J. of Cardiovasc. Trans. Res. (2014) 7:677–691
DOI 10.1007/s12265-014-9581-5

Use of mHealth Systems and Tools for Non-Communicable Diseases in Low- and Middle-Income Countries: a Systematic Review

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Received: 1 June 2014 / Accepted: 27 July 2014 / Published online: 11 September 2014

Abstract With the rapid adoption of mobile devices, mobile health (mHealth) offers the potential to transform health care delivery, especially in the world's poorest regions. We systematically reviewed the literature to determine the impact of mHealth interventions on health care quality for non-communicable diseases in low- and middle-income countries and to identify knowledge gaps in this rapidly evolving field. Overall, we found few high-quality studies. Most studies narrowly focused on text messaging systems for patient behavior change, and few studies examined the health systems strengthening aspects of mHealth. There were limited literature reporting clinical effectiveness, costs, and patient acceptability, and none reporting equity and safety issues. Despite the bold promise of mHealth to improve health care, much remains unknown about whether and how this will be fulfilled. Encouragingly, we identified some registered clinical trial protocols of large-scale, multidimensional mHealth interventions, suggesting that the current limited evidence base will expand in coming years.

Keywords mHealth · Mobile health · Non-communicable diseases · Low and middle income countries · Evidence · Quality · Evaluation

Abbreviations

NCD	Non-communicable diseases
LMIC	Low- and middle-income countries
CVD	Cardiovascular disease
UN	United Nations
WHO-PEN	World Health Organization Package of Essential NCD interventions
PHC	Primary health care
mHealth	Mobile health
EMBASE	Excerpta Medica database
CINAHL	Cumulative Index to Nursing and Allied Health Literature
LILACS	Latin American and Caribbean Health Science Literature Database
WHO	World Health Organization
RCT	Randomized controlled trial

Introduction

The rising disease burden from non-communicable diseases (NCDs), particularly in low- and middle-income countries (LMICs), constitutes a major threat to the health and well-being of communities worldwide. The "big four NCDs" (cardiovascular disease (CVD), diabetes, cancer, respiratory disease) account for 87 % of all NCD deaths and 54 % of NCD disability adjusted life years [1]. The United Nations (UN) high-level meeting on NCDs in 2011 demonstrated a historic commitment to NCD control, and in 2012, the World Health Assembly set in its 2013–2020 Global Action Plan a voluntary target of 25 % relative reduction in mortality due to NCDs by 2025 ("25×25 target") [2]. Recent modeling

Associate Editor Daniel P. Judge oversaw the review of this article

Electronic supplementary material The online version of this article (doi:10.1007/s12265-014-9581-5) contains supplementary material, which is available to authorized users.

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suggests that a 25 % reduction in the prevalence of six NCD risk factors alone (tobacco, alcohol, salt, blood pressure, obesity, and glucose) could almost achieve the 25×25 target [3].

Although public health interventions will play a critical role in meeting this target, improved access to appropriate health care will also make a major contribution [4]. The World Health Organization Package of Essential NCD interventions (WHO-PEN) is a systems-oriented framework to tackling NCDs in low-resource primary health care settings [5]. It outlines (1) a conceptual framework for improving PHC equity and efficiency; (2) identification of core technologies, essential medicines, and risk prediction tools; (3) evidence-based protocols for implementation of a set of essential cost-effective NCD interventions; and (4) a technical and operational outline for integration into PHC and for monitoring and evaluation purposes [5]. Despite the potential for comprehensive primary health care (PHC) to deliver reductions in NCD burden, spiraling costs both to system planners and to consumers themselves is making health systems unsustainable to meet the growing NCD burden. Innovative strategies to implementing WHO-PEN are urgently needed in order to meet the 25×25 target.

Such strategies cannot merely duplicate the paths taken to improve health care quality in high-income countries, which are beset by rising costs, variation in care, and low uptake of evidence-based practices. LMICs are looking to "leap frog" some of the dilemmas experienced by high-income countries through novel health care delivery models that leverage low-cost, innovative technologies [6]. Just as mobile phones overcame barriers to communication caused by limited fixed line access, these technologies are now being applied to assist in health care delivery where access to traditional health care services is limited. mHealth is a multidimensional field encompassing a wide variety of tools, technologies, and models of health care delivery. Despite the bold promise of mHealth to be transformational, delivering high-quality care at a fraction of the cost incurred in high-income countries, there is a paucity of evidence to substantiate such a claim. mHealth is accused of being afflicted with "pilotitis" [7], in which piecemeal seed projects have been conducted with a lack of attention to scalability, poor integration into health care systems, sparse robust studies demonstrating effectiveness, and few evaluations of costs and benefits [8, 9].

Most reviews into the effectiveness of mHealth interventions have been dominated by studies conducted in high-income country settings. Although the number of studies included in these reviews have been few in number, improvements have been observed in health care service delivery processes [10], behavior change (particularly smoking cessation) [10, 11], and use of geographic information systems to support improved health care [12]. In LMIC settings, the mHealth literature is dominated by interventions in maternal and child health and sexual health, with a particular focus on use of mobile phones for data collection [13–15]. Braun et al. identified 25 studies exploring community health workers' use of mobile technology [14]. Most studies were small scale and of the few that reported outcome evaluations, some demonstrated improvements in quality of care. Goel et al. conducted a narrative synthesis of 28 studies to examine the role of mHealth in bridging human resource gaps [15]. The authors found mHealth to be widely used in PHC settings for varying purposes including data collection, health surveillance, health education, supervision, and monitoring. Despite the breadth of use, there were little data on the impact of these interventions. Only one review has specifically looked at mHealth and NCDs in LMICs, and this focused only on the use of text and automated voice interventions [16]. Of the nine controlled studies analyzed, there were significant improvements in clinical outcomes (e.g., glycemic control for diabetics, lung function for asthmatics, and heart failure symptoms) and processes of care (e.g., attendance rates for follow-up appointments), and a limited number of studies showed improvements in costs and quality of life measures.

Although these reviews have looked at specific components of mobile health interventions, they have not examined the full breadth of mobile interventions as health care system strengthening tools. In this review, we take a systems-oriented approach to critically appraising the role of mHealth in improving health care quality for NCDs in LMICs. Specific aims are to the following: (1) characterize the spectrum of mobile health interventions that have been used for NCD management and prevention in LMICs, (2) evaluate the impact of mobile health interventions on health care quality, and (3) identify gaps in knowledge around mHealth research that need to be addressed.

Methods

Database Search

A systematic search of the literature was performed current to May 2014 using the following electronic databases: PubMed, PsychInfo, EMBASE, CINAHL, Cochrane, and the Latin American and Caribbean Health Science Literature Database (LILACS). A gray literature search was also conducted examining articles and websites from relevant organizations including WHO, International Telecommunications Union, the m-Health Alliance (mhealthalliance.org), HealthUnbound (healthunbound.org), mHealthKnowledge (mhealthknowledge.org), Global mHealth Initiative (jhumhealth.org), and Google and Google Scholar searches. We also searched for registered trial protocols in the WHO International Clinical Trials Registry Platform which includes 15 approved trial registries and supplementary searches in Clinicaltrials.gov. Keywords used in these

searches included the following: cellular phone, mobile phone, telecommunication, mHealth, telehealth, telemedicine, patient education, point of care system, medical registries, electronic health records, clinical decision support system, data collection, provider-provider communication, provider scheduling, provider training, human resource management, supply chain management, financial transactions, primary prevention, secondary prevention, developing countries, underserved areas, and all of the LMIC names. Details of the search can be found in supplementary Tables S1, S2, S3, S4, S5, S6, and S7.

Inclusion/Exclusion Criteria

We included articles on any mobile technology health care interventions used in LMICs that were relevant to NCD management and prevention. LMICs were defined based on World Bank criteria [17]. NCDs included CVD, respiratory disease, cancer, diabetes ("the big four"), and mental health. Articles were included if they were (1) randomized controlled trials (RCTs), (2) quasi-experimental empirical studies with or without a comparator group, (3) descriptive studies without any outcome measures reported, (4) reviews of mHealth interventions (systematic or non-systematic), or (5) registered RCT protocols. There was no language exclusion to the articles retrieved. Telehealth, telemonitoring, and telephone coaching studies were only included if they explicitly drew on mobile technologies as part of the overall intervention strategy. If these interventions were delivered via a standard fixed phone line or via the internet using a desktop computer, they were excluded.

Classification Framework

The mHealth interventions used in each study were characterized using a framework proposed by Labrique et al. in an analysis of maternal and child health mHealth interventions (Table 1) [18]. A key strength of this framework is its focus on health systems rather than specific technologies. The framework was developed in consultation with mHealth stakeholders including academics and program and policy implementers. It was then applied to illustrate where mHealth opportunities and health system constraints lie across a continuum of care for maternal and child health. It is useful in determining who might be the beneficiary targets of particular mHealth strategies and making explicit the particular health system barriers that are being targeted.

Outcome measures were assessed according to the WHO dimensions of quality of care (Table 2) [19]. These domains serve as building blocks for identifying tools and strategies for quality improvement at the level of policy makers, service providers, and consumers across whole health systems. Assessing outcomes in these particular domains allowed us to identify where the gaps were in the evidence base for mHealth interventions across the whole health system.

Data Extraction

Two reviewers independently evaluated and excluded articles at the title/abstract review stage. Full-text articles whose abstracts met the inclusion criteria were then reviewed. An Excel template was developed which outlined study characteristics, the mHealth domains, and WHO quality outcome domains. The reviewers performed test data extractions using this template to check for any inconsistency in interpretation of definitions, and the extraction template was refined following this. If the article met the final inclusion criteria, reviewers populated the data extraction template. For the RCTs, methodological quality was assessed using the Cochrane Risk of Bias Assessment Tool. Discrepancies in article inclusion, data extraction, and bias assessment were solved by team consensus.

Results

We retrieved 1,569 articles using the search terms, and 177 articles were selected for full-text review (Fig. 1). Of these, 129 articles were excluded for the following reasons: not specifically using mobile technology, in particular internet and fixed line telemedicine interventions (n=86); not pertaining to LMICs (n=29); not relevant to NCDs (n=12) and study protocols (n=2) (see supplementary Table S8 for more details on excluded studies).

The 24 included non-protocol studies, their characteristics and the mHealth domains are summarized in Table 3. The majority of studies came from middle-income country settings with a mixture of urban- and rural-based studies. The most common disease areas were either diabetes (n=8) [20–27] or CVD and risk factors for CVD (n=9) [22, 28–35]. Thirteen studies tested specific mHealth interventions, but only seven used a RCT design [23, 25, 26, 33, 36–38], with the remainder using quasi-experimental designs to assess outcomes [24, 27, 28, 34, 39, 40]. Six exploratory studies were identified which described, validated, or pilot-tested various mHealth interventions but did not provide any substantive outcome data [29–32, 35–41]. Five reviews were also identified [16, 20–22, 42], of which two systematically appraised the literature [16, 21].

Of the intervention and exploratory studies (n=19), the following mHealth domains were identified: client education and behavior communication (n=13) [23–27, 33, 34, 36–41], sensors and diagnostics (n=5) [28–30, 32, 35], registries (n=1) [34], data collection (n=3) [28, 29, 34], electronic health records (n=1) [28], decision support (n=1) [31],

Table 1 Common mHealth applications

	Domain	Description/Examples
1	Client education and behavior change communication	Consumer-directed strategies to improve knowledge, attitudes, motivations, and health-seeking actions
2	Sensors and point-of-care diagnostics	Technologies that can store and forward biometric data via a mobile device
3	Registries and vital events tracking	Facilities that enable identification and enumeration of populations for specific services or programs (e.g., pregnancy and birth registration)
4	Data collection and reporting	Integration of field-based data collection to aggregated data repositories for monitoring and evaluation purposes
5	Electronic health records	Shared record systems that support multiple users and multiple sites interacting with patient data
6	Electronic decision support	Protocols, algorithms, and checklists to support adherence to a particular standard of health care
7	Provider-provider communication	Communication via voice, SMS, and cloud-based systems to support patient care from multiple providers
8	Provider work-planning and scheduling	Reminders, alerts, and prompts to assist health workers in the prioritization of workflow tasks
9	Provider training and education	Workforce professional development activities assisted through use of mobile platforms
10	Human resource management	Employees' dashboards to identify, support, and monitor workforce activity
11	Supply chain management	Tools to track and manage stocks and supplies of essential commodities such as medications
12	Financial transactions and incentives	Tools to assist in payment for services and supplies. Also includes incentive and insurance schemes and stock payment systems

Source: Labrique et al. [18]

provider communication (n=3) [28, 29, 34], provider work-planning (n=5) [28, 36–38, 40], and supply chain management (n=1) [28]. There were no studies pertaining to provider training and education, human resource management, or financial transactions and incentives. Most studies tested only one or two mHealth domains (n=16) with only three studies using multifaceted interventions involving three or more domains [28, 29, 34].

Table 2 WHO quality outcome dimensions

Quality dimension	Definition
Effective	Delivering health care that is adherent to an evidence base and results in improved health outcomes for individuals and communities, based on need
Efficient	Delivering health care in a manner which maximizes resource use and avoids waste
Accessible	Delivering health care that is timely, geographically reasonable, and provided in a setting where skills and resources are appropriate to medical need
Acceptable/patient-centered	Delivering health care which takes into account the preferences and aspirations of individual service users and the cultures of their communities
Equitable	Delivering health care which does not vary in quality because of personal characteristics such as gender, race, ethnicity, geographical location, or socioeconomic status
Safe	Delivering health care which minimizes risks and harm to service users

Source: WHO [19]

The outcomes of the 13 studies that did test particular interventions are shown in Table 4. Six studies reported effectiveness of the intervention for clinical outcomes (n=6) [23–26, 33, 34], and three reported improvements in processes of care, particularly improved knowledge, attitudes, and behaviors such as medication adherence (n=3) [23, 36, 39]. Three studies addressed costs [26, 33, 37], with one study reporting improvements in health-related quality of life [33]. Four studies reported improvements in clinical attendance rates [28, 36–38], and four studies reported various self-reported metrics related to acceptability of the intervention [24, 25, 27, 36]. No studies reported outcomes related to equity or safety, and similarly, no studies reported any qualitative or process evaluations of the interventions. For the RCTs, the majority of the risk of bias criteria was classified as either low or unclear (Fig. 2).

The search of registered clinical trial protocols identified 24 additional mHealth RCT protocols for NCD prevention in LMICs (Table 5). Although eight of these studies were listed as being complete, we were unable to find published results for any of these. As with the published RCTs, the majority of studies focused on client education strategies using SMS systems (Table 5).

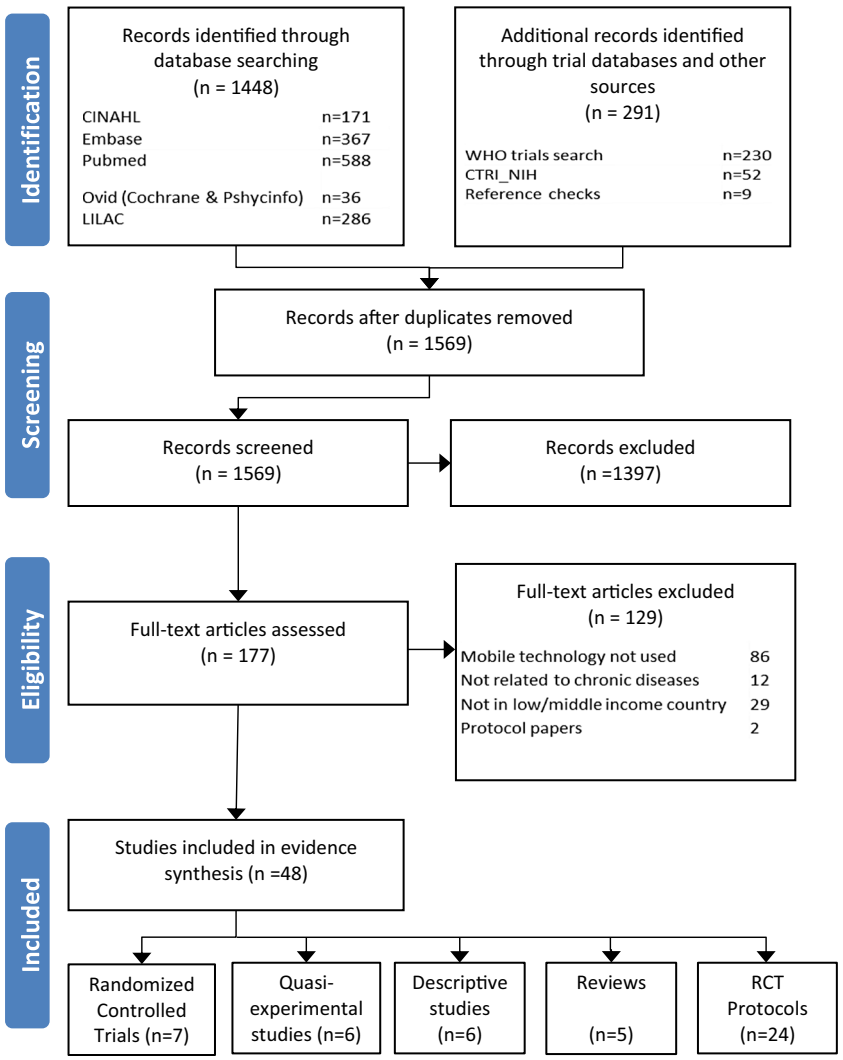

Fig. 1 Included/excluded studies

Discussion

In this review, we examined the ability of mHealth interventions to improve health care quality in LMIC settings for NCD management and prevention. Specifically, we sought to identify which mHealth components have been associated with the greatest impact on health care quality dimensions. We build on previous reviews by updating searches in a rapidly evolving field, but more importantly, we examine how mHealth has been used to strengthen health care systems to address the growing NCD burden.

A number of key findings were observed from this review. The first and most important is that mHealth for NCD management remains a relatively under-explored area. The literature is characterized by a limited number of high-quality studies, mainly conducted in middle-income country settings and mainly focused on two NCDs—CVD and diabetes. Despite mHealth having a wide variety of applications, studies so far are dominated by behavior change interventions through use of text messaging systems. Few studies have applied mHealth tools as a means of strengthening health systems. Although the studies that have reported effectiveness are encouraging, few have examined outcomes across multiple dimensions of health care quality, and none have looked at equity and safety issues. Related to this, there is a dearth of process evaluations to understand the contextual factors that promote or hinder effectiveness of the interventions. Consequently, there remains a major gap in our understanding of the factors that may influence scalability, replication of outcomes in different settings, and sustainability of outcomes beyond controlled trial settings.

The paucity of literature suggests that mHealth for NCD management is still at an early stage of development. There are, however, several relevant registered studies, all of which are RCTs, which are actively recruiting. This suggests that the evidence base will grow substantially in the coming years. These registered studies generally have larger sample sizes, longer follow-up periods, and are using designs such as cluster and stepped-wedge cluster RCTs which are more conducive to understanding health system impacts. Unfortunately, most of

Table 3 Included studies

Author	Country	Setting	NCD area	Population	Follow-up	Intervention	mHealth domain
Descriptive studies							
Campos Neto 2008 [29]	Brazil	Rural	CVD	Rural and remote patients in Brazil requiring ECG	NA	Tele-ECG transmitted via cellular network with remote physician review	Sensors and POC diagnostics, data collection, provider-provider communication
Eren 2008 [31]	Turkey	Rural	CVD DM	Not described	NA	Mobile decision support tool using a mobile telecommunications platform	Decision support
Yu 2013 [35]	China	Not stated	CVD, Others	*n*=11 health volunteers	NA	Health examination tool kit (M-HELP) involving sensors and upload of data into an Android phone	Sensors and point-of-care diagnostics
Choi 2011 [30]	Honduras	Rural	CVD	*n*=89 patients with clinical indications for echocardiography	NA	Mobile upload of echocardiography images for remote review on a Smartphone	Sensors and point-of-care diagnostics
Garcia 2012 [32]	India	Rural	CVD	Not described	NA	Handheld ultrasonography for echocardiogram assessment	Sensors and point-of-care diagnostics
Hung 2007 [41]	China	Not stated	RD	Not described	NA	COPD endurance training delivered via a mobile phone	Client education
Quasi-experimental studies							
Agrawal 2013 [28]	India	Rural	CVD, others	*N*=3,677 general village patients Chausala	NA	Transportable e-health center with EMR and telemedicine consults via mobile network	Sensors and point-of-care diagnostics, electronic health records, provider-provider communication, provider work planning and scheduling, supply chain management
Lua 2012 [40]	Malaysia	Urban/Rural	Neuro	*N*=51 patients with epilepsy, ≥18 years of age	3-month	follow-up	Mobile epilepsy educational system (MEES)
Client education, provider work planning and scheduling							
Kingue 2013 [34]	Cameroon	Rural	CVD	*N*=268 adult subjects (or individuals aged 15 years and above) with hypertension not at target level (SBP (or DBP) ≥140 (90) mmHg or ≥130 (80) mmHg (for those with diabetes or nephropathy)	6-month	duration	Multifaceted telecare intervention (TELEMED-CAM) comprising training, protocol based treatment, and telemedicine support using SMS or voice mail and, immediate physician feedback from a central location
Client education, registries/vital events tracking, data collection, provider-provider communication							
Piette 2011 [24]	Honduras	Rural	DM	*n*=85 diabetes patients	6-week	duration	Cloud-based interactive voice response disease management calls and automated email to clinicians
Client education							
Khokhar 2009 [39]	India	Urban	CA	*n*=106 female volunteer employees in one	6-month	duration	SMS reminder system to conduct breast self-examination

Table 3 (continued)

Author	Country	Setting	NCD area	Population	Follow-up	Intervention	mHealth domain
				workplace aged >20 years			
Client education							
Kulnawan 2011 [27]	Thailand	Not stated	DM	*n*=112 DM patients; >20 years of age; HbA1C >7 %	5-week	duration	Telephone-linked care system for diabetes self-management using an interactive voice response system
Client education							
		Randomized controlled trials					
Lua 2013 [36]	Malaysia	Urban/Rural	Neuro	*n*=144 patients with epilepsy, ≥18 years of age	3-month	follow-up	Brief, frequent SMS to patients for epilepsy education
Client education, provider work planning and scheduling							
Goodarzi 2012 [23]	Iran	Not stated	DM	*n*=81 patients with diabetes ≥30 years	12-week	follow-up	Educational program via SMS for self-management
Client education							
Grancelli 2007 [33]	Argentina	Urban/Rural	CVD	*n*=1,518 stable chronic heart failure patients, aged ≥18 years	Mean	follow-up of 16 months (range 7–27 months)	Two-week nurse telephone intervention and cardiologist support to promote education, disease monitoring and treatment adherence
Client education							
Liew 2009 [38]	Malaysia	Urban	Multiple diseases	*n*=931 patients with at least one chronic disease	NA	SMS appointment reminders to visit the health center	Client education, provider work planning and scheduling
Leong 2006 [37]	Malaysia	Not stated	Multiple diseases	*n*=993 patients who required follow-up at the clinics between 48 h and 3 months from the recruitment date	NA	SMS reminders 24–48 h prior to scheduled appointments	Client education, provider work planning and scheduling
Wong 2013 [26]	China	Not stated	DM	*n*=104 Chinese professional drivers with pre-diabetes (FPG level of 5.6–6.9 mmol/L or a 2HPPG of 7.8–11.0 mmol/L after a 75-g glucose load)	24-month	follow-up	SMS intervention to prevent patients with pre-diabetes developing diabetes
Client education							
Shetty 2011 [25]	India	Not stated	DM	*n*=215 type 2 diabetic patients with five or more years of diabetes and having HbA1c between 7.0 and 10 %	12-month	follow-up	SMS to promote medication adherence
Client education							
Reviews							
Mohammadzadeh 2013 [42]	Iran	Not stated	CA	NA	NA	Cancer care management through a mobile phone health approach: key considerations	Electronic health record, human resource management
Ajay 2011 [20]	India	Urban/Rural	DM	NA	NA	Use of mobile phones for diabetes management in LMICs	Client education, registries/vital events tracking, data collection, electronic health records, electronic decision support system, provider-provider

Table 3 (continued)

Author	Country	Setting	NCD area	Population	Follow-up	Intervention	mHealth domain
							communication, provider training and education
Feder 2010 [22]	Mexico	Not stated	CVD, DM, HIV	NA	NA	Use of mobile phones for health care in LMICs	Client education
Ali 2011 [21]	Multiple LMICs	Urban/Rural	DM	NA	NA	Systematic review of use of electronic decision support tools for diabetes care in LMICs	Decision support
Beratarrechea 2014 [16]	Multiple LMICs	Urban/Rural	Multiple diseases	NA	NA	Systematic review of use of SMS interventions for NCDs in LMICs	Client education, data collection, electronic decision support system, provider-provider communication, provider work planning and scheduling

NA not applicable

these newer interventions remain narrowly focused on behavior change using text messaging systems. However, there are some notable exceptions which are taking a systems-oriented approach using mHealth domains such as decision support, electronic health records, and workforce-oriented strategies such as provider-provider communication. Several completed studies have not published results which raises concerns about publication bias. For high-income countries, the mHealth research landscape is certainly changing. In 2012, Labrique and colleagues identified 215 mHealth intervention studies registered in clinicatrials.gov with 176 involving an RCT design [7]. Publications arising from these trials will result in major shifts in the quantity and quality of research evidence becoming available and may cure mHealth of its chronic “pilotitis.” Although this will be useful, it may take up to a decade before there is more clarity on the role of mHealth in strengthening health systems in LMIC settings.

Limitations

There are a number of limitations to this review. Although the classification framework we used was very useful, many studies lacked sufficient detail to characterize them in finer detail. For example, there may be considerable variation in the design and delivery of SMS behavior change interventions, and hence, it is difficult to appreciate differences between interventions within any particular mHealth domain. Similarly, we had limited ability to analyze specific technical approaches used and were unable to make conclusions regarding the similarities and difference between platforms used. This is important because there is a clear need for standardized and approved architectures for mHealth tools. Recent US Food and Drug Administration guidance on regulatory requirements may facilitate this [43]. Another limitation was that owing to the paucity and heterogeneity of RCTs in the review, we were unable to conduct a quantitative meta-analysis of the outcomes. This may be addressed in coming years as more trial results in this field are published. Although we examined the leading contributors to NCD mortality, we did not examine other NCD areas such as musculoskeletal conditions which are a major contributor to disability. It is important that research on both disease-specific and non-disease primary health care strategies are conducted to enable a more nuanced understanding of both the disease management and systemic challenges that mHealth may be able to address.

Conclusion

On balance, despite the promising findings demonstrated by some mHealth interventions in this review, we

Table 4 Outcome measures by WHO quality domains (intervention studies)

Author	Effectiveness	Efficiency	Accessibility	Acceptability/patient centeredness
Quasi-experimental studies				
Agrawal 2013 [28]	Not reported	Not reported	~50 % of village accessed in 5 months	Not reported
Lua 2012 [40]	Not reported	Not reported	Not reported	50 % found intervention very useful, 24.0 % quite useful, 18.0 % useful, 8.0 % of "little use." 88.2 % would recommend intervention to other patients
Kingue2013 [34]	10.1 % absolute improvement in target BP attainment in HTN stage III patients	Not reported	Not reported	Not reported
Piette 2011 [24]	1.1 % reduction in HBA1C (10.0 vs 8.9 %)	Not reported	Not reported	55 % completed majority of IVR tasks. 33 % completed 80 % of more of tasks. 89 % reported better foot care as a result of the program. 56 % reported better glycemic management. 92 % would use the service again.
Khokhar 2009 [39]	32 % increase in self-reported breast self-examination from month 1 to month 6 (42 % at month 1, 72 % at month 6)	Not reported	Not reported	Not reported
Kulnawan 2011 [27]	Not reported	Not reported	Not reported	72 % responders completed responses to the TLC. 89.4 % of 95 responders reported satisfaction.
Randomized controlled trials				
Lua 2013 [36]	Adjusted mean difference between intervention and control at follow-up—awareness 2.3 (95 % CI 1.2–3.3, $p<0.01$); knowledge: 0.7 (95 % CI 0.1–1.5, $p=0.07$); attitudes 0.4 (95 % CI 0.3–1.1, $p=0.276$); total AKA 1 (95 % CI 0.4–1.7, $p=0.003$); medication adherence 0.1 (95 % CI 0.1–0.2, $p=0.591$).	Not reported	Clinic attendance increased by 27 % ($p<0.05$)	Not reported
Goodarzi 2012 [23]	Mean change in knowledge of 53.95 (7.97 pre-test to 10.83 after 3 months, $p<0.001$), and practice of 38.57 (3.72 pre-test to 4.93 after 3 months, $p<0.001$) for the exposure group and percentage change in self-efficacy with a mean change of 13.19 (15.34 pre-test to 17.02 after 3 months, $p<0.001$). Significant change in HbA1C ($p=0.024$), LDL ($p=0.19$), cholesterol ($p=0.002$), BUN ($p\leq 0/001$), micro-albumin ($p<0.001$) for the exp. group	Not reported	Not reported	Not reported
Grancelli 2007 [33]	20 % relative risk reduction in the primary endpoint of overall death or hospitalization for heart failure compared with the control group (95 % CI 3–34, $p=0.026$). 29 % relative risk reduction in	Cost-benefit analysis. Lower average cost per patient ($3,005.99 vs. 2,795.19; $p=0.05$) generated savings of $210.80 per surgical patient. Patients assigned to the program had a better quality of life than patients in the control group, with a mean	Not reported	

Table 4 (continued)

Author	Effectiveness	Efficiency	Accessibility	Acceptability/patient centeredness
	hospitalizations for heart failure (95 % CI 9–44, p=0.005)	difference of 4.4 (95 % CI 1.8–6.9, p=0.001) (score of 30.6 in the intervention group vs 35.0 in the control group)		
Liew 2009 [38]	Not reported	Not reported	The differences in non-attendance rates between telephone and control groups (9.3 %, p=0.003) and between text messaging and control groups (7.4 %, p=0.020)	Not reported
Leong 2006 [37]	Not reported	The cost-effectiveness analysis showed that it cost RM 0.45 per attendance for text messaging reminder as compared with RM 0.82 per attendance for mobile phone reminder. The ratio of cost per unit attendance of text messaging versus mobile phone was 0.55.	Attendance to clinics: text messaging versus control—59.0 versus 48.1 % (p=0.005, OR 1.59 (1.17–2.17), NNT 9 (6–25)); mobile phone versus control—59.6 versus 48.1 % (p=0.003, OR 1.55 (1.14–2.11), NNT 9 (6–32)); text messaging versus mobile phone—59.0 versus 59.6 % (p=0.874, OR 0.98 (0.72–1.33), NNT (not applicable))	Not reported
Wong 2013 [26]	At the 24-month follow-up, T2DM was diagnosed in six (out of 54) in the intervention group and nine (out of 50) in the control group. The RR for T2DM onset was 0.35 (95 % CI 0.10–1.24) at 12-month and 0.62 (95 % CI 0.24–1.61) at 24-month assessments, while the NNT for preventing one case of T2DM at 12 month was 9.6 and at 24 month was 10.6.	Low monetary cost with a budget of HK$39.60=US$5.08 per subject	Not reported	Not reported
Shetty 2011 [25]	At the end of 1 year, the mean FPG (185+57 mg/dl to 166+54, p<0.002) and 2 h PG 263+84 mg/dl to 220+67, p<0.002) levels decreased significantly in the SMS group. There was no significant difference in the mean HbA1C values in both groups. Serum TC decreased significantly in both groups (control, 175+47 mg/dl to 164+38 mg/dl, p<0.03 and SmS,179+42 mg/dl to 164+31 mg/dl, p<0.03)	Not reported	Not reported	SMS was acceptable to the patients and the median number requested was 2 per week

