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ORIGINAL ARTICLE

A META-ANALYSIS OF MOBILE HEALTH AND RISK REDUCTION IN PATIENTS WITH DIABETES MELLITUS: CHALLENGE AND OPPORTUNITY

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Purpose: To examine scientific evidence on the effectiveness of mobile phone technology in Diabetes Mellitus (DM) care management.

Methods: A systematic review was conducted through literature searches from three electronic databases and was restricted to English-language articles published between January 2002 and March 2012. Studies that used mobile phone intervention and reported changes in diet, physical activity, and blood glucose and /or glycosylated hemoglobin (HbA1c) levels were retrieved. A meta-analysis was conducted for studies with HbA1c measures.

Results: More than 50 articles were screened. Of them, 15 met the review criteria. Of the 15, study sample sizes ranged from 12 to 130 participants aged 8 to 70 years old. Duration of intervention ranged from 1 to 12 months. Overall, significant improvements were observed in blood glucose and/or HbA1c concentration, adherence to medication, healthy lifestyle, and self-efficacy. Twelve of 15 trials, which had serum HbA1c measures, showed an average 0.39% (95%CI: -0.067, -0.721) HbA1c reduction from studies with pre- to post-tests (p=0.018).

Conclusion: Findings from the study provide the evidence that health reminders, disease monitoring and management, and education through mobile phone technology may significantly help improve glycaemic control patients with DM.

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Introduction

There has been a rapid escalation in the rate by which mobile technology has been adopted in the United States and globally[1, 2]. More recently, as of June 2011, the U.S had an estimated 331.6 million wireless subscribers (Cellular Telecommunications & Internet Association (CTIA), 2011) and 4.6 billion mobile cellular subscriptions worldwide[3].

As mobile phone technology continues to expand and electronic medical and personal health records (PHRs) grow simultaneously, mobile phones will become increasingly important in the strategic implementation of chronic disease management [1, 4]. Research evidence suggests that mobile phone technology may be beneficial in diet and weight management [5, 6], physical activity involvement [7, 8], asthma control [9, 10], and diabetes management [11, 12].

Diabetes Mellitus (DM) is a highly prevalent chronic disease in the United States and in the world [13-15]. Although several methods of patient care have been well established to improve clinical profile and complications associated with DM, effectiveness of novel interventions remains to be evaluated [16].

The purpose of this review is to identify the impact of mobile phone technology interventions on DM care and patient outcomes, recognize potential challenges and limitations associated with performing healthcare practice and conducting research in this field, and examine practical ways of incorporating mobile phone technology in DM management.

Methods

Data sources

Electronic literature searches were conducted extensively to identify all eligible observational and randomized controlled clinical trials. Searches were performed on three major databases including PubMed, Ovid MEDLINE, and Google scholar using combined terms of 'diabetes', 'diabetes mellitus', 'cellular phone' 'mobile phone', and 'text message'. In addition, manual searches were completed by screening the bibliographies and citations of published articles. The search was restricted to English-language articles published between January 2002 and March 2012.

Eligibility criteria

Studies were selected for the review based on the following criteria: (1) participants had clinically diagnosis of DM (either type II or type I); (2) the study evaluated use of mobile phones for DM self management; (3) effect was measured in the process or outcome of DM care; and (4) the studies with designs of randomized controlled trial, quasi-randomized trial, crossover randomized clinical trial, or observational cohort studies. Studies were excluded if (1) they were case reports, and (2) if other communication technologies such as the Internet, e-mail, or video messaging were used as the primary mode of communication instead of mobile phone technology.

Data extraction

Relevant data from each eligible published paper were extracted into a structured spreadsheet. Authors, year of publication, study setting, sample size, study design, age group, race, duration of intervention, outcomes, method of self-management, intervention details, and reported results were reviewed.

Meta-analysis

Studies with a randomized controlled trial design and having pre- and post-intervention measures of serum HbA1c concentration were further analyzed using meta-analysis random effect modeling approach to quantitatively estimate the overall effect from multiple studies.

Results

Characteristics of included studies

In the initial review, more than 50 articles were screened. After excluding studies that did not meet the eligibility criteria, 15 studies were reviewed intensively. Of them, studies took place in several countries including Korea [17, 17-20], U.S [11, 21-23], Austria [24], Finland [12], Iran [25], U.K [26-29], and multi center (Italy, England, and Spain)[30]. Patients were recruited from primary clinics, tertiary hospitals and community settings. Figure 1 shows the selection of studies.

