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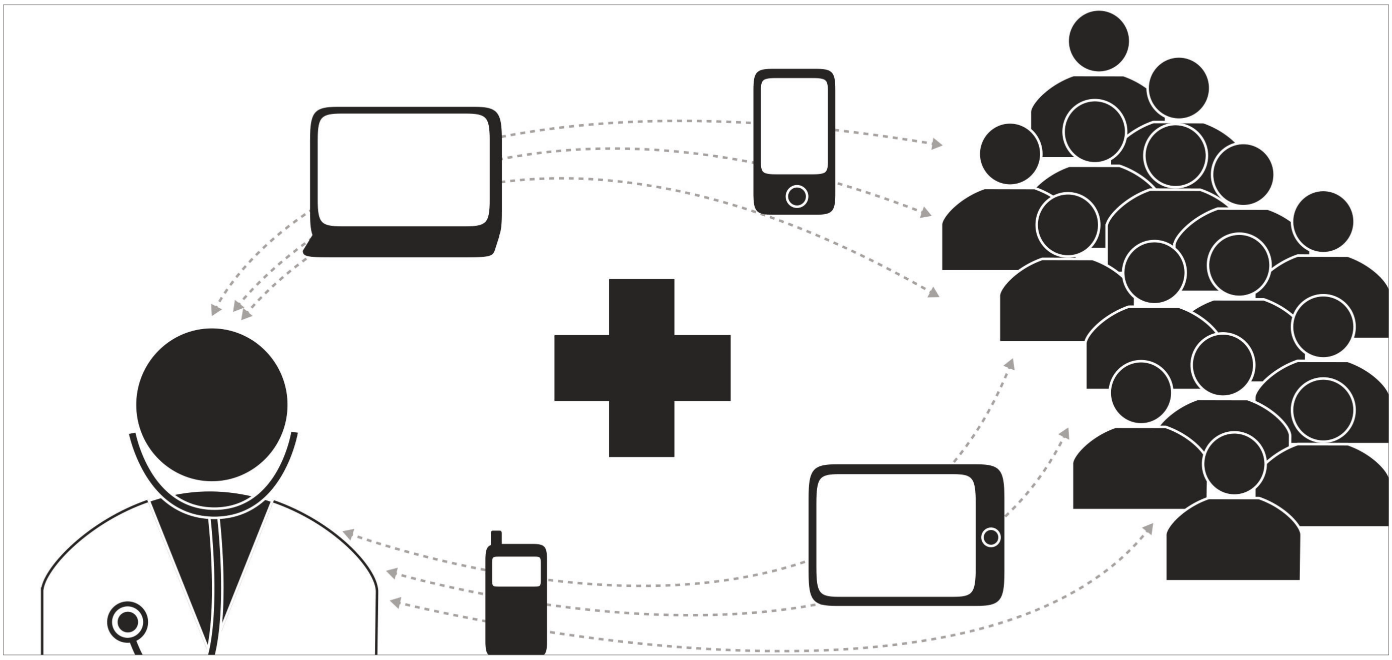
A systematic review of randomized controlled trials



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Zusammenfassung

Hintergrund: Die Todesursachen in Entwicklungsländern verschieben sich kontinuierlich von übertragbaren hin zu nicht-übertragbaren Krankheiten (NCDs). Deshalb werden in diesem systematischen Review, gesundheitsbezogene Einflüsse von mobile Health (mHealth) Interventionen zur Bekämpfung von NCDs in Entwicklungs- und Schwellenländern (LAMICs) untersucht, um Einschätzungen zur bisherigen und Empfehlungen zur weiteren Entwicklung zu geben.

Methode: Eine systematische Literatursuche in drei großen Datenbanken wurde durchgeführt um randomisiert-kontrollierte Studien (RCTs) von mHealth Interventionen in LAMICs zu identifizieren. Die ermittelten RCTs wurden hinsichtlich der Effekte von mHealth Interventionen auf gesundheitsbezogene Parameter ausgewertet.

Resultate: Von insgesamt 733 erfassten Titeln wurden 6 RCTs mit 1850 Teilnehmern einbezogen. Es wurde festgestellt, dass mHealth einen positiven Einfluss auf klinische Resultate, Compliance-Raten, sowie Lebensqualitätsbezogene Aspekte hat. Zudem verbesserten sich im Rahmen der Interventionen weitere Faktoren wie das Vertrauen zwischen Patient und Arzt oder die Patienten Angst. Ferner wurde festgestellt, dass individualisierte Interventionen bessere Resultate als generalisierte Interventionen erzielen. Limitierende Faktoren bei diesem Review waren die geringe Anzahl an RCTs, die Heterogenität der evaluierten Parameter und der Umstand, dass fast alle inkludierten Studien in urbanen Gebieten von Schwellenländern durchgeführt worden sind.

Schlussfolgerung: mHealth kann zu einem wichtigen Instrument bei der Bekämpfung von NCDs in LAMICs heranwachsen. Dazu ist jedoch eine stärkere Unterstützung insbesondere von staatlichen Institutionen unumgänglich. Zudem müssen zukünftige Forschungen einen Fokus auf Langzeit-Effekte insbesondere in einkommensschwachen Ländern haben.

Abstract

Background: mHealth refers to the use of mobile phones for health care and public health practice. The reasons of deaths in developing countries are shifting from communicable diseases towards non-communicable diseases (NCDs). We review studies assessing the health-related impacts of mobile health (mHealth) on NCDs in low- and middle-income countries (LAMICs) with the aim of giving recommendations for their further development.

Methods: A systematic literature search of three major databases was performed in order to identify randomized controlled trials (RCTs) of mHealth interventions. Identified RCTs were reviewed concerning effects of the interventions on health-related outcomes.

Results: The search algorithms retrieved 733 titles. 6 RCTs were included in the review, including a total of 1850 participants. mHealth was found to have positively influenced clinical outcomes, compliance rates, as well as quality of life related aspects. Furthermore, other outcomes such as patients' anxiety or patient-physician trust improved significantly. We also found that tailored interventions using a single service for the transmission (e. g. only SMS) showed the most positive effect. Limiting factors of the evaluation however, were the few numbers of RCTs, the heterogeneity of outcome measures and the fact that all included studies were conducted in middle income countries and mostly in urban areas.

Conclusions: Although mHealth is still in its infancy, it can emerge as an important tool for fighting NCDs in LAMICs. Therefore, further support by governmental institutions for coordinating and promoting the development of the required tools, as well as further research especially in low-income economies, with a focus on the evaluation of the long-term effects of mHealth is needed.

Content

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Abbreviations

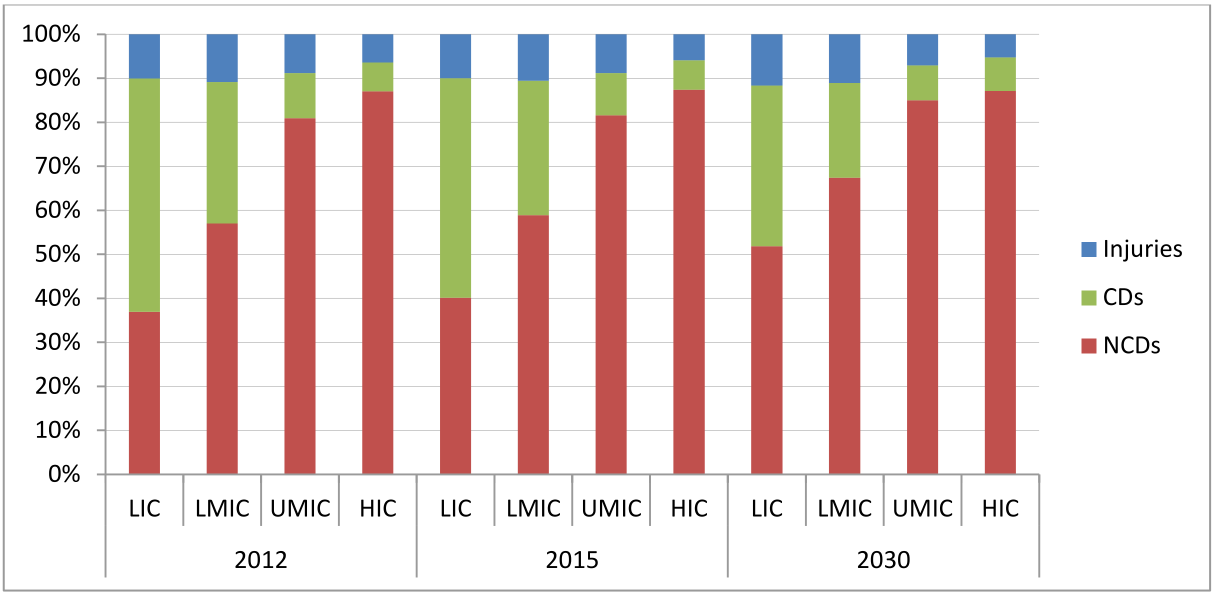
BMI	Body Mass Index
BP	Blood Pressure
CDs	Communicable Diseases
CENTRAL	Cochrane Central Register of Controlled Trials
EMBASE	Excerpta Medica Database
FEV1	Forced Expiratory Volume in 1 Second
GOe	Global Observatory for eHealth
HCW	Healthcare worker
HDL-C	High-Density Lipoprotein Cholesterol
HICs	High Income Countries
ICS	Inhaled Corticosteroids
LAMIC	Low and Middle Income Countries
LDL	Low Density Lipoprotein
LIC	Low income countries
LMICs	Lower Middle Income Countries
MEDLINE	Medical Literature Analysis and Retrieval System Online
mHealth	Mobile Health
MIC	Middle income countries
NCDs	Non Communicable Diseases
NGO	Non Governmental Organization
PCAS	Primary Care Assessment Survey
PEF	Peak Expiratory Flow
PEFR1	Peak Expiratory Flow Rate
PPG	Postprandial Plasma Glucose Test
QoL	Quality of Life
RCT	Randomized Controlled Trial
SMS	Short Message Service
TC	Total Cholesterol
UMIC	Upper Middle Income Countries

WHO	World Health Organization
WLAN	Wireless Local Area Network

A. Introduction

As of 2011, 66.4 % of world-wide deaths were caused by illnesses like cardiovascular disease, diabetes or cancer – classified as non-communicable diseases (NCDs), while 24.5 % were due to infectious or communicable diseases (CDs) (WHO 2013). High-income countries (HICs) have a larger proportion of deaths caused by NCDs than low- and middle-income countries (LAMICs) (see figure 1). However, as a result of increasing life-expectancy and growing welfare in LAMICs, there is a steady shift away from infectious to non-infectious diseases, which are most of the time chronic (Weiser et al. 2008). It is estimated that more than 50 % of deaths in LAMICs will be caused by NCDs in 2030. In absolute numbers, the developing world already bore 80 % of the world-wide burden of NCDs in 2011 (WHO 2011).

Figure 1: Causes of death in 2012 with estimates for 2015 and 2030 for low (LICs), lower-middle (LMICs), upper-middle (UMICs) and high-income countries (HICs) (WHO 2013)

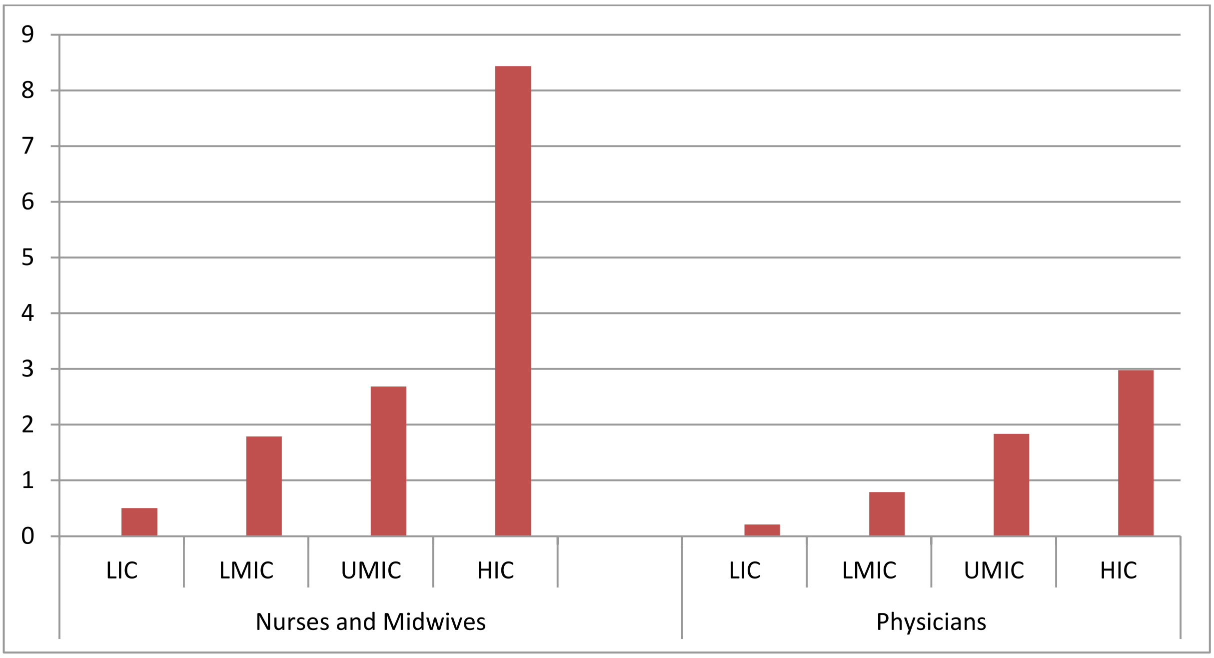


Health-care workers in LAMICs

The ability of the developing world to fight and overcome this increasing burden is limited. A main reason for that is the shortage of health-care workers (HCWs): It is estimated that the developing world has a deficit of 2.4 million nurses and doctors (Naicker et al. 2009). In fact, the number of nurses and physicians per population in low-income countries (LICs) is ten times lower than in HICs, with less than 1 health care worker per 1000 citizens (see figure 2). According to estimates of the World Health Organization (WHO) the current health-care workforce would need to be scaled up by 140 % in order to reach targets such as those written in the millennium declaration (Kinfu et al. 2009).

Moreover, many professionals emigrate from developing countries to richer countries. This brain drain significantly contributes to the shortage of the health-care workforce (Stilwell et al. 2004; Meinardi et al. 2001).

Figure 2: Nurses & Midwives and Physicians per 1000 inhabitants in low (LICs), lower-middle (LMICs), upper-middle (UMICs) and high-income countries (HICs) in 2010 (WHO 2014a)



MOBILE PHONES IN LAMICS

The mobile phone subscriptions have grown rapidly since the 1980ies – in the developed as well as in the developing world (Kaplan 2006) and today there are almost as many mobile phone subscriptions in the world as people (95 % of the world's population). While the developed world subscriptions average is above 100 %, the developing world is catching up with very high growth rates (see figure 3) – Africa has the fastest growing cellphone subscriber market in the world, while fixed telephone lines are being replaced by cellular connections in this region (Hamilton 2003).

A similar trend can be seen concerning mobile broadband connections – even if they remain relatively infrequent in the developing world (Kochi 2012), with around 19.8% compared to 75% in the developed world. Growth rates of above 80 % have been registered within the last two years. Although prices for mobile connections remain high in the developing world, there are ambitions to promote the wireless broadband infrastructure in rural areas and to drive broadband prices down in these regions (GSMA 2014). These numbers demonstrate the unique position mobile phones have in these countries, where other resources and infrastructure remain scarcer.

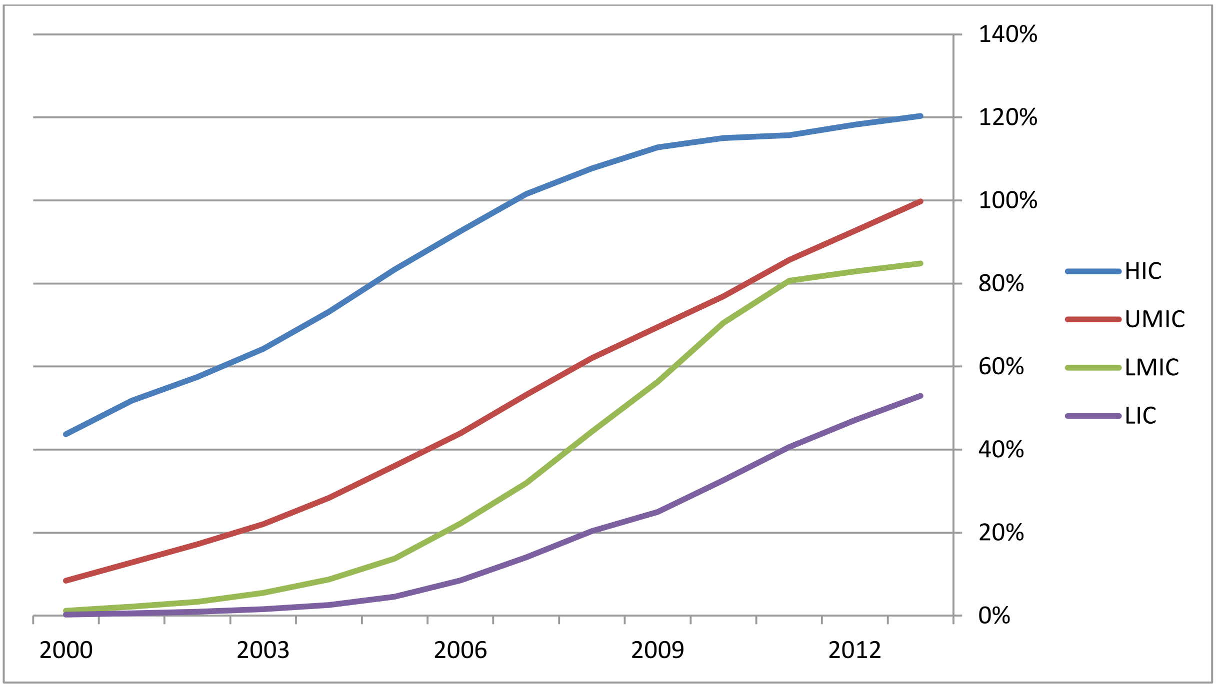
Mobile Health

The ubiquity of mobile phones in the developing world has already brought improvements in accesses to financial, agricultural and educational services (Kochi 2012). Also, there are more mHealth projects in the developing world, especially in Africa, than anywhere else in the world (GACD 2014). But what is mHealth?