Fig. 2 Risk of bias for randomized controlled trials

conclude that the current evidence base is insufficient to guide decisions on policy and practice. There is a lack of research on end-to-end health care systems where multifaceted strategies are taken to improve patient care. Restricting mHealth to patient-level behavior change initiatives on its own will not be adequate to promote reductions in NCD burden in LMICs. Mechael et al. recommend that mHealth move from single-solution-focused approaches to become an integrator of health information across the entire continuum of care [8]. In particular, the development of mHealth tools to strengthen workforce capacity, communication, and workflows is of particular importance. This would lead to better alignment with WHO-PEN and support practical links between the use of mHealth tools and national and international policy frameworks. It should be noted, however, that we are not advocating for a departure from "grassroots" approaches to intervention development. Such approaches are critical in maximizing user-responsiveness and sensitivity to context, and when companioned with other measures to address system gaps, their likelihood of lasting success is increased.

We recommend four priority areas to improve the mHealth research agenda: (1) comparative effectiveness studies examining mHealth versus other "traditional" health care improvement strategies; (2) large, multinational studies powered on "hard" clinical endpoints such as mortality and hospitalizations that enable cross-country comparisons; and (3) process and economic evaluations of effective and failed interventions to determine contextual opportunities and constraints for scale-up. A fourth more complex research priority area is the need to examine policy-level barriers to large-scale adoption of promising mHealth interventions. Factors such as mobile network coverage, data governance and consumer rights, patient identifiers, inter-operability and standards, regulatory approval, medical advice liability, and sustainable business models tend not to be considered in traditional research studies and yet are of crucial relevance to delivery of promising interventions at scale. Greater engagement with policy makers in study design and implementation is needed to ensure that research does not occur in a policy vacuum and that interventions can be integrated with existing national and local initiatives. Similarly, greater engagement with the private health care sector, including insurance providers, is needed. Given private investors are likely to be major payers for mHealth systems and that a large proportion of health care in LMICs is sought privately, it is critical that research and business agendas are better aligned [6]. While there is every reason to be optimistic about the transformative power of mHealth to reduce NCDs in LMICs, there is much work to do to convert the rhetoric into reality.

Table 5 RCT protocols registered in clinical trials databases

Database	Year registered	Trial status	Country	NCD	Population	Int/Cont (*n*)	Follow-up	Intervention	mHealth domain
CHICTR	2009	Unsure	China	DM	250 diabetic patients; 30–70 years; willing to take oral antidiabetic drug (or inject insulin) and perform glucose self-monitoring	125/125	3 years	Mobile technology-based self-monitoring	Client education
WHO_ICTRP	2011	Completed	Iran	DM	100 diabetic patients; 30–70 years; HbA1C>7	50/50	3 months	Health education delivered remotely via mobile phone	Client education
ANZCTR	2011	Completed	Taiwan, Australia	CVD, DM	182 diabetic patients ≥18 years with a cardiac event admitted to acute care hospital	91/91	4 weeks	Three face-to-face sessions as well as telephone and SMS follow-up over a 4-week period delivered in two countries	Client education
IRCT	2011	Completed	Iran	DM	66 diabetic patients; 18–55 years	33/33	3 months	SMS and phone education on laboratory results	Client education
Clinicaltrials.gov	2011	Ongoing	Argentina, Guatemala, and Peru	CVD	636 adults; aged 30–60 years; SBP values in the 120–139 mmHg range or DBP in the 80–89 mmHg range	212 per country (106/106)	18 months	SMS and one-to-one telephone calls to promote lifestyle modification and blood pressure reduction	Client education, registries/vital events tracking
ANZCTR	2011	Ongoing	Pakistan	CVD	3,400 patients admitted to hospital with their first event (non-fatal MI, CABG, PCI, stable, and unstable angina)	770/770	18 months	SMS, voice, and multimedia messages to promote behavior change/lifestyle modification health messages over a 6-month period	Client education
ISRCTN	2011	Ongoing	Congo, Cambodia, and the Philippines	DM	1,320 patients diagnosed as having (pre-) diabetes; 18 years and above	480/country (240/240)	2 years	Personalized SMS messages for self-management	Client education
Clinicaltrials.gov	2011	Ongoing	Tibet, China, and Haryana India	CVD	39 villages (27 in Tibet, 12 in India) involving patients ≥40 years with CVD, diabetes, or systolic BP >160 mmHg	1,043/1,043	1 year	Community health worker delivered lifestyle and medication management plan using a Smartphone decision aid	Client education, electronic health records, decision support system
WHO_ICTRP	2012	Completed	Iran	CVD	120 post-menopausal women; 40–60 years; BMI >25	60/60	4 months	SMS instructions on physical activity and healthy food choices via SMS, 3 times/week over 4-month intervention	Client education
WHO_ICTRP	2012	Completed	India	DM	200 participants at high risk of diabetes; diabetes risk score >21; 30–60 years of age	100/100	4 weeks	A Smartphone diabetes application to promote awareness of risk of diabetes (D-CHECK)	Client education
ISCRTN	2012	Completed	Jordan	CVD	156 patients diagnosed of coronary heart diseases; 18–70 years	78/78	8 months	Improvement in physical activity. SMS and phone follow-up to increase physical activity	Client education
Clinicaltrials.gov	2012	Ongoing	India, UK	DM	1,050 adults 35–55 years; HbA1c 6.0 to <6.5 %;	525/525	2 years	SMS lifestyle modification intervention to improve education, treatment targets, and provide support	Client education
IRCT	2013	Completed	Iran	CVD	99 patients post-cardiac valve replacement surgery	33/33/33 (int 66/cont 33)	3 months	SMS and telephone support service for post-surgery care	Client education
PACTR	2013	Ongoing	Kenya	CA	286 females; 25–69 years who have never had cervical cancer screening performed	143/143	12 months	Multiple SMS reminders for cervical cancer screening	Client education
Clinicaltrials.gov	2013	Ongoing	Kenya	CVD	5,424 patients >18 years with a blood pressure >140/90 mmHg	2,712/2,712	5 years	Multifaceted intervention with community health workers (CHWs), who are provided with a tailored behavioral communication strategy and a Smartphone-based tool linked to an electronic health record to promote improved blood pressure management	Client education, Registries/vital events tracking, data collection, electronic health records, decision support system
Clinicaltrials.gov	2013	Ongoing	India	CVD, DM	40,500.5consenting adults of age >30 years attending the community health centers and the district hospital in Himachal Pradesh	20,250/20,250	3 years	Multifaceted intervention involving workforce training,, health education, optimizing care pathways and use of a Smartphone-based decision support system (m-Power Heart)	Client education, Registries/vital events tracking, electronic decision support system

Table 5 (continued)

Database	Year registered	Trial status	Country	NCD	Population	Int/Cont (*n*)	Follow-up	Intervention	mHealth domain
ANZCTR	2013	Ongoing	Taiwan	RD	94 asthma patients between 12 and 18 years	47/47	4 weeks	Self-management program: involving face-to-face meetings, SMS reminders for medication intake, and motivational messages	Client education
CTRI	2013	Ongoing	India	CVD	18 primary health care centers, 54 villages, ~16,000 patients aged 40–84 years with or at high risk of CVD	16,000	2 years	Multifaceted intervention with decision support, health care worker training, building of referral linkages to medical care, reminder systems for patient follow-up [44]	Client education, registries/vital events tracking, data collection, electronic health records, decision support system, provider-provider communication, provider work-planning and scheduling
IRCT	2013	Ongoing	Iran	CVD	36 patients, 35–65 years with class II or III heart failure and an ejection fraction less than 40 %	12/12/12 (int 24/cont 12)	3 months	SMS and telephone follow-up to assist with treatment regimen adherence	Client education
CHICTR	2013	Unsure	China	RD	600 participants; 40–75 years; with post-bronchodilator FEV1 (forced expiratory volume in first second of expiration)/forced vital capacity (FVC) ratio was less than 0.70	300/300	Details not provided	Mobile phone-based internet intervention for respiratory self-management	Details not provided
DRKS	2013	Unsure	Bangladesh	DM	216 diabetes patients on medication, 18–65 years	108/108	6 months	Daily SMS for 6 months providing reminders for medication and clinic attendance in addition to health education advice	Client education
ISRCTN	2014	Completed	Mexico	DM	300 diabetic patients aged 18–75 years with an HbA1C ≥8 %	100/100/100 (Int: 200/Cont: 100)	10 months	Multifaceted intervention with clinical management support, self-management, data collection and uploading, motivational videos, patient registries, and provider communication	Client education, Registries/vital events tracking, Data collection, electronic health records, electronic decision support system, Provider-provider communication
Clinicaltrials.gov	2014	Ongoing	China	CVD	300 patients aged18–80 years presenting to emergency department with acute ischemic stroke within 4.5 h of symptom onset	150/150	3 months	Telemedicine support from a hub hospital using a mobile platform to guide thrombolysis treatment decisions	Provider communication, decision support
IRCT	2014	Ongoing	Iran	MH	66 war veteran males with post-traumatic stress disorder	33/33	6 months	Telenursing program using mobile calls and SMS to reduce recidivism and promote improve quality of life	Client education

Acknowledgments DPe is supported by an Australian National Health and Medical Research Council Fellowship (ID 1054754). DPr is supported by a scholarship from the Australian Agency for International Development (AusAID).

Conflict of Interest DPe has received research grant(s) number 1047508 and 1040147 from Australia's National Health and Medical Research Council to develop and test m-health interventions in Australia and India. No human studies were carried out by the authors for this article. There was no funding obtained in the development and writing of this article.

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