Title
The Efficacy of Mobile Technology to Promote Medication Adherence

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The Efficacy of Mobile Technology to Promote Medication Adherence

by

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DISSERTATION

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Dedication

I dedicate this dissertation to my children, Ethan and Noah Park. You are my most treasured gifts from God, and I love you dearly. Thank you for your unconditional love and reminding me to laugh, play, and enjoy my highest calling and greatest privilege of being your mom during my doctoral journey.

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I have experienced firsthand what the proverb “It takes a village” means. I will be forever grateful for the generosity and kindness I have received from so many individuals and in so many different forms during my doctoral studies.

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The Efficacy of Mobile Technology to Promote Medication Adherence

Linda Park, PhD, MS, FNP-BC

Background: Adherence to medications is critical to prevent morbidity and mortality in patients with coronary heart disease (CHD). Mobile technology may provide an innovative, practical, and inexpensive means to promote medication adherence.

Objectives: The primary aim of this randomized controlled trial was to compare adherence to antiplatelet and statin medications among patients after myocardial infarction and/or coronary stent procedure who: 1) received text messages (TM) for medication reminders and health education (TM Reminders + TM Education), 2) received TM for health education (TM Education Alone), and 3) did not receive TM (No TM). Secondary aims were to: 1) explore feasibility and patient satisfaction, 2) compare self-efficacy, and 3) identify predictors of medication adherence.

Methods: Customized TM were delivered over 30 days. Adherence was assessed with electronic devices [Medication Event Monitoring System (MEMS)], two-way TM response rates, and the Morisky Medication Adherence Scale. Questionnaires on patient satisfaction with TM and self-efficacy were administered.

Results: Among 90 patients (76% male, mean age 59.2 years), MEMS revealed a significant difference in adherence among groups for antiplatelets only ($p < .05$). The TM Reminders + TM Education group had a higher percentage of correct doses taken (88.0 ± 14.0 vs. 72.4 ± 27.6; $p = .016$) and a higher percentage of prescribed doses taken on schedule compared to the No TM group (86.2 ± 15.4 vs. 69.0 ± 29.2; $p = .01$). The TM Education Alone group had a higher percentage number of doses taken compared to the No TM group (95.8 ± 9.5 vs. 79.1 ± 27.7; $p = .01$). Two-way TM response rates were higher for antiplatelets than statins (90.2 ± 9 vs. 83.4 ±15.8; $p = .01$). Self-reported adherence improved for all groups over time, but did not differ among groups, similar to findings with self-efficacy. Feasibility was established and high patient satisfaction reported. Less depression and higher social support predicted higher medication adherence at 30 days.

Conclusions: TM increased adherence to antiplatelet therapy demonstrated by MEMS and TM responses. Addressing depression and social support in clinical practice should be a priority to improve medication adherence. Further research is needed to explore the full potential of mobile health.

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Chapter 1

Introduction

Chapter 1

Introduction

Coronary Heart Disease

Coronary heart disease (CHD), which includes coronary artery disease, myocardial infarction (MI) and angina, is the leading cause of death and loss of disability-adjusted life years worldwide [World Health Organization (WHO), 2004]. The rates of cardiovascular disease have risen greatly in low-income and middle-income countries, with about 80% of the burden now occurring in these countries (WHO, 2004; Yusuf, Reddy, Ounpuu, & Anand, 2001). In the United States, the prevalence of CHD in 2010 was 15.4 million, claiming the lives of 1 of every 6 Americans (Go et al., 2013). In our country, someone dies approximately every minute from a coronary event, while an individual experiences a coronary event approximately every 34 seconds (Go et al., 2013). The incidences of first and recurrent MI were 635,000 and 280,000 in 2009, respectively, including an additional 150,000 silent first MIs (Go et al., 2013).

The decline in CHD related deaths over the past four decades has been attributed to improved modification of cardiac risk factors and availability of pharmacologic and invasive therapies [i.e., percutaneous coronary intervention (PCI)] (Ford et al., 2007; Lloyd-Jones et al., 2010). Extensive research and clinical guidelines in the management of MI and CHD support the role of pharmacologic treatment for secondary prevention of CHD (Jneid et al., 2012; O'Gara et al., 2013; Smith et al., 2006).

Medication Adherence

Medication adherence is defined as the degree to which a patient follows the instructions for taking the prescribed medication (Osterberg & Blaschke, 2005). Medication nonadherence is the number one problem in treating illness as more than half of individuals with chronic diseases do not take any or all of their medications correctly (American Heart Association, 2009; Osterberg & Blaschke, 2005). One study comparing cohorts of patients found two-year adherence rates of statin medications were only 40.1% following acute coronary syndrome (i.e., MI or unstable angina), 36.1% for stable CHD, and 25.4% for primary prevention (Jackevicius, Mamdani, & Tu, 2002).

Medication nonadherence in patients with CHD is closely linked to adverse clinical outcomes such as rehospitalization, morbidity, and mortality (Dunbar-Jacob, Bohachick, Mortinmer, Sereika, & Foley, 2003; Ho et al., 2008; Ho, Bryson, & Rumsfeld, 2009). After PCI with drug-eluting stents, patients who discontinue antiplatelet therapy before the recommended time period of 12 months have a significantly greater incidence of overall major adverse cardiac events, stent thrombosis, and death (Rossini et al., 2011). In one study, the premature interruption of antiplatelet therapy in nearly 1 in 7 individuals resulted in 9 times greater mortality (Spertus et al., 2006).

Mobile Health

Behavioral change interventions have attempted to promote medication adherence over many decades as reported in a Cochrane review of 83 studies; however, even the most effective interventions did not result in large improvements in adherence and treatment outcomes (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008). Because the reasons for medication nonadherence are complex and multifactorial, diverse solutions are required with tailored interventions for different populations and conditions. In the recent decade, novel behavioral interventions have introduced the use of technology by applying mobile health (mHealth) solutions to enhance adherence. The focus of this dissertation will be on an mHealth intervention to promote medication adherence.

The positive impact of mobile technology in the management of CHD may be substantial for patients, caregivers, health care providers, and society. The use of mobile phones is highly popular and widespread throughout developed and underdeveloped nations including individuals with low socioeconomic status (Fjeldsoe, Marshall, & Miller, 2009; Krishna, Boren, & Balas, 2009). The growth and popularity of mobile phones over the past decade has been astounding. Mobile phones have the potential to reach many populations given their pervasive and widely accepted use.

The benefits of using mobile phones for health promotion and self-management of chronic diseases are multifold. Mobile phones by nature are portable, lightweight, easily accessible, and does not produce a sick-role stigma (Welch, Dowell, & Johnson, 2007). Furthermore, text messaging, also referred to as short message service (SMS), is fast, direct, efficient, user-friendly, traceable, popular, and provides easy data transfer (Franklin, Waller, Pagliari, & Greene, 2006). Text messaging is nonintrusive, relatively simple, and lower in cost compared to mobile voice communication (Cocosila, Archer, Haynes, & Yuan, 2009). The four key functions of mobile phone use in healthcare include providing health education, monitoring health status, enhancing self-management, and facilitating communication.

Mobile phones can allow remote access and provide medical advice in areas with a disproportionate lack of health care providers (de Jongh, Gurol-Urganci, Vodopivec-Jamsek, Car, & Atun, 2008). In addition, mobile phones can benefit populations that are not typical users of health services such as pediatric patients, teenage females, and young adult males (Miloh et al., 2009). The use of handheld phones among patients can provide all of these benefits along with a more convenient and efficient way to communicate with health care providers while still providing personalized care.

Text messaging interventions can enhance self-efficacy through reminders and feedback on treatment success, provide a form of social support, and establish social networks (de Jongh et al., 2008). In turn, increased self-efficacy and support systems may influence health behaviors and improve self-management of chronic diseases (de Jongh et al., 2008).

Dissertation Aims

The overall objective of this dissertation manuscript is to present the impact of a mobile phone intervention on medication adherence and self-efficacy among patients with CHD. An overview of the significance of medication adherence, previous mobile phone interventions, theoretical framework, and measurement considerations are presented to support this objective in the following chapters.

The primary purpose of the intervention was to establish the efficacy of an intervention using mobile phone technology, specifically text messaging, to improve adherence to cardiac medications (i.e., antiplatelet and statin) among patients with a recent MI and/or PCI. The primary and secondary aims along with their associated hypotheses were:

Primary Aim:

1) To compare medication adherence in patients who receive text messages (TM) on medication reminders and health information ("TM Reminders + TM Education" group), patients who receive TM on health information alone ("TM Education Alone" group), and patients who do not receive TM ("No TM").

H1: Patients who receive TM to take medications and/or health education (TM Reminders + TM Education and TM Education Alone) will have better adherence to their medication regimen as compared to patients who do not receive TM (No TM).

Secondary Aims:

2) To compare self-efficacy among the TM Reminders + TM Education, TM Education Alone, and No TM groups.

H2: Patients who receive TM (TM Reminders + TM Education and TM Education Alone) will have increased self-efficacy as compared to patients who do not receive TM (No TM).

3) To identify the personal (sociodemographic and clinical characteristics) and social support factors that are related to medication adherence.

H3: The following variables will be positively related to medication adherence: older age (>65 years), living with a spouse/partner, higher level of education, less depression, and higher social support.

4) To explore the feasibility and patient satisfaction with using mobile phones to improve medication adherence.

H4: Patients who receive medication reminders and/or health education (TM Reminders + TM Education and TM Education Alone) will consider mobile phones to be positive, effective, and practical in improving medication self-administration.

Presentation of Dissertation

This dissertation is presented in six chapters. This introduction chapter has reviewed the problems of CHD and medication nonadherence with the potential for mobile phone technology to address the latter issue. Chapter 2 is a systematic review of mobile phone interventions that have been implemented to address medication adherence in a variety of settings, conditions, and populations. The theoretical framework of Self-Efficacy Theory, which undergirds the research intervention, is described in Chapter 3. Chapter 4 includes a review of electronic measures of medication adherence and presents more innovative measurement tools apart from traditional forms.

The intervention study using text messaging for medication reminders and health education is fully described in Chapter 5. The impact of the intervention study on self-efficacy is presented in Chapter 6 as well as other predictors (sociodemographic, clinical, and social support variables) of medication adherence. Chapter 7 is a conclusion of the topics and research findings of this dissertation. Current and future clinical, social, policy, and research implications are discussed.

Chapters 2, 4, 5, and 6 have been or will be submitted to journals for publication and are presented in this dissertation manuscript to the specifications of the journals.

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Chapter 2

A Systematic Review of the Efficacy of Mobile Phone Interventions To Improve Medication Adherence

Chapter 2

A Systematic Review of the Efficacy of Mobile Phone Interventions To Improve Medication Adherence

Abstract

Aims: To evaluate the efficacy of mobile phone interventions to improve medication adherence and to describe the characteristics of the interventions. Secondary aims are to explore acceptability and satisfaction of mobile phone interventions as well as evaluate the selected studies in terms of study rigor, impact, cost and resource feasibility, generalizability, and implications for nursing practice and research.

Background: Medication nonadherence is a major global challenge. Mobile phones are the most commonly used form of technology worldwide and have the potential to promote medication adherence.

Design: Guidelines from the Centre for Reviews and Dissemination were followed to develop this systematic review.

Data Sources: A comprehensive search of databases (PubMed, Web of Science, CINAHL, PsycInfo) and bibliographies from related articles was performed from January 2002 through January 2013 to identify the studies included in this review.

Review Methods: A systematic review was conducted and the selected studies were critically evaluated to abstract and summarize pertinent characteristics and outcomes.

Results: The literature search produced 29 studies related to mobile phones and medication adherence. The studies were conducted for prevention purposes as well as management of acute and chronic illnesses. All studies used short message service (SMS), while no studies used applications (apps). Eighteen studies found significant improvement in medication adherence.

Conclusion: While the majority of investigators found improvement in medication adherence, long-term studies characterized by rigorous research methodologies, appropriate statistical and economic analyses, and the test of theory-based interventions are needed to determine the efficacy of mobile phones to influence medication adherence.

Key Words: medication adherence, mobile phone, short message service (SMS), text messaging

STUDY SUMMARY

Why is this research or review needed?

- Medication nonadherence is a major global challenge and leads to increased morbidity and mortality.
- Mobile phones are the most commonly used form of technology worldwide and have significant potential to promote health-related behavioral change and self-management of acute and chronic disease.
- Mobile phone interventions have been conducted to improve medication adherence with the recent advent of mobile health.

What are the key findings?

- A comprehensive systematic review found 18 out of 29 studies using text messaging improved medication adherence.
- Text messaging interventions are feasible and acceptable with the majority of studies reporting high participant satisfaction (>80%) in receiving text messages for health management.

How should the findings be used to influence policy / practice / research / education?

- Nurses will be instrumental in developing strategies to include mobile health resources to promote medication adherence with patients and their caregivers in clinical practice and research settings.

- Further research is recommended to determine the efficacy of different mobile health approaches over time as well as to explore topics on patient acceptance, clinical outcomes, cost-effectiveness, and theory supporting medication adherence behavior.

Introduction

Medication nonadherence is a major global challenge [World Health Organization (WHO) 2003]. More than half of Americans with chronic diseases do not take any or all of their medications correctly (Osterberg & Blaschke 2005). In developing countries with limited resources and access to health care, medication nonadherence is assumed to have even greater magnitude and impact than industrialized countries (WHO 2003). A strong association between medication adherence and clinical outcomes such as rehospitalization, morbidity, and mortality has been demonstrated in observational studies (Smith *et al.* 2006). In addition, in the United States, medication nonadherence results in an estimated $290 billion in healthcare costs (New England Health Institute 2009).

The factors that influence medication adherence behavior are complex and unique to each individual, thereby requiring numerous multifactorial strategies to remove barriers and promote adherence (Brown & Bussell 2011). Behavioral strategies such as self-monitoring, positive reinforcement, and including coaches or partners (i.e., caregivers, health care providers) can be employed to facilitate adoption and integration of medication taking into daily life patterns (Bosworth *et al.* 2011). Mobile health can promote the implementation of these behavioral strategies and improve adherence in order to provide meaningful impact on primary and secondary prevention of chronic diseases.

Mobile Health

The evolution of mobile health, frequently referred to as mHealth, has taken shape in the past decade and refers to the use of mobile devices that are used to promote health. Mobile health has "… the potential to advance research, prevent disease, enhance diagnostics, improve treatment, reduce disparities, increase access to health services and lower health care costs in ways previously unimaginable" (Nilsen *et al.* 2012, p. 6). Mobile phones are the most commonly used form of technology worldwide (International Telecommunication Union 2011) and have the greatest potential to influence large populations. The growth of mobile phones over the past decade has been astounding with worldwide mobile phone subscriptions growing from 12.4 million to 5.9 billion in 2011 with global penetration of 87% of individuals, including 79% in the developing world (International Telecommunication Union 2011).

Applying mobile phones in health care is a relatively young field of research with intervention studies being published just within the past decade. Text messaging interventions using short message service (SMS) have been most widely applied, while some investigators have tested interventions using a mobile phone application (app) (Meltzer, Kelley, & Hovell 2008). Previous reviews have described the breadth of research that has been conducted with mobile phones (de Jongh, Gurol-Urganci, Vodopivec-Jamsek, Car, & Atun 2012; Fjeldsoe, Marshall, & Miller 2009; Ingerski, Hente, Modi, & Hommel 2011; Krishna, Boren, & Balas 2009; Militello, Kelly, & Melnyk 2012; Wei, Hollin, & Kachnowski 2011). These reviews introduced initial studies using mobile phones to promote health-related behavioral change as well as managing acute and chronic disease. Recently, there has been a transition within mHealth and global health, as well as in funding agencies, to move beyond the exploration phase of research (e.g., pilot studies, proