Features, Outcomes, and Challenges in Mobile Health Interventions for Patients Living with Chronic Diseases: A Review of Systematic Reviews

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Abstract

Background: Mobile health (mHealth) technology has the potential to play a key role in improving the health of patients with chronic non-communicable diseases.

Objectives: We present a review of systematic reviews of mHealth in chronic disease management, by showing the features and outcomes of mHealth interventions, along with associated challenges in this rapidly growing field.

Methods: We searched the bibliographic databases of PubMed, Scopus, and Cochrane to identify systematic reviews of mHealth interventions with advanced technical capabilities (e.g., Internet-linked apps, interoperation with sensors, communication with clinical platforms, etc.) utilized in randomized clinical trials. The original studies included the reviews were synthesized according to their intervention features, the targeted diseases, the primary outcome, the number of participants and their average age, as well as the total follow-up duration.

Results: We identified 5 reviews respecting our inclusion and exclusion criteria, which examined 30 mHealth interventions. The highest percentage of the interventions targeted patients with diabetes (n=19, 63%), followed by patients with psychotic disorders (n=7, 23%), lung diseases (n=3, 10%), and cardiovascular disease (n=1, 3%). 14 studies showed effective results: 9 in diabetes management, 2 in lung function, and 3 in mental health. Significantly positive outcomes were reported in 8 interventions (n=8, 47%) from 17 studies assessing glucose concentration, one intervention assessing physical activity, 2 interventions (n=2, 67%) from 3 studies assessing lung function parameters, and 3 mental health interventions assessing N-back performance, medication adherence, and number of hospitalizations. Divergent features were adopted in 14 interventions with significantly positive outcomes, such as personalized goal setting (n=10, 71%), motivational

feedback (n=5, 36%), and alerts for health professionals (n=3, 21%). The most significant found challenges in the development and evaluation of mHealth interventions include the design of studies with high quality, the construction of robust interventions in combination with health professional inputs, and the identification of tools and methods to improve patient adherence.

Conclusions: This review found mixed evidence regarding the health benefits of mHealth interventions for patients living with chronic diseases. Further rigorous studies are needed to assess the outcomes of personalized mHealth interventions toward the optimal management of chronic diseases.

Keywords: Mobile health, chronic disease, review

1 Introduction

Chronic non-communicable diseases such as diabetes, lung diseases, cardiovascular disease and mental disorders, are by far the leading causes of mortality in the world, killing 40 million people each year, equivalent to 70% of all deaths globally [1]. Patients with chronic conditions are in need of support to cope with their disease and take actions related to change of their behavior and lifestyle, thereby improving their health status and everyday wellness [2]. However, the institution-based model of healthcare faces enormous challenges imposed by such a disease burden, and its cost-effectiveness has come under question [3].

Mobile health (mHealth) technology has recently been shown to provide useful means of daily self-management of chronic diseases by the patients themselves [4], or remote medical management [5]. The enormous processing, sensing and communication capabilities of mobile devices (e.g., smartphones and tablet computers) along with their wide availability and uptake, have allowed their use as the main technology for provision of pervasive health services [6]. In

this regard, several research works have shown the value of mobile devices in facilitating patient independent living and improving quality of life [7–9].

As the peer-reviewed literature on mHealth grows exponentially, there is a substantial need to develop an evidence base for the effectiveness of mHealth [10]. In this direction, we present a review of systematic reviews of mHealth for patients living with chronic non-communicable diseases, aiming to explore the features and outcomes of mHealth interventions, and synthesize recent research evidence along with the associated challenges in this rapidly developing field. The review focuses on the study of an emerging class of networked electronic interventions [11], which use advanced technical capabilities of mobile phones (e.g., native or Internet-linked apps, interoperation with sensors, communication with clinical platforms, etc.) for chronic disease management according to the definition by WHO [12], and therefore it has a different scope from other reviews which consider the typical operation of mobile phones through voice or short messaging service (SMS) only [13–15]. Furthermore, this review targets at several chronic conditions rather than a single disease [16], in order to obtain a broader view of the diverse characteristics of mHealth interventions. By systematically identifying the current state of application of mHealth interventions, their effectiveness and shortcomings, this review will improve the understanding of researchers, engineers, clinical practitioners, and policy makers toward better designed, developed, and impactful interventions.

2 Methodology

We searched the bibliographic databases of PubMed, Scopus and Cochrane to identify systematic reviews of the effectiveness of mHealth interventions for diabetes, cardiovascular disease, lung diseases, and mental disorders, as reported in manuscripts published since 2008. The

inclusion criteria were: a) the review should be defined as systematic, focus on the effectiveness of the interventions, and follow reporting guidelines such as the Preferred Reporting Items for Systematic review and Meta-Analyses (PRISMA) [17], or the Cochrane guidelines [18], b) the review should include only mobile-based interventions which were evaluated in a randomized (or