Due to its relatively young history, there is no standardized, international definition yet (e. g. by the International Organization for Standardization). However, mHealth can be seen as a sub-segment of the field of electronic health (Vodafone 2009). The WHO uses the working-definition of the Global Observatory for eHealth (GOe), which defines mHealth as ”...*medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices*” (Kay et al. 2011).

This definition implies a very broad field of possible applications because it includes all mobile devices such as physicians’ laptops with a satellite internet connection or medical students’ tablets connected with the wireless local area network (WLAN) of their university. But since the focus of this paper lies on the ubiquity of the cellular network, we define mHealth more narrowly as the usage of mobile phones and their core functionality (such as the Short Message Service (SMS) or data transmissions) for the support of for health care and public health practices.

Figure 3: Mobile phone subscriptions as percentage of the overall-population, sorted by low (LICs), lower-middle (LMICs), upper-middle (UMICs) and high-income countries (HICs) (Worldbank 2014)



Objectives of this Study

An important question is whether mHealth can be used to address the increasing burden of NCDs. The major focus of most mHealth research projects in the past has been on CDs instead on NCDs. This paper aims to fill the gap and to systematically review the available literature on mHealth in the field of NCDs in LAMICs Therefore, the main research question is:

What are the health-related effects of mHealth interventions used for the treatment of NCDs in low- and middle-income countries?

In addition, we will identify different options for using mHealth interventions in the fight against NCDs in low- and middle-income countries.

B. Method

In order to answer the main research question, a systematic literature review was conducted, following the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0, (Higgins JPT, Green S 2014)). Peer-reviewed publications were screened and the data of eligible studies were gathered and assessed. In the following sections: the eligibility criteria, the method of the screening, the data collection and the quality assessment are described in detail.

B.1 Eligibility criteria

Eligibility criteria for the inclusion of studies were defined in terms of participants, observed interventions, outcomes of interest and types of studies. In addition, report characteristics were specified.

B.1.1 Types of participants

Only participants from LAMICs were taken into consideration. The World Bank classification for income groups was used (WHO 2014).[1] The World Bank definition distinguishes for middle income countries between lower and upper middle income countries (UMICs). Upper middle income countries were included because of the following two reasons:

- Most of the UMICs still have big differences among their populations' living conditions, especially between rural and urban areas. This is expressed by high Gini-coefficients for income and consumption (e. g. 74 in Namibia or 63.1 in South-Africa) (WHO 2014)
- Previous systematic reviews about mHealth in developing countries included also UMICs and showed that a lot of projects have been conducted in countries such as South-Africa, Brazil, Mexico, China and Namibia (Deglise et al. 2012; Piette et al. 2012). Therefore, including this income group might result in a higher number of high quality studies of mHealth.

Only participants with NCDs were included. WHO's definition of NCDs was used (WHO 2014). It was required that the disease was explicitly mentioned. Otherwise the study was excluded. No other restrictions regarding the type of participants were applied. All kinds of groups, in terms of age, profession or place of living (urban or rural) were included. Also, interventions for both patients and health-professionals were included.

B.1.2 Types of interventions

All mHealth interventions for NCDs were taken into consideration based on the above mentioned definition (chapter A): the intervention should use the mobile phone network for at least one of the mobile phones' core functions. If a study did not clearly mention what kind of telecommunication was used or the source of its connectivity could not be derived from

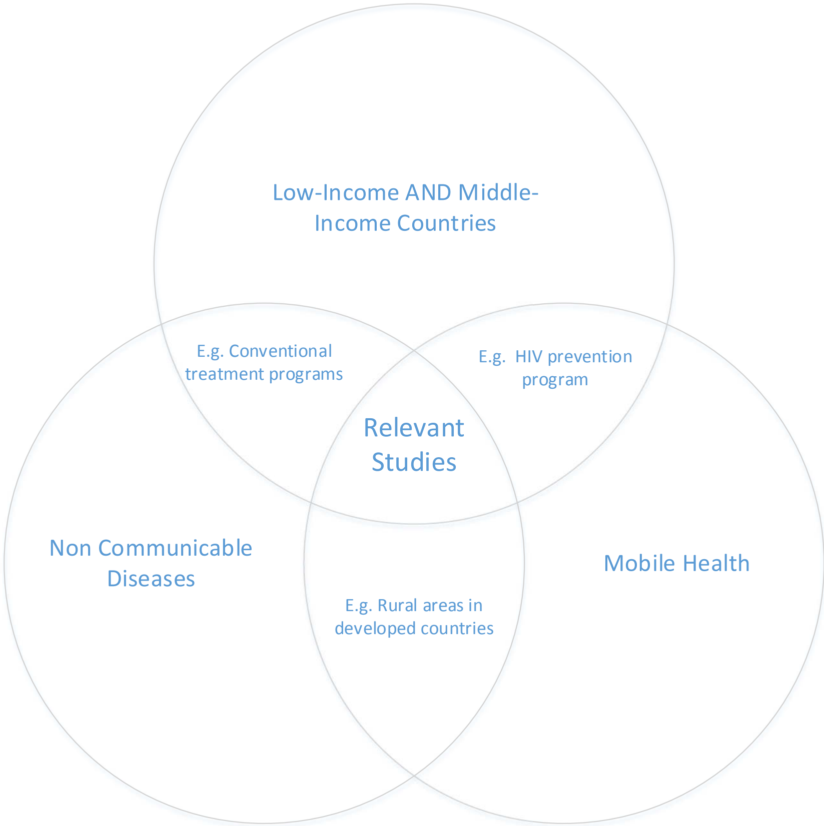
[1] e. g. for 2013: countries identified by the World Bank as having an annual per capita gross national income of less than $12,615 were UMICs and $1,035 or less were LMICs

the context, the study was excluded. Other systematic reviews used similar definitions in order to narrow the term mHealth, such as a restriction for SMS-interventions (Deglise et al. 2012).

B.1.3 Types of outcome measures

All outcomes that are likely to be meaningful to clinicians, consumers, the general public, administrators and policy makers were included. Therefore this review included a diverse set of outcomes, such as clinical events, patient-reported outcomes, economic outcomes or other outcomes such as depression or anxiety level.

Figure 4: Search set with the different terms of interest



B.1.4 Types of studies

Only randomized-controlled trials (RCTs) were included because they provide the highest quality of evidence.

B.1.5 Study characteristics

In addition, only studies published in scientific journals in English and in German were included. Grey literature was excluded.

B.2 Search method for identification of studies

CENTRAL – a Central Register of Controlled Trials, that is regarded as the largest literature-base for doing systematic reviews (DIMDI 2014) – and the Medical Literature Analysis and Retrieval System Online (MEDLINE) databases were searched. In addition, the database Business Source Complete was searched in order not to miss studies published in economic journals.

No Google-search was performed because a preliminary search-attempt revealed the infeasibility of doing a systematic search in Google. The search-mask did not allow complex search-request and the use of third party programs was impossible because Google limited the number of search-requests per day.

For transforming the above mentioned criteria, each of them were grouped into one of the following three terms (see figure 4):

1. **NCDs**: non-communicable, chronic, cancer, neoplasms, diabetes, mental, neuro-logical, sense organ, ophthalmology, cardiology, cardiovascular, heart, digestive, genitourinary, skin, dermatology, musculoskeletal, congenital, oral, pathology, psychiatry
2. **mHealth**: mHealth, mobile Health, mobile, SMS, tele*
3. **Low and middle-income countries**: developing countries, developing world, rural areas, low-resource, lower-income, middle-income, middle-resource

Search terms for the operationalization of NCDs were derived from the list of NCDs in WHO's Global Burden of Disease Report (WHO 2014). In addition, commonly known terms such as *cancer* were added. Similar to other systematic reviews in this field (e. g. Beratarrechea et al. (2014) the aim at this stage was to have a high sensitivity and a low specificity. No filter for the study design was set.

B.2.1 CENTRAL-search

The search conducted with the CENTRAL-database can be examined in table 1. It was carried out using the free text search with Boolean-operators and MeSH descriptors (with the enabled option of *exploding all trees*).

Table 1: Search method conducted with the CENTRAL-database

ID	Search	Hits
#1	MeSH descriptor: [Telemedicine] explode all trees	1066
#2	MeSH descriptor: [Developing Countries] explode all trees	717
#3	#1 and #2	2
#4	("m-Health" or "mHealth" or mobile or SMS or tele*)	13041
#5	"developing countries" or "developing world" or "rural areas" or "low-resource" or "low-income" or "mid-income"	4685
#6	"non-communicable" or noncommunicable or chronic or cancer or neoplasms or diabetes or mental or neurological or "sense organ" or ophthalmology or cardiology or cardiovascular or heart or digestive or genitourinary or skin or dermatology or musculoskeletal or congenital or oral or pathology or psychiatry	372756
#7	#4 and #5 and #6	658
#8	#7 or #3	659

B.2.2 Medline-search

First of all, the above defined words were used for the free text search using Boolean operators and Truncations. MeSH-tags using the terms *Telemedicine* [Mesh] AND *Developing Countries* [Mesh] were then included.

B.2.3 Business Source Complete-search

The database Business Source Complete was searched using the *Boolean/Phrase Search-Mode* with the activated option of *apply related words*. Due to a very low number of results, it was feasible to exclude the field of terms for *health-condition of interest* (all search-terms for NCDs) and to include solely the location and the intervention of interest.

B.2.4 Hand-search

Reference lists of included studies and of existing reviews in the field of mHealth and NCDs were screened with the aim of identifying studies missed by our search algorithm.

B.3 Study selection and data analysis

After the iterative search steps were completed, the included titles were collected and analyzed. For this process, the reference-management software Citavi was used, which allowed sorting and labeling of the titles.

The screening process was divided into three parts: title, abstract and full-text screening. Studies whose titles clearly indicated that they were not concerned with mHealth for NCDs in LAMICs were excluded. Publication dates were also checked at this stage. Subsequently, abstracts were screened to determine if studies fulfilled the inclusion criteria for the review. Also, the language of publications was verified. Finally, full texts of selected studies were screened to determine whether they fully met the inclusion criteria. Studies identified during hand search of reference lists were taken into a second abstract-screening phase and scanned for inclusion.

B.3.1 Analysis of included studies

The included studies were analyzed for all data of interest. Main characteristics of the studies were gathered (e. g. number of the participants, mean age, area of disease) and basic information about the study design were extracted (e. g. inclusion/exclusion criteria or the place of recruitment). On this basis the outcome-data were gathered, classified and discussed in terms of their significance.

B.4 Risk of bias in individual studies

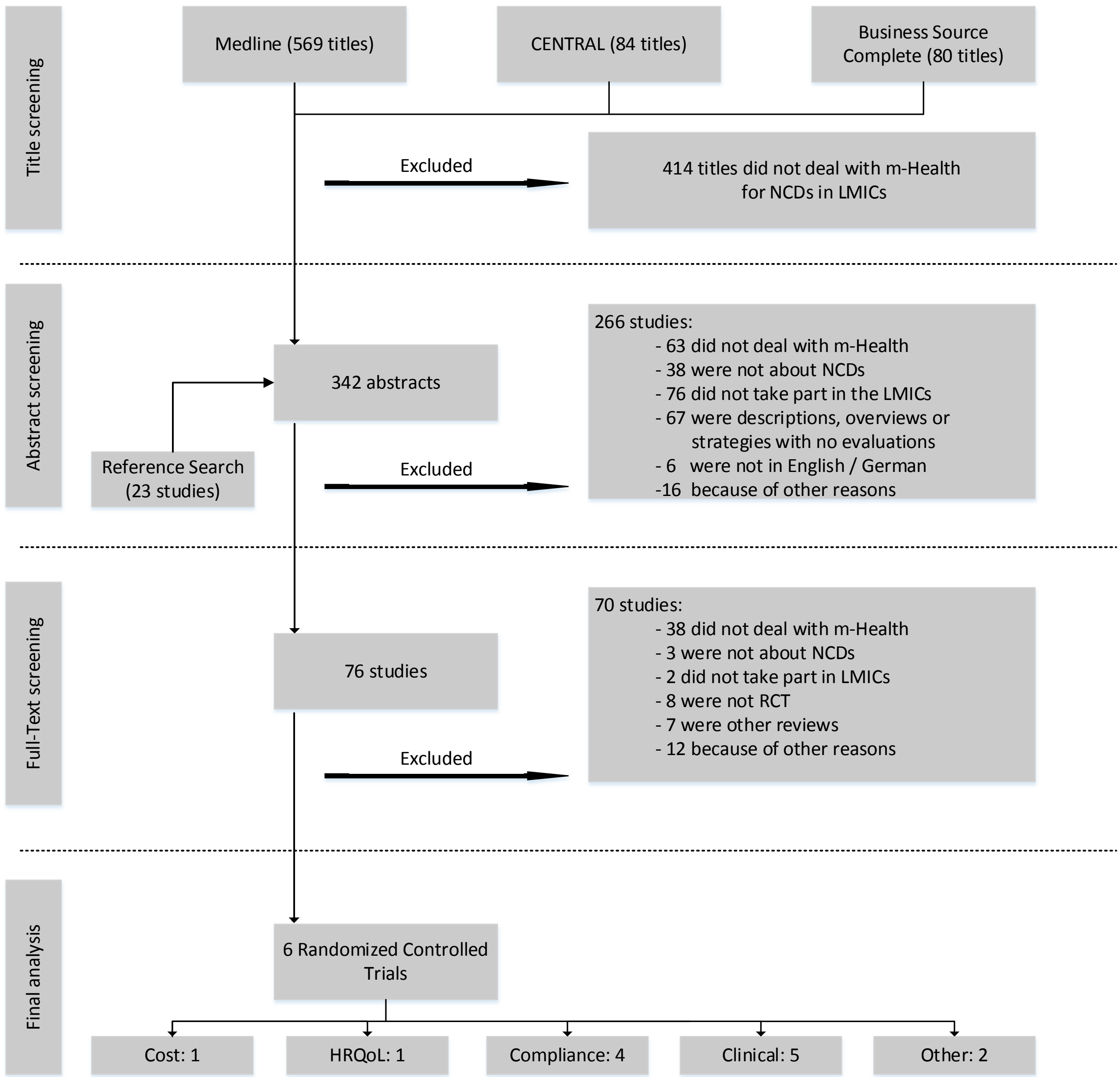
A systematic assessment of the risk of bias was conducted to ascertain the validity of the RCTs. The risk of election, performance, detection, attrition, reporting and other biases were assessed. The risk of bias of individual studies was summarized in a risk of bias table, giving a classification for every study as having an either low, high or unclear risk.

C. Results

Figure 5 illustrates the process of the literature search and highlights the main reasons for exclusion. The search identified a total of 733 studies in the three databases (without counting of duplicates) and 414 studies were excluded during title screening, mostly because titles indicated that studies did not focus on LAMICs. In step two, abstracts were screened and 266 studies were excluded. The most important reasons for exclusion were: 1) Studies did not deal with the definition of mHealth (n=63), 2) they were not about NCDs (n=38) and 3) they did not focus on

LAMICs (n=67). Additionally, editorials and letters were excluded. Studies that did not include any form of evaluation (n=67) or were not written in English or German language (n=6) were excluded. Other reasons for exclusion (n=16) were for instance the absence of a comparison group.

Figure 5: Overview of the screening process with the different steps (title-, abstract-, fulltext-screening) and the main reasons for exclusion



23 studies were identified from references of other studies or systematic reviews and their abstracts were also screened for inclusion in the review. Full texts of 76 studies were screened of which 70 were excluded because (1) they did not deal with mHealth (n=38), (2) were no RCT (n=8), (3) did not focus on NCDs (n=3), (4) focused on high-income countries (n=2), or (5) other reasons (n=12), such as redundancy (different reports of the same evaluations). Consequently, out of the 733 studies retrieved from the primary literature search, 727 studies were excluded and only 6

studies met all inclusion criteria. (The 77 studies included in the title screening can be reviewed in the appendix).

General Overview

Table 2 and table 3 summarize the main characteristics of the six included studies, as well as their study designs. Following Howitt et al. (2012), the studies are categorized into two groups of interventions: (1) Applications that provide one or two way communications to monitor health-conditions, maintain caregiver appointments, or ensure medication regimen adherence are summarized under the category *remote monitoring and integrated care interventions*. (2) The one-way delivery of health information or awareness raising and (mass-oriented) tele-education are classified as *health promotion and awareness.*

Three studies were conducted in LMICs, four in UMICs. One study reported results of two trials, where one was conducted in an UMIC (Mexico) and the other one was proceeded in a LAMICs (Honduras).One study was conducted in Uruguay, which today is classified as an HIC, but during the time the study was conducted, it was categorized among the UMICs. The participating population came mostly from urban areas and were recruited mainly from primary care centers or urban hospitals. One study was conducted in a semi-rural/rural area.

In almost all the studies, the participants needed to own a cellphone, be able to use it and read its messages. Thus, most of the interventions required the participants to read SMS. Most participants had some years of formal education. Only one study provided a subgroup analysis for people with low literacy and/or higher information needs about their disease.

In most of the studies the participants had to own a cellphone, to use it and read its messages. In one study (Liu et al. 2011) participants were loaned a telephone if they did not have a compatible one. In another study (Liew et al. 2009), it was not mandatory that the participants own a phone as long as they had an accompanying person with a phone who would be able to contact the patient at any time.

Two studies dealt with diabetes, two with asthma, one with severe forms of hypertension and one with different NCDs, including hypertension, asthma and diabetes. In the majority of cases, the participants were diagnosed with their disease at least six months before the intervention started.

A total of 1849 participants were included in all six studies. 780 participants received an mHealth intervention. One study contained a second intervention group (Liew et al. 2009) with 314 participants. Overall, the control group consisted of 755 participants and the mean age was 56.1 years.

Narrative summary

Balsa and Gandelman (2010) conducted their study in Uruguay and tested the effects of an internet-based/SMS-supported information system on patients with type 2 diabetes. Participants were recruited from waiting rooms of specialists for internal medicine treating diabetic patients in Montevideo between April and July 2009. It was mandatory for the intervention-participants to have access to the internet and a mobile phone, at least once a week. The intervention consisted of an internet-based platform informing the participants about type 2 diabetes, healthy lifestyle and providing links to additional internet-based sources where they could ask questions regarding their disease (via forums, chats, wikis). The patients in the intervention-group received in addition periodic reminders about new topics through SMS. Before the beginning of the intervention, all patients in the intervention group were invited to participate in a short workshop, instructing them how to use the internet-platform. At baseline, the patients were interviewed. Follow-up interviews were conducted six months after the intervention started (after the initiation of the distance phase). Beside the impact on knowledge about type 2 diabetes, behavioral changes and self-perceived overall health, systolic/diastolic blood-pressure and different glucose-metabolism related parameters were evaluated.

Shetty et al. (2011) studied the effects of using SMS to ensure the adherence to prescriptions by diabetic patients. Patients within the intervention group received an SMS once in three days. The messages consisted of varied instructions on medical nutrition therapy, physical activity, healthy living habits as well as reminders of the drug intakes. Outcome measures were followed for one year and were compared to the baseline-data. Beside the acceptance of the SMS and the frequency of visits, the adherence to the prescription was observed. The latter included behavioral changes, such as enhanced physical activity, diet modifications and the use of pharmaceutical drug. Moreover, health outcomes, HbA1c level and other glycemic parameters, were measured.

Liew et al. (2009) studied the effect of SMS-reminders on the attendance rate in follow-up visits of patients with chronic diseases and compared them to telephone-calls and no reminders in Malaysia. Patients were recruited from two different urban clinics in Kuala Lumpur, if they had at least one chronic (non-communicable) disease and owned a mobile phone. Furthermore, it was demanded that the patients were able to read and understand text messages on their cellphone. Reminder-messages were sent to the patients of the SMS-group 24-48 hours before their scheduled appointment. Standardized telephone calls were made within the same period. If the call was not successful, 3 other attempts were made. Main outcome measure was the number of attenders, defined as those who showed up for their appointment or changed/canceled it.

Liu et al. (2011) investigated the effect of a mobile-phone based self-care system on patients with moderate-to-severe persistent asthma in Taiwan. Participants were recruited from outpatient-clinics. All of them received education on asthma and were asked to measure and record their daily peak expiratory rate and their asthma symptoms in a diary. The intervention-group received an interactive self-care software for their cell-phones (but if they did not have a compatible cell-phone, they could loan one). Patients were taught how to use the software, in which they followed an interactive questioning system about their peak expiratory flow rate (PEFR), their quality of sleep, severity of coughing, difficulty in breathing and their daily activities affected by asthma. The patients received corresponding management advice via General Packed Radio Service (GPRS) immediately. The control-group patients were asked to record their PEFR on a daily basis and received an individualized asthma action plan with instruction for their self-management in the beginning of the study. The study was conducted over a period of six months. Clinical outcomes were compared to the PEFR, the Quality of Life, and medications used.

Table 2: Randomized controlled trials of mHealth interventions in LAMICs

Study	Location	Disease	Intervention	Sample Size	Mean Age	Outcome
Liew et al. (2009)	Malaysia (urban)	Diabetes, Asthma, Hypertension, Dyslipidaemia, Coronary Artery Disease	SMS reminders for follow-up attendance	314 (telephone) 398 (SMS) 309 (control	58.19	Attendance rate
Liu et al. (2011)	Taiwan (urban)	Asthma	Recording of daily symptoms with interactive phone-software with corresponding management advises	60 (intervention) 60 (control)	24.6	FEV (1)[a], Forced Vital Capacity, cost of money and time
Ostojic et al. (2005)	Croatia (urban)	Asthma	Sending daily data about the asthma to a doctor who responded with individualized advises	8 (intervention) 8 (control)	24.6	FEV (1)[a], Forced Vital Capacity, cost of money and time
Piette et al. (2012)	Honduras (rural), Mexico (urban)	Hypertension	Home blood pressure monitoring in combinations with automatic mobile ph one calls	99 (intervention) 101 (control)	56.1	SBP[c], number of medication problems, depressive symptoms, overall health, satisfaction with HTN and overall care

Table 2: Randomized controlled trials of mHealth interventions in LAMICs

Study	Location	Disease	Intervention	Sample Size	Mean Age	Outcome
Balsa and Gandelman (2010)	Uruguay (urban)	Type 2 Diabetes	Information and material related to diabetes provided on a website and via a weekly SMS reminder	195 (intervention) 193 (control)	n/d	Knowledge about type 2 diabetes, behavior changes, self perceived overall health , BP, Glucose parameter
Shetty et al. (2011)	India (urban)	Diabetes	Frequent SMS-reminders reminding the patient of drug intakes and other behavioral habits	110 (intervention) 105 (control)	50.1	HbA1C[d] values, annual follow up

a: Forced Expiratory Volume in 1 second

b: Peak Expiratory Flow Rate

c: Systolic Blood Pressure

d: Glycated hemoglobin

Table 3: Study design of the included randomized controlled trials

		Criteria		Care-type	
Study	**Place of Recruitment**	**Exclusion**	**Inclusion**	**Intervention**	**Control**
Liew et al. (2009)	Two primary care clinics in Kuala Lumpur	Illiteracy, Inability to read or understand text messaging	Registered with the clinics for at least 6 months, return appointment between 1 and 6 months, ownership of a mobile phone	SMS-appointment reminder & Telephone appointment reminder	No reminder
Liu et al. (2011)	Outpatient clinics of Chang Gung Memorial Hospital, Linkou, northern Taiwan		Moderate to severe Asthma	Mobile Phone based interactive self-care software	Booklet for written asthma diary and action plan,
Ostojic et al. (2005)	General Hospital “Sveti Duh”, Zagreb, Croatia	Non-smoking, chronic bronchitis or emphysema	Moderate Asthma for at least 6 months, consistent access to a cellphone, able to use SMS	Weekly therapeutic advise	No weekly therapeutic advise
Piette et al. (2012)	Four private and two public clinics in Cortes, Honduras and one primary care center in Real de Monte, Mexico		SBP >= 130 mm Hg if diabetic and SBP >= 140 mm Hg if non-diabetic, between 18 and 80 years, access to a cellphone and able to use it	Mobile blood pressure monitors in combination with weekly therapeutic advises	No weekly therapeutic advise

Table 3: Study design of the included randomize controlled trials

		Criteria		Care-type	
Study	**Place of Recruitment**	**Exclusion**	**Inclusion**	**Intervention**	**Control**
Balsa and Gandelman (2010)	Waiting rooms of internists treating diabetic patients or endocrinologists at three HMOs in Montevideo	Diabetes 1; pregnant, taking insulin, under dialysis treatment	Adult patients with Diabetes 2; Access to Internet (at least once a week)	Internet-based/SMS-supported	Brief educational brochure
Shetty et al. (2011)	Patients at a diabetes centre in Chennai, India	Inability to read and to make clinic visits at 3 months interval	Type 2 Diabetes with a minimum duration of 5 years; Minimum of high school education, HbA1c value ranging between 7 % to 10 %	SMS once in 3 days reminding the patient about the prescriptions	Oral advises on diet modification and physical activity

Ostojic et al. (2005) ascertained the impact of weekly sent SMS as an additional tool for asthma-control. Participants with persistent asthma were recruited from a clinic in Croatia. All of them had a 1-hour asthma education session and were advised to measure and note their daily peak expiratory flow rate (PEFR), their medication use and symptoms in general. A spirometry was done in the beginning of the study. Participants in the intervention group were instructed to send their records via SMS to a doctor. They received weekly SMS from an asthma specialist with advice for their treatment, based on the data they sent before. The study was conducted over a period of 16 weeks and at the end, the forced expiratory volume in 1 second (FEV1) was measured, the daily consumption of inhaled medication and the cost of time and money for the monitoring were assessed. Moreover, the daily self-recorded symptoms were compared among the two groups.

Piette et al. (2012) observed the effect of home blood pressure monitoring in combination with structured mobile phone calls among hypertensive patients in Honduras and in Mexico. Participants with Systolic Blood-Pressure (SBP) suggestive of hypertension were recruited from different rural and semi-rural clinics, a primary care practice and a diabetes clinic. The intervention group received mobile blood pressure monitors and they were instructed to measure their blood pressure several times in a week and to record it. They received weekly automated calls regarding their measured blood-pressure and based on these values, advice and medication reminders were given. After six weeks, both groups were visited by trained research associates who measured the patients' SBP. Additionally, surveys were conducted regarding their perceived general health, depressive symptoms, medication-related problems and the overall satisfaction with care. A sub-group analysis was performed among patients with low-literacy or high hypertension information needs.

C.1 Outcomes

Table 4 provides an overview of all relevant study outcomes by showing the intervention-group results compared to the control-group results (the values of the different parameters with their P values can be retrieved from the Appendix). In the second part the outcomes will be summarized and classified according to their type of outcome. The following classifications were chosen: Clinical outcomes, Compliance, Quality of Life, Costs and other outcomes.

C.1.1 Clinical Outcomes

Five studies observed the impact of mHealth on clinical outcomes.

Balsa and Gandelman (2010) compared the impact of a web-based education and SMS reminder for patients with type 2 diabetes with a conventional paper-based education form. They found no impact on clinical outcome variables; neither regarding blood pressure (systolic and diastolic) nor regarding glucose level (fasting and two hours after eating).

Shetty et al. (2011) studied the impact of motivational SMS, consisting various instructions on medical nutrition therapy. He found no significant difference in the percentage of obesity among the two groups. The percentage of patients with abnormal glycaemic parameters and cholesterol level decreased significantly in the SMS-group, as well as the percentage of people having hypertriglyceridaemia.

Piette et al. (2012), who studied the impact of individualized weekly mobile phone calls with advices for hypertension, found a non-significant difference (4.2 mm Hg relative decrease; p=0.09) in systolic blood pressure among patients in the intervention-group as compared to the control group. Furthermore, they discovered a large reduction among the subgroup of intervention-participants with low-literacy or high information needs (a reduction of 8.8 mm Hg with 95 % CI [p=0.002].

Effects of mHealth interventions on patients with asthma were monitored by Liu et al. (2011) and Ostojic et al. (2005). The former found a significant increase of forced expiratory volume in 1 second (FEV1) values and a significant increase of the peak expiratory flow-rate (PEFR) for patients within the intervention group, who were supported by an interactive mobile phone software on a daily basis. Ostojic et al. (2005), who studied the effect of weekly reminder SMS, could not observe a significant difference in the absolute PEF or FEV1 values between both groups. However, patients in the SMS group had lower symptom scores for cough and night symptoms although they had similar scores for wheezing or limitation of activity.

C.1.2 Compliance

Compliance can be defined here as how the patients adhere to the prescribed treatment program. Examples are clinical attendance-rates for scheduled appointments, adherence to the drug regimen or adherence to recommended behavioral changes.

Among the included studies, four reported compliance-outcomes. Shetty et al. (2011) observed a satisfying compliance with the drug prescription for both the intervention and the control group but unfortunately without giving any more details. Liu et al. (2011) and Ostojic et al. (2005) found no significant differences in the consumption of steroids, antileukotrienes or ICSs between the intervention and the control-group. Furthermore, Liu et al. (2011) found no significant differences in adherence to the prescribed asthma-plan. Over 70 % of the intervention-patients were still adherent to the interactive self-care system after 3 and 6 months, likewise the control group, which kept on recording their asthma in diary booklets and kept on with their action plan. With respect to the attendance rate of scheduled appointments, Shetty et al. (2011) found a non-significant difference in the annual follow-up rate between intervention and control-group. Liew et al. (2009), who compared SMS reminders with telephone reminders and no reminders, ascertained a significantly lower non-attendance for patients in the SMS and the telephone group than those in the control group. But there was no difference found between the two interventions.

Table 2: Overview of intervention-group outcomes compared to control-group outcomes; grey: no difference; light-green (+): superior to control group without significance; dark-green (++): superior to control group with significance (p<0.05); red (-): inferior to control group

	Study	Balsa and Gandelman (2010)	Shetty et al. (2011)	Ostojic et al. (2005)	Liu et al. (2011)	Piette et al. (2011)	Liew et al. (2009)
Outcomes	**Disease**	**Diabetes**		**Asthma**		**Hyper-tension**	**-**
Clinical	SBP[a] (mm Hg)					++[b]	
	Fasting blood glucose level						
	BMI[c] <26 kg/m^2						
	PPG[d] <180 mg		++				
	HbA1c[e] <8 %		++				
	TC[f] <150 mg/dl		++				
	HDL-C[g] >40 mg/dl						
	LDL-C[h] <100 mg		++				
	FEV1 %[i] predicted			+	++		
	PEFR[j] L/min			+	++		
	PEF[k] variability			++			
	Coughing			++			
	Night symptoms			++			
	Wheezing						
	Limitation of activities						
Compliance	Attendance		+				++
	ICS[l] dosage				+		
	Systemic steroids				+		
	Antileuktorine						
	Long-acting beta2-agonist						
	Adherence to diet prescription						
	Adherence to physical activity		+				

	Study	Balsa and Gandelman (2010)	Shetty et al. (2011)	Ostojic et al. (2005)	Liu et al. (2011)	Piette et al. (2011)	Liew et al. (2009)
Outcomes	**Disease**	**Diabetes**		**Asthma**		**Hyper-tension**	**-**
QoL[m]	Physicial component				++		
	Mental component				++		
Cost	Monetary			-			
	Timely			-			
Other	Knowledge						
	Perception of health quality						
	Health-related behaviors						
	Physician-Patient relationship						
	Depression scores					++	
	Perceived overall health					++	
	Overall satisfaction with care					++	
	Number of medication problems					++	

a: Systolic Blood Pressure

b: Subgroup of low-literacy people/people with higher education needs

c: Body Mass Index

d: Postprandial Plasma Glucose Test

e: Glycated hemoglobin

f: Total Cholestorol

g: High-Density Lipoprotein Cholesterol

h: Low Density Lipoprotein

i: Peak Expiratory Flow Rate

j: Forced Expiratory Volume in 1 second

k: Peak Expiratory Flow

l: Inhaled Corticosteroid

m: Quality of Life

Regarding the adherence to other prescriptions, Shetty et al. (2011) observed no significant changes in the adherence of diet prescriptions or physical activities.

Quality of Life

One study observed the effects of mHealth on Quality of Life. Liu et al. (2011) used the SF12 questionnaire, and discovered an increase of the physical component score for patients who received the intervention (changes were observed two months after the start of study). No significant change was found for the mental component among the mobile telephone group. Interestingly a significant decrease in the mental component was found in the control group, which started after a study period of four months.

C.1.3 Costs

Only one study observed the impact of the intervention on costs for patients and physicians. Ostojic et al. (2005) estimated that the intervention would lead to additional monetary costs per patient and extra-time spend per week. The physician’s time per patient was 2 minutes per week at a cost of 1 Euro.

Other Outcomes

Piette et al. (2012) measured depression scores, as well as the perceived overall health and overall satisfaction with the care of all participants. Compared with the control group, patients in the intervention had lower depression scores, were more satisfied with their care, and reported better overall health.

Balsa and Gandelman (2010) looked at the physician-patient relationship and assessed the patient trust as well as doctor-patient communication with the help of the Primary Care Assessment Survey (PCAS). Comparison of the baseline and the follow-up values revealed that the intervention had no effect on these variables. Other variables showed the same results such as patients knowledge about their disease, perception of their health-care and health-related behaviors.

C.2 Bias

A closer look was taken at the study-designs in order to identify -possible source of bias (table 5). This was done following the criteria defined by the Cochrane Collaboration, which distinguish between selection-, performance- detection- and reporting-bias.

C.2.1 Sequence generation – Selection bias

Four studies used computer-supported randomization for allocating the participants to the different groups (e. g. ”randomized [...] using a computer-generated random number” Shetty et al. (2011)). Two studies (Balsa and Gandelman, 2010; Liu et al., 2011) do not provide information about how the randomization was achieved (e. g. ”the patients were randomized into two groups” (Liu et al. (2011)). The risk of bias for the sequence generation of these two studies is therefore unclear.

C.2.2 Allocation sequence concealment – Selection bias

None of the studies explicitly mentions measures taken to ensure concealment of the allocation sequence. Thus, the risk of bias is unclear. In one study (Liew et al. 2009), the risk of bias is perceived as low because of the kind of intervention; automatically generated SMS were sent 24-48 h before the next scheduled appointment to the participants who were provided beforehand with an anonymous identification code. This procedure seems so automatized that a risk of bias is unlikely.

C.2.3 Blinding of participants and personnel – Performance bias

Given the characteristics of the interventions, blinding of the participants was barely possible. Also, blinding of the study personnel was difficult because it was often necessary to explain to the participants how the mHealth intervention worked or how to use the mHealth application. E. g. Piette et al. (2012) states that, ”it was not possible to blind patients or their clinicians to their experimental assignment because research associates needed to demonstrate the use of the blood-pressure monitor to ensure that low-literacy patients understood the procedure”. Although this is reasonable, a standardization of the explanation-process could have reduced the risk of bias.

Other studies also lack information about the explanation process. They do not describe whether the study personnel responsible for care used standardized guidelines. The risk of bias for all of these studies is therefore unclear.

Ostojic et al. (2005) state that the study personnel was not blinded, but highlights the fact that standardized guidelines were used for explanation. Furthermore, the author emphasizes the low risk of bias on that point. Liew et al. (2009) is the only study where personnel was explicitly blinded, which was due to the fact that no explanation of the system was needed. In these two studies, the risk of performance bias is therefore reduced to a low level.

C.2.4 Blinding of outcome assessment – Detection bias

No study mentions if the outcome assessors were blinded. Therefore, the detection bias related to different outcome measure was taken into account: In the study of Liew et al. (2009), the non-attendance rate which was clearly defined by the authors was recorded. It is an objectively measurable outcome and the knowledge about the intervention should not have influenced the outcome assessment. Similar to Ostojic et al. (2005) where the way of assessing the outcome uses standardized techniques such as using office spirometry for FEV1 and PEF testing, the risk of bias is low.

Other studies have similar, standardized outcome assessments (e. g. electronic BP monitoring in Piette et al. (2012), although some outcome assessments lack detailed descriptions in the studies, for example the QALYs (e. g. Liu et al. (2011)), the depressive symptoms in Piette et al. (2012) or the data about physical activity, dietary adherence in Shetty et al. (2011). Despite the fact that almost all the main outcome parameters were standardized the risk of bias is unclear especially due to the vague description for some other outcomes assessments.

Table 3: Bias of the included studies; grey: unclear risk of bias; red (-): high risk of bias; green (+): low risk of bias

	Sequence generation – Selection bias	Allocation sequence concealment – Selection bias	Blinding of participants and personnel – Performance bias	Blinding of outcome assessment – Detection bias	Incomplete outcome data	Selective outcome reporting – Reporting bias	Other bias
Balsa and Gandelman (2010)					+	+	+
Liew et al. (2009)	+	+	+	+	+	+	+
Liu et al. (2005)					-	+	+
Osotjic et al. (2005)	+		+	+	+	+	+
Piette et al. (2012)	+		-		+	+	+
Shetty et al. (2011)	+				-		+

C.2.5 Incomplete outcome data

Shetty et al. (2011) report a high drop-out rate for the annual follow-up with 29 % in the intervention and 37 % in the control group. Similarly, Liu et al. (2011) recorded a drop-out rate of 28.3 % (intervention-group) and 23.3 % (control-group). These relatively high drop-out rates may result in a high risk of bias. All other studies had a moderate drop-out rate and all studies used intention-to-treat analysis instead of per-protocol analysis.

C.2.6 Selective Outcome Reporting – Reporting bias

All studies presented all listed variables, including their significance levels. Only Shetty et al. (2011) did not report about one outcome (Use of drugs) and just states *"were followed satisfactorily by both groups"*. This implies a certain risk of bias. However, a biased reporting about mHealth in general was not detected. Due to the low study sample size and the variety of outcomes, it was not possible to use instruments such as funnel plots.

C.2.7 Other bias

Only the study of Piette et al. (2012) showed some imbalances in baseline-characteristics of the different groups. More patients in the intervention group than in the control group reported taking anti-hypertensive medication at baseline (89 % vs. 77 %, p=0.04). The baseline medication usage was therefore included, as a co-variate in the analysis of intervention-effects. This resulted in an unclear risk of bias.

D. Discussion

D.1 Summary of evidence

CLINICAL OUTCOMES

Two studies (Liu et al., 2011; Ostojic et al., 2005) found improvements in pulmonary functions for patients with Asthma (FEV1 and PEF values), though, some parameters improved only non-significantly which may be explained by the studies' small sample size (see limitations). Both studies show more improvements in night symptoms and episodes of coughing.

With regard to diabetes, Shetty et al. (2011) showed a non-significant higher percentage of people with better glycemic levels when compared to the conventional treatment. Other parameters showed significant improvements for people receiving frequent SMS reminders, such as the lipid profiles or number of patients with HbA1C values <8 %.

Balsa and Gandelman (2012) found no impact on clinical outcome variables. Their interventions was using a generalized information system.

The home blood pressure monitor combined with advisory weekly sent SMS for patients with hypertension (Piette et al., 2012) revealed no differences for mean blood pressure measures between the two groups but showed larger improvements for the low-literacy subgroup with high need of education. Although the study tends to be partially imprecise (see limitations), it indicates the impacts mHealth can have on different groups of people.

These effects on clinical outcomes reveal a clear tendency of mHealth being a useful supporting tool for NCD management.

COMPLIANCE

Two studies (Liu et al., 2011; Ostojic et al., 2005) observed the compliance of patients with their physicians' prescriptions, such as behavioral or drug prescriptions. In terms of drug prescription, most of the parameters did not show any significant inter-group differences. Although some of them showed improvements for the intervention group (with no statistical significance) and only the mean daily dosage of inhaled corticosteroids increased significantly for the mHealth group. The non-significant results could be caused by study limitations, such as Liu et al. (2011) high dropout rates and Ostojic et al. (2005) small study sample size (see limitations).

Two other studies (Shetty et al., 2011; Liew et al., 2009) observed the attendance rate of follow up appointments. Both showed better rates for people who received mobile phone reminders, although one did not show significant improvements (Shetty et al., 2011). The quality of the study with significant improvements is high, while the other one has study limitations (see limitations). Previous evaluations also presented improvements of mobile interventions on follow-up attendance rates and therefore, emphasize the results of this review (Chen et al. 2008; Beratarrechea et al. 2014).

Concerning the compliance with behavioral and drug prescriptions, the study results are too vague when taking the study limitations into consideration. With regard to the attendance-rate for follow-up appointments, on the other hand, there is a higher level of evidence that mHealth is significantly improving it.

COSTS

Only one trial assessed the costs of mHealth by calculating the amount of extra-time and money needed for a patient compared to the usual healthcare delivery. Unfortunately, no further evaluation of the cost-effectiveness of mHealth' was made, but it is only assumed here that the SMS intervention may produce greater savings than costs.

Previous evaluations on mHealth interventions for CDs have shown their potential cost-effectiveness. For example Mahmud et al. (2010) estimated the fuel-savings and time-savings for HCWs and nurses who were equipped with a cellphone for general healthcare delivery including all kinds of tele-diagnoses and appointment reminders.

At the end of the pilot study, the hospital saved 2048 hours of health worker time and doubled the capacity of the tuberculosis treatment program. Zurovac et al. (2012) assessed the costs of an mHealth intervention where all health workers received text messages on their personal mobile phones on malaria case-management. They calculated the cost per child being managed correctly on different implementation-scales: 0.50 USD under study conditions, 0.36 USD if implemented by the Ministry of Health in the same area and 0.03 USD if implemented nationally.

QUALITY OF LIFE (QOL)

Only one study observed the impact of mHealth on QoL. The health-related quality of life of the participants revealed to be significantly better with mHealth than with usual care, according to both their physical and their mental components. Looking at the already mentioned positive impacts of mHealth, this is not particularly surprising because it is likely that quality of life values increase with an effective chronic disease management (Cafazzo et al. 2012). For the future, it would be important to have more studies evaluating the impact of mHealth on QoL because, QoL measures are critical for decision-making in the health-care sector (Santana and Feeny 2008).

OTHER OUTCOMES

Other outcomes including doctor-patient communication and health-care satisfaction were evaluated by two trials. One study, Balsa and Gandelman (2010), did not find any improvements; neither for the patient-trust in physicians, nor in the doctor-patient communication.

In contrast, Piette et al. (2012) discovered improvements for various parameters, including depressive symptoms, the number of medication problems, satisfaction with care and perceived overall health.

Both studies have some limitations . However, other studies which have observed positive impacts of mHealth on parameters such as patients' anxiety or satisfaction with care. For example Jareethum et al. (2008) found that explanatory SMS for pregnant women can reduce their fears which were caused by the effects of pregnancy (such as nausea and frequent urination).

With NCDs, messages which explain the course of a disease or the side-effects and consequences of treatment could help to demystify them (e. g. loosing hair when having a chemotherapy). The impact of diseases and the side-effects of medication therapies, which are widely known among the people in HICs, are not necessarily known among the people in LAMICs (Grady 2013, 2013). Therefore mHealth could play a crucial role in accompanying a patient in the time between the appointments with health professionals.

D.2 Comparison of different types of mHealth

Another way of looking at mHealth's efficiency is by taking the kind of intervention into consideration. All of the six studies used different types of mHealth, such as SMS and phone-calls.

The most basic intervention, where a single SMS as an appointment reminder has been used (Liew et al. 2009), proved its efficiency (this has been underlined by other studies – see above). The question then arises; why was it so effective?

Table 4: Health-related impacts depend on the kind of mHealth intervention, green implies improvements, red implies no changes compared to the intervention group and gray means no conducted observations so far; number of +/- indicate the number of studies with these results

<table>
<tr><th>Outcomes / Intervention</th><th colspan="2">Clinical</th><th>Compliance</th><th>QoL-related</th><th>Costs</th></tr>
<tr><td>Tailored
(Piette et al. (2011); Liew et al. (2009); Ostojic et al. (2005); Liu et al. (2011))</td><td colspan="2">+++</td><td>+++</td><td>+</td><td>-</td></tr>
<tr><td>Generalized
(Balsa and Gandelman (2010); Shetty et al. (2011)</td><td>+</td><td>-</td><td>-</td><td>-</td><td></td></tr>
</table>

One basic characteristic of the SMS-reminder intervention was that it was tailored for the patients, that is, the SMS were sent to them individually (24–28 hours prior to their appointment). Beside of that, it used only one channel/platform for transmitting the messages. These two basic characteristics were also noticed in three other studies. In one study (Liu et al., 2011), the patients recorded their daily symptoms, sent them via SMS to a HCW who responded with a tailored advice. In another study (Piette et al., 2012), the patients received calls with individualized advices based on home-blood-pressure data they gathered. And in a third study (Ostojic et al., 2005), the participants used an interactive phone-software (comparable to a smart-phone application) where they entered specific daily data about their disease and received automatically tailored advises on their phone. Looking at the results of these studies reveals that all of them improved the health-status in terms of clinical-outcomes (such as pulmonary functions for people with asthma or the blood pressure for low-literacy people with hypertension) or quality of life related outcomes (such as depression scores, the satisfaction level with the health-care systems or the patient-physician trust). Some of the outcomes, however, did not improve significantly which can be explained by some study limitations (see below).

In contrast, the study by Balsa and Gandelman (2010), which used different platforms (the SMS in combination with a web-page) for reminding/supplying patients with general information about their disease did not show any significant improvements for the measured outcomes. Here we have opposite characteristics: 1) the information on these platforms were general and not individualized for the patients. And 2) it combined two different systems (Internet and SMS). Another intervention (Shetty et al., 2011) focused on one platform but used SMS to supply the patients with general, non-tailored information. Here, mHealth showed partially significant improvements for some of the clinical outcomes as well as some compliance outcomes. Others were not significant; this might be as a result of the non-tailored messages. The motivation for the participants to follow the advices seems to be lower than for tailored messages.

In a nutshell, tailored mHealth interventions seem to have a better health-related impact than general, non-tailored messages.

D.3 Limitations

D.3.1 Validity

The quality of the included studies varies, but remains acceptable. The randomization was adequate in all trials (only 2 studies did not mention the kind of randomization used). Two studies, Shetty et al. (2011) and Liu et al. (2011), had a high drop-out rate which lowers the quality of the presented outcomes and raises the possibility that the observed effect is biased. However, all of the studies used intention-to-treat analysis. Liew et al. (2009) reveals a very low level of risk of bias due to its standardized outcomes.

Liu et al. (2011) and Ostojic et al. (2005) had very small sample sizes with 89 and 16 participants, respectively. Especially in the latter, the number of participants leads to considerable uncertainty which limits the findings of the study.

Another possible limitation is related to the relatively short time-span of one study. Piette et al. (2012) has only a time-span of 6 weeks from baseline to follow-up measures. This might be too short a period for measures of effects on chronic diseases such as hypertension. The other studies have longer observation periods, starting from 4 months until 1 year.

Another problem is related to the difficulty of allocating an effect to the mHealth part of an intervention. Piette et al. (2012) studied a combination of a BP monitor with a mobile phone connection. It is likely that the measured effects are dependent on both systems and therefore, can’t be reproduced with just one of it. Furthermore, the intervention of Balsa and Gandelman (2010) was about a combined webpage/SMS-reminding system. In this case it is very likely that effects here were more a result of the SMS part of the intervention, because most of the participants were reached by SMS and barely visited the web-page.

D.3.2 Review process

Considering the limitation of the review process, it has to be pointed out that only peer-reviewed, but **no grey literature**, publications were included. As mentioned in chapter C, several tests were made with the Google-search, especially with 3rd party applications (e. g. Publish or Perish). But it turned out that the Google search has some major limitations, compared to professional literature search interfaces:

The Google-scholar searching-mask-field is limited to 256 characters. It was barely possible to specify all the inclusion criteria in that field. Additionally, no truncation operators can be used. That resulted in a very low precision of the results. The result-page of Google is limited to 20 results per page and the search-results can't be conveniently saved. This makes 3rd party programs inevitable (in this case Public or Perish has been used). Unfortunately, it was, due to the functionalities of these programs which are likely to get blocked by Google after a specific number of search-requests for 48 hours. The searching-process was therefore inconvenient. These and other limitations of Google-scholar as a replacement for systematic literature searches were also mentioned by (Boeker et al. 2013).

Other limitations of the review process might have been the restriction to the two **languages** German and English, although only 6 studies were excluded because of the language.

A difficulty in the study selection process was the distinction between **what mHealth is** and what it is not. Although it is clearly defined in the beginning, some interventions combined mHealth components with non mHealth components.

One important limitation is that our review focused exclusively on **randomized-controlled trials**. Other intervention trials using less rigorous methods, such as quasi-experimental or non-randomized trials might provide information, which could be useful for fully understanding the impact of mHealth on NCDs. More than 500 mHealth pilot projects in LAMICs were mentioned by (Collins 2012). Nevertheless, our focus on RCTs guarantees the strongest and most unbiased estimation of effects.

EXCLUDED STUDIES

The evaluations that were excluded during full-text screening because they were no RCT are presented in table 7 with a summary of the kind of interventions, the results and the reasons for exclusion.

The reasons for exclusion varied from study to study: There was either no randomization conducted (Quinley et al. 2011; Fruhauf et al. 2013: Tran et al. 2011) no control group and the design was only a single-group, pre-post design (Desai et al. 2003); Khokhar et al. 2009; Piette et al. 2011; Nakashima et al. 2013), or control group participants were not representative (Odigie et al. 2012).

Looking at the small number of studies even when including non-RCTs, the lack of evaluation among the peer-reviewed literature is evident. This deficit is much bigger for mHealth regarding

NCDs than mHealth regarding CDs, where a much broader base of non-RCTs exists among the peer-reviewed literature (Howitt et al. 2012).

Some of the findings of the excluded non-RCT studies underline the results of this review. For example Piette et al. (2011) who observed the impacts of an interactive voice-call management found that patients with diabetes felt much better with their disease, they were less anxious and could decrease their HbA1c values significantly. Odigie et al. (2012) observed the effect of a continuous possibility for patients with cancer to call their doctors. The authors noticed, once more, an increase in attendance at the follow-up appointments and furthermore, a high acceptance among the intervention group of which almost 60 % had no formal education. Nevertheless, the findings of these studies should be carefully taken into consideration, because their study-designs have bigger potential for risks of bias.

Interestingly, three of the excluded studies (Tran et al. 2011; Fruhauf et al. 2013; Quinley et al. 2011) offer a glance on a so far not mentioned way of mHealth being used to support and educate HCWs, instead of interacting directly with patients. They will be presented in more detail in chapter F.

Table 5: Excluded studies because of no RCT-design with reasons for exclusion

Study	Intervention	Results	Exclusion Reason
Desai et al. (2003)	Telepathology between a tertiary cancer center and a rural cancer hospital	Diagnosis could be offered in 98.9 % of all cases	Observational study
Khokhar et al. (2009)	SMS reminder for conducting Breast self examination (BSE)	BSE increased significantly	Single group, pre-post study
Piette et al (2011)	An interactive voice response call management for patients with diabetes	Diabetes management improved; HbA1c values decreased significantly	Single group, pre-post study
Nakashima et al. (2013)	Different data were transmitted to a remote clinic, which conducted a diagnose and made a prescription	3 % of the participants could be classified as being an emergency	Single group, pre-post study
Odigie et al. (2012)	Participants were advised to call their doctors at any time	97 % had sustained their follow-up appointment against 19.2 %	The control group participants were dropped-out intervention participants

Study	Intervention	Results	Exclusion Reason
Tran et al. (2011)	Comparison of Face-2-Face consultation with remote diagnosis (using a smart-phone)	Overall agreement of 73 %	No randomization
Fruhauf et al. (2013)	Comparison of Face-2-Face with remote expert diagnosis (using a smart-phone)	Concordance between off- and on-site diagnosis was 74 %	No randomization
Quinley et al. (2011)	Comparison of on- and off-site diagnosis (using a smart-phone) for cervical cancer screening	Concordance between on- and off-site diagnosis was 70 %	No randomization

D.3.3 Applicability

All of the studies took place in MICs and none of them was conducted in LICs. Furthermore, most of the interventions took place among the urban population of the countries and not so much in the rural parts. Given the fact that a major part of the population in LICs still lives in rural areas (Satterthwaite 2003) the portability of the results might be limited. Moreover, low-literacy remains high among the LICs, as well as information needs about NCDs (Grady 2013). However, just one study did a subgroup analysis and observed interestingly different (or better) results than with the overall group analysis. Therefore, an enhanced focus on the group of people with higher information needs has to be done.

A wide field of outcomes are included in this study, starting from HbA1C measures and ending at patient-physician trust. This gives an interesting and good overview of mHealth effects on different diseases, but it limits the comparability of the effects. In addition, the mHealth interventions differ – three SMS, one interactive software, one system with automated calls and one combined Internet and SMS reminder. This makes it even more difficult to compare the results or the interventions. Nevertheless it is still possible to compare and highlight specific/common characteristics of the different interventions.

D.3.4 Other systematic reviews

Other systematic reviews within the field of mHealth and LAMICs exist and even if there has not been a review which evaluated solely the impact on NCDs, it is interesting to take a look and to see what methods were used, how many studies were found (and how many RCTs), what diseases they dealt with and what impacts were observed.

Deglise et al. (2012) conducted a review which observed only SMS-supported interventions for surveillance, management and treatment compliance of CDs. The authors did not restrict their search to RCTs and found in their screening process over 90 studies which reported the usage of SMS. A third of them included some sort of evaluation and only three of them were RCTs. The majority of the mHealth applications focused on HIV and mostly one-way messages (push-messages) were used. Most of the outcomes measured were about the process and the satisfaction. Both showed promising results and the SMS was well accepted by both the HCWs and the patients who looked at mHealth in an optimistic way, thinking that it can bring new opportunities to their health. Furthermore, it was observed that most people were familiar with how to use a phone. The authors concluded that the SMS (especially the one-way messages) may be one of the most cost-efficient methods of reaching a mass audience. However, the review lacked high quality evaluations and an evaluation of clinical outcomes. Nevertheless, the authors evaluated an important way of using mHealth. In the current review most of the studies worked with a two-way system where the sent SMS were mostly individualized and personalized for the patients, no mass messages were used. But sending mass-messages could be transferred to the field of NCDs for health promotion and education, such as calling the attention for the consequences of smoking or explaining complicated diseases like cancers.

Gurman et al. (2012) focused on the effects of mHealth on behavior change and found 16 articles which reported evaluations in developing countries, mostly in African countries. Almost all of them were about treating HIV or addressing family planning/pregnancy issues. The majority of the included studies used two-way communication systems. Similar to Deglise et al. (2012), the authors found positive results regarding the adherence to a prescribed treatment. They also discovered that mHealth is an effective tool for maintaining behavioral patterns, but less effective for changing behavioral patterns on its own. They therefore view mHealth as a promising tool but mention the need for stronger evidence on that topic. The insight that tailored two-way messages should not stand alone when establishing behavioral changes has important implications for the treatment of NCDS (such as cancer, diabetes and hypertension), where behavioral changes are most of the time necessary.

Kaplan et al. (2006) conducted a systematic review about mobile interventions within the developing world and the developed world in general. Over 90 % of the observed literature was from the developed world and of the few literature dealing with developing countries, almost none was about the usage of mobile phone for NCDs. Beside the small number of studies, the authors mentioned the difficulty to generalize the observed and measured outcomes because of their variety. Furthermore, they noted that the transfer of mobile interventions from the developed to the developing world is difficult, because the usage of mobile phones is different from each other – while in the developed world most of the people own a mobile phone, people in less developed are used to share it. In the end, with regards to the increasing prevalence of NCDs in the less developed world, the authors concluded that possible mHealth interventions need to be dynamic and sustainable over time as patients' lives will change. Kaplan (2006) gives more general suggestions and therefore, the implications for the context of NCDs in LAMICs is low. But it shows once more how young the field is. Moreover, it would be interesting to see if the model of a shared phone in these countries is still the case, giving the increasing numbers of mobile phone subscriptions within the last years.

A very large systematic review was published by the Lancet in 2012 (**Howitt et al. 2012**), where a literature search with 9212 articles from peer-review journals was conducted. Only 9 RCTs could be found, most of them for CDs. Mostly they used the basic mobile phone functions such as the SMS or the voice function. The analysis concludes how the communication between the different actors among a health-care system could be improved and lists several examples of positive results for different areas of mHealth. Unfortunately, this publication which is only part of an appendix, does not give a systematic overview of all results of the included studies and presents the possible applications in a more general way. However, a closer look at the findings will be done in the next chapter, where the most important results will be presented.

Another systematic review was conducted by **Beratarrechea et al. (2014)**. The authors focused on the impact of mHealth on chronic disease outcomes in developing countries. They found numerous positive results, such as the improvements on attendance rate as well as benefits of SMS in the support of the self-management for long-term illnesses. Concerning mHealth's cost effectiveness, it is noted that SMS are more cost effective than telephone interventions. Clinical outcomes were partially improved and reductions in symptoms and physical impairment were also observed. In the end, it is mentioned that more high quality studies – especially focused on longterm follow up measurements – are needed in order to get a better understanding of the impacts of mHealth on long-term diseases. Although Beratarrechea's systematic review has similarities to our review, some significant differences exist:

1) Beratarrechea et al. (2014) focused on the field of chronic diseases and not NCDs 2) They used different databases for their literature-search (e.g no search was conducted on the Business Source Complete database) 3) They had more exclusion criteria (e. g. restrictions regarding the included outcomes and 4) Beratarrechea et al. (2014) used a different definition of mHealth. Hence they included studies, which we would have excluded (e. g. Ramachandran et al. (2007), an intervention which used conventional telephones, instead of cellphones).

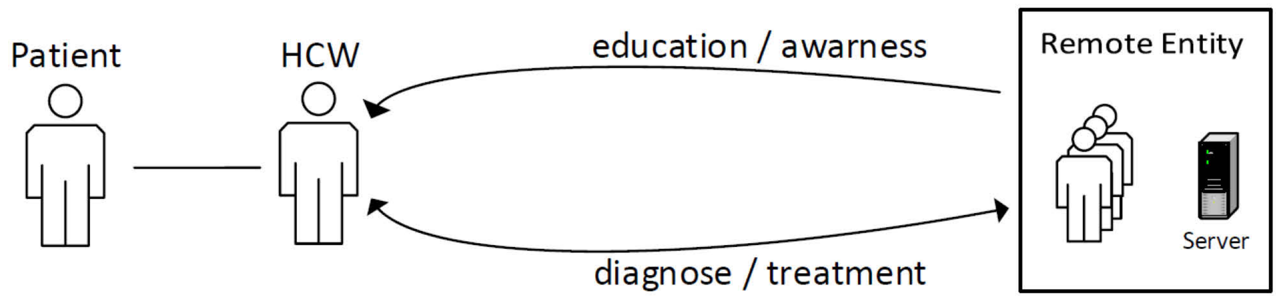
E. A broader view

So far the review has included six studies. However, as mentioned in the previous chapters, more evaluations exist within other related fields. Drawing conclusions and making recommendations without considering the insights of these other results would be incomplete and maybe not satisfying. Because some of the other results may be applicable to the context being discussed in this review or may have important implications for it.

E.1 Expert to Expert mHealth

The results presented so far dealt with mHealth for patients' remote monitoring and their care. But mobile phones can also be used for supporting the clinicians instead of interacting directly with the patients. Either it can be used to support the health-care worker/nurse in making their diagnoses or it can be used for remote education and awareness (e. g. about a new disease outbreak) (see figure 6).

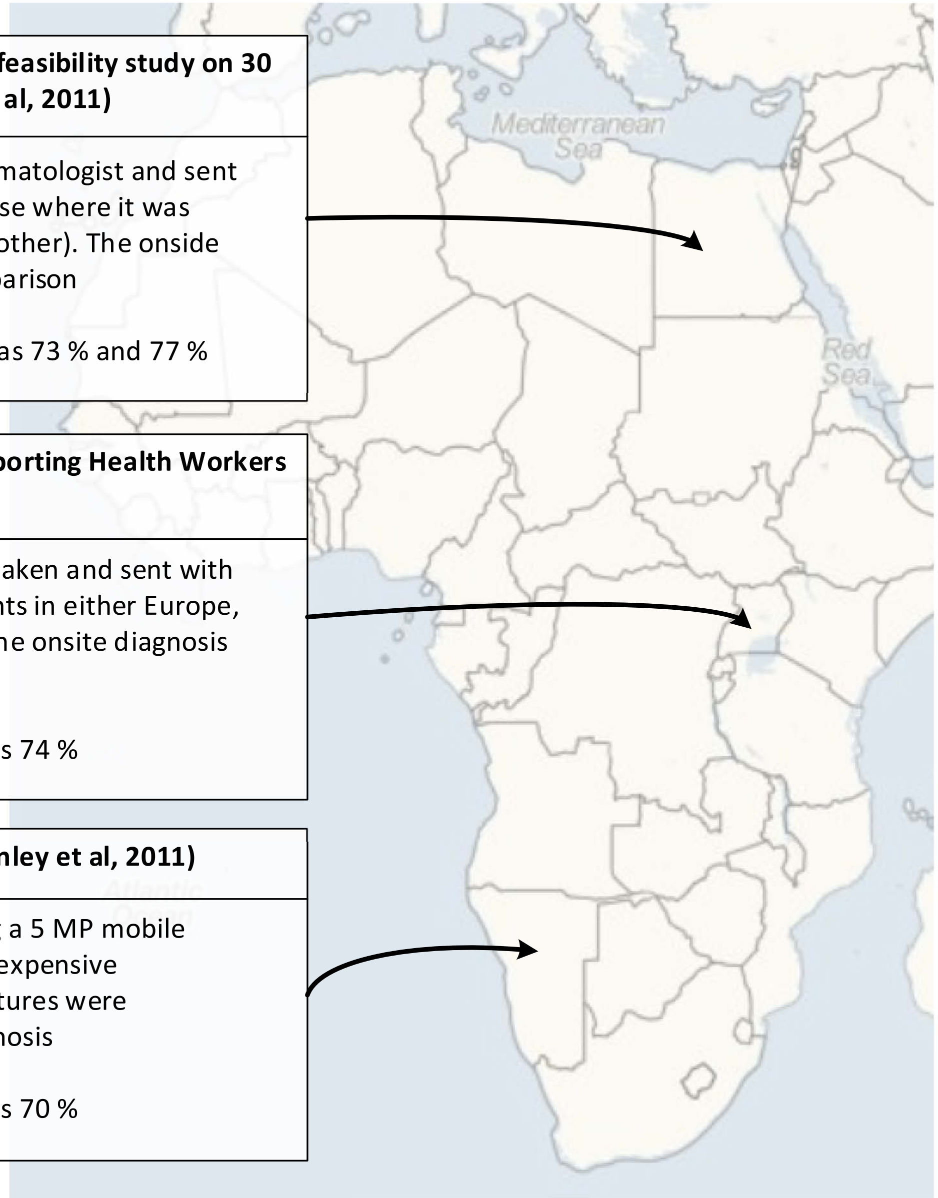
Figure 6: Functioning of expert to expert mHealth



The following three studies were detected during the screening process of the systematic review, but were excluded because they were non-randomized controlled trials (see chapter E.3). Nevertheless, their results contain interesting findings in relation to expert-to-expert mHealth. Figure 7 gives a brief overview of the studies, which will be discussed afterwards.

Two interventions (Fruhauf et al. 2013; Tran et al. 2011) dealt with dermatological issues, whereas one intervention (Quinley et al. 2011) was about the detection of cervical cancer. All the interventions used smart phones, mainly the camera-functionality.

Figure 7: Examples of expert-to-expert mHealth studies



Mobile teledermatology in the developing world: implications of a feasibility study on 30 Egyptian patients with common skin diseases (Tran et al, 2011)	
Intervention:	Mobile phone photographs were taken by a junior dermatologist and sent with relevant medicial information to an online database where it was evaluated by 2 senior dermatologists (blinded to each other). The onside diagnosis by the junior dermatologist served as a comparison
Outcomes:	The concordance between on and off-site diagnoses was 73 % and 77 %

Mobile Teledermatology in Sub-Saharan Africa: A Useful Tool in Supporting Health Workers in Low-resource Centres (Fruhauf et al, 2013)	
Intervention	Using an app, up to 3 different pictures per case were taken and sent with relevant text-information to dermatological departments in either Europe, USA or Autralia, where a specialist made a diagnosis. The onsite diagnosis served as a comparison
Outcomes:	The concordance between on and off-site diagnosis was 74 %

Use of mobile telemedicine for cervical cancer screening (Quinley et al, 2011)	
Intervention:	Medical students took photos of women‘s cervix (using a 5 MP mobile phone camera) after applying 4 % of acetic acid – an inexpensive alternative to cytology based screening. The stored pictures were diagnosed by a nurse and compared to the onsite diagnosis
Outcomes:	The concordance between on and off-site diagnosis was 70 %

RESULTS

The comparison between the on- and the off-site dermatological expert-diagnoses revealed a concordance between 73 % and 77 % (Tran et al. 2011). In a second study (Fruhauf et al. 2013) the concordance between on- and off-site diagnoses was 74 %. These results may imply a higher risk of bias, because the onsite diagnosis was proceeded by HCWs and not by a dermatological specialist. However, these comparable findings were reached in two different settings; in a low-income and a lower-middle-income country. The authors of both studies claim that their findings confirm the results of trials within other settings (developed world). This may imply that, taking pictures of skin diseases and sending them to remote experts is an effective tool for different settings. These results appear to be logical, because most skin diseases can be diagnosed with a simple visual inspection (Ruocco et al. 2011). This first visual inspection could be therefore supported by mHealth technology. Moreover, it could be assumed that a further development of smart-phones' cameras and a more intensive training on how to take pictures could improve the concordance. Nevertheless the few existing publications in that field were performed with a relatively small number of participants (Tran et al. 2011). In order to support the evidence of its usefulness, further investigations on a larger scale are necessary. For the screening of cervical cancer, a concordance of over 70 % was reached. The offsite-diagnoses were done by the same nurse-midwife who proceeded the onsite-diagnoses (but who was blinded to it). However, mHealth was combined with the application of acetic acid, a practical alternative to cytology-based Pap smear screening for low-resource settings (Sritipsukho and Thaweekul 2010). The pictures were taken by two medical students, who had one day of special training for that. However, the quality of some pictures was later classified as insufficient (for instance due to the glare from the metal speculum or hair between the camera lens and the cervix). When those pictures were excluded, the concordance of the on- and the off-site diagnoses increased to 81 %. This shows that a special focus should be placed on the training of how to take pictures. Another solution could be creating a short checklist and/or even an application which immediately identifies specific characteristics of already taken pictures.

E.2 mHealth for communicable diseases in LAMICs

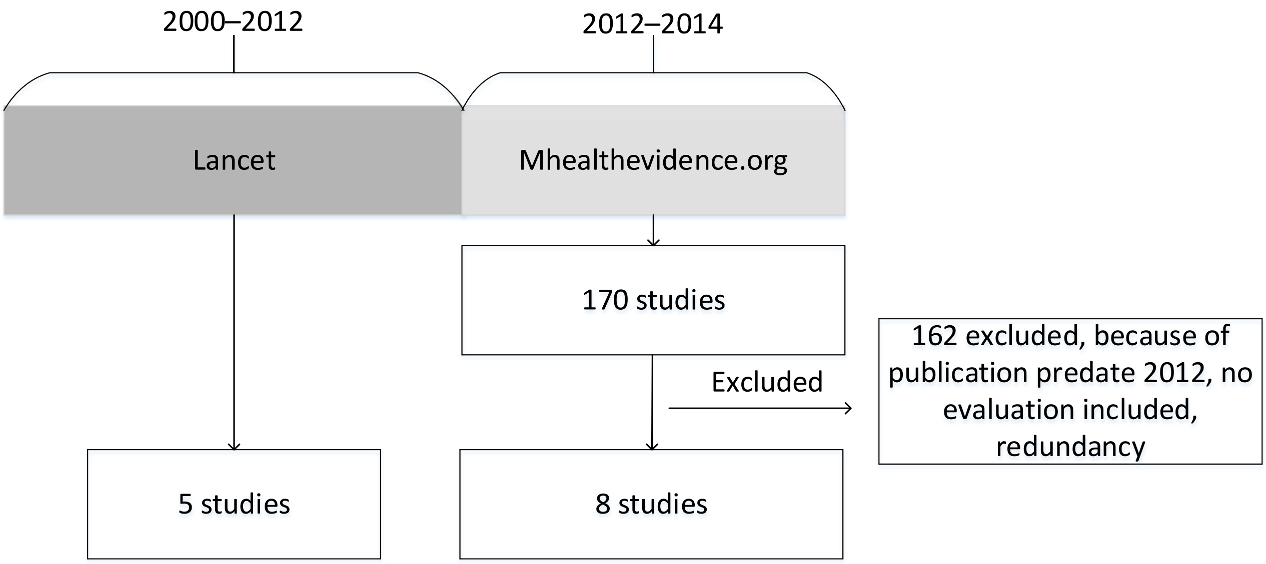
As already mentioned, the field of communicable diseases is more explored in the peer-reviewed literature. Some of those studies have been mentioned already in the previous chapter, but in order to get a fuller picture of that field, another systematic overview was conducted, which is presented in the following sections.

E.2.1 Method

The screening process for the CDs used the same method as the systematic review for NCDs, but was less complex. As a basis for the search, a study by Howitt et al. (2012) was taken, which was published in the Lancet. The study deals with health technologies in general and how the global health-care systems can benefit from it.

However, in the appendix of the article, a large review of already implemented mHealth systems – mainly for Communicable Diseases– in LAMICs was presented. Over 9000 study titles which were published between 2000 and 2012 were screened. All the included studies were evaluations, although not all of them were RCTs. To begin with, all the included studies of Howitt et al. (2012) were screened. The report analyzed the literature from 2000 until 2012. However, because mHealth evaluations in LAMICs have rapidly increased within the last few years, an updated search was conducted. The screening process for articles published in the period between January 2012 and January 2014 was conducted on www.mhealthevidence.org web-page (webpage access: 30.01.2015). The studies were title-, abstract- and full-text-screened and checked for inclusion criteria, which were similar to those of the systematic review in chapter 3, though – of course – instead of NCDs solely CDs (defined by the WHO) were included. Furthermore, non-randomized controlled trials were also considered in order to get a broader evidence base.

Figure 8: Screening method for mHealth evaluations for CDs in LAMICs



E.2.2 Results

The screening phase resulted in 170 studies. 104 of them were excluded due to a publication date before 2012. Of the 66 remaining studies the major proportion took place in Africa (n=27) and the south-American LAMICs (n=28). The big share of studies published between 2012 and 2014, compared to the overall time-span, is an indicator for a raising focus on evidence-based mHealth publications. However, a lot of articles still present, explain or discuss systems instead of evaluating them. Finally, eight articles were included and added to the five articles from the Lancet report. Of these thirteen studies, ten were conducted in Africa and most of the studies dealt with supporting the treatment of HIV, followed by programs which support pregnant women and Malaria or Tuberculosis treatment. Six interventions were about educating and supporting health-care workers in making their clinical decisions, three studies were about the collection of remote data, two dealt with health promotion & awareness for patients and the remaining two were about remote monitoring and integrated care.

Figure 9: mHealth for education, clinical decision support & remote data collection

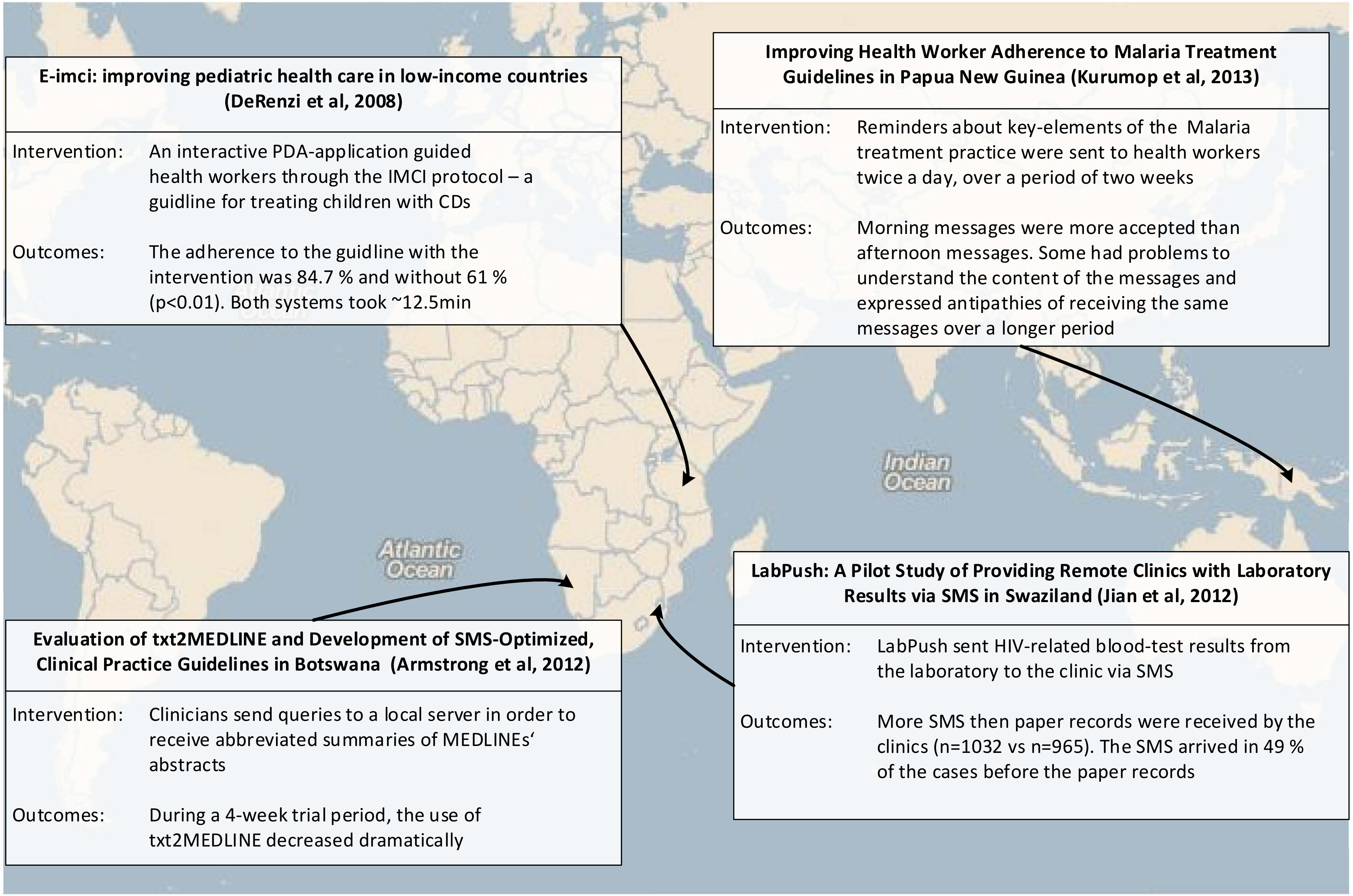
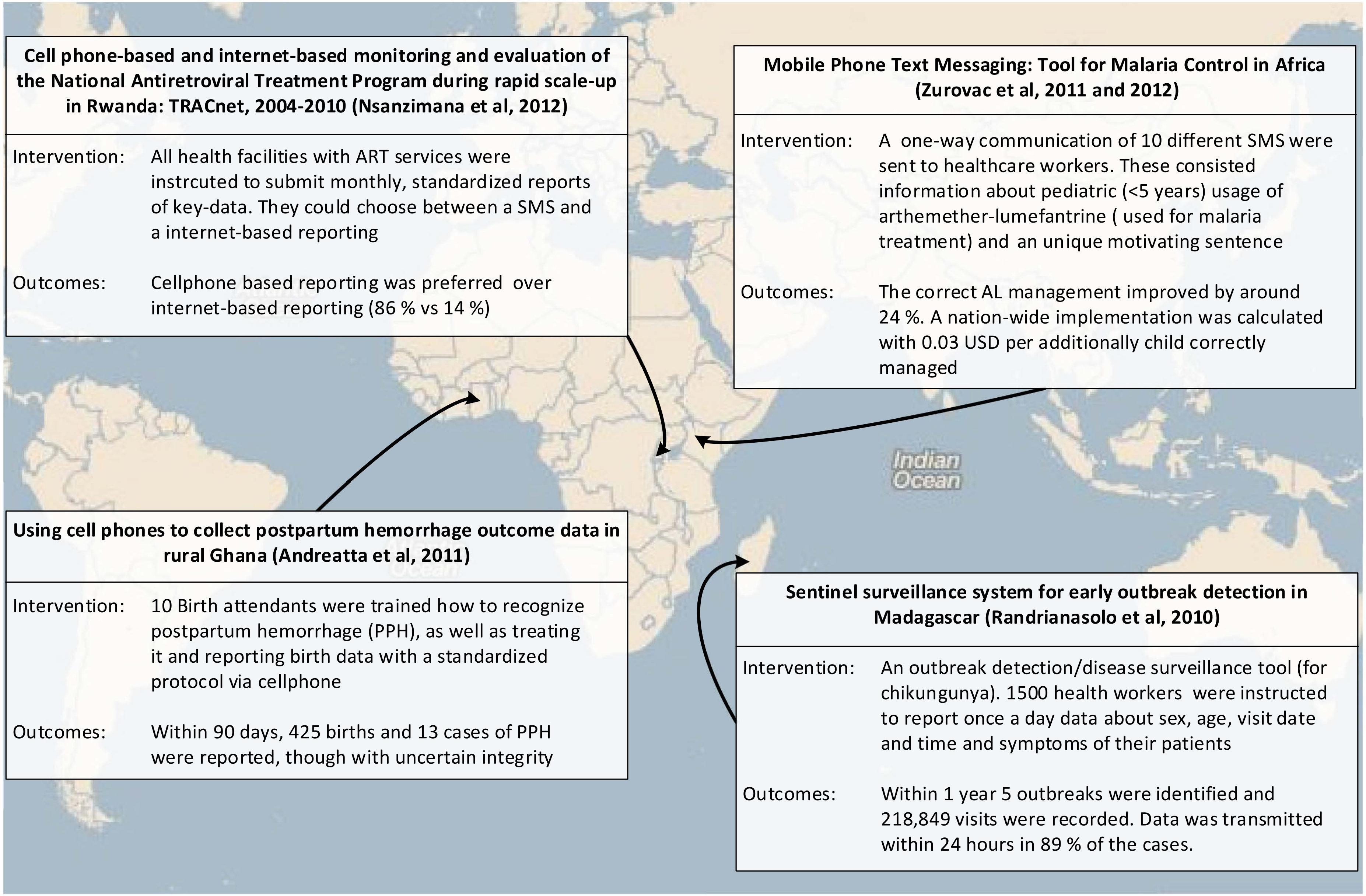


Figure 10: mHealth for education, clinical decision support & remote data collection



Education of and Support for clinical decision-making by health-care workers

Zurovac et al. (2011 & 2012) and Kurumop et al. (2013) showed the effectiveness and acceptability of systems which are improving CHWs knowledge about correct treatments and drug prescriptions. Zurovac et al. (2012) highlights the improved adherence to official treatment guidelines, when reminding HCWs with SMS. Moreover, the authors point out the increasing cost-effectiveness of mHealth, if implemented on a nationwide scale by a ministry, compared to a local implementation. Kurumop et al. (2013) looks more at the acceptance of reminder-SMS by HCW. Generally, HCW approve of it, although they emphasize the importance of the sending-time, its interval and the importance of the contents being understood. An example for a non-accepted SMS-tool was given by (Armstrong et al. 2012) who showed that an SMS-based access to abstracts of the MEDLINEs database was not accepted due to its poor ease of use.

However, another way of using mHealth is shown by Jian et al. (2012) who was using SMS as a tool for sharing information (here blood test results) between health-care institutions. It turned out to be much faster and safer, due to a loss rate of up to 10 % of all sent paper records.

Under this theme, only one intervention used smart-phones (DeRenzi et al. 2008), but had promising results as well. It resulted in an increase in adherence to treatment guidelines and taking the same time it would take for a conventional treatment.

Collection of remote data

Three studies showed that cellphones can be helpful tools for collecting remote data. Andreatta et al. (2011) implemented a system for collecting data from traditional birth attendants. Randrianasolo et al. (2010) used mobile data collection for disease surveillance and disease-outbreak detection. Furthermore, Nsanzimana et al. (2012) showed that for reporting data a cellphone-based reporting system is preferred over an internet-based reporting.

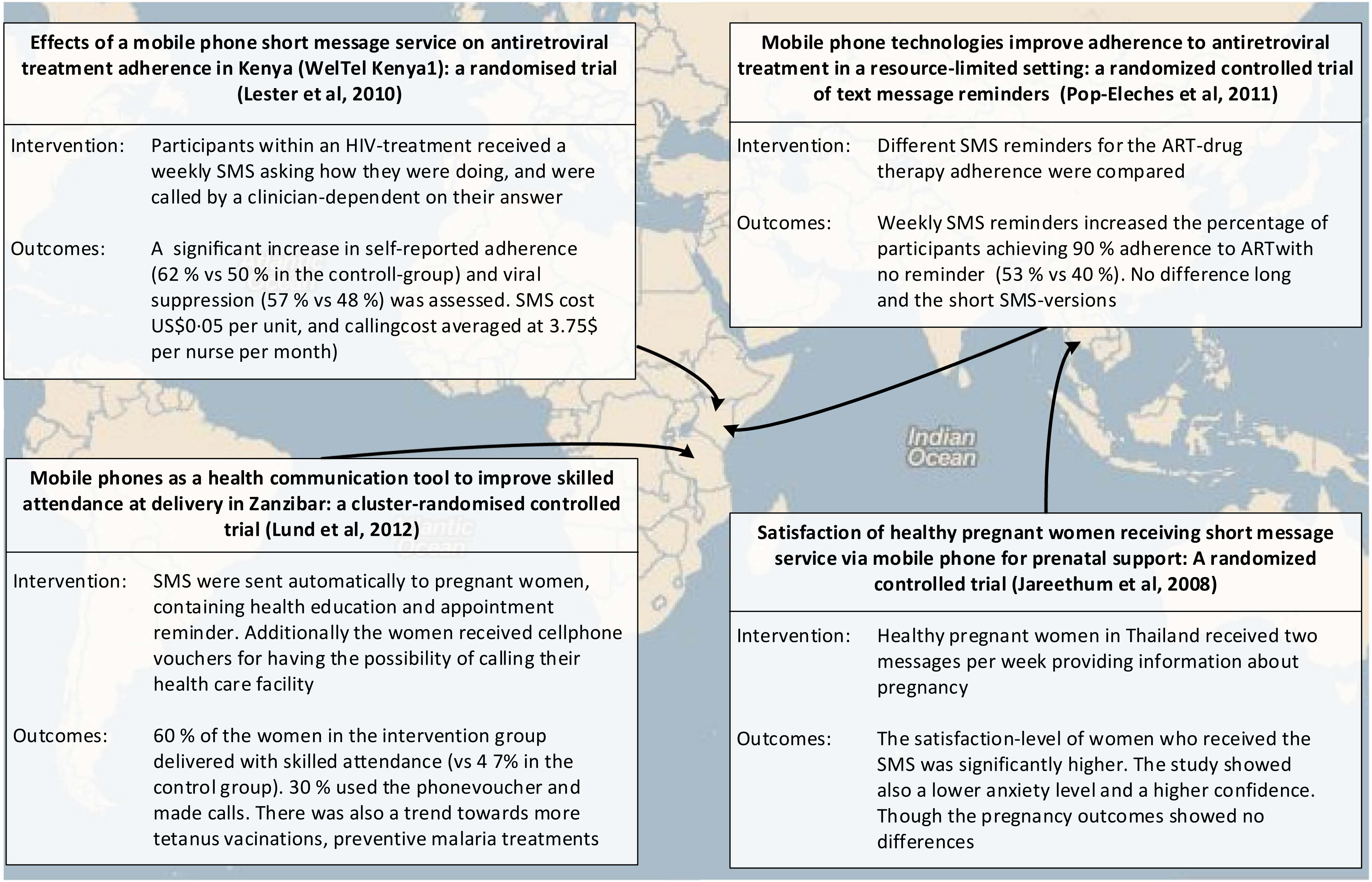
Health promotion and awareness

Jareethum et al. (2008) showed that, SMS can raise the confidence about pregnancy side-effects (such as nausea) and can lower anxiety levels, although the intervention brought no differences in anxiety or depression during the perinatal or postnatal period. Lund et al. (2012) also found improvements for pregnant women and increased skilled delivery attendance amongst those with health information support via SMS.

Remote monitoring and integrated care

The two other studies deal with remote monitoring and integrated care, which can help to overcome the fragmented access to health facilities in LAMICs, especially in the rural parts. The possibility of asking patients about their perceived health-status via SMS was well perceived and many patients reported that they felt “like someone cares” (Lester et al. 2010). Once again, the frequency of sent SMS revealed to be an important factor; daily reminders were less effective for drug-adherence than weekly reminders, while no differences were obtained between long and short messages. Nontheless it should not be forgotten that some participants were provided with money for charging their cellphones (Pop-Eleches et al. 2011)

Figure 11: Health promotion and awareness remote monitoring and integrated care



E.3 Summary

This broader view on other studies confirms and extends findings of our review. It was shown that mHealth can also support clinicians, either as a remote diagnostic support for cervical cancer and dermatological diseases or in the form of messages, which refresh clinicians' knowledge about drug usage or as an interactive software on a smart-phone which guides through the official treatment guideline. However, the tools were found to be useless when the ease of use was poor.

mHealth also showed its potential as a data collector, which could be used by different kinds of health-care workers. Positive results for direct patient mHealth interventions, such as appointment reminders were observed also for CD. This includes, reducing patients' anxiety level about usual side-effects and reminding them to take their medicine/to adhere to their medication treatment.

F. Conclusion

F.1 Summary

Our systematic review of RCTs on the effects of mHealth in the field of NCDs identified only six studies, which met all our inclusion criteria. All of them took place in upper middle income countries and lower middle income countries, mostly in urban areas. The studies included 1850 participants, of whom 780 received an mHealth intervention. Two interventions dealt with diabetes (Balsa and Gandelman 2010; Shetty et al. 2011), two with asthma (Liu et al. 2011; Ostojic et al. 2005), one with severe hypertension (Piette et al. 2012) and one with several NCDs (Liew et al. 2009). The interventions differed: three studies combined external devices (such as a blood pressure monitor and peak expiratory flow meter) with a mobile phone/smart-phone for supplying the patients with tailored advice (Piette et al. 2012; Osotjic et al. 2005; Liu et al. 2011), one study used SMS as an appointment reminder (Liew et al. 2009), one study utilized SMS and a web-page for informing the patients about their diseases (Balsa and Gandelman 2010) and another used frequent SMS to remind patients of their prescribed treatment-plan (Shetty et al. 2011).

Most of the **clinical outcomes** indicated at least some improvement for the mHealth intervention groups. Pulmonary functions for people with asthma and glycemic levels for patients with diabetes improved significantly for those who received mHealth interventions. One study (Piette et al. 2012) showed a higher improvement of blood-pressure values in a subgroup analysis of low-literacy people with diabetes when compared with the overall group. Only one study found no (significant) differences between the intervention and the control group.

The results associated with **compliance** also showed better attendance-rates, and improved adherence to behavioral and drug prescriptions given by physicians for the intervention groups. However, some of these results should be interpreted with care because of study limitations (such as a small study sample size and a high drop-out rate). Regarding **quality of life** related outcomes, the patients with mHealth showed significantly better parameters at follow-up appointments, according to both, their physical and their mental component.

Also **other outcomes**, including patients' satisfaction levels with their healthcare, their depression levels or even the trust between patients and physicians revealed to be better in the intervention groups than in the control-groups.

Unfortunately, no particular observations were made on the **cost-effectiveness** of mHealth interventions. Costs were estimated for one intervention, with the assumption that the intervention might have produced greater savings than costs.

Overall, tailored interventions were found to work better than interventions which used generalized messages.

The small number of included studies in our review implies certain limitations. Relevant information may be available in grey literature or from non-RCTs, which were excluded by our review. Therefore, the results of the systematic review were supplemented with information from other studies, which had been originally excluded, with the aim of obtaining a broader view on the potential impact of mHealth on NCDs:

Some of the excluded studies showed that mHealth can also be used to support healthcare workers (instead of interacting directly with the patients). Remote diagnoses with pictures sent via mobile phones proved to have sufficiently reliable results (and resulted in a concordance of around 70 % between on- and off-site diagnoses). A review of the impact of mHealth on CDs in LAMICs showed that mHealth can be used for a wide range of purposes: (1) as an **educational tool,** (2) as a **clinical decision supporter,** (3) to improve **health-care workers knowledge** for specific treatment guidelines (with SMS reminder, interactive phone applications) and (4) to **share information** between different clinical institutions, and (5) to **collect remote data**. Finally, two studies (Zurovac et al. 2012; Lester et al. 2010) estimated that costs can be saved when scaling-up m Health interventions from a village level to a country-wide, ministry supported program.

F.2 Recommendations for policy makers

Based on our systematic review and on insights from the broader literature, we developed a framework of the main participants and actors who create and maintain mHealth (figure 12). On top of the figure are the actors, who are necessary at the organizational level. Beneath them, there are the entities which are in charge for the technical aspects of mHealth. And at the bottom, the process of mHealth itself is illustrated, including all actors who are connected to it.

Support by government institutions, such as the **ministry of health**, is extremely important. Most of the programs so far were developed on a small scale (such as villages) by NGOs or scientific institutions – often independent and with no government support. In order to sustain mHealth interventions in the long-term, a strong domestic institution with a wide range of competence is needed to ensure adequate support after the end of project based interventions.

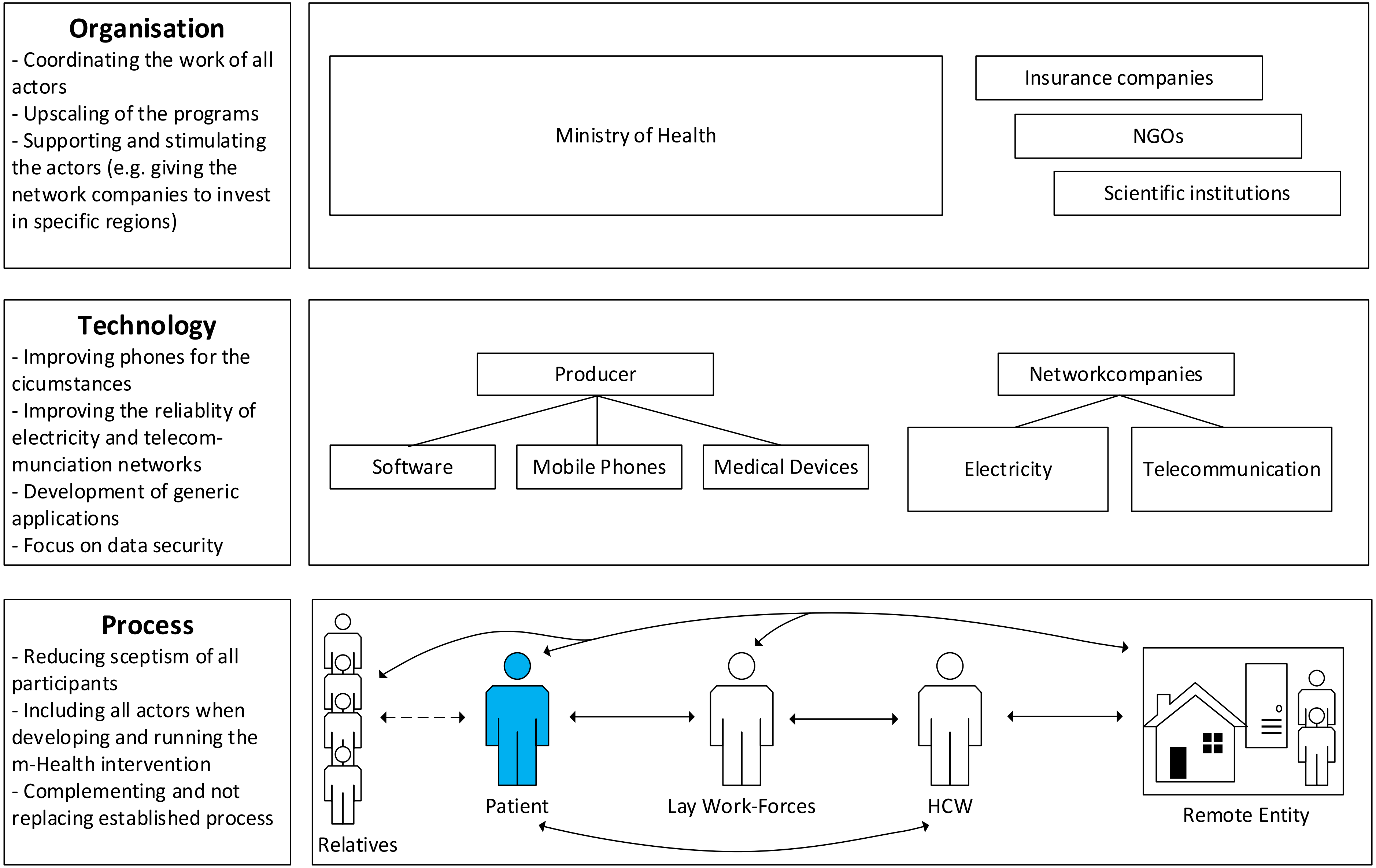
Insurance companies may also play a role although their relevance has not yet been discussed in the literature.

Nevertheless, in the short-term knowledge and experiences **of NGOs and scientific institutions** is needed to move mHealth to a larger level. For the technical aspects of mHealth close collaboration between **manufacturers** (hard and software) and **network companies** (electricity and mobile-network) is advisable. It is likely that **smartphones** will soon replace conventional cellphones. Therefore, an intensified orientation on smartphone-based mHealth tools should be considered now. Using all technical features of smartphones enlarges the possibilities of mHealth (see Box 1). Different studies have demonstrated how a digital picture (such as a .jpeg file) can be useful for replacing a face-two-face visit (Szot et al. 2004).

Furthermore, low-literacy people could possibly be better reached with smartphone tools. They could be provided with applications that are designed with pictograms instead of text.

A further point for a government supported development of mHealth tools could be the focus on generic software instead of disease-specific tools. **Generic tools**, which can be individually

Figure 12: Involved actors for mHealth' process and its organizational and technical aspects



extended (according to the disease) but which have a consistent interface could get a much broader acceptance as well as be better to understand by patients/HCWs. Another point, which has not been much analyzed in the literature so far, is **data-security**. The data transferred via

Box 1: Examples for medical low-cost devices combined with mobile phones:

•**A mobile ophthalmoscope**: Pictures of the retina can be taken and transferred to a mobile phone and send to remote experts who can analyze the photographs and send results via SMS to the patient. The quality of the pictures is perceived as good by the clinical experts (Blanckenberg et al. 2011)

•**Mobile low-cost blood pressure device**: A simple, low cost pressure sensor on the skin sends information automatically to the mobile phone which saves the blood pressure and the heart rate and which then sends the data to a remote server where they can be analyzed (Arteta et al. 2012)

•**Mobile phone mounted light microscope**: A microscope-apparatus with a LED-Light, an objective, and an eyepiece at which a smartphone-camera get installed. Pictures are good enough to detect the microorganisms morphology. Furthermore automated image analysis software can count the numbers of bacillus automatically (Breslauer et al. 2009)

•**Low Cost ECG-monitor**: Built with electrodes made from scap material and a low power amplifier of high gain. The data can be sent to a mobile phone where the ECG can be displayed and analyzed (Walker et al. 2009)

•**Medication compliance reminder SIMPILL**: A medication-bottle which contains a SIM-card, which automatically sends a message with its unique box-identification number to a remote server. If no message is received by the server a medication-reminder SMS will be send to the patient (www.simpill.org).

cellular networks contain sensitive information. For example, if a laboratory company sends blood test results via SMS, there is a need to code these messages. Also, it should be ensured that patients are aware they are receiving sensitive content on their phones. Mobile phones are often used by several members of a household in LAMICs (Aspen Institute 2014) and messages can be read by family, friends, seat-neighborhoods in the bus etc.

In LAMICs, especially in rural areas, the **electricity network coverage** is often unreliable (Winkler et al. 2011). Solutions can be by manufacturing phones with low power-consumptions, solar-modules for recharging the phones or supporting a network of 'recharging-shops' with electric generators. Besides the durability of phones, they should be outdoor proven and first and foremost, affordable.

Another aspect is the cellular **mobile network coverage**. Although network coverage in LAMICs is progressively increasing, there are still several regions without any cellular-signal. This can be included into future developments. Firstly, the government could support network companies in providing important regions with fast and reliable mobile phone connections and secondly, the software should be designed with on- and off-line modes, where data could be kept on the phone as long as the phone is offline and sends/receives the important data automatically when it is online again.

Furthermore, when an mHealth tool is developed, a careful analysis of the **involved participants** has to be performed. This should not only focus on patients but should include others such as relatives who also need to be informed about a patient's condition and the implications (e. g. the loss of hair for patients in a chemo-therapy). This is particularly important because stigmatization and misinformation remain high in the developing world. People could be isolated and abandoned by their society for having unusual behavioral patterns or suffering from unknown disease conditions/symptoms.

mHealth is more than a hype. It has proven its various application fields and shown its efficacy for a broad spectrum of diseases. A careful implementation, which takes all the obstacles, anxieties and skepticism of all protagonists into consideration, is needed. Although mHealth should not be considered as the silver bullet for solving the developing worlds' burden of NCDs, it has to be considered as a complement for an existing, always evolving health-care system.

F.3 Implications for research

In view of the limited number of available high quality evaluations, more RCTs are needed to confirm the potential benefits of mHealth. Such studies should try to measure all relevant impacts, but should focus on clinical outcomes, in particular. As non-communicable-diseases often demand lifestyle changes in order for health related outcomes to change, studies will require long-term follow-ups. Multi-country studies would be helpful to explore the relationship between different environments and impacts. Future research should also investigate the position of smart-phones in combination with affordable, external devices (see box above).

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H. Appendix

Table 6: Excluded studies of the full-text screening with reason for exclusion

Title	Author	Year	Reason for Exclusion
No RCTs			
Experience with telepathology at a tertiary cancer centre and a rural cancer hospital	Desai, Sangeeta; Patil, Rajasa; Chinoy, Roshni; Kothari, Ashok; Ghosh, T. K.; Chavan, Manoj; Mohan, Ashok; Nene, B. M.; Dinshaw, K. A.	2004	Observational study
Mobile teledermatology in sub-Saharan Africa: a useful tool in supporting health workers in low-resource centres	Fruhauf, Julia; Hofman-Wellenhof, Rainer; Kovarik, Carrie; Mulyowa, Grace; Alitwala, Caroline; Soyer, H. Peter; Kaddu, Steven	2013	No randomization
Short text messages (SMS) as a reminder system for making working women from Delhi Breast Aware	Khokhar, Anita	2009	Single group, pre-post study
Evaluation of "Portable Health Clinic" with BAN standard for 10K subjects in Bangladesh	Nakashima, Naoki; Hiramatsu, Tatsuo; Ghosh, Partha Pratim; Islam, Rafiqul; Kobayashi, Kunihisa; Inoguchi, Toyoshi	2013	Single group, pre-post study
The mobile phone as a tool in improving cancer care in Nigeria	Odigie, V. I.; Yusufu, L M D; Dawotola, D. A.; Ejagwulu, F.; Abur, P.; Mai, A.; Ukwenya, Y.; Garba, E. S.; Rotibi, B. B.; Odigie, E. C.	2012	control group participants were dropped-out intervention participants
A preliminary study of a cloud-computing model for chronic illness self-care support in an underdeveloped country	Piette, John D.; Mendoza-Avelares, Milton O.; Ganser, Martha; Mohamed, Muhima; Marinec, Nicolle; Krishnan, Sheila	2011	Single group, prepost study
Use of mobile telemedicine for cervical cancer screening	Quinley, Kelly E.; Gormley, Rachel H.; Ratcliffe, Sarah J.; Shih, Ting; Szep, Zsofia; Steiner, Ann; Ramogola-Masire, Doreen; Kovarik, Carrie L.	2011	No randomization
Mobile teledermatology in the developing world: implications of a feasibility study on 30 Egyptian patients with common skin diseases	Tran, Kathleen; Ayad, Mohamed; Weinberg, Jennifer; Cherng, Augustin; Chowdhury, Mridul; Monir, Saadeddin; El Hariri, Mohamed; Kovarik, Carrie	2011	No randomization
Other Reasons			
Mobile phones as mediators of health behavior change in cardiovascular disease in developing countries	Chan, Connie V.; Kaufman, David R.	2009	Discussion about the opportunities of mobile phones in supporting behavior modification in developing countries.
Comparison of an SMS text messaging and phone reminder to improve attendance at a health promotion center: a randomized controlled trial	Chen, Zhou-Wen; Fang, Li-Zheng; Chen, Li-Ying; Dai, Hong-Lei	2008	Patients diseases are not mentioned

Title	Author	Year	Reason for Exclusion
Enhancing 'MHealth' With South-To-South Collaborations	Curioso, Walter H.; Mechael, Patricia N.	2010	Discussion of mHealth' opportunities
E-health's promise for the developing world	Dentzer, Susan	2010	An editorial
Telehealth in Sub-Saharan Africa: Lessons for Humanitarian Engineering	Foster, Kenneth R.	2010	Discussion of mHealth' opportunities
Cyber sight--ORBIS telemedicine	Helveston, Eugene M.; Kopecky, Gwen; Smallwood, Lynda	2004	A description of the network ORBIS
'Mobile' Health Needs And Opportunities In Developing Countries	Kahn, James G.; Yang, Joshua S.; Kahn, James S.	2010	Discussion of mHealth
Health help 4 u: Mobile telephone technologies come of age	Kaufman, Michele B.	2009	Description of a teledermatology system
The use of text messaging to improve attendance in primary care: a randomized controlled trial	Leong, Kwok Chi; Chen, Wei Seng; Leong, Kok Weng; Mastura, Ismail; Mimi, Omar; Sheikh, Mohd Amin; Zailinawati, Abu Hassan; Ng, Chirk Jenn; Phua, Kai Lit; Teng, Cheong Lieng	2006	The patients diseases are not mentioned
Lifelink: 3G-based mobile telemedicine system	Alis, Christian; del Rosario, Carlos; Buenaobra, Bernardino; Mar Blanca, Carlo	2009	Description of a phone based system
Implementation of mHealth applications in Botswana: telemedicine and education on mobile devices in a low resource setting	Littman-Quinn, Ryan; Mibenge, Chikoti; Antwi, Cynthia; Chandra, Amit; Kovarik, Carrie L.	2013	Description of the implementation of an mHealth intervention with no evluation
Scientific publishing in non industrialized countries: a pilot wireless internet project for Africa	Azzi, Angelo	2005	Proposal of a mHealth system
Experiences in mHealth for Chronic Disease Management in 4 Countries	Piette, J. D., Blaya, J. A., Lange, I., & Sanchis, J. B. B.	2011	Description of a system
Opportunities in Mobile Health	SANDHU, JASPAL S.	2011	Discussion of mHealth
Not mHealth			
International telepharmacy education: another venue to improve cancer care in the developing world	Alfaar, Ahmad S.; Kamal, Sherif; Abouelnaga, Sherif; Greene, William L.; Quintana, Yuri; Ribeiro, Raul C.; Qaddoumi, Ibrahim A.	2012	Connection was established with a DSL with 25 megabites per second
Mobile primary healthcare services and health outcomes of children in rural Namibia	Aneni, Ehimen; De Beer, Ingrid H; Hanson, Laura; Rijnen, Bas; Brenan, Alana T.; Feeley, Frank G.	2013	mobil unit=mobile clinic without usage of mobile technology
Teleophthalmology-based rural eye care in India	Bai, V. Thulasi; Murali, V.; Kim, R.; Srivatsa, S. K.	2007	The intervention uses a satellite connection
Teleconsultation in paediatric orthopaedics in Djibouti: evaluation of response performance	Bertani, A.; Launay, F.; Candoni, P.; Mathieu, L.; Rongieras, F.; Chauvin, F.	2012	Landline internet connection to an e-mail address
iPath - a Telemedicine Platform to Support Health Providers in Low Resource Settings	Brauchli, K.; O'mahony, D.; Banach, L.; Oberholzer, M.	2005	No focus on the mobile communication network

