Evidence for mHealth

A Market Research Project

conducted in collaboration with GSMA

Lisa Stroux
Wolfson College
Supervised by: Dr Gari Clifford

Trinity Term 2012

ABSTRACT

Mobile Health (mHealth) raises high hopes to positively contribute to health care challenges faced by health authorities, clinicians and patients alike. MHealth interventions promise the potential to improve personalised and individual health monitoring, to reduce costs of disease management and support health systems with convenient data transfer and storage solutions.
An application area of particular interest is chronic disease management where it is believed mHealth programs can have a particularly significant impact. Given the optimistic reports on mHealth it is surprising that large scale uptake of interventions has been slow. One barrier to wider roll out frequently highlighted is a lack of robust evidence to support developer's claims.

The primary objective of this report is to provide an overview and assessment of the most recent evidence base of mHealth for diabetes as an example of high burden chronic conditions. The report furthermore aims to inform the reader on the particular characteristics of the disease and the challenges of strong evidence building as a good understanding may influence the effect of future mHealth interventions.

A comprehensive PubMed search was conducted to retrieve evidence published in 2011 and the first half of 2012. 35 primary research articles were found to be relevant; 8 randomised controlled trials (RCTs) and 27 observational or descriptive reports.
The RCTs were assessed using the Jadad soring system and four trials were identified as very robust evidence.
The remaining observational studies were evaluated applying a quality assessment tool developed by the McMaster University and six articles were considered good evidence.

The interventions identified all used a variety of technologies, most prominently voice, Internet and text messaging, or combination therefore. These channels demonstrated significant improvements in the measured health outcomes (predominantly glycaemic control) and good acceptance amongst users.

In summary the analysis found mHealth for diabetes a highly active research area demonstrating promising results. Moving forward the assessment identified a number of aspects requiring further investigation, such as cost-benefit calculations and the role and impact of stakeholders other than the patient.

Contents

Table of Contents

Contents 3

Introduction 4
- Definition of mHealth 4
- The potential of mHealth 4
- Diabetes as an example of mHealth 4
- Evidence for mHealth 5
- Purpose of the report 5

Diabetes 5
- Prevalence of diabetes worldwide 5
- The disease pattern of diabetes 6
- The potential impact of mHealth 7

Study designs 8
- Study designs – an overview 8
- Classification of study designs 9
- Evidence hierarchy 10

Evidence for mHealth interventions targeting diabetes 11
- PubMed search 2011 - present 11
- Total number and origin of relevant evidence found, 2011-present 12

Evidence evaluation 13
- Evaluation methodology for Randomised Controlled Trials (RCTs) 13
- Evaluation outcome RDTs 14
- Evaluation of observational studies 14
- Evaluation outcome observational studies 14
- Summary of outcomes supported by high quality evidence 15

Conclusion 18
- Summary of findings 18
- The evidence base – considerations for future research 20

Bibliography 22

Introduction

Definition of mHealth

Mobile health (mHealth) is a subcategory of electronic health (eHealth) and related to telemedicine. There is no standardised definition for mHealth available, however, generally accepted descriptions include:

> *Telemedicine (also telecare or telehealth): medical practices mediated remotely, such as over the phone, by video, or asynchronously through a web service.*
> *mHealth: mobile healthcare, generally referring to telemedicine using a mobile phone* [8] .
>
> The World Health Organization defines mobile health as follows:
> *The practice of medical and public health through the usage of mobile devices* [36].

For the context of this report a mobile device may be a mobile phone, a personal digital assistant (PDA), or any medical device enabled to communicate wirelessly with mobile networks.
Mobile health interventions can span the entire patient pathway as well as be a tool for health system strengthening. The functionality of mHealth solutions includes personal wellness monitoring and disease management, information provision and education, decision support, data management and access, or results consultation [27] .

Typically, mHealth aims to utilise the inherent capabilities of mobile devices for health care purposes. A review commissioned by the GSMA found the existing evidence on mHealth to be based on the more familiar technologies such as text messaging, handset applications, the internet, voice, video, or a combination thereof; less frequently found, mHealth has the potential to equally exploit integral technologies such as global positioning systems or accelerometers.

The potential of mHealth

The advances in mobile phone technology, the continuous decrease in cost and the rapidly increasing use of mobile phones worldwide have driven the desire to develop new mHealth interventions in recent years. Mobile health interventions promise opportunities to extend health care delivery and improve outreach, to integrate data more easily with existing eHealth services and to allow for independent and personal health monitoring, to name a few of the promising applications available [36].
The key characteristics of mHealth, such as ‘continuous’, ‘personal’ and ‘mobile’, appear to be particularly promising when applied to the challenges of chronic disease management, where constant condition monitoring is crucial to successful health outcomes.

Diabetes as an example of mHealth

This report focuses on mHealth in the context of diabetes management as the field represents a significant global disease burden, and is relatively well-reported upon. The report provides an introduction to the disease pattern and the prevalence of diabetes and

subsequently investigates the most recent evidence base available for mobile health applications for diabetes management.

Evidence for mHealth

As highlighted above mobile health is an increasingly active area of medical product and service development. However, the large scale implementation of mHealth initiatives lag behind in pace [1] . This is particularly true in lower resource environments where mHealth initiatives often are small-scale pilots [16] . One aspect influencing the adoption of novel health delivery methods is the evidence base available to decision makers. It has been argued repeatedly that rigorous evaluations of mobile health interventions that support the developers' claims are still scarce [1, 4] .

Purpose of the report

The following report aims to provide a brief overview of the most recent evidence base published on mHealth interventions for diabetes.
The first part sets the context by discussing the global burden of diabetes; it introduces the disease pattern, the challenges particular to the disease, and why mHealth is believed to have the potential of positive impact. The report also aims at familiarising the reader with common tools to classify and evaluate evidence. Those tools are used subsequently to assess the evidence published between 2011 and May 2012.

Diabetes

Prevalence of diabetes worldwide

Non-communicable diseases are an increasing health burden worldwide and have hence been the focus of attention of the most recent World Health Statistics report, released by the World Health Organization (WHO) in May 2012 [38] . According to the latest figures, the WHO estimates that one in ten adults has diabetes, with diabetes being responsible for 3.5% of deaths due to non-communicable diseases. Raised fasting blood glucose is believed to be responsible for 6% of deaths worldwide, being not only the underlying cause of diabetes, but also a risk factor that may lead to cardiovascular death.

Surveys show that diabetes, of both type 1 and 2, has dramatically risen in the past years. The number of people with diabetes worldwide is estimated to have increased from 153 million in 2008 to 347 million in 2010; the increase has been attributed to population growth and aging (70%) as well as epidemiological factors (30%) [9] .

The current prevalence of diabetes (all types) is highest in China and India, followed by the United States; a particularly high burden is also recorded in Russia, Brazil and Mexico, as reported by the Word Diabetes Foundation in their most recent diabetes atlas (figure 1).

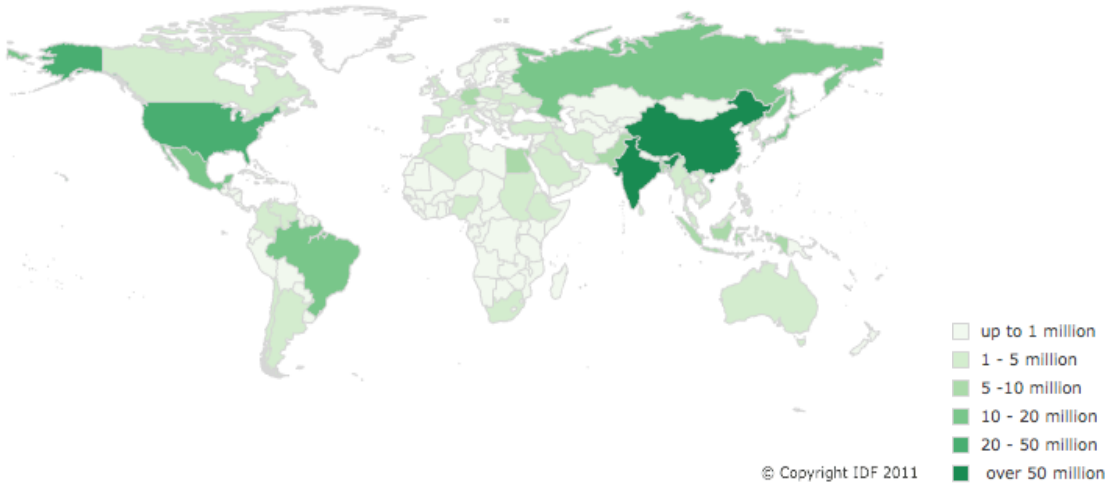

Figure 1: Estimated diabetes prevalence worldwide, 2011. Adapted from the Diabetes Atlas 2012. [37]

The disease pattern of diabetes

Diabetes is a metabolic disease, characterized by defects in insulin production and insulin action. Insulin is required to support the processing of glucose, the main source of energy to the body. With too little insulin present or an inappropriate insulin response by the cells, glucose accumulates in the blood, passes into the urine and gets secreted 'unused'.

There are three main types of diabetes: Type 1 diabetes, type 2 diabetes and gestational diabetes.
Type 1 diabetes (T1B) typically develops during childhood and adolescence, but not exclusively. T1B is classified as autoimmune disease whereby the immune system prohibits the production of insulin or a sufficient amount of insulin. Symptoms of T1B include increased thirst, hunger and urination, weight loss, vision impairment and fatigue. If not treated appropriately type 1 diabetes may ultimately result in life-threatening coma (ketoacidosis).
T1B patients are dependent on daily lifelong insulin intake with possibly complex treatment regimes. Type 1 diabetes is treated by insulin injections and a healthy lifestyle to regulate blood glucose levels. Blood glucose levels must be monitored by checking blood glucose, typically with a glucometer and occasionally complemented by a laboratory blood test.

Type 2 diabetes (T2B) occurs more frequently and accounts for about 90% of diabetes cases [35]. T2B is often related to obesity, an unhealthy diet and insufficient physical activity; it is also associated with a family history of diabetes and earlier gestational diabetes.
In type 2 diabetes insulin is typically available but not effectively used by the body. In comparison to T1B symptoms develop gradually over time, they include the same key indicators of fatigue, thirst and hunger, weight loss, blurred vision and slow wound healing process.
Type 2 patients can manage their diabetes by diet and physical exercise as well as regular blood glucose monitoring. Patients may require additional medication, such as insulin.

Gestational diabetes, characterized by high blood sugar levels (hyperglycemia) is diagnosed during pregnancy. Even though women with gestational diabetes are likely to go back to

normal after several weeks post delivery, once contracted, their chances of subsequently developing type 2 onset increase to 40-60% [24] .
Symptoms are comparable to those of type 1 and type 2 diabetes and can be managed by following dietary and exercise recommendations as well as regular monitoring of blood glucose levels.

Managing diabetes requires day-to-day metabolic control of blood glucose levels for symptom relief and the prevention of complications. Treatment can include injections of insulin, oral medication, dietary and exercise plans, as well as eye and foot care. Continuous monitoring is essential as both high and too low glucose content can have severe health implications [35]. In sever cases of diabetes the recommended medical support may include an extensive list of specialist doctors [24] :

1. A primary care provider such as an internist, a family practice doctor, or a paediatrician;
2. An endocrinologist (specialist in diabetes care);
3. A dietitian, a nurse, and other health care providers who are certified diabetes educators and experts in providing information about managing diabetes;
4. A podiatrist (foot care);
5. An ophthalmologist or an optometrist (eye care).

The potential impact of mHealth

There are several factors that underpin hopes that mHealth interventions have the potential to effectively alleviate the burden of diabetes disease by achieving greater health care coverage and equal access, improving personal health monitoring, supporting behavioural change, decreasing cost and reducing patient discomfort. The following issues are particularly noteworthy:

Monitoring and support:

- Diabetes is a chronic condition that requires continuous supervision and adjustment in condition management.
- Diabetes, and in particular type 2 diabetes, can be positively influenced by changing behavioural patterns. Education and continuous disease management support can be crucial in achieving a healthy lifestyle, such as an appropriate diet and physical exercise [25] .

Cost:

- Diabetic patients incur high costs to health care systems. The health care expenditure on diabetes in 2010 has been estimated to lie between 376 and 672 billion dollars globally, 12% of the total health expenditure worldwide. Global expenditure is predicted to rise by up to 34% by 2030 [39, 40] .

Increased coverage and equal access:

- Diabetes affects people on all continents and across all income groups. Required patient care is often not available in remote locations and low-resource settings [39] .
- Health expenditure in not equally distributed. An estimate of 91% of health care expenditure related to diabetes is spent in developed nations, with only 9% of the total spent in developing countries [40] .

- Total expenditure is not necessarily related to prevalence (figure 3). The highest spender by far is the United States, spending an average of 7382 USD on each diabetic patient. The two countries with the highest prevalence (almost 50% higher than the US), China and India, only spend 115 USD and 55 USD respectively [40] .

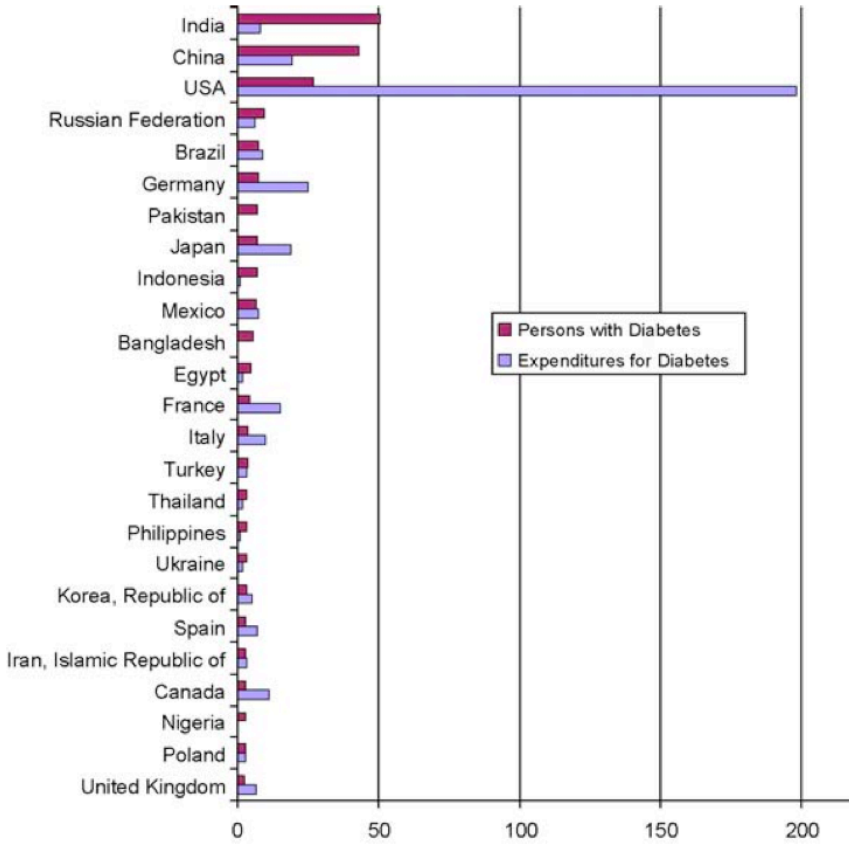

Figure 2: Health expenditure for diabetes (billions of ID) and the number of persons (millions) with diabetes in the 25 countries with the largest number of persons with diabetes in 2010. Adapted from Zhang et al. [40] .

Study designs

Evidence, its appropriateness and quality, is depended on the underlying study design and research method chosen. The following paragraphs provide an overview of the building blocks of research design, the different types of studies available and the hierarchy of resulting evidence.

Study designs – an overview

Study designs have a greater chance of successfully answering the relevant question by following a structured design approach. One such approach is the 'Patient Intervention Comparison and Outcome' framework (PICO) as described by the Centre for Evidence Based Medicine (CEBM) at Oxford University. [7]
The four PICO elements explained in table 1 aim to guide the researcher in considering the appropriate study design and execution.

(P) Patients/population	• Which patients or population of patients are we interested in? • How can they be best described? • Are there subgroups that need to be considered?
(I) Intervention / (E) Exposure	• Which intervention, treatment or approach should be used?
(C) Comparison	• What is/are the main alternative/s to compare with the intervention?
(O) Outcome	• What is really important for the patient? • Which outcomes should be considered, such as intermediate or short-term measures; mortality; morbidity and treatment complications; rates of relapse; late morbidity and readmission; return to work, physical and social functioning? • Should other measures such as quality of life, general health status and costs be considered?

Table 1: The PICO guide [7, 23] .

Classification of study designs

Research may be differentiated into primary and secondary evidence. Primary evidence investigates the intervention in question, whilst secondary research summarises and evaluates available primary studies. Primary research can be described as 'basic', 'epidemiological' or 'clinical 'research', Basic research may describe animal studies, cell studies or genetic investigations; Epidemiological research examines frequency in disease occurrence and its origins. Clinical studies encompass research into the impact and effects of certain interventions; the majority of mHealth diabetes evidence will primarily fall into the latter category, even though epidemiological data often plays a secondary role.
Secondary research is typically published in the form of reviews and meta-analyses. Primary as well as secondary clinical research is of interest when investigating mHealth evidence [30] .

A variety of study design exists in primary clinical research. The diagram below provides an overview of possible study choices and may serve as a classification tool.