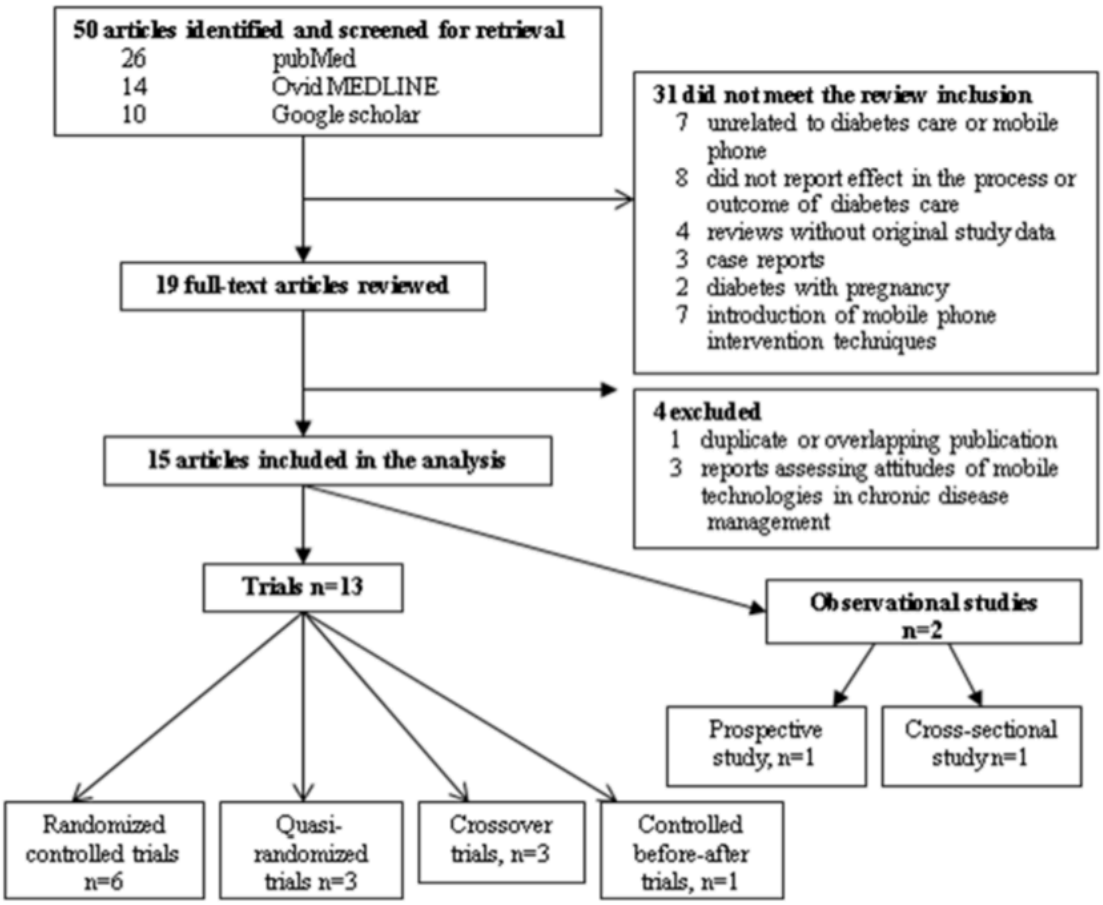

Figure 1 - Papers selected for the systematic review of mobile phone technologies involving diabetes care and management

Of the 15 studies, 2 were observational studies (one cross-sectional and one prospective cohort study) and the other 13 were randomized controlled trials. The minimum duration of intervention in these studies was 1 month and maximum of 12 months. Sample size ranged from 12 to 130 participants at the end of the follow-up period and all studies included both males and females. Gender was distributed almost equally in all the studies. Participants were aged 8-70 years old. Five studies examined patients with Type 1 DM, eight studies observed patients with Type 2 DM, and two studies included patients with both Type 1 and Type 2 DM.

Approach of mobile phone intervention

Mobile phone intervention in the included studies showed a wide range of technological innovations. Three of the studies developed software or an application programmed for diabetes care management [11, 21, 28]. The others used both mobile phone technology and Internet to provide support for self-monitoring blood glucose, continuous education, reinforcement of diet, exercise, and medication adjustment [12, 17, 17-20].