Title	Author	Year	Reason for Exclusion
Effectiveness and feasibility of telepsychiatry in resource constrained environments? A systematic review of the evidence	Chipps, J.; Brysiewicz, P.; Mars, M.	2012	Landline-bandwithes
A review of telemedicine in Uzbekistan	Doarn, Charles R.; Adilova, Fatima; Lam, David	2005	Landline-bandwithes
Effectiveness of research training workshop taught by traditional and video-teleconference methods in a developing country	Dodani, S.; Kazmi, K. A.; Laporte, R. E.; Wilson, J. P.	2009	Landline internet connection
Building research capacity in developing countries: cost-effectiveness of an epidemiology course taught by traditional and video-teleconferencing methods in Pakistan	Dodani, Sunita; Songer, Thomas; Ahmed, Zakiuddin; LaPorte, Ronald E.	2012	Landline internet connection
Digital pathology - implementation challenges in low-resource countries	Fontelo, Paul; Faustorilla, John; Gavino, Alex; Marcelo, Alvin	2011	Tablet, which used schools WiFi
Digital pathology - implementation challenges in low-resource countries	Fontelo, Paul; Faustorilla, John; Gavino, Alex; Marcelo, Alvin	2012	Tablet, which was connected with the WLAN of an university
Randomised trial of telephone intervention in chronic heart failure: DIAL trial	Gesica Investigators	2005	Telephon calls; no indication, that mobile phones were used
Screening for CKD and cardiovascular disease risk factors using mobile clinics in Jalisco, Mexico	Gutierrez-Padilla, Jose Alfonso; Mendoza-Garcia, Martha; Plascencia-Perez, Salvador; Renoirte-Lopez, Karina; Garcia-Garcia, Guillermo; Lloyd, Anita; Tonelli, Marcello	2010	mobil unit=mobil clinic
The Sankara Nethralaya mobile teleophthalmology model for comprehensive eye care delivery in rural India	John, Sheila; Sengupta, Sabyasachi; Reddy, Sumanth J.; Prabhu, Pearlson; Kirubanandan, Krishan; Badrinath, Sengamedu S.	2012	Satellite-connection
Effectiveness of Tele-guided Interceptive Prosthodontic treatment in rural India: A comparative pilot study	Keeppanasserril, Arun; Matthew, Anil; Muddappa, Sapna	2011	Satellite telemedicine linkage or broadband internet
Preventing diabetes blindness: cost effectiveness of a screening programme using digital non-mydriatic fundus photography for diabetic retinopathy in a primary health care setting in South Africa	Khan, Taskeen; Bertram, Melanie Y.; Jina, Ruxana; Mash, Bob; Levitt, Naomi; Hofman, Karen	2013	Mobile photocamera, but no usage of the cellular network
Cancer diagnosis and telemedicine: a case study from Cambodia	Kvedar, J.; Heinzelmann, P. J.; Jacques, G.	2006	Satellite-connection
A study of a rural telemedicine system in the Amazon region of Peru	Martinez, Andres; Villarroel, Valentin; Seoane, Joaquin; del Pozo, Francisco	2004	Radio
Opportunistic screening for skin cancer using a mobile unit in Brazil	Mauad, Edmundo C.; Silva, Thiago B.; Latorre, Maria R D O; Vieira, Rene A C; Haikel, Raphael L Jr; Vazquez, Vinicius L.; Longatto-Filho, Adhemar	2011	Mobile unit = mobile clinic

Title	Author	Year	Reason for Exclusion
Telemedicine in pediatric cardiac critical care	Munoz, Ricardo A.; Burbano, Nelson H.; Motoa, Maria V.; Santiago, Gabriel; Klevemann, Matthew; Casilli, Jeanne	2012	Landline bandwith connection
Virtual surgical pathology in underdeveloped countries: The Zambia Project	Pagni, Fabio; Bono, Francesca; Di Bella, Camillo; Faravelli, Agostino; Cappellini, Anna	2011	Satellite connection
Telemedicine diffusion in a developing country: the case of India (March 2004)	Pal, Amrita; Mbarika, Victor W A; Cobb-Payton, Fay; Datta, Pratim; McCoy, Scott	2005	ISDN connection
eC3--a modern telecommunications matrix for cervical cancer prevention in Zambia	Parham, Groesbeck P.; Mwanahamuntu, Mulindi H.; Pfaendler, Krista S.; Sahasrabuddhe, Vikrant V.; Myung, Daniel; Mkumba, Gracilia; Kapambwe, Sharon; Mwanza, Bianca; Chibwesha, Carla; Hicks, Michael L.; Stringer, Jeffrey S A	2010	Nurses stored digital images on a laptop
Supporting hospital doctors in the Middle East by email telemedicine: something the industrialized world can do to help	Patterson, Victor; Swinfen, Pat; Swinfen, Roger; Azzo, Emil; Taha, Husen; Wootton, Richard	2007	E-Mail telemedicine over landline connection
Reinforcement of endocrine surgery training: impact of telemedicine technology in a developing country context	Pradeep, P. V.; Mishra, Anjali; Mohanty, B. N.; Mohapatra, K. C.; Agarwal, Gaurav; Mishra, Saroj Kanta	2007	ISDN connection and satellite based connectivity
Impact of a comprehensive telephone-based disease management programme on quality-of-life in patients with heart failure	Ramachandran K		Its it not clearly whether a mobile phone was used
Comparison of store and forward method of teledermatology with face-to-face consultation	Rashid, Eanas; Ishtiaq, Osama; Gilani, Salman; Zafar, Asif	2003	pictures sent via E-Mail but its not clear whether the cellular network was used
Telecardiology: effective means of delivering cardiac care to rural children	Sekar, Prem; Vilvanathan, Vairan	2007	Satellite connection
The role of information communication technology (ICT) towards universal health coverage: the first steps of a telemedicine project in Ethiopia	Shiferaw, Fassil; Zolfo, Maria	2012	Dial-up connection
Integrated regional networks for ST-segment-elevation myocardial infarction care in developing countries: the experience of Salvador, Bahia, Brazil	Solla, Davi Jorge Fontoura; Paiva Filho, Ivan de Mattos; Delisle, Jacques Edouard; Braga, Alecianne Azevedo; Moura, Joao Batista de; Moraes, Xavier de Jr; Filgueiras, Nivaldo Menezes; Carvalho, Marcela Embirucu; Martins, Mariana Steque; Manganotti Neto, Orlando; Roberto Filho, Paulo; Roriz, Pollianna de Souza	2013	Not clear whether the mobile network was used
Telepsychiatry in Chennai, India: the SCARF experience	Thara, Rangaswamy; John, Sujit; Rao, Kotteswara	2008	Satellite connection

Title	Author	Year	Reason for Exclusion
Feasibility and diagnostic accuracy of Internet-based dynamic telepathology between Uganda and Germany	Wamala, Dan; Katamba, Achilles; Dworak, Otto	2011	No usage of mobile network
What we can really expect from telemedicine in intensive diabetes treatment: results from 3-year study on type 1 pregnant diabetic women.	Wojcicki, JM		Modem
A model for online interactive remote education for medical physics using the Internet	Woo, Milton K.; Ng, Kwan-Hoong	2003	Classroom with PCs and a conventional telephone landline
Prospective case review of a global e-health system for doctors in developing countries	Wootton, R.; Youngberry, K.; Swinfen, P.; Swinfen, R.	2004	Not clear whether the mobile network was used
Comparative performance of seven long-running telemedicine networks delivering humanitarian services	Wootton, Richard; Geissbuhler, Antoine; Jethwani, Kamal; Kovarik, Carrie; Person, Donald A.; Vladzymyrskyy, Anton; Zanaboni, Paolo; Zolfo, Maria	2012	No usage of the mobile communicatiion network
Other Reviews			
The Impact of Mobile Health Interventions on Chronic Disease Outcomes in Developing Countries: A Systematic Review	Beratarrechea, Andrea; Lee, Allison G.; Willner, Jonathan M.; Jahangir, Eiman; Ciapponi, Agustin; Rubinstein, Adolfo	2013	Review on chronic diseases (includes HIV etc.)
E-health technologies show promise in developing countries	Blaya, Joaquin A.; Fraser, Hamish S F; Holt, Brian	2010	a systematic review of evaluations of e-health implementations in developing countries, with a broad e-health context and no specific area of diseases (a lot of the studies deal with HIV, tubercolosis or Malaria)
SMS for disease control in developing countries: a systematic review of mobile health applications	Deglise, Carole; Suggs, L. Suzanne; Odermatt, Peter	2012	Majority of studies about communicable diseases, such as HIV
Mobile phone messaging for facilitating self-management of long-term illnesses	Jongh, Thyra de; Gurol-Urganci, Ipek; Vodopivec-Jamsek, Vlasta; Car, Josip; Atun, Rifat	2012	Review about mHealth interventions in developed countries
Impacts of e-health on the outcomes of care in low- and middle-income countries: where do we go from here?	Piette, John D.; Lun, K. C.; Moura, Lincoln A Jr; Fraser, Hamish S F; Mechael, Patricia N.; Powell, John; Khoja, Shariq R.	2012	About a broad field of e-Health interventions; more a summery on different projects and their impacts
Telemedicine: current status in developed and developing countries	Rao, Babar; Lombardi, Adriana 2nd	2009	Review of the telemedicine-literature, with a focus on teledermatology and the developed world

Title	Author	Year	Reason for Exclusion
A systematic review of telemedicine projects in Colombia	Rey-Moreno, Carlos; Reigadas, Javier Simo; Villalba, Estrella Everss; Vinagre, Juan Jose; Fernandez, Andres Martinez	2010	Review/master thesis about e-Health
	No NCD-context		
Performance factors of mobile rich media job aids for community health workers	Florez-Arango, J. F.; Iyengar, M. S.; Dunn, K.; Zhang, J.	2011	No specific NCD context
A text message-based intervention to bridge the healthcare communication gap in the rural developing world	Mahmud, Nadim; Rodriguez, Joce; Nesbit, Josh	2010	Focus on Communicable Diseases: HIV, Tuberculosis, Prevention of Mother to Child Transmissions
Cost Effectiveness of Personal Digital Assistants in Health Information System in Rakai and Lyantonde Districts, Uganda	Tumwesigye; Mbona, Nazarius	2013	No specific NCD context
No developing country			
A comparative study of teledermatoscopy and face-to-face examination of pigmented skin lesions	Ishioka, Priscila; Tenorio, Josceli M.; Lopes, Paulo Rl; Yamada, Sergio; Michalany, Nilceo S.; Amaral, Marcio B.; Pisa, Ivan T.; Hirata, Sergio H.; Almeida, Fernando A.	2009	Telemedicine from Italy to Austria
Do automated calls with nurse follow-up improve self-care and glycemic control among vulnerable patients with diabetes?	Piette, John D.; Weinberger, Morris; McPhee, Stephen J.; Mah, Connie A.; Kraemer, Fredric B.; Crapo, Lawrence M.	2000	No developing country context

Table 7: Outcome-data of the included Randomized Controlled Trials

Study	Disease	Intervention	Outcomes
Balsa and Gandelman (2010)	Diabetes	Educational SMS plus an informative internet platform compared to a paper-based brochure	65 were reached by SMS, 44 % were reached by the internet platform no significant impact on any of the variables
Liew et al (2009)	Different NCDs	SMS reminders for follow-up appointments were compared to telephone-reminder and no reminder	**Non-attendance** of *mHealth intervention vs control group*: 15.6 % vs 23:0 % [p=0.020]; telephone reminder vs control group: 13.7 % vs 23 % [p=0.003]
Piette et al (2012)	Hyper-tension	Home-blood pressure monitor and weekly calls with life-style advice and medication reminder were compared to the usual care	*Intervention vs control group, from baseline to follow-up (6 weeks):* **SBP** (mm Hg): 154.0 to 138.3 vs 150.5 to 144.1; SBP (mm Hg) for the subgroup of people with low-literacy/higher information needs: 153.2 to 142.5 vs 150.0 to 143.6; **Depressive symptoms scores**[a]: 11.1 to 8.3 vs 10.7 to 10.6 [p=0.004]; **Number of medication problems**[b]: 3.9 to 2.8 vs 3.7 to 3.6 [p=0.0001]; **Perceived overall health**[c]: 1.9 to 2.5 vs 2.0 to 2.1 [p=0.0001] **Satisfaction with care**[d]: 1.7 to 1.8 vs 1.5 to 1.4 [p=0.0001]; **Overall satisfaction with HTN care**[d]: 1.7 to 1.8 vs 1.7 to 1.4 [p=0.004]
Liu et al (2011)	Asthma	Interactive selfcare phone-software with instant advice were compared to paper-based individualized action plans	*From baseline to follow-up, intervention vs control*: **FEV1 % predicted**: 57.9 to 65.2 vs 56.2 to 56.5 [p<0.05]; **PEFR (L min^{-1})**: 352.2 to 382.7 vs 350.1 to 343.5 [p<0.05]; **Medication used: ICS dosage µg**: 605 to 709 vs 620 to 630; **Systemic steroids(mg)**: 1.16 to 2.38 vs 1.30 to 1.25; **Antileukotrine**: 19 to 17 vs 14 to 16; **Quality of life: Physical component**[e]: 41.6 to 45.5 vs 43.2 to 40.0 [p=0.01]; **Mental component**[f]: 48.6 to 50.4 vs 48.6 to 44.4 [p=0.01]

Study	Disease	Intervention	Outcomes
Ostojic et al (2005)	Asthma	Weekly SMS with advice for selfcare were compared to usual care	*From baseline to follow-up, intervention vs control*: **FVC % predicted**: 88.66 to 87.63 vs 86.63 to 89.00; **FEV1 % predicted**: 77.63 to 81.25 vs 78.88 to 78.25; **PEF variability**: 14.12 to 27.24 [p=0.049]; **PEF by time of day (L min^{-1})** in the morning: 380.00 vs 365.15; afternoon: 405.35 vs 385.48; evening: 415.27 vs 395.60; Average-scores on symptoms[f]: **Coughing**: 1.42 vs 1.85 [p=0.028]; **Night symptoms**: 0.85 vs 1.22 [p=0.021]; **Wheezing**: 0.80 vs 0.89; **Limitations of activities**: 0.54 vs 0.84; **Costs (in Euro) per week**, intervention vs control: for patient: 0.67 vs 0; for physician: 1.00 vs 0; **Time (in min) per week**: for patient: 26.2 vs 14.7; for physician: 2.0 vs 0; **Daily consumption of inhaled medication (μg); of steroid**: 625 vs 530; of **long-acting β2s-agonist**: 118 vs 84
Shetty et al (2011)	Diabetes	SMS (every three days) with advice for nutrition, physicial activity and other relevant living habits were compared to usual care	*From baseline to follow-up, intervention vs control*: **Attendance rate at annual follow up**: 71% vs 63%; **Adherence to diet prescription**: 60.3% to 58.4% vs 54.5% to 52%; **Adherence to physical activity**: 47% to 56% vs 47% to 52%; **BMI <25kg/m^2**: 30.8% to 24.4% vs 31.8% to 28.8%; **PPG <180mg/dl**: 14.1% to 43.6% vs 13.6% to 19.7% [p<0.007]; **HbA1c <8 %**: 30.8% to 55.1% vs 31.8% to 58.5% [p<0.007]; **TC <200mg/dl**: 79.5% to 89.7% vs 80.3% to 92.4%; **TC <150mg/dl**: 53.8% to75.6% vs 66.7% to 78.8% [p<0.007]; **HDL- C >40 mg/dl**: 55.1% to 64.1% vs 66.7% to 74.2%; **LDL-C <100 mg/dl**: 59.0% to 78.2% vs 60.6% to 81.8% [p<0.02]

a: 10-item Center for Epidemilogical Studies-Depression Scale

b: Scale from 0 (no problems) to 7 (severe problems)

c: 1=poor, 2=fair, 3=good, 4=very good, 5= excellent

d: 0= not receiving care for blood pressure control; 1=receiving care but dissatisfied; 2=satisfied

e: Using the SF-12

f: Scale from 0 (none symptoms) to 3 (severe symptoms)

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Does mHealth contribute to improved care for people with non-communicable diseases in developing countries?

The reasons of deaths in developing countries are shifting from communicable diseases towards non-communicable diseases (NCDs). We review studies assessing the health-related impacts of mobile health (mHealth) on NCDs in low- and middle- income countries (LAMICs) with the aim of giving recommendations for their further development. A systematic literature search of three major databases was performed in order to identify randomized controlled trials (RCTs) of mHealth interventions.
6 RCTs were included in the review, including a total of 1850 participants. mHealth was found to have positively influenced clinical outcomes, compliance rates, as well as quality of life related aspects. Furthermore, other outcomes such as patients' anxiety or patient-physician trust improved significantly. We also found that tailored interventions using a single service for the transmission showed the most positive effect. Limiting factors of the evaluation however, were the few numbers of RCTs, the heterogeneity of outcome measures and the fact that all included studies were conducted in middle income countries and mostly in urban areas. However, mHealth can emerge as an important tool for fighting NCDs in LAMICs. Therefore, further support by governmental institutions for coordinating and promoting the development of the required tools, as well as further research especially in low-income economies, with a focus on the evaluation of the long-term effects of mHealth is needed.

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