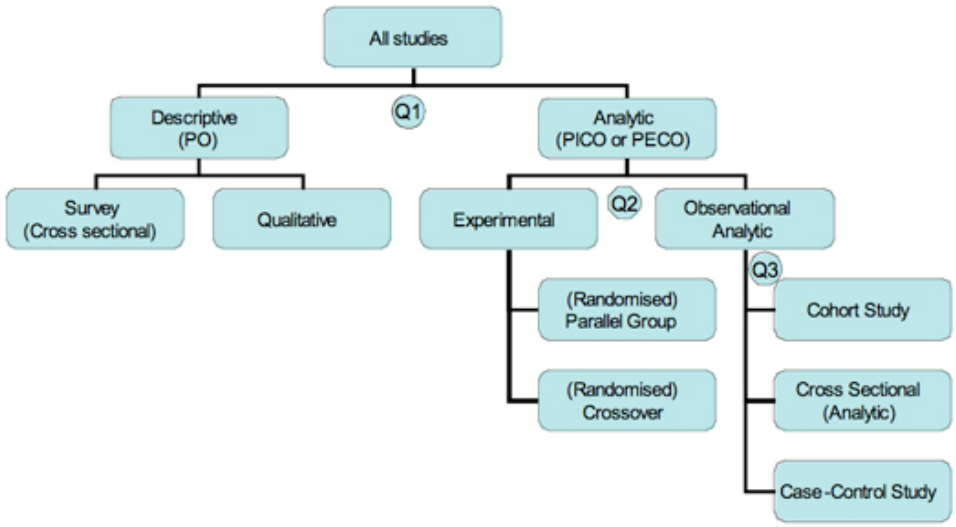

Figure 3: Different types of studies. Adapted from the Centre for Evidence Based Medicine [7] .

Studies may be categorised non-analytic or analytic. Whilst non-analytic studies are a descriptive record of, for example, incident rates or experiences in a group, analytic research will attempt to capture the interdependence of two factors, the effect of an intervention on the outcome of interest.

The Centre of Evidence Based Medicine at the University of Oxford proposes a simple three-question process to categorise the evidence under investigation.
Using the flow chart in figure 4, the questions in table 2 may guide the identification of the type of evidence.

Q1. What was the aim of the study?	To simply describe a population (PO questions)	➔ Descriptive
	To quantify the relationship between factors (PICO questions)	➔ Analytic.
Q2. If analytic, was the intervention randomly allocated?	Yes?	➔ Randomised Controlled trial (RCT)
	No?	➔ Observational study
Q3. If observational, when were the outcomes determined?	Some time after the exposure or intervention?	➔ Cohort study ('prospective study')
	At the same time as the exposure or intervention?	➔ Cross sectional study or survey
	Before the exposure was determined?	➔ Case-control study ('retrospective study' based on recall of the exposure)

Table 2: Guiding questions to determine type of study design [7] .

Evidence hierarchy

Mobile health interventions can target a variety of health care challenges, such as compliance and disease monitoring (improving health outcomes), as well as health information system support (health system strengthening) [36] . Depending on the intervention type different evidence requirements may apply. Health outcomes are considered best measured employing analytic and ideally experimental study designs. Interventions of health system strengthening however may be sufficiently supported by descriptive or observational reports.
Mobile health for diabetes appears particularly strong in the area of condition management to positively impact health outcomes. Study designs and evidence hierarchy related to this type of intervention will be the focus of the following paragraph.

Study designs are not equal in their risk of introducing error or bias. It has to be understood prior to establishing a trial design and conducting the research which methods provide the best evidence given the resources available. This includes being aware of the limitations the approach may hold.
Clinical evidence has been classed into different types, as outlined above, and ranked according to how close to the 'truth' the results are likely to be. Most rankings have focussed on effectiveness, investigating how well the intervention works, what the health impact is, who benefits and to what extend. However, more recent approaches distinguish between effectiveness, appropriateness and feasibility.

'Appropriateness', for example, concerns how suited the intervention is in a given environment and how acceptable it is to the intended user. 'Feasibility' on the other hand evaluates how easily the intervention in question can be implemented given the organisational and financial constraints encountered.

	Effectiveness	Appropriateness	Feasibility
Excellent	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies	• Systematic review • Multi-centre studies
Good	• RCT • Observational studies	• RCT • Observational studies • Interpretive studies	• RCT • Observational studies • Interpretive studies
Fair	• Uncontrolled trials with dramatic results • Before and after studies • Non-randomized controlled trials	• Descriptive studies • Focus groups	• Descriptive studies • Action research • Before and after studies • Focus groups
Poor	• Descriptive studies • Case studies • Expert opinion • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality	• Expert opinion • Case studies • Studies of poor methodological quality

Table 3: Hierarchy of evidence for health outcomes: ranking of research evidence evaluating health care interventions. Adapted from Evans, D. 2003 [11] .

In the context of evaluating evidence for mHealth interventions, impacting on health outcomes, this distinction seems particularly suited. MHealth interventions are likely go beyond the patient interaction but affect the system of health care delivery. Mobile health applications may imply the introduction of entirely new channels of health care delivery; they introduce potentially novel technology to the users and new modes of interaction between patients and health care providers. In addition to the effectiveness of a device or service, its appropriateness and chance of successful implementation are equally of interest and crucial to determine.

Evidence for mHealth interventions targeting diabetes

PubMed search 2011 - present

The following analysis collates and evaluates most recent mHealth interventions for diabetes. A PubMed search has been carried out to retrieve all evidence published in the period January 2011 to May 2012.

* Exclusion criteria: Entries were excluded for which the following criteria applied:
  - No abstract was available (5);
  - Article was not available in English (2);
  - mHealth was not a primary research focus (7);
  - Diabetes was not a primary research focus (9);

- System was primarily based on data transmission through telephone line and/or stationary computer (12). (Internet based or hybrid interventions (including for example both, mobile phones and data transmission through stationary home pc; or interventions that could easily be transferred to a mobile device) were not excluded.);
- The abstract was not conclusive regarding the technology used and access to the article was not available. (1)
- Articles classified as 'Commentary and opinion' (11), 'Review' (6) and 'Market research' (1) have been excluded from the set of evidence.

	PubMed search terms	Entries found	Entries excluding duplicates	Entries excl. unrelated or unsuitable *	Date exported
Diabetes + telemedicine	("diabetes mellitus"[MeSH Terms] AND "telemedicine"[MeSH Terms]) AND ("2011"[PDAT] : "3000"[PDAT])	64	62	20	10th May 2012
Diabetes + mobile phone	("diabetes mellitus"[MeSH Terms] AND ("cellular phone"[MeSH Terms] OR ("cellular"[All Fields] AND "phone"[All Fields]) OR "cellular phone"[All Fields] OR ("mobile"[All Fields] AND "phone"[All Fields]) OR "mobile phone"[All Fields])) AND ("2011"[PDAT] : "3000"[PDAT])	26	15	12	10th May 2012, updated 18th May 2012
Diabetes +Wireless technology	("diabetes mellitus"[MeSH Terms] AND ("wireless technology"[MeSH Terms] OR ("wireless"[All Fields] AND "technology"[All Fields]) OR "wireless technology"[All Fields])) AND ("2011"[PDAT] : "3000"[PDAT])	1	0	0	10th May 2012
Diabetes +Telemetry	("diabetes mellitus"[MeSH Terms] AND ("telemetry"[MeSH Terms] OR "telemetry"[All Fields])) AND ("2011"[PDAT] : "3000"[PDAT])	13	10	2	10th May 2012
Diabetes + Videoconferencing	("diabetes mellitus"[MeSH Terms] AND ("videoconferencing"[MeSH Terms] OR "videoconferencing"[All Fields])) AND ("2011"[PDAT] : "3000"[PDAT])	1	1	0	10th May 2012
Diabetes + Electronic mail	("diabetes mellitus"[MeSH Terms] AND ("electronic mail"[MeSH Terms] OR ("electronic"[All Fields] AND "mail"[All Fields]) OR "electronic mail"[All Fields])) AND ("2011"[PDAT] : "3000"[PDAT])	5	3	1	10th May 2012
TOTAL		110	92	35	

Table 4: PubMed search results for mHealth for diabetes, 2011-present.

Total number and origin of relevant evidence found, 2011-present

In the period 2011 to present 35 articles were found that describe evidence related to mHealth interventions for diabetes patients. Of the total evidence base, only eight were randomised controlled trials whilst the remaining may be described as observational studies.

Total relevant evidence	Randomised Controlled Trials	Observational Studies
35	8	27

Table 5: Relevant mHealth evidence for further evaluation.

By far the most trials originated in the US, followed by Poland, South Korea and The Netherlands. The majority of research was conducted in developed nations, with only three studies implemented in low-resource countries (Kenya, South Africa, Honduras).

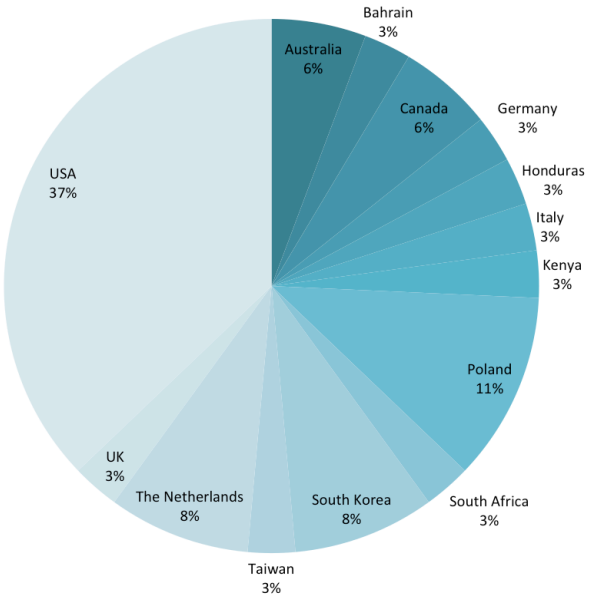

Figure 4: Country origin of evidence found 2011-present.

Evidence evaluation

Evaluation methodology for Randomised Controlled Trials (RCTs)

A well-established and relatively fast method of evaluating the methodological quality of randomised controlled trials is the Jadad scoring system (Jadad scale). The score, developed by Alejandro R. Jadad and his team, assigns a numerical score between 0 (weak) and 5 (strong) to describe the quality of study design and reporting using the framework presented in table 6 [14] .

	Scoring questions	**Score**
1.	Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1
2.	Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc)?	0/1
3.	Was the study described as double blind?	0/1
4.	Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc)?	0/1
5.	Was there a description of withdrawals and dropouts?	0/1
6.	Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc).	0/-1
7.	Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	0/-1

Table 6: Jadad scoring system.

It has to be considered that in the context of mHealth evidence evaluation randomised controlled trials are unlikely to be blinded, as patients will always be aware of technology based interventions. For the purpose of this report, 'blinded' will be acknowledged if neither the research staff or health care providers involved, nor the patients knew of the group assignment prior to the participant's consent; or if the assessing staff has been blinded to the intervention status of the patient.

Evaluation outcome RDTs

Eight randomised controlled trials were assessed using the Jadad scoring system (Appendix A). Only two provided maximum strength evidence (5), followed by two with medium scores (3), the remaining four were of weak evidence (2), or could not be analysed due to restricted access to the full article (2). The mHealth systems assessed were predominantly diabetes monitoring, management and educational applications or a combination therefor, measuring the outcome of glycaemic control. Six out of eight focussed on type 2 diabetes explicitly. Most interventions utilise a combination of technologies and products, such as a mobile phones in conjunction with other medical devices (e.g. glucose meters) or stationary computers.
All randomised controlled trials originated in developed countries, predominantly the US and South Korea.

Evaluation of observational studies

Tools for the evaluation of non-randomised studies are less established. This may be due to the common notion that observational research is not, or is less suited to provide evidence to decision making in clinical practice, given the greater potential of selection bias. However, several assessment instruments have been developed and evaluated for their suitability. [10]

For the evaluation of retrieved observational evidence in this report, a tool produced by the Effective Public Health Practice Project (EPHPP) at Mc Master University (Ontario, Canada) has been chosen. (Also referred to as 'Thomas tool', named after the primary developer Thomas H.). This particular 'quality assessment tool for quantitative studies' was selected for its wide application range as well as its simplicity in use [22] .

The freely available assessment tool is designed to be applicable to any type of study, rating the methodological quality of evidence under assessment as either strong, moderate or weak. The tool guides the evaluation of several crucial study components, the following have been assessed in the context of this review: 1. Selection bias; 2. Study design; 3. Confounders; 4. Blinding; 5. Data collection methods; 6. Withdrawals and dropouts.

To identify the type of observational study the decision tree outlined earlier in this report under 'classification of study designs' was used.

Evaluation outcome observational studies

Non-randomised research is often considered weaker evidence compared to randomised controlled trials due to the increased risk of bias introduced. In the hierarchy of evidence observational research typically ranks below systematic reviews and randomised controlled trials. It is advisable to keep this in mind when using assessment tools designed to cover

both RDTs and non-randomised study designs, as observational methods with lower score may still provide good evidence.

Appendix B summarises the evidence retrieved for mHealth interventions in diabetes patients, 2011 to present, which included 27 research papers. 22 studies were found to be cohort studies including one or more groups. The remaining five articles were categorised 'intervention description' and not assessed for their quality as they delivered a descriptive rather than analytic report only. Six cohort studies have been found of moderate quality and 15 of weak quality, one articles could not be accessed in full for further analysis. Two studies were classified product evaluation reports, focussing on the technical feasibility.

The majority of the research papers presented in the table (Appendix B) are small-scale studies focussed on the feasibility of the intervention and the user acceptability of the product or service. No study was found that investigates cost-effectiveness or the implications of larger-scale implementation.

Internet, voice and text message based interventions were most commonly observed. A small number of medical devices were included in last year's publications. Almost all diabetes interventions found provided monitoring and/or educational services, such as means of blood glucose level monitoring and supervision, or advice on dietary and physical activity. Compared to the randomised controlled trials, both type 1 and type 2 diabetes patients were addressed equally.

Summary of outcomes supported by high quality evidence

Four randomised controlled trials, assigned a score between 3 and 5 on the Jadad scale (table 7), and six observational studies with at least 'moderate' rating and supported by a good journal impact score (table 8), were considered suitable evidence. All randomised controlled studies reported a significantly positive effect of the intervention on the recorded outcomes. Five out of the six cohort studies could demonstrate the potential benefit of the intervention.

Three out of the four RCTs had the objective to improve glycaemic control and reduce A1c (glycated haemoglobin) levels compared to the available standard treatment schemes. The studies employed varying technologies to allow for monitoring of glucose levels and/or communication with the patient. Interventions assessed were the approach of a mobile application combined with a web-portal; video visits combined with uploads of glucose levels; and uploads of glucose levels combined with personalised text messaging. All studies reported a successful blood glucose control with a resulting significant decrease in A1c levels. The intervention of mobile application coaching assessed in addition diabetes related symptoms, such as distress or blood pressure; no beneficial effect was reported. The trial investigating the effects of video visits and glucose level monitoring also demonstrated the potential to reduce disparity in diabetes management.
One study described the use of web-based depression treatment having a significant effect in the reduction of depression symptoms and emotional stress. No effect could be reported on the secondary outcome, glycaemic control.

Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized, controlled trial [33].
Objective: To investigate whether depression can be effectively treated with web-based cognitive behaviour therapy (online lessons). Primary outcome: Reduction in depressive symptoms. Secondary outcome: Reduction in diabetes-specific emotional stress and glycaemic control. Results: The intervention was effective in reducing depressive symptoms. The interventions also reduced emotional stress; no beneficial effect was recorded on glycaemic control.

Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control [28] .
Objective: To investigate whether mobile application coaching and patient/provider web portals reduce glycated haemoglobin compared to standard treatment in type 2 diabetes patients. Primary outcome: Change in glycated haemoglobin (A1c) levels over a one-year period. Secondary outcome: Changes in symptoms related to diabetes. Results: Significant decline in glycated haemoglobin, no difference in diabetes related symptoms such as distress, depression or blood pressure and lipid levels could be measured.

Glycemic control and health disparities in older ethnically diverse underserved adults with diabetes: five-year results from the Informatics for Diabetes Education and Telemedicine (IDEATel) study [34].
Objective: To investigate the effect on glycaemic control of video visits and glucose level uploads. Update on existing IDEATel study with new study component: To analyse the intervention potential in reducing health disparities. Outcome: Improvement in glycaemic control, reduction in health disparities. Results: A significant decrease in A1c levels was reported. The study also reported the potential to reduce disparity in diabetes management.

Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system [18] .
Objective: To assess the improvement of glycaemic control without hypoglycaemia through a clinical-decision-support system (CDSS). (Glucose meter combined with individualised SMS). Outcome: Change in glycated haemoglobin (A1c) levels, improved glycaemic control. Results: A1C levels were reduced after 6 months in all groups. Better glycaemic control with less hypoglycaemia was achieved for the CDSS group.

Table 7: Strong evidence – Randomised controlled trials.

In contrast to the randomised controlled trials previously discussed, most of the observational studies selected investigated interventions related to type 1 diabetes. One explanation may be that a group of particular interest in type 1 diabetic patients are children and adolescents; randomised controlled trials can involve higher ethical barriers when including young patients. All five selected interventions (two studies were based on the same intervention) are mobile phone centred, most using inherent capabilities: voice (calls), a mobile application, or upload of glucose levels in combination with a web portal (integrated mobile phone and glucose meter), respectively. One application employed an integrated sensor to monitor physical activity. Except two, all discussed studies aimed to demonstrate improvement of blood glucose management and reduction in A1c levels.

The study performed using the integrated glucose meter and mobile phone could not validate any reduction in A1c levels. The same research group conducted a second trial marrying the intervention with a behavioural contract between child and parents, which interestingly demonstrated significant improvements in the patient's diabetes management profile and glucose levels. The group's hypothesis was that the technology might be enhanced and made effective by introducing the contractual component. The researchers found the intervention to be well received, however, technical usability issues were reported.

The remaining 'mobile app' (calculator for insulin bolus) and 'voice' (coaching) intervention studies both reported improvements in A1c levels. The acceptability of the calculator was reported high. Implementing the phone coaching could also demonstrate the effectiveness in decreasing blood pressure and body mass index (BMI).

One research article described the use of mobile phones to measure disease management and insulin administration of adolescents. The outcomes highlighted the potential of mobile

phones to survey management patterns; the authors suggested translating the insights gained into meaningful interventions to improve self-care.
The article describing a mobile phone intervention with integrated sensor to assess the physical activity of adolescents reported promising outcomes related to acceptability and the ability to link exercise (physical activity) to glucose levels. The authors suggested the system should ultimately support individual insulin dose adjustment. However, further trials are recommended given the small sample size (n=16) and short test period (three days).

Using mobile phones to measure adolescent diabetes adherence [21].
Objective: Determine the feasibility of using mobile phones to sample the behaviour of Type 1 diabetes patients (ecological momentary assessment) and identify patterns of adherence. Conclusions: Mobile phones are a feasible tool to measure monitoring and insulin administration in adolescents. Recommendation: Collect and use insights to develop targeted interventions to improve self-care.

An evaluation of Birmingham Own Health telephone care management service among patients with poorly controlled diabetes. A retrospective comparison with the General Practice Research Database [15].
Objective: Evaluation of nurse-delivered motivational coaching and support for self-management and lifestyle change, telephone-based. Conclusions: The study demonstrated the effectiveness in reduction of HbA1C levels, blood pressure and BMI. The changes observed were greater in patients with poorer baseline values. The intervention is reported to be effective in the most deprived areas.

Preliminary application of a new bolus insulin model for type 1 diabetes [26].
Objective: To investigate the feasibility of implementing a new calculator for insulin bolus on a mobile phone (for type 1 patients). Conclusions: Outcomes are indicative for patient acceptability and improvement of blood glucose control. The authors recommend the promising results should lead to more extensive clinical trial.

Using a cell phone-based glucose monitoring system for adolescent diabetes management [6].
Objective: To investigate the feasibility and acceptability of mobile phone glucose monitoring. Conclusions: The technology was reported to have been well received, however, several users had technical issues. The intervention did not have a positive effect on diabetes management, glycaemic control, quality of life or conflict with parents. It was suggested to test the intervention in conjunction with a behavioural contract (see study below).

Contracting and monitoring relationships for adolescents with type 1 diabetes: a pilot study [5].
Objective: Evaluate the effect on the diabetes management of adolescents by glucose monitoring via mobile phone in conjunction with a behavioural contract between adolescent and parents. Conclusions: Significant improvements were recorded in the diabetes management profile and for the reduction of A1c. Previous work has shown a reduction in A1c levels, it is hence hypothesised that behavioural contracts can enhance the technology. Further trials are required to confirm the preliminary data.

An Innovative Telemedical Support System to Measure Physical Activity in Children and Adolescents with Type 1 Diabetes [31] .
Objective: Evaluate the feasibility of a telemedical support sys- tem To assess physical activity in patients with type 1 diabetes. Results: High acceptability was reported with no complaints or usability issues recorded. In some patients correlation between activity and glucose levels could be shown. Conclusions: The study demonstrated the feasibility of using proposed device to document physical activity in association with glucose levels. The authors propose to use the system for insulin-dose control. Further trials are required to confirm outcomes.

Table 8: Good evidence – Observational studies.

In summary, the evidence found strongly supports the notion that mHealth for diabetes has the potential to be effective, feasible and acceptable to the end users. Personal monitoring tools and web or phone-based clinical coaching and support appear to have a positive impact on the patients' blood glucose levels, physical and mental wellbeing.

Cost-effectiveness and the wider implications of implementing the interventions into existing health systems have not been covered by the identified research. In particular non-randomised study articles have highlighted the importance of additional and larger scale trials to be conducted to assure bias reduction and translation of findings to a greater population size and divers settings.

Conclusion

Summary of findings

High research activity

The total amount of relevant (not quality-assessed) evidence found is substantial compared to the research output recorded in the last ten years. Figure 6 shows the number of articles published on mHealth for diabetes between 2001 and 2010 (as reported by A.T.Kearney and GSMA [2]), and 2011 (as found by the analysis described in this report). It is likely that there were differences in search and selection method between this report and the document prepared by A.T. Kearney in 2010, however, even with potentially slight variation in degree, the trend appears to continue rapidly upwards.

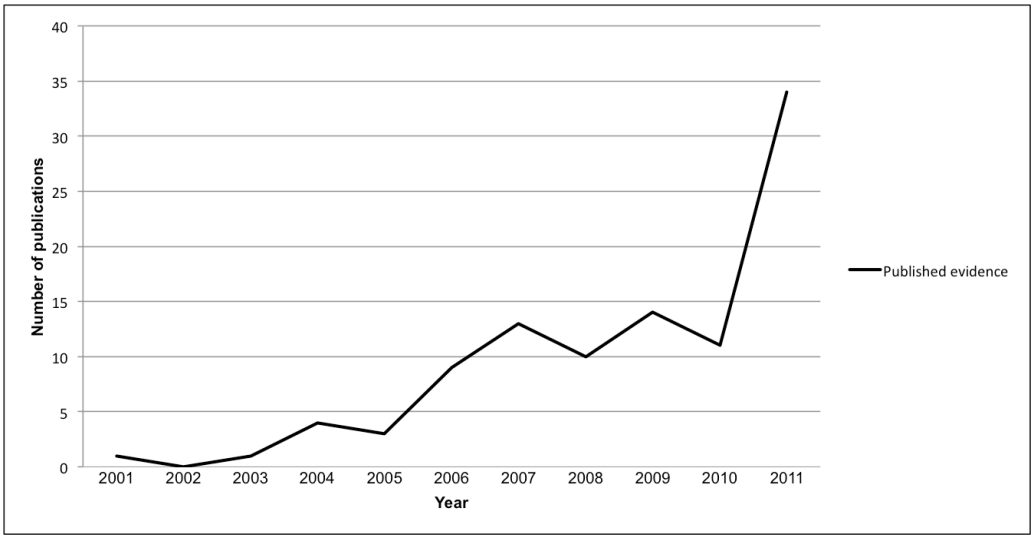

Figure 5: Number of studies on mHealth for diabetes published 2001-2011.

Quality of evidence

50% of RCTs were classified as good quality evidence, compared to 29% of the total of selected non-randomised studies (taking into account that one article could not be accessed for thorough analysis and five articles were categorised 'descriptive' upon further investigation and not assigned a score (see appendix B)). It should be reiterated that the quality assessment tools used in this document typically apply to clinical study designs; hence they will naturally rank research with reported low bias and rigorous quantitative approach higher than less stringent evidence reports. Strong evidence is an important tool to support uptake and dissemination of interventions. The assessment in this report however does not imply that mHealth solutions described in the remaining articles do not have the potential of making a positive impact on diabetes management.

Research focus

The majority of mHealth applications for diabetes reviewed are self-monitoring and management tools, frequently including an educational component and often using existing equipment, such as personal mobile phones or computers or a combination thereof. The primary focus of those monitoring applications was to supported glucose level management.

A small number of systems also have been described aiming to facilitate foot and eye care, typically involving a home-based screening device. Most frequently developers used voice, text, mobile app and Internet functionalities.

Less than a third of the total of selected interventions address type 1 diabetes. It has been argued previously that in the case of RCTs (1 out of 8) this may be due to higher barriers when involving adolescents, a group of particular interest in type 1 diabetes. The focus on type 2 diabetes, however, may also be explained by the fact that: 1. The prevalence of type 2 diabetes is much higher; 2. Type 2 diabetes can be prevented and dramatically influenced by behavioural change, such as dietary management and physical exercise. MHealth may hence promise a higher impact on type 2 disease outcomes.

The cost/benefit ratio of implementing the respective mHealth intervention has been neglected by most investigations.

Outcomes compared to published reviews

The results of this report are in agreement with a recent meta-analysis on the effect of mobile phone intervention for diabetes on glycaemic control [17] . The analysis assessed results of 22 studies including both type 1 and 2 patients over the last eight years and showed that mobile phone supported self-management successfully reduced A1c levels. Interestingly, the analysis found that there was a significantly greater effect on type 2 patients (figure 7), which supports the hypothesis above. Other differences in patients, such as age, weight and baseline A1c, or differences in technologies and frequency used did not have an impact. Similar to the findings of this report, cost-effectiveness was only researched and demonstrated by a small number of studies. Early meta-analyses could not report significant positive effects on diabetic management (Franc, Daoudi et al. 2011, Farmer, Gibson et al. 2005). The more recent evidence base however, as discussed in this report and most recent meta-analyses, provides a promising outlook [12, 13] .

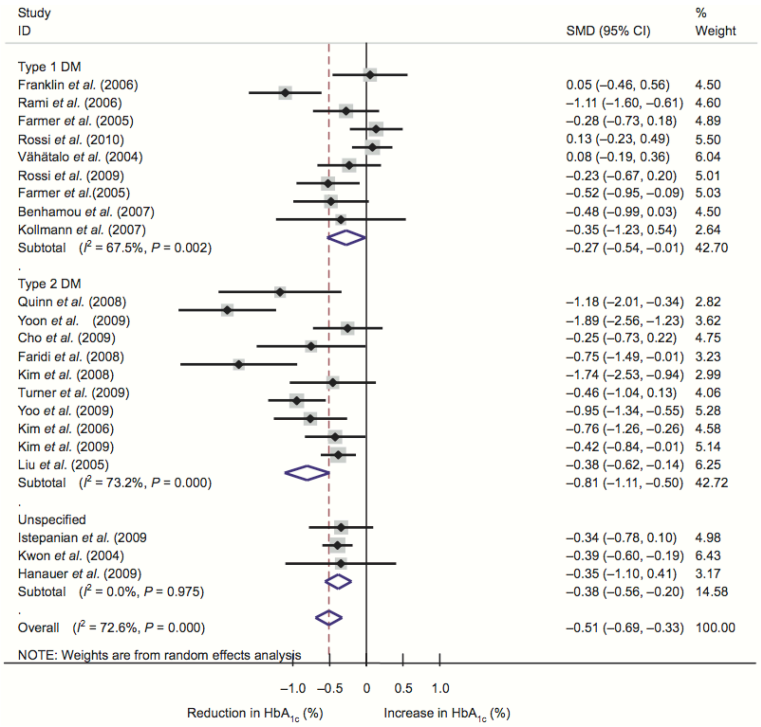

Figure 6: The reduction in HbA1c values by the type of diabetes. Adapted from Liang, Wang et al.2011.

The evidence base – considerations for future research

Research gaps

The evidence base for mobile technology to support mHealth diabetes interventions is steadily growing, particularly for glycaemic control.

However, there are several aspects to mobile health interventions, which are poorly represented in the studies reviewed. Only a very limited amount of research is available on the cost-effectiveness of the interventions proposed. A better understanding of the cost-benefit of mobile health programs could positively impact decision makers and the uptake of mHealth on a larger scale.

Few accounts are available describing the role of medical personnel in mHealth interventions. For interventions relying on clinical staff involvement it can be assumed beneficial to also understand the interaction of nurses and doctors with the proposed solution to ensure acceptance and a successful outcome. Many of the studies that included medical guidance in the form of text messages, calls or video consultations did not provide detailed information on the content of the educational intervention or the cost-benefit ratio of human interaction. A qualitative review has recently been published highlighting the latter, and included several other recommendations on successful mHealth intervention design [3] .

Knowledge of educational or consultation content is also considered important since it will co-determine the effect of the mHealth intervention – described by Liang et al. [17] .

Alternative approaches to evidence building

As discussed earlier in this report randomised controlled trials are considered the 'gold standard' of clinical study design when measuring health outcome. Few RCTs are available on mHealth for diabetes and mHealth in general. It can be assumed this is due to a number of reasons, such as limited funds and access to a larger group of potential subjects, the typically long timeframe (possibly unsuitable for rapid technology development) or simply the notion that an RDT is not the appropriate measure to evaluate the intervention in question given the resources available.

Particularly in the case of a technology-based intervention it may be argued that RCTs have their limitations, as mentioned earlier in the document; blinding is difficult to achieve and the effectiveness of the intervention may depend on the active participation of the patient and their preferences. The validity may be compromised if the intervention's success is dependent on a clinician or nurse, as it will affect the generalizability of the outcomes [19] .

It is commonly acknowledged that strong evidence is of ultimate importance. Which methods are most applicable to the assessment of mHealth, however, is a continuous discussion between stakeholders. Of particular interest are methods that are equally or even better suited than RCTs to improve the body of robust research for mHealth [29] . Suggestions for alternative methods include:

Step-wedge design: Step wedge randomised studies roll out the intervention subsequently over time to the respective patients or patient groups. The design is relevant in situations where randomization at the patient level is unsuitable and where simultaneous implementation of the experimental intervention is impossible due to ethical, logistic or financial reasons [20] .

N-of-1 trials: N-of-1 studies are single patient randomised controlled multi-crossover studies that aim to provide a rigorous assessment of the individual patient's outcome. They have been suggested as a flexible and efficient research alternative, as when combining individual effectiveness measures, they can form a convincing evidence base [41] .

Practice-Based evidence: Practice-based research measures outcomes as they occur in practice rather than in a tightly controlled study set-up. Patients are not assigned study groups prior to outcome recording, but according to the commonalities they share. It is favoured by those who feel the intervention in question does not necessarily fit the "cause and effect" model [32].

Not all mHealth interventions necessarily require an RCT or alternative randomised study approach. Mobile health programs may not necessarily target the improvement of a health outcome directly but provide support for data transmission, information storage and other health system challenges. The benefit and superiority of these applications may well be demonstrated by future feasibility studies and cost benefit calculations.

Bibliography

[1] A.T. KEARNEY, 2011. *Improving the evidence for mobile health.* GSMA.

[2] A.T. KEARNEY and GSMA, 2010-last update, GSMA mHealth Evidence Knowledge Bank [Homepage of GSMA], [Online]. Available: http://www.gsm.org/connectedliving/mhealth/evidence-knowledge-bank/ [May 14, 2012].

[3] AJAY, V.S. and PRABHAKARAN, D., 2011. The scope of cell phones in diabetes management in developing country health care settings. *Journal of diabetes science and technology,* **5**(3), pp. 778-783.

[4] BULLETIN OF THE WORLD HEALTH ORGANIZATION, 2012. *Establishing an evidence base for e-health: the proof is in the pudding* . 90:322-322A. World Health Organization.

[5] CARROLL, A.E., DIMEGLIO, L.A., STEIN, S. and MARRERO, D.G., 2011. Contracting and monitoring relationships for adolescents with type 1 diabetes: a pilot study. *Diabetes technology & therapeutics,* **13**(5), pp. 543-549.

[6] CARROLL, A.E., DIMEGLIO, L.A., STEIN, S. and MARRERO, D.G., 2011. Using a cell phone-based glucose monitoring system for adolescent diabetes management. *The Diabetes educator,* **37**(1), pp. 59-66.

[7] CENTRE FOR EVIDENCE BASED MEDICINE, 22 January 2009, 2009-last update, Study Designs [Homepage of Centre for Evidence Based Medicine], [Online]. Available: http://www.cebm.net/index.aspx?o=1039 [May 18, 2012].

[8] CLIFFORD, G.D. and CLIFTON, D., 2012. Wireless technology in disease management and medicine. *Annual Review of Medicine,* **63**, pp. 479-492.

[9] DANAEI, G., FINUCANE, M.M., LU, Y., SINGH, G.M., COWAN, M.J., PACIOREK, C.J., LIN, J.K., FARZADFAR, F., KHANG, Y., STEVENS, G.A., RAO, M., ALI, M.K., RILEY, L.M., ROBINSON, C.A., EZZATI, M. and GLOBAL BURDEN METAB RISK FACTORS C, 2011. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet,* **378**(9785), pp. 31-40.

[10] DEEKS, J.J., DINNES, J., D'AMICO, R., SOWDEN, A.J., SAKAROVITCH, C., SONG, F., PETTICREW, M. and ALTMAN, D.G., 2003. *
Evaluating non-randomised intervention studies.* Volume 7: No. 27. Health Technology Assessment.

[11] EVANS, D., 2003. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. *Journal of Clinical Nursing,* **12**(1), pp. 77-84.

[12] FARMER, A., GIBSON, O.J., TARASSENKO, L. and NEIL, A., 2005. A systematic review of telemedicine interventions to support blood glucose self-monitoring in diabetes. *Diabetic medicine : a journal of the British Diabetic Association,* **22**(10), pp. 1372-1378.

[13] FRANC, S., DAOUDI, A., MOUNIER, S., BOUCHERIE, B., DARDARI, D., LAROYE, H., NERAUD, B., REQUEDA, E., CANIPEL, L. and CHARPENTIER, G., 2011. Telemedicine and diabetes: Achievements and prospects. *Diabetes & metabolism,* **37**(6), pp. 463-476.

[14] JADAD, A.R., MOORE, R.A., CARROLL, D., JENKINSON, C., REYNOLDS, D.J.M., GAVAGHAN, D.J. and MCQUAY, H.J., 1996. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled clinical trials,* **17**(1), pp. 1-12.

[15] JORDAN, R.E., LANCASHIRE, R.J. and ADAB, P., 2011. An evaluation of Birmingham Own Health telephone care management service among patients with poorly controlled diabetes. A retrospective comparison with the General Practice Research Database. *BMC public health,* **11**, pp. 707.

[16] LEMAIRE, J., 2011. *Scaling up mobile health - elements necessary for the successful scale up of mHealth in developing countries.* Geneva: ADVANCED DEVELOPMENT FOR AFRICA.

[17] LIANG, X., WANG, Q., YANG, X., CAO, J., CHEN, J., MO, X., HUANG, J., WANG, L. and GU, D., 2011. Effect of mobile phone intervention for diabetes on glycaemic control: a meta-analysis. *Diabetic Medicine,* **28**(4), pp. 455-463.

[18] LIM, S., KANG, S.M., SHIN, H., LEE, H.J., WON YOON, J., YU, S.H., KIM, S.Y., YOO, S.Y., JUNG, H.S., PARK, K.S., RYU, J.O. and JANG, H.C., 2011. Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system. *Diabetes care,* **34**(2), pp. 308-313.

[19] LOKE, Y.K., PRICE, D., HERXHEIMER, A. and COCHRANE ADVERSE EFFECTS METHODS GROUP, 2007. Systematic reviews of adverse effects: framework for a structured approach. *BMC medical research methodology,* **7**, pp. 32.

[20] MDEGE, N.D., MAN, M.S., TAYLOR NEE BROWN, C.A. and TORGERSON, D.J., 2011. Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation. *Journal of clinical epidemiology,* **64**(9), pp. 936-948.

[21] MULVANEY, S.A., ROTHMAN, R.L., DIETRICH, M.S., WALLSTON, K.A., GROVE, E., ELASY, T.A. and JOHNSON, K.B., 2012. Using mobile phones to measure adolescent diabetes adherence. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association,* **31**(1), pp. 43-50.

[22] NATIONAL COLLABORATING CENTRE FOR METHODS AND TOOLS, 13 April, 2010, 2010-last update, *Quality Assessment Tool for Quantitative Studies* [Homepage of Hamilton ON: McMaster University], [Online]. Available: http://www.nccmt.ca/registry/view/eng/14.html [May 22, 2012].

[23] NICE, June 13, 2007, 2007-last update, Guideline Development Methods - Chapter 5: Developing clinical questions [Homepage of National Institute for Health and Clinical Excellence], [Online]. Available: http://www.nice.org.uk/niceMedia/pdf/GDM_Chapter5_0305.pdf [May 20, 2012].

[24] NIH, April 4, 2012, 2012-last update, National Diabetes Clearing House [Homepage of National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)], [Online]. Available: http://www.diabetes.niddk.nih.gov/dm/pubs/overview/index.aspx [May 17, 2012].

[25] NIH, August 1, 2011, 2011-last update, Diabetes - Successes and Opportunities for Population-Based Prevention and Contro [Homepage of National Center for Chronic Disease Prevention and Health Promotion], [Online]. Available: http://www.cdc.gov/chronicdisease/resources/publications/AAG/ddt.htm [May 24, 2012].

[26] PELZER, R., MATHEWS, E.H. and LIEBENBERG, L., 2011. Preliminary application of a new bolus insulin model for type 1 diabetes. *Diabetes technology & therapeutics,* **13**(5), pp. 527-535.

[27] PING YU, WU, M.X., YU, H. and XIAO, G.Q., 2006. The Challenges for the Adoption of M-Health, *Service Operations and Logistics, and Informatics, 2006. SOLI '06. IEEE International Conference on* 2006, pp. 181-186.

[28]QUINN, C.C., SHARDELL, M.D., TERRIN, M.L., BARR, E.A., BALLEW, S.H. and GRUBER-BALDINI, A.L., 2011. Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control. *Diabetes care,* **34**(9), pp. 1934-1942.

[29] ROBERT WOOD JOHNSON FOUNDATION, MCKESSON FOUNDATION, NATIONAL SCIENCE FOUNDATION and NIH, August 16, 2011, 2011-last update, mHealth Evidence Workshop [Homepage of National Institues of Health], [Online]. Available: http://videocast.nih.gov/launch.asp?16799 [May 24, 2012].

[30] ROHRIG, B., DU PREL, J.B., WACHTLIN, D. and BLETTNER, M., 2009. Types of study in medical research: part 3 of a series on evaluation of scientific publications. *Deutsches Arzteblatt international,* **106**(15), pp. 262-268.

[31] SCHIEL, R., THOMAS, A., KAPS, A. and BIEBER, G., 2011. An innovative telemedical support system to measure physical activity in children and adolescents with type 1 diabetes mellitus. *Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association,* **119**(9), pp. 565-568.

[32] SWISHER, A.K., 2010. Practice-based evidence. *Cardiopulmonary physical therapy journal,* **21**(2), pp. 4.

[33] VAN BASTELAAR, K.M., POUWER, F., CUIJPERS, P., RIPER, H. and SNOEK, F.J., 2011. Web-based depression treatment for type 1 and

type 2 diabetic patients: a randomized, controlled trial. *Diabetes care,* **34**(2), pp. 320-325.

[34] WEINSTOCK, R.S., TERESI, J.A., GOLAND, R., IZQUIERDO, R., PALMAS, W., EIMICKE, J.P., EBNER, S., SHEA, S. and IDEATEL CONSORTIUM, 2011. Glycemic control and health disparities in older ethnically diverse underserved adults with diabetes: five-year results from the Informatics for Diabetes Education and Telemedicine (IDEATel) study. *Diabetes care,* **34**(2), pp. 274-279.

[35] WHO, 2012-last update, Diabetes Programme [Homepage of World Health Organization], [Online]. Available: http://www.who.int/diabetes/action_online/basics/en/index.html [May/17, 2012].

[36] WHO GLOBAL OBSERVATORY FOR EHEALTH, 2011. *
mHealth
New horizons for health through mobile technologies.* Volume 3. Geneva: World Health Organization.

[37] WORLD DIABETES FOUNDATION, May 15, 2012, 2012-last update, Diabetes Atlas [Homepage of World Diabetes Foundation], [Online]. Available: http://www.worlddiabetesfoundation.org/composite-35.htm [May 23, 2012].

[38] WORLD HEALTH ORGANIZATION, 2012. *World Health Statistics 2012.* Geneva: WHO Press.

[39] WORLD HEALTH ORGANIZATION, 2010. *Global status report on noncommunicable diseases 2010 - Description of the global burden of NCDs, their risk factors and determinants.* Geneva: WHO Press.

[40] ZHANG, P., ZHANG, X., BROWN, J., VISTISEN, D., SICREE, R., SHAW, J. and NICHOLS, G., 2011. Global healthcare expenditure on diabetes for 2010 and 2030. **92**(2),.

[41] ZUCKER, D.R., SCHMID, C.H., MCINTOSH, M.W., D'AGOSTINO, R.B., SELKER, H.P. and LAU, J., 1997. Combining single patient (N-of-1) trials to estimate population treatment effects and to evaluate individual patient responses to treatment. *Journal of clinical epidemiology,* **50**(4), pp. 401-410.

Appendix A - RDTs 2011- present, assessed using the Jadad score.*

Journal	Year	PubMed ID	Country	Title	mHealth Category	Technology	Type of evidence	Study design	Population	Sample size	Research focus	Journal impact score (2010)	Jadad score
Telemedicine and e-health	2011	21375410	Poland	The impact of telehome care on health status and quality of life among patients with diabetes in a primary care setting in Poland.	Monitoring	Combination (Internet, SMS, voice)	Primary	RCT	Type 2	100	Health outcomes	1.297	1
Diabetes Care	2011	21270184	USA	Glycemic control and health disparities in older ethnically diverse underserved adults with diabetes: five-year results from the Informatics for Diabetes Education and Telemedicine (IDEATel) study.	Monitoring	Combination (Video, internet)	Primary	RCT	Not specified	1665	Health outcomes	7.141	3
Diabetes Care	2011	21216855	The Netherlands	Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized, controlled trial.	Monitoring, Education	Internet	Primary	RCT	Type 1 and 2	286	Health outcomes	7.141	5
Journal of Telemedicine and Telecare	2011	21933896	South Korea	Effects on diabetes management of a health-care provider mediated, remote coaching system via a PDA-type glucometer and the Internet.	Monitoring	Medical device (PDA-type blood glucometer)	Primary	RCT	Type 2	71	Health outcomes	1.274	2
Journal of Telemedicine and Telecare	2011	21628421	South Korea	Effectiveness and safety of a glucose data-filtering system with automatic response software to reduce the physician workload in managing type 2 diabetes.	Monitoring, Prioritisation	Internet	Primary	RCT	Type 2	79	Efficacy and safety	1.274	2
Perspectives in Health Information Management	2011	21307985	USA	A patient-centric, provider-assisted diabetes telehealth self-management intervention for urban minorities.	Monitoring	Internet (Laptop equipped with peripherals)	Primary	RCT	Type 2	47	Health outcomes	Not available	2
Diabetes Care	2011	21788632	USA	Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control.	Monitoring, Education	Handset App, Internet	Primary	Cluster-randomized clinical trial	Type 2	163	Health outcomes	7.141	5
Diabetes Care	2011	21270188	South Korea	Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system.	Monitoring	Combination (medical device connected via PSTN, SMS)	Primary	RCT	Type 2	144	Health outcomes	7.141	3

** Assessment limitation: Evidence has been evaluated by one reviewer only.*

Appendix B – Non-randomised trials 2011- present. Assessed using described quality assessment tool for quantitative studies.**

Journal	Year	PubMed ID	Country	Title	mHealth Category	Technology	Type of evidence	Study design	Population	Sample size	Declared research focus	Journal impact score (2010)	Quality assessment rating
Journal of Medical Internet Research	2011	21959968	The Netherlands	Factors influencing the use of a Web-based application for supporting the self-care of patients with type 2 diabetes: a longitudinal study.	Monitoring	Website application, email	Primary	Cohort study (longitudinal)	Type 2	50	Usability	4.663	Weak
Telemedicine and health	2011	21882998	Taiwan	One-year efficacy and safety of the telehealth system in poorly controlled type 2 diabetic patients receiving insulin therapy.	Monitoring	Medical device, Internet, Voice	Primary	Cohort study (two groups)	Type 2	64	Efficacy, safety	1.297	Weak
Experimental and Clinical Endocrinology & Diabetes	2011	21472657	Germany	An innovative telemedical support system to measure physical activity in children and adolescents with type 1 diabetes mellitus.	Monitoring	Medical device	Primary	Cohort study	Type 1	16	Feasibility, acceptance	1.826	Moderate
BMC Public Health	2011	21929804	UK	An evaluation of Birmingham Own Health telephone care management service among patients with poorly controlled diabetes. A retrospective comparison with the General Practice Research Database.	Monitoring	Voice	Primary	Case-control study	Not specified	473	Effectiveness	2.364	Moderate
Telemedicine and eHealth	2011	21492033	USA	Diabetes population management by telephone visits.	Monitoring	Voice	Primary	Cohort study (two groups)	Not specified	167 (baseline), 143 (study)	Feasibility	1.297	Weak
Journal of Health Communication	2011	21294020	USA	Expanding the walls of the health care encounter: support and outcomes for patients online.	Monitoring	Internet, email	Primary	Cohort study (one group)	Type 1 and 2	109	Feasibility	1.314	Weak
The Diabetes Educator	2011	21106908	USA	Using a cell phone-based glucose monitoring system for adolescent diabetes management.	Monitoring	Medical device	Primary	Cohort study (one group)	Type 1	40	Usability, satisfaction	1.947	Moderate
Journal of Health Care for the Poor and Underserved	2011	22102311	USA	Socio-demographic psychosocial and clinical characteristics of participants in e-HealthyStrides ©: an interactive ehealth program to improve diabetes self-management skills.	Monitoring, Educational	Internet	Primary	Cohort study (one group)	Not specified	146	Acceptance, efficiency	1.033	Weak
Telemedicine and eHealth	2011	21565846	USA	A pilot project for improving paediatric diabetes outcomes using a website: the Pediatric Diabetes Education Portal.	Education	Internet	Primary	Cohort study	Type 1	52	Feasibility	1.274	Weak

*** Assessment limitation: Evidence has been evaluated by one reviewer only.*

Journal	Year	PubMed ID	Country	Title	mHealth Category	Technology	Type of evidence	Study design	Population	Sample size	Declared research focus	Journal impact score (2010)	Quality assessment rating
Health Psychology	2012	21967662	USA	Using mobile phones to measure adolescent diabetes adherence.	Monitoring	Voice	Primary	Cohort study (one group)	Type 1	50	Feasibility	3.982	Moderate
Diabetes Research and Clinical Practice	2011	21840079	Bahrain	Effectiveness of mobile phone short message service on diabetes mellitus management; the SMS-DM study.	Monitoring	SMS	Primary	Cohort study (two groups)	Type 2	32	Feasibility, acceptance	2.134	Weak
Journal of Diabetes Science and Technology	2011	22027326	USA	Feasibility and usability of a text message-based program for diabetes self-management in an urban African-American population.	Monitoring	SMS	Primary	Cohort study	Not specified	18	Feasibility, usability	Not available	No access to full article
Diabetic Medicine	2011	21434996	Australia	Mobile phone support is associated with reduced ketoacidosis in young adults.	Monitoring	Voice	Primary	Cohort study	Type 1	Group 1(285) Group 2 (31) Group 3 (15) Group 4 (19)	Feasibility	3.036	Weak
American Journal of Preventive Medicine	2011	21565655	Honduras/ USA	A preliminary study of a cloud-computing model for chronic illness self-care support in an underdeveloped country.	Monitoring	Voice, internet	Primary	Cohort study (one group)	Not specified	85	Feasibility, satisfaction	4.11	Weak
Diabetes Technology & Therapeutics	2011	21410336	South Africa	Preliminary application of a new bolus insulin model for type 1 diabetes.	Monitoring, treatment	Handset application	Primary	Cohort study (one group)	Type 1	11	Product description, feasibility	2.146	Moderate
Diabetes Technology & Therapeutics	2011	21406018	USA	Qualitative evaluation of a mobile phone and web-based collaborative care intervention for patients with type 2 diabetes.	Monitoring	Internet	Primary	Cohort study (one group)	Type 2	8	Acceptance, feasibility	2.146	Weak
Diabetes Technology & Therapeutics	2011	21406011	USA	Contracting and monitoring relationships for adolescents with type 1 diabetes: a pilot study.	Monitoring	Internet, SMS	Primary	Cohort study (one group)	Type 1	10 (parent-adolescent pairs)	Effectiveness	2.146	Moderate

Journal	Year	PubMed ID	Country	Title	mHealth Category	Technology	Type of evidence	Study design	Population	Sample size	Declared research focus	Journal impact score (2010)	Quality assessment rating
Journal of Telemedicine and Telecare	2011	21844173	Australia	Trial of a mobile phone method for recording dietary intake in adults with type 2 diabetes: evaluation and implications for future applications.	Monitoring	Mobile phone application,	Primary	Cohort study	Type 2	10	Feasibility, acceptability, ease-of-use	1.274	Weak
Journal of Diabetes Science and Technology	2011	21880237	Canada	Remote monitoring technologies for the prevention of metabolic syndrome: the Diabetes and Technology for Increased Activity (DaTA) study.	Monitoring	Internet, data transmission	Primary	Cohort study (one group)	Type 2	24	Usability and feasibility	Not available.	Weak
Journal of Diabetes Science and Technology	2011	21880236	Canada	Diabetes and Technology for Increased Activity (DaTA) study: results of a remote monitoring intervention for prevention of metabolic syndrome. (SAME AS ABOVE)	Monitoring	Internet, data transmission	Primary	Cohort study (one group)	Type 2	24	Feasibility	Not available.	Weak
PRODUCT EVALUATIONS													
Diabetes Technology & Therapeutics	2011	21751890	Poland	Area of the diabetic ulcers estimated applying a foot scanner-based home telecare system and three reference methods.	Monitoring	Medical device	Evaluation of system or product	Cohort study (one group)	Type 1 and 2	23	Technical feasibility	2.146	Weak
Diabetes Technology & Therapeutics	2011	21568750	Poland	A new imaging and data transmitting device for telemonitoring of diabetic foot syndrome patients.	Monitoring	Medical device	Evaluation of system or product	Cohort study (one group)	Type 2	10	Technical feasibility	2.146	Weak
DESCRIPTION OF INTERVENTION													
Journal of Health Communication	2011	21916721	USA	The potential of an online and mobile health scorecard for preventing chronic disease.	Monitoring	Internet	Article	Product description	Chronic disease patients	NA	Product description	1.5	NA
The International Journal of Artificial Organs	2011	20946304	Poland	Monitoring of diabetic foot syndrome treatment: some new perspectives.	Monitoring	Medical device	Article	Product description	Not specified	NA	Product description	1.719	NA
Journal of Diabetes Science and Technology	2011	21303625	Italy	Utilizing information technologies for lifelong monitoring in diabetes patients.	Monitoring	Network architecture	Article	Product description	Chronic disease patients	NA	Product description	Not available	NA
Studies in Health Technology and Informatics	2011	21893723	The Netherlands	Development of a web-based decision support system for insulin self-titration.	Decision-support	Internet	Article	Product description	Type 2	NA	Product description	Not available	NA
The Annals of Pharmacotherapy	2011	21558485	Kenya	The evolution of diabetes care in the rural, resource-constrained setting of western Kenya.	Monitoring	Voice	Primary	Programme description	Not specified.	NA	Programme description	2.166	NA