Among the 15 included studies, 12 used a mobile phone Short Message Service (SMS) to deliver blood glucose test results and self-management information. These studies adopted a short message service alone, or SMS combined with other intervention strategies, which included transmitting self-monitored blood glucose to mobile phone via a Bluetooth wireless link. One study [26], combined mobile phone with clinical visits that consisted of medical advice and structured counseling from a diabetes specialist nurse in response to real-time blood glucose test. The combined intervention appeared achieving a greater reduction in HbA1c than isolated mobile phone intervention.

Table 1 summarizes the key features of studies included in the systematic review. Outcome measures varied across individual studies, including HbA1c concentration, insulin and lipid profile levels, changes in body weight, blood pressure values, self-efficacy, and perception of the use of mobile phone technology.

Table 1. Characteristics of studies included in the present review

Author/Yr (Country)	Study design	Duration (months)	Sample size	Age group	Type	Approach	Intervention
Vahatalo *et al.* 2004 (Finland)	Q-RCT	12	100	43.1	T1DM	Mobile phone & internet	SMBG support and therapy recommendation through SMS
Farmer *et al.* 2005, (U.K)	CBA	9	93	18-30	T1DM	Mobile phone	Drug advice, nutrition, & physical activity from a DSN in response to real-time blood glucose test results
Franklin *et al.* 2006, (U.K)	RCT	12	92	8-18	T1DM	Mobile phone	Sweet Talk SMS-Care delivered by a multidisciplinary team & drug advice
Rami *et al.* 2006, (Austria)	COT	3	36	10-19	T1DM	Mobile phone	Telemedicine system and SMS weekly advice on diet, exercise, SMBG, & drug advice for 3 months
Kim & Jeong, 2007, (Korea)	CBA	6	51	C: 47.5 I: 46.8	T2DM	Mobile phone & internet	Web-based intervention using SMS by a nurse
Yoon *et al.* 2008, (Korea)	RCT	12	51	C: 47.5 I: 46.8	T2DM	Mobile phone & internet	SMS- education, diet, exercise, medication adjustment, & SMBG
Faridi *et al.* 2008, (U.S)	RCT	3	30	C: 56.7 I: 55.3	T2DM	Mobile phone	NICHE-provides patient specific tailored feedback and reminders, glucometer, & pedometer
Kim *et al.* 2009 (Korea)	RCT	3	100	>18	T2DM	Mobile phone & internet	Automatic adjustment of insulin dose
Turner *et al.* 2009, (U.K)	CBA	3	23	58	T2DM	Mobile phone	Telehealth monitoring and support for insulin initiation and adjustment by nurses, SMBG
Cho *et al.* 2009, (Korea)	RCT	3	69	C: 45.2 I: 51.1	T2DM	Mobile phone & internet	The phone group communicated with medical staff and received medical recommendations and glucose monitoring via SMS. The Internet group used the internet based glucose monitoring system.
Rossi *et al.* 2010, (Italy, Spain, UK)	RCT	6	130	35.7	T1DM	Mobile phone	Diabetes Interactive Diary (DID)-education, managing medication, &SMBG
Arsand *et al.* 2010, (U.S)	PCS	6	12	44-70	T2DM	Mobile phone	Few touch application
Dick *et al.* 2011, (U.S)	CS	1	18	Average age: 55	T1DM T2DM	Mobile phone	Automated SMS with personalized medication, foot care, and appointment reminders and text messages were received from participants on adherence
Fischer *et al.* 2012, (U.S)	Q-RCT	3	47	40-69	T1DM T2DM	Mobile phone	Cell phone text messaging that provided blood sugar measurements prompts and appointment reminders
Zolfaghari *et al.* 2012, (Iran)	Q-RCT	3	77	18-65	T2DM	Cellular phones & telephones	SMS group: received information about diet, exercising, medication, SMBG, and stress management. Telephone group: counseling, continuous education & reinforcement of diet, exercise, medications taking, & SMBG

CBA, controlled before-after trial; COT, randomized crossover trial; CS, cross-sectional study; DSN, diabetes specialist nurse; NICHE, Novel Interactive Cell-phone technology for Health Enhancement; PCS, prospective cohort study; Q-RCT, quasi-randomized trial; RCT, randomized controlled trial; SMBG, self-monitoring of blood glucose.

Effects of intervention

Glycosylated hemoglobin (HbA1c) levels were measured in 12 studies (Fig 2). The effects of the intervention in each study was calculated as the difference in the mean percentage change of HbA1c value from pre-intervention to post-intervention in the intervention and control groups. The minimum difference reported at the end of the study period in the intervention group was -0.1 (6.4% pretest to 6.3% at 3 months) while the maximum difference was -2.4 (9.8% pretest to 7.4% at 3 months). Ten studies showed lower HbA1c levels among participants in the intervention group at the end of the intervention, although only seven [17, 19, 20, 25, 27, 28, 30] reported significant reduction in HbA1c levels ($p < 0.05$). Meta-analysis suggests that during an average follow-up of 6.3 years, an overall net effect of HbA1c reduction of the 12 studies in intervention groups was 0.39% (95%CI: -0.067, -0.72, p=0.018) after taking off the reduction in control groups.

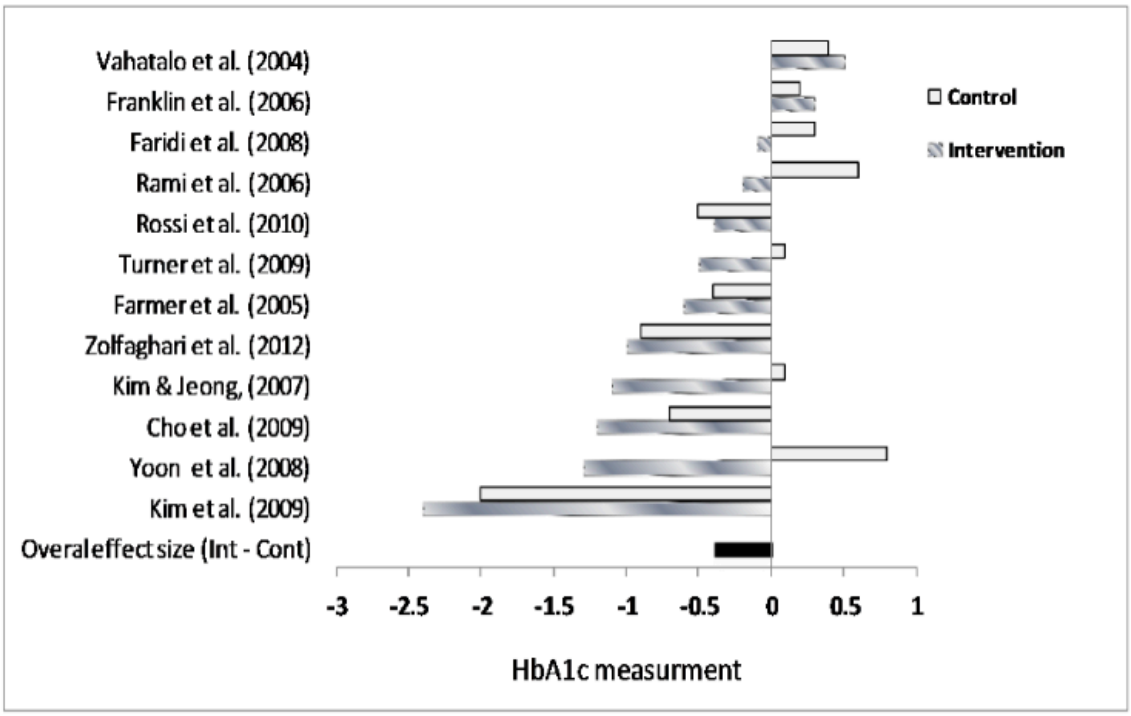

Figure 2 - Meta-analysis for studies with HbA1c measures

Discussion

Maintaining health lifestyle in patients with DM is fundamental to their health status and welfare. Mobile phone technology may be essential in interventions that target behavioral and lifestyle changes, particularly, those associated with chronic diseases management. Our study reviewed fifteen studies that assessed the effect of mobile phone interventions on the self monitoring and management of DM provides evidence that there is a significant effect on DM management using mobile technique. This result is consistent with existing literature [17-19].

The main contribution of the present review provides the most recent evidence of mHealth studies, and the findings are based on studies from different countries. Among the reviewed studies, most applied randomized controlled designs, which enhanced the comparability of the outcomes. Also, most studies applied quantitative measures of key outcomes, including HbA1c, weight loss and serum glucose concentration measurement.

Despite the strengths of mobile phone technology use, several potential limitations should be kept in mind when interpreting these results. First, although findings from the reviewed studies showed promise in mobile phone use and improvement of DM management, some of these studies had small sample sizes. Therefore, future studies that utilize large

sample size are needed to determine whether the increased patient-providers' communication via mHealth have significant impacts on clinical outcomes and public health. Secondly, it is unknown what kind of modalities of mobile technology (SMS, mobile phone calls, application, etc) play a better role in improving outcomes in patients with DM. Thirdly, since most studies had a short period of intervention, the long-term effects of mHealth are still unclear. Fourthly, the current review paper is done by the authors in searching for the relevant literatures. We may have missed some papers during the search. If any, it will cause potential selection bias. Further studies should be continued to confirm the findings. Lastly, as with all systematic reviews, the present study is subject to publication bias [31].

It should be noted that our present study aims to review the studies in the last decade and to evaluate the feasibility of using mobile phone technology to promote patients' DM management and improve healthy lifestyle. It is clear that although mHealth techniques may offer new opportunities in disease control, we still face several challenges. First, the application of mHealth is a new approach in real-world practice. Most studies are still in the exploratory stages. Therefore, it is essential to find the link between practice and scientific knowledge, which come from studies with vigorous study designs and a large-scale sample size. Secondly, continuous adherence and compliance to mobile phone technology in DM management is crucial to the outcomes. The mobile phone use intervention relies heavily on behavioral change theory. In other words, the innovation is based on a patient's willingness to fully participate in every aspect of the intervention. Thus, the intervention may not be suitable for all patients with DM, such as those who may have difficulties operate smart phone. Several studies observed that some patients withdrew from an intervention study due to the inconvenience of using the assigned mobile phones on a regular day-to-day basis. Therefore, findings observed in most studies are based on participants who may be highly motivated [1]. Thirdly, mobile phone technology raises important questions about how to protect patients with DM while simultaneously promoting its development and implementation [1]. This includes challenges associated with privacy and confidentiality of information collected and stored by mobile devices and/or transmitted to cyber infrastructure databases. For notification and intervention purposes, additional privacy and confidentiality concerns arise when sending health-related data to mobile devices [32]. For example, interventions can be interrupted and privacy may be breached if the mobile phone is lost or stolen. However, similar limitations are present with other communication modes (e.g., postal mail or emails may be delivered to the wrong address) [31]. It is important to ensure that information gathered and transmitted via mobile devices remains secure [1]. Fourthly, although mobile phone technology promises unprecedented opportunities to reach DM patients anytime and anywhere, mHealth interventions may result in the marginalization of certain populations, such as illiterates or those without access to a mobile phone [31]. These drawbacks may greatly affect the impact of such interventions in such population. In the United States, mobile handset ownership differs among different ethnic groups and access is lower among those with lower socioeconomic status (defined as those with less than a high school graduate). Similarly, evidence points to disparity between younger and older patients [1]. Possible explanations for this disparity might be related to age, urban and rural, and economy; although neither of these reasons has been definitively determined. Fifthly, mobile phones and Internet technology are advancing rapidly and are ubiquitously available worldwide [16]. However, the costs to participants and healthcare providers are still difficult to estimate. Moreover, the question remains as to who will be responsible for covering the attributable costs of this innovation in the real world. Unfortunately, only three studies [24, 28, 30] in this review had cost/benefit analysis information, in which they reported that self-monitoring and management of diabetes via mobile phone technology would be cost-effective at approximately €4/month, 2 pence/text, and €1.4/month respectively. Nevertheless, the applicability of mobile technology in low resources settings is still questionable in terms of its overall cost (phone, internet and operation). Furthermore, patients with DM are disproportionately distributed in those with low socioeconomic status. The application of mobile technology calls for healthcare system and health policy reforms to meet an urgent need of an increasing trend of DM in the United States and worldwide[13, 15, 33, 34].

Conclusion

The results from the present study indicate significant improvements in gylcaemic control and self-management with mobile phone intervention methods for DM care. Most reviewed studies demonstrated the promise of mHealth to aid patients and to reduce HbA1c by the use of mobile phone technology. Further research with a longer duration and larger sample size is needed to examine several key issues including the benefits of mHealth interventions for patients and healthcare providers' perceptions, and

how mHealth integrating appropriately into healthcare practice, and the cost effectiveness of intervention in improving self-management in patents with diabetes.

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