essential to organize their work properly and follow a specific plan. Mobile phones have proven to be a valuable tool in scheduling health providers. In Tanzania, a m-health application was tested, sending SMS reminders to community health workers of their appointments, while further reminders and notification calls from supervisors were delivered in cases of missed appointments [133]. This method was successful in enhancing commitment to their work and reducing delays in home visits. Positive outcomes seemed to justify the costs of implementing and sustaining this application, but further research is necessary to determine whether this solution is financially sustainable [133]. Moreover, utilization of a mobile phone application in Thailand, through which health providers registered Malaria patients during their first treatment and generated a follow-up schedule, resulted in increased follow-up rates and time efficiency of patient data collection, showing promise in improving malaria management [134]. Concerns arise though involving the completeness, reliability and timeliness of the collected data in cases of hard-to-reach groups [134].

Applications incorporating multiple m-health components have also been developed aiming at assisting healthcare providers. An m-health system was piloted at a hospital in Malawi, including various functionalities such as sending appointment reminders to health workers, adherence reporting, query submission to physicians, requests for medication and drug dosage estimation [135]. Several benefits were observed by utilizing this application, such as reduced workload among health workers, increased operational capacity of the hospital, as well as financial gains. Another complex m-health practice was developed and trialed in rural India, in order to support maternal and neonatal services delivered by Accredited Social Health Activists (ASHA), by integrating work scheduling, behavior change intervention, data collection and reporting, decision support and communication with supervisors into a single application (ImTeCHO) [136]. Implementation of this system proved to be feasible and accepted. Combining various m-health complementary interventions shows great potential for improving the performance of health workers, and therefore the performance of the healthcare system in the developing world.

TABLE IX
SUMMARY OF RANDOMIZED CONTROL TRIALS INCLUDED IN THE PRESENT STUDY FOR HEALTH WORKERS SUPPORT (CATEGORY E: HEALTH WORKER EDUCATION, CONSULTATION AND WORK PLANNING). IG AND CG DENOTE INTERVENTION GROUP AND CONTROL GROUP, RESPECTIVELY

Study/Location	M-health delivery system and purpose	Participants/ Intervention Duration	Intervention Description	Primary Outcomes
D. Zurovac et al, 2011 [126]. Kenya.	Text messages to improve the skills of health workers in Malaria management.	**n=119** health workers and **n= 2,269** children and in need for malaria treatment; IG: n=1157 children; CG: n=1112 children. Duration: 6 months.	IG health workers received 2 text messages with guidelines for malaria treatment and assessed the IG children.	Correct management of malaria cases at the end of the intervention period: Improvement of 23.7 % points in the IG compared to the CG. Correct management of malaria cases 6 months after the end of the intervention period: Improvement of 24.5 % points in the IG compared to the CG. (See [126] for more information on the used measures for correct management).
CG Gill et al, 2016 [129]. Vietnam.	Text messages to improve medical knowledge of community health workers.	**n=638** community health workers; IG1: n=214; IG2: n=212; CG: n=212. Duration: 6 months.	IG1 received a daily educative SMS and replied to confirm receipt; IG2 received a daily SMS including a multiple choice quiz; CG received a random SMS once a week with no response required;	Health related knowledge based on exams performed after the end of the intervention period: No changes were observed among the 3 groups. Time spent by the health workers on studying and use of related knowledge material: No changes were observed among the 3 groups.

V. DISCUSSION

The large number of studies evaluating the potential of mobile technologies to improve health in low resource settings reflects the wide interest of the scientific community and industry in m-health. The sample of 98 studies included in the present review paper demonstrated a large variety of m-health deployment and a wide range of results. The positive results reported outnumber the negative or moderate ones, indicating that the health care system in the developing world may benefit from proper utilization of m-health. However, robust and statistically significant conclusions cannot be drawn, given that in the majority of cases evaluation was conducted through pilot and/or small scale trials, and a limited number of studies assessed long term effects. All those experiments have provided valuable information on the advantages, disadvantages and challenges involving m-health, which is essential in order to determine future research directions.

Results have been reported from a wide variety of countries (Table II). The majority of the studies have been conducted in Africa, suggesting that this continent has received the most of attention for experimenting with m-health. Second is Asia, where a focus on India is observed, while the least of the research according to our sample has been undertaken in Latin America.

The "citizen education and behavior change communication" is the most investigated category, represented by 32 articles. Several means such as SMS messages, IVR calls, or direct calls from physicians have been utilized to induce health-related behavior changes to the citizens. The vast majority of the m-health applications under study used SMS messages, which present significant advantages due to their low cost. Although the outcomes were mixed, such interventions seemed to be effective in motivating patients suffering from chronic diseases to adhere to their treatment and appointments, in supporting healthy lifestyle (e.g nutrition, safe sexual practice), as well as in promoting uptake of proper health services (e.g. HCT, antenatal care, vaccination).

Efficient and timely data collection and management is crucial for the health care system to function properly. Mobile communications have demonstrated several benefits in this domain, such as enhanced disease surveillance, efficient patient data collection and processing leading to improved patient monitoring and follow-up, reduction in turn-around-time involving laboratory examinations, better performance of clinical research, improved supply chain management of medical products, as well as increased efficiency in administration and logistics procedures involving bone marrow transplantation and blood transfusion. Such positive signs encourage future efforts to supplement, or replace traditional paper based methods for data collection with novel m-health tools.

Advances in sensors technologies have enabled the development of low cost diagnostic tools that demonstrate great potential in providing point-of-care diagnostic tests, such as tuberculosis testing, ultrasound imaging, hearing screening,

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ECG examination, and routine health check-ups to remote populations with limited access to health facilities. Wireless capabilities supported by such systems can also offer real time transmission of patient data, increasing significantly the efficiency of diagnostic procedures. Capturing and transmitting smartphone pictures to remote physicians, has shown promise for diagnosing dermatological conditions and cervical cancer, but this method is still at a very early stage.