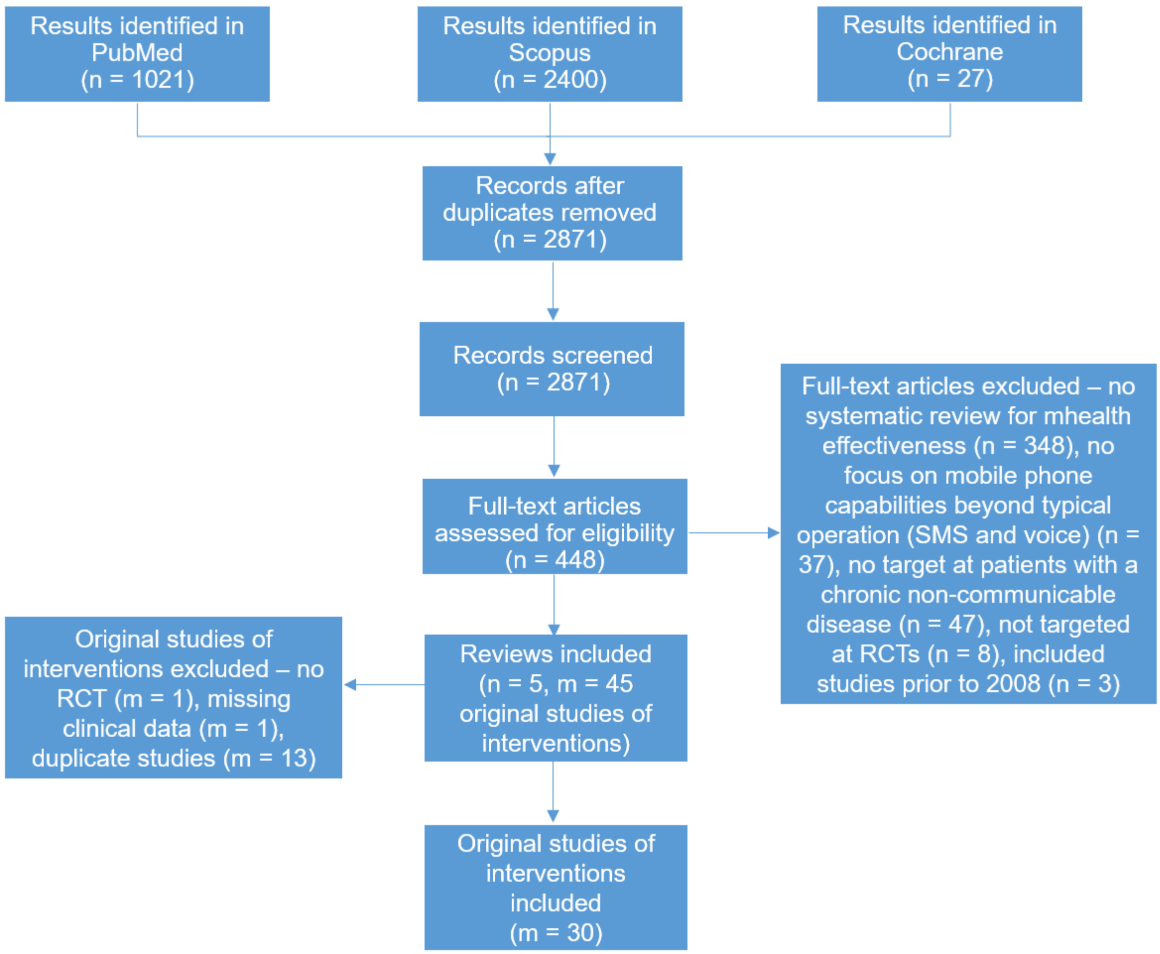

Figure 1 Flow diagram for study inclusion.

quasi-randomized) controlled trial (RCT), c) the review should report interventions targeted at chronically ill individuals diagnosed with diabetes, cardiovascular disease, lung diseases, or mental disorders, d) the paper should be written in English. We used the keyword query *("mobile health" OR "mhealth" OR "smartphone" OR "mobile phone" OR "mobile applications" OR "mobile apps")* for search within the title, abstract and keywords of the manuscripts, and restricted

the search to a review type of articles. Reviews examining interventions which used the typical mobile phone utilities of voice and SMS only, were excluded. Furthermore, reviews which included one or more studies (of any type of mobile intervention) conducted before 2008 were excluded, because we considered that a significant boost of the mobile phone industry occurred thereafter, e.g., the first commercial Android device as well as the Apple iTunes Store were both released in 2008 [19]. Reviews not examining quantitative outcomes, surveys, and protocol papers were also excluded from the review.

The papers were selected and reviewed independently by two reviewers (AT and HK) in order to verify their relevance according to the inclusion and exclusion criteria, and minimize possible errors or bias in their selection. After receiving the results of the literature search, the abstracts and the full manuscripts were screened. Reviews not meeting the inclusion criteria were excluded and reviews were included only if consensus between the reviewers could be reached.

Quality assessment of the methodology applied in the included reviews was conducted by the two reviewers using the first version of the AMSTAR tool (A Measurement Tool to Assess Systematic Reviews), which has been found to be reliable [20]. The original studies of interventions in the included reviews were synthesized (AT) according to the target disease, the features of the intervention and the form of health professional involvement, the theoretical model for health behaviour change, the primary outcome and whether this had a significant positive change, the number of enrolled participants and their average age, and the total follow-up duration.

3 Results

3.1 Literature Search Outcomes

Our search on December, 2017 yielded 1021 results from the PubMed database, 2400 results from Scopus, and 27 results from the Cochrane database. After removing all duplicates in the Mendeley© bibliography management software [21], and applying our eligibility and exclusion criteria, 448 articles remained for full manuscript reading. Finally, 5 papers (systematic reviews) were included. Reasons for paper exclusion are shown in Fig. 1.

3.2 Quality Assessment of Reviews and Original Studies

The average score in the 11-item AMSTAR quality assessment tool (one point earned for each met criterion) of all included systematic reviews was 8 (range 7–11), which means that they were of moderate to high quality (Table 1) [22].

The quality of the 30 original studies of interventions examined in the reviews (after removal of 13 duplicates, the study by Seto et al. [23] which used a pre-post design, and the study by Takenga et al. [24] in which clinical data was missed), was found to be diverse. More specifically, in the review of asthma interventions [25,26] by Belisario et al. [27], the studies were

Table 1 Quality assessment of the included reviews according to AMSTAR criteria (1: Yes, 0: No) of included studies (A: 'A priori' design, B: Duplicate study selection and extraction, C: Comprehensive literature search, D: Status of publication used as an inclusion criterion, E: List of studies provided, F: Characteristics of included studies provided, G: Scientific quality of included studies assessed, H: Scientific quality of included studies used appropriately in conclusions, I: Methods used to combine the findings of the studies are appropriate, J: Likelihood of publication bias assessed, K: Conflict of interest stated).

Study	**AMSTAR Criteria**											**Global Rating**
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	
Belisario et al. [27]	1	1	1	1	1	1	1	1	1	1	1	11
Cui et al. [8]	1	1	1	0	0	1	1	0	1	1	1	8
Gire et al. [48]	1	1	1	0	0	1	1	0	0	1	1	7
Hou et al. [56]	1	1	1	1	0	1	1	1	1	1	1	10
Whitehead et al. [60]	1	1	1	0	0	1	1	0	0	1	1	7

found to have high risk of bias according to the Cochrane collaboration risk of bias instrument [28] in the blinding of the study participants and the personnel (study participants and personnel should not have knowledge of which intervention a participant received, for judging a study to be at low risk of performance bias). The review of diabetes interventions [29–40] by Cui et al. [8], showed the quality assessment of 6 studies which were included for meta-analysis. Even though only one study showed blinded assessment of outcomes [34], the studies were reported to have low risk of bias [29,30,33–36]. The review of psychotic disorder interventions [41–47] by Gire et al. [48] showed that only the study by Spaniel et al. [47] was found to have low risk of bias, whereas the studies by Ainsworth et al. [41], Dang et al. [42], and Pijnenborg et al. [46] showed high risk of bias. The review of diabetes interventions [30,33–35,37,39,49–55] by Hou et al. [56], showed that 3 studies [34,39,55] were of poor quality according to the quality rating tool proposed by the U.S. Preventive Services Task Force [57]. Finally, the review of CVD [58], diabetes [30,34,50,54,55], and lung diseases [25,26,59] interventions by Whitehead et al. [60], showed that there was a high risk of bias in the blinding of participants and personnel in all studies.

3.3 Population and Primary Outcomes

The largest percentage of original interventions targeted patients with diabetes [29–40,49–55] (n=19, 63%), followed by patients with psychotic disorders [41–47] (n=7, 23%), lung diseases [25,26,59] (n=3, 10%), and CVD [58] (n=1, 3%) (Table 2). All interventions targeted adults. The largest percentage of interventions was conducted in Europe [26,29,30,33,36,39–41,44–47,51–54] (n=16, 53%), followed by USA [31,32,34,37,43,49] (n=6, 20%), Asia [25,35,38,42,50,59] (n=6, 20%), and Australia [55,58] (n=2, 7%). Study primary outcomes included glycosylated hemoglobin (HbA1c) for all diabetes interventions, except for the study by Quinn et al. [31] which focused on exploring differences in medication prescription, and the study by van der Weegen et

al. [40] which examined physical activity. The primary outcomes for the studies of the psychotic disorder interventions were diverse, i.e., positive and negative symptom scale [41], N-back cognitive performance [42], suicidal ideation [43], patient preferences [44], medication adherence [45], cognitive scale [46], and number of hospitalizations [47]. The primary outcome for the studies of two asthma interventions and one Chronic Obstructive Pulmonary Disease (COPD) intervention was lung function [25,26,59]. Finally, the study of CVD intervention by Varnfield et al. [58] had exercise capacity as primary outcome. The average number of enrolled participants in the included studies was 132 (range 14–562), their mean age was 49 years (range 25–72), and the average follow-up duration of the studies was 172 days (range 6–365).

Table 2 Table with the characteristics of original studies of interventions included in the reviews (TD: Target disease, AG: Mean age of all participants, MO: Main modality, FE: Features of the intervention, HI: Health professional involvement in the intervention, TM: Theoretical model for the development of the intervention, PO: Primary outcome, NP: Number of participants, FU: Follow-up duration in days, SPO: Significantly positive outcome reported, IC: Implications for clinical practice). *: Target disease of study not examined by included review.

	TD	AG	FE	MO	HI	TM	PO	NP	FU	SPO	IC
Varnfield et al. [58]	CVD	56	Physical activity tracking, personalized goal setting, motivational feedback, education	Smartphone	Yes (review of patient data by mentors prior to telephone consultations)	No	Exercise capacity	120	42	No	Effective cardiac rehabilitation through an alternative model of care delivery
Charpentier et al. [54]	Diabetes	34	Glucose reporting, personalized goal setting, motivational feedback	Smartphone	Yes (teleconsultations with doctors based on monitored data every 2 weeks)	No	HbA1c	180	180	Yes	Improved glycemic control in type 1 diabetes
Cho et al. [38]	Diabetes	48	Glucose reporting, personalized goal setting	Mobile phone	Yes (bi-directional communication between doctors and patients)	No	HbA1c	69	90	No	Effective glycemic control in type 2 diabetes through an alternative model of care delivery
Faridi et al. [49]	Diabetes	56	Glucose reporting, physical activity tracking, personalized goal setting	Mobile phone	Yes (review of patient data by providers)	No	HbA1c	30	90	No	Effective glycemic control in type 2 diabetes after required technology upgrades
Holmen et al. [30]	Diabetes	57	Glucose reporting, personalized goal setting, motivational feedback	Mobile phone	Yes (phone-based health counseling with a diabetes	Yes (transtheoretical model of stages of	HbA1c	151	120	No	Effective glycemic control in type 2 diabetes, which

					specialist nurse every month)	change, problem-solving model)					can be adopted even from older patients
Hsu et al. [32]	Diabetes	54	Glucose reporting, personalized goal setting, education	Tablet computer	Yes (shared decision making interfaces in which patient data and adherence is displayed, virtual visits, text messages)	Yes (model of cognitive apprenticeship that is informed by the situated learning theory)	HbA1c	40	84	Yes	Improved glycemic control in type 2 diabetes
Istepanian et al. [39]	Diabetes	59	Glucose reporting, personalized goal setting	Mobile phone	Yes (treatment recommendations by clinicians based on monitored data)	No	HbA1c	137	270	No	Effective glycemic control in type 2 diabetes
Karhula et al. [29]	Diabetes (and heart disease*)	66	Glucose reporting, personalized goal setting	Mobile phone	Yes (phone-based health coaching based on monitored data every 4-6 weeks)	Yes (Wagner's Chronic Care Model)	HbA1c	250	365	No	No beneficial effect of health coaching supported by telemonitoring in type 2 diabetes patients
Kirwan et al. [55]	Diabetes	35	Glucose reporting, personalized goal setting, motivational feedback, education	Smartphone	Yes (review of patient data from a certified diabetes educator every week)	No	HbA1c	72	180	Yes	Improved glycemic control in type 1 diabetes
Nagrebetsky et al. [51]	Diabetes	58	Glucose reporting, personalized goal setting	Mobile phone	Yes (review of patient data by nurses twice a week)	No	HbA1c	14	180	No	Feasibility of self-titration of oral glucose-lowering medication in type 2 diabetes with self-monitoring and remote monitoring of blood glucose levels
Orsama et al. [33]	Diabetes	62	Glucose reporting, personalized goal setting, motivational feedback	Mobile phone	Yes (alerts)	Yes (Information-Motivation-Behavioral Skills Model)	HbA1c	48	300	Yes	Improved glycemic control in type 2 diabetes
Quinn et al. (2008) [37]	Diabetes	51	Glucose reporting, personalized goal setting, education	Mobile phone	Yes (computer-generated logbooks)	No	HbA1c	30	90	Yes	Improved glycemic control in type 2 diabetes
Quinn et al. (2011) [34]	Diabetes	53	Glucose reporting, personalized goal setting motivational feedback, education	Mobile phone	Yes (summary reports sent to clinicians, web portal to view patient data)	No	HbA1c	163	365	Yes	Improved glycemic control in type 2 diabetes
Quinn et al. (2014) [31]	Diabetes	53	Glucose reporting, personalized goal setting	Mobile phone	Yes (summary reports sent to clinicians, web portal to view patient data)	No	Difference in medication prescription	117	365	No	Feasibility of medication prescription in type 2 diabetes through virtual patient-provider communication
Rodrı´guez-Idı´goras et al. [36]	Diabetes	64	Glucose reporting	Mobile phone	Yes (alerts)	No	HbA1c	328	365	No	Feasibility of effective glycemic

											control in type 2 diabetes
Rossi et al. (2010) [53]	Diabetes	36	Glucose reporting, personalized goal setting, education	Mobile phone	Yes (prescription changes by physician)	No	HbA1c	130	180	No	Effective glycemic control in type 1 diabetes
Rossi et al. (2013) [52]	Diabetes	36	Glucose reporting, personalized goal setting, education	Mobile phone	Yes (prescription changes by physician)	No	HbA1c	127	180	No	Effective glycemic control in type 1 diabetes
van der Weegen et al. [40]	Diabetes (and COPD*)	58	Physical activity tracking, personalized goal setting, motivational feedback	Smartphone	Yes (Face-to-face consultations (4) with a practice nurse based on activity results in 4-6 months)	Yes (”Five ‘A’s Cycle” counseling technique)	Physical activity (minutes/day)	199	180	Yes	Improved physical activity in patients with type 2 diabetes
Waki et al. [50]	Diabetes	57	Glucose reporting, personalized goal setting (lifestyle modification)	Smartphone	Yes (alerts for missed readings sent to nurses, dietary evaluation by a dietician according to meal photos)	No	HbA1c	54	90	Yes	Improved glycemic control in type 2 diabetes
Yoo et al. [35]	Diabetes (and hypertension*)	58	Glucose reporting, personalized goal-setting, motivational feedback	Mobile phone	Yes (personalized recommendations sent by physicians based on monitored data)	No	HbA1c	123	90	Yes	Improved glycemic control in overweight patients with type 2 diabetes
Liu et al. (2011) [25]	Asthma	52	Reporting of symptoms/peak flow, personalized goal-setting	Mobile phone	Yes (review of patient data by medical staff)	No	Lung function parameters - Asthma	120	180	Yes	Improved asthma control
Ryan et al. [26]	Asthma	49	Recording of symptoms/drug use/peak flow, personalized goal-setting	Mobile phone	Yes (review of patient data by clinician and alerts)	No	Lung function parameters - Asthma	288	180	No	No cost-effectiveness of mobile phone-based care delivery model compared to paper-based model in asthma
Liu et al. (2008) [59]	COPD	72	Exercise training via a mobile phone	Mobile phone	Yes (review of adherence to the training programme every week and phone calls)	No	Lung function parameters - COPD	48	90	Yes	Improved exercise training for COPD patients
Ainsworth et al. [41]	Psychotic disorders	33	Health status tracking (assessment questionnaires via smartphone app)	Smartphone	No	No	Positive and Negative Symptom Scale	24	6	No	Real-time assessment of patients with schizophrenia is valuable after required technology updates
Dang et al. [42]	Psychotic disorders	25	Games for cognitive training	Tablet computer	Yes (Nurses assistance)	No	N-Back performance	17	28	Yes	Improved cognitive rehabilitation for patients with schizophrenia

Kasckow et al. [43]	Psychotic disorders	51	Education	Custom messaging device	Yes (clinical staff everyday remote monitoring of patient response to questions)	No	Suicidal Ideation (Beck Scale)	51	90	No	Feasible model of monitoring patients with schizophrenia or suicidal ideation
Kauppi et al. [44]	Psychotic disorders	39	SMS reminders	Mobile phone	No	No	Patient preferences	562	365	N/A	Acceptable model of health reminders in patients with antipsychotic medication
Montes et al. [45]	Psychotic disorders	40	SMS reminders	Mobile phone	No	No	Medication adherence	254	90	Yes	Feasible and acceptable model to improve medication adherence in patients with schizophrenia
Pijnenborg et al. [46]	Psychotic disorders	27	Personalized goal setting via SMS	Mobile phone	No	No	Cognitive scale, social functioning scale, self-esteem	62	35	No	Effective model to reinforce appointments with mental health workers and leisure activities in patients with schizophrenia
Spaniel et al. [47]	Psychotic disorders	30	Recording of symptoms via SMS	Mobile phone	Yes (email alerts for clinicians)	No	Number of hospitalizations	146	283	Yes	Relapse prevention in patients with schizophrenia

3.4 Features of Interventions

The main modality for the delivery of the intervention was a mobile phone [25,26,29–31,33–39,44–47,49,51–53,59] (n=21, 70%), i.e. a previous-generation cellphone which was not reported to be a smartphone, followed by a smartphone [40,41,50,54,55,58] (n=6, 20%), i.e. a new-generation mobile device acting as a miniature computer, tablet computer [32,42] (n=2, 7%), and other custom-made messaging device [43] (n=1, 3%). The most common feature of the interventions was personalized goal setting through computer-tailored programs [25,26,29–35,37–40,46,49–55,58] (n=22, 73%), followed by motivational feedback sent to the patients [30,33–35,40,54,55,58] (n=8, 27%). Glucose reporting was a feature of all diabetes interventions except for the study by van der Weegen et al. [40], in which the focus was on physical activity tracking. The interventions for lung diseases included symptom and peak flow tracking [25,26], as well as

exercise training [59]. The CVD intervention by Varnfield et al. included physical activity tracking [58]. The interventions for psychotic disorders included features for health status tracking [41], cognitive training via games [42], education [43], medication reminders [44,45], goal setting [46], and recording of symptoms [47]. Theoretical models for health behaviour change to drive the development of the intervention, were used in five studies [29,30,32,33,40] (n=5, 17%), all targeted at diabetes.

3.5 Health Professional Involvement

Health professional involvement was present in the vast majority of interventions [25,26,29–40,42,43,47,49–55,58,59] (n=26, 87%), and it was at different forms. Alerts for health professionals to view patient data or contact the patient in the case of detected abnormal health status or missed readings, were employed in interventions for diabetes [33,36,50], psychotic disorders [47], and asthma [26] (n=5, 17%). In other studies, health professionals were enabled to review patient data or reports at specific time points [43,51,55] or before vocal communication (or telecommunication) with the patient [29,40,54,58,59]. In other interventions, patients could receive recommendations sent by health professionals (e.g., through SMS or letters) based on monitored data [35,39].

3.6 Evidence of Effectiveness in Health Outcomes and Implications for Clinical Practice

None of the reviews demonstrated strong evidence regarding the effectiveness of mHealth interventions in health outcomes for any chronic condition (Table 3). More specifically, the review by Belisario et al. [27] for asthma self-management, showed that the current evidence is not sufficient to advise clinicians. The reviews for diabetes self-management by Cui et al. [8] and Hou

et al. [56], both demonstrated moderate beneficial effect of mHealth interventions on glycemic control. The review by Gire et al. [48] for the assessment and treatment of psychotic disorders, showed no sufficient evidence of effectiveness of mHealth (although showing evidence of feasibility). Finally, the review by Whitehead et al. [60] for diabetes, lung disease and cardiovascular disease self-management, showed only the potential of mobile apps to improve symptom management.

14 original studies included in the reviews, showed effective results (Figure 2): 9 in diabetes management, 2 in lung function (COPD and asthma), and 3 in mental health (psychotic disorders). Significantly positive health outcomes were reported in 8 diabetes interventions [32–35,37,50,54,55] (n=8, 47%) from 17 studies assessing glycosylated hemoglobin, one diabetes intervention [40] assessing physical activity, and 2 lung disease interventions [25,59] (n=2, 67%) from 3 studies assessing lung function parameters.

Table 3 Characteristics of included reviews in terms of focus, number of RCTs examined, total number of participants and reported evidence of effectiveness of mHealth interventions.

	Focus	**Number of RCTs**	**Number of Participants**	**Evidence**
Belisario et al. [27]	Asthma self-management	2	408	Current evidence base is not sufficient to advise clinicians
Cui et al. [8]	Type 2 diabetes self-management	13 (6 studies were included for meta-analysis)	1022	Smartphone apps offered moderate beneficial effect on glycemic control
Gire et al. [48]	Assessment and treatment of psychotic disorders	7	1105	Evidence regarding effectiveness in health outcomes is not sufficient
Hou et al. [56]	Diabetes self-management	14	1360	Moderate beneficial effect on glycemic control for type 2 diabetes
Whitehead et al. [60]	Effectiveness of self-management in diabetes, chronic lung disease, and cardiovascular disease	9 (5 for diabetes, 3 for lung disease, 1 for cardiovascular disease)	1196	Mobile apps have potential to improve symptom management (6/9 RCTs reported a statistically significant difference in the primary clinical outcome of interest)

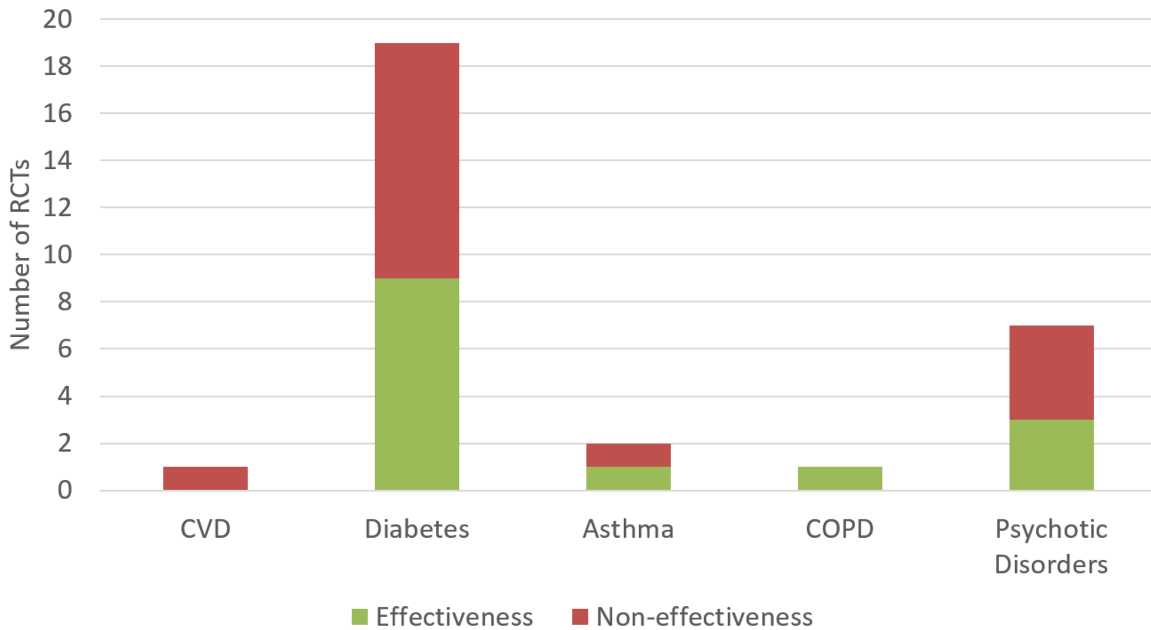

Figure 2 Effectiveness vs non-effectiveness (in terms of significantly positive outcomes reported) of mHealth interventions in RCTs.