Smartphone based clinical decision support systems and interactive guidelines that break complicated diagnostic procedures down to simple and small steps have proven to be a valuable tool in supporting lesser trained front line health workers to assess patients.

Finally, given the significance of services provided by health workers in improving the availability and quality of health services in rural areas, m-health has been utilized to train them and aid with their work. Applications providing access to health related information, mobile phone interventions with educational context, communication with higher level health providers, software tools scheduling their work, or combinations of the above have demonstrated to be effective in improving the performance of health workers.

VI. Challenges and Opportunities

Based on the analysis performed so far for each different category considered, it is evident that m-health technologies seem to have the potential to improve the public health situation in developing countries. However, there are still various hurdles that need to be overcome and many challenges that have to be addressed towards adopting m-health projects. In general, implementing m-health strategies can be quite complicated given the target group and the location. It is of major importance to take into account factors such as cultural, socioeconomic and educational characteristics of the various vulnerable groups when implementing m-health strategies. In the case of "citizen education and behavior change communication", the effectiveness of m-health can vary significantly with respect to the condition of the patient (e.g. hypertension, diabetes, HIV), while some behaviors (e.g. uptake of physical exercise) may be more difficult to change and may require more robust kinds of interventions. Moreover, confidentiality issues were present in cases of delivering reminders to HIV and Tuberculosis patients. Another concern involving such interventions is the fact that very low income groups might not be able to have Internet connectivity or afford a mobile phone with Internet services, and using it as a means to provide health information might intensify the gaps in knowledge due to economic status [56]. In cases of applications aiming at shifting tasks to lesser trained health workers, or establishing new patterns of communication and organization among health staff, it is essential to consider the educational background and skills of health workers, existing resources, healthcare infrastructure and organization systems, as well as the willingness of medical staff accept m-health and allow its utilization for enhancing the healthcare system.

The GOe, based on its third global survey, made an analysis on barriers and the degree in which they hinder m-health implementations (Fig. 10) [23]. Insufficient funding was reported by the majority of the 125 participating WHO member states (71%) as an extremely significant barrier, followed by lack of legal policies and procedures involving m-health programs (51%), lack of prioritizing m-health policies (51%) and insufficient evidence of cost efficiency. Such barriers are even more important in developing countries, given that m-health strategies, though potentially cost effective in the long term, would entail increased costs during the implementation which could be prohibitive due to the lack of financial resources, the prioritization of other needs and the uncertainty on the financial sustainability [23].

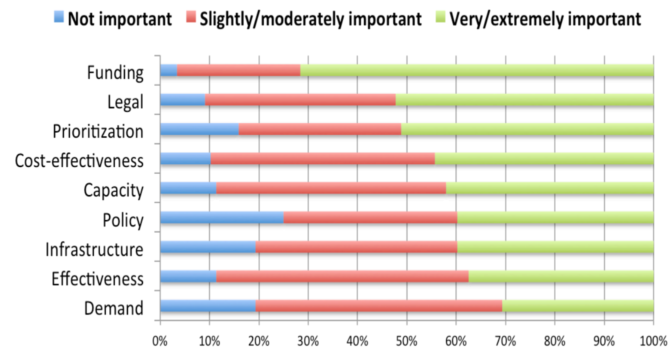

Fig. 10: Significance of barriers hindering the implementation and proper function of m-health strategies based on the GOe's third global survey [23].

The reviewed studies revealed some important open issues that have to be considered in the future towards designing more effective m-health solutions. As reported in several studies, the private sector can substantially contribute to the successful implementation and sustainability of m-health interventions by forming partnerships with and financially supporting the public sector (e.g. reduction of costs for delivering SMSs and mobile phone calls through partnerships with communication companies [51]). Furthermore, several programs have been developed aiming at supporting the economy and the health care system in developing countries, as well as promote technological innovation among vulnerable populations, which could bridge the technology gap between low- and high- income countries and essentially enhance the establishment of m-health ([137], [138], [139], [140]). Also, governments, and in particular national health authorities, can play a significant role towards implementing and improving such strategies by advertising and promoting the integration of m-health in the healthcare system, advancing m-health standards and interoperability, offering guidance regarding privacy and security matters, supervising and supporting data ownership [23]. Finally, since mobile technologies constitute an ever-expanding research area, new tools and applications will emerge that may assist users in their daily lives [141]. Significant research should be conducted on issues related to behavioral theories and particular attention should be given on how such theories can be exploited to achieve improvements in self-care and help the design of optimal m-health strategies at both personal and community level [142], [143].

VII. Conclusion

In conclusion, this review of m-health in developing countries has provided a summary of the evidence involving its effectiveness. Robust and statistically significant conclusions cannot be drawn, given that in the majority of cases evaluation was conducted through pilot and/or small scale trials, and a limited number of studies assessed long term effects. However, many positive signs have been identified towards the utilization of m-health for improving the health care system. The contribution of SMS messages towards supporting healthy lifestyle and promoting uptake of health services has been highlighted. Advances in sensors technologies, decision support systems and data collection have shown promise for replacing traditional methods with novel m-health tools that may favor clinical practice. Apart from the population of developing countries, healthcare workers have been shown to benefit from such technologies, having more opportunities to improve their performance. Even though the benefits of m-health interventions are subject of debate and require further investigation, this paper provides essential elements needed for the design and deployment of m-health strategies, which is essential to orient relevant future research and enhance its impact.

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