In psychotic disorder interventions, significantly positive health outcomes were reported in the study by Dang et al. [42] which assessed the N-back cognitive performance, the study by Montes et al. [45] which assessed medication adherence, and the study by Spaniel et al. [47] which assessed the number of hospitalizations, all targeted at patients with schizophrenia. In effective interventions (n=14), personalized goal setting was the most common feature (n=10, 71%), followed by delivery of motivational feedback (n=5, 36%) and alerts for health professionals (n=3, 21%). Health professional involvement (e.g., review of patient data or alert notifications) was reported in 13 effective interventions (n=13, 93%). Theoretical models for health behaviour change were adopted in two effective diabetes interventions assessing glycosylated hemoglobin (the model of cognitive apprenticeship [32] and the information-motivation-behavioural skills model [33]), and one diabetes intervention assessing physical activity (the "Five 'A's cycle" counceling technique [40]). The cost-effectiveness of mHealth compared to typical care was

examined only in the study for asthma self-monitoring by Ryan et al. [26], in which the mobile technology was not found to be cost-effective.

The implications for clinical practice in terms of interpretation of the interventions' health outcomes can be grouped into the following 3 categories: a) studies which showed statistically significant health outcomes of the intervention compared to the control group, had the clear implication for improved patient condition, e.g., improved glycose control or asthma control, through the mobile-based model of therapy; b) another category of studies, although not showing significant health outcomes of their intervention compared to the control group, had implications for similar effectiveness of their technology-based therapy model with the traditional one, which could be used alternatively - for example in the study by Varnfield et al. [58], it was noted that their smartphone-based therapy model could be used as a feasible alternative to traditional cardiac rehabilitation requiring physical visits to specialized centers, for patients who have no access to them; c) finally, there were two studies, one for patients with diabetes [29], and another for patients with asthma [26], which clearly indicated no added benefits of the mHealth intervention, mainly because of lack of social support, or introduction of significant costs.

3.7 Challenges

Several challenges in evaluation of mHealth interventions have been reported in the included reviews. Most importantly the methodological limitations of the studies (e.g., blinding of outcome assessors to the intervention status of participants, blinding of study participants to the exact research question to protect from performance bias, use of an active control group, etc.), prevent from drawing safe conclusions on the effectiveness of mHealth interventions [27,48,56]. The efficacy of mHealth applications as interventions needs to be further explored, since in most studies these are part of complex interventions in which significant health professional input is

also employed [27,56,60]. The incorporation of computer-generated feedback supplemented with personalized feedback from health professionals, seems to bring better outcomes for the patients compared to typical care, and therefore this area needs also to be investigated in future studies [8,56]. Tools and methods to improve patient adherence in studies of suitable duration is also important [27,56], since improved outcomes (e.g., better symptom control) are more likely to occur when adherence is high [60]. Other challenges include: The consideration of the seasonal nature of the patient condition as happens for example in asthma [27], the increase of patient awareness for regular health self-management [8], usability [48], incorporation of behaviour change theories, inclusion of game elements, and consideration of the needs of older patients [56], as well as iterative design with end-users, patient safety and privacy, and rigorous analysis of cost-effectiveness [60].

4 Discussion

4.1 Main Findings

This review examined the features, outcomes, and challenges in mHealth interventions for patients living with chronic non-communicable diseases, by drawing, exploring, and synthesizing the findings of systematic reviews in this vast area of research. The effectiveness of mHealth interventions on the condition of patients with diabetes, cardiovascular disease, lung diseases or psychotic disorders, was found to be mixed, since in total 14 out of 30 RCTs (47%) reported a significantly positive outcome compared to standard care. If we consider the quality assessment of the studies of interventions, we can identify that from 12 studies with fair or high quality targeted at patients with diabetes (extracted by the reviews of Cui et al. [8] and Hou et al. [56]), 5 studies reported significantly positive outcomes (42%), which also shows that mHealth has a mixed effect

for this population. The study by Spaniel et al. [47] for patients with schizophrenia, was found to be the only one with high quality, among the studies for chronic conditions other than diabetes, and had a positive effect on the number of hospitalizations for the patients. In summary, this review could not identify superior effectiveness of mHealth interventions compared to standard care for any chronic condition. However, given the small number of studies identified in this review (especially for diseases other than diabetes), and the fact that there have been several studies reporting improved disease control for patients, e.g., [54], [25], or implying the feasible and effective use of mHealth as an alternative model of therapy, e.g., [38,58], further investigation of the clinical usefulness of mHealth is warranted.

The mHealth interventions were found to employ features such as personalized goal setting via computer-tailored plans, or delivery of motivational feedback to the patients. Interestingly, personalized goal setting was found to be an integral component of a large number of effective interventions for different chronic diseases, i.e., diabetes, lung diseases, and psychotic disorders. Further longitudinal studies are needed to explore the impact of such features on mHealth effectiveness for specific patient groups, and therefore increase our understanding towards implementing successful, less complex, and lower cost interventions. In this direction, the use of factorial designs could facilitate insights [61].

Health professionals were involved in the vast majority of mHealth interventions demonstrating positive outcomes, e.g., through the reception of alerts when patient readings were found to be abnormal, or patient data reports. This suggests that mHealth interventions can be considered as tools complementing the care services delivered by medical staff. The level of health professional involvement was different in the mHealth interventions, e.g., medical staff reviewed adherence of COPD patients every week in the study by Liu et al. [59], and doctors had

teleconsultations with diabetic patients every two weeks based on monitored data in the study by Charpentier et al. [54]. Therefore, the target professional group and the form of health professional inputs, need to be carefully considered when designing mHealth studies, since these are likely to have a substantial impact on the health outcomes. Interestingly, the intensity of support by health professionals did not appear to be vital in affecting patient outcomes [60]. For example, the study by Kasckow et al. [43] for schizophrenia, in which the clinical staff monitored patient data every day, and the study by Nagrebetsky et al. [51] for diabetes, in which nurses monitored patient readings twice a week, did not note significant improvement on patient health outcomes compared to standard care.

A more careful look at the effective mHealth interventions which involved interactions with health professionals and incorporated personalized goal setting, shows that health professionals were not always engaged in the selection of goals for their patients. For example, in the study by Orsama et al. [33], goals in terms of blood glucose, blood pressure, weight, and activity were automatically determined through a rule-based decision support system, while in the study by Liu et al. [25], a scoring system was developed, based on which patients could be automatically assessed on their level of asthma control and provided with management goals. On the contrary, in other studies health professionals seemed to have a more active role in goal selection, as for example in the study by Hsu et al. [32], in which shared decision-making computer interfaces were provided for both diabetic patients and health professionals, enabling them to review data and choose desired goals. In this context, more studies would be needed to compare the efficacy between computerized goal setting alone (e.g., through rule-based [62] or machine learning approaches [63]) and collaborative goal setting with health professionals [64].

Several challenges for designing and evaluating mHealth interventions drawn from this review can be highlighted. First of all, there is a significant space to improve the methodological quality of the mHealth studies. Through the conduction of high quality studies which introduce low risk of bias, the evidence of effectiveness or non-effectiveness of interventions can be established, and recommendations to guide research and clinical practice can be made [65]. Proper incorporation of clinical feedback into mHealth interventions is another major challenge, since this can bring added value in the delivery of personalized health services to the patients if implemented correctly, but it could require dedicated support and effort by health professionals which may not always be possible mainly due to organizational factors [66]. Patient adherence to using mHealth interventions which could possibly lead to the gain of positive health outcomes, needs to be further investigated. However, such explorations would require studies of long duration (even more than the average 6-month duration of the examined studies in this review), which cannot always be feasible, due to limited resources in terms of funds, time, or available infrastructure. Theoretical models for health behaviour change need to be employed in a wider scale in future studies, considering the low number of found interventions incorporating them in this review, since these can guide the design of conceptually coherent and effective mHealth interventions, possibly also increasing the rate of their adoption [67].

4.2 Limitations

This review was based on the findings from systematic reviews of mHealth interventions and different populations in terms of disease, age, education and socioeconomic level were studied in different settings, which prevented the conduction of a meta-analysis. The limitations of the included systematic reviews (introduced for example in their inclusion and exclusion criteria) might have affected the representation of the progress of mHealth interventions, even though the

methodological quality of the reviews was found to be moderate to high. This review presented features and outcomes of mHealth interventions for patients diagnosed with diabetes, cardiovascular disease, lung diseases, or mental disorders considering their global burden. Interventions for other chronic conditions such as cancer, arthritis, or liver disease were not examined. Terms related to mHealth, such as telemonitoring and telemedicine, are broader, and they were not used in our literature search. Furthermore, the original studies of the interventions included in the reviews were all reported after 2008, in order to depict the recent progress. Different results could emerge if older studies were also included. All original studies included in this review, were examined based on the specific disease identified by a published systematic review, even though there were studies which examined more than one disease [35,40]. Another limitation is that our search was conducted in a limited number of bibliographic databases (PubMed, Scopus and Cochrane), and not updated to include reviews published after December, 2017. Only primary (and not secondary) outcomes of the original studies of interventions were collected and analyzed. The review did not focus on potential harms of mHealth, which can be considered as an appropriate area of research for future studies.

5 Conclusion

Our review showed mixed evidence regarding the outcomes of mHealth interventions for patients living with chronic diseases. However, the outcomes indicated by a number of studies, demonstrate the potential and value of mHealth. In this context, future studies of mHealth interventions, can explore the use of features such as personalized goal-setting, as well as the form or level of health professional involvement, toward meeting patients’ individualized needs and improving their health.

Authors' Contributions

Author AT was responsible for the study conduction; Authors AT and HK reviewed the literature and assessed the quality of the included studies; AT synthesized the literature according to the described methodology; AT wrote a first draft of the manuscript and all other authors contributed to the final version. All authors have read and agreed to the paper being submitted as it is.

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Conflicts of Interest

The authors of this manuscript declare no conflicts of interest.

Summary Points

What was already known on the topic?

- Mobile health interventions are often employed to improve the condition of patients living with chronic diseases.

What this study added to our knowledge?

- Mobile health interventions for diabetes, cardiovascular disease, lung diseases, and mental disorders, have shown mixed evidence regarding their superior effectiveness in the management of chronic diseases compared to standard care.
- Personalized goal setting was found to be an integral component of a large number of effective interventions.

- In the vast majority of effective interventions, there was health professional involvement at different levels and frequency.
- The development of most interventions was not driven by a theoretical model.
- Further rigorous studies are needed to assess the benefits of personalized mobile health technology across different settings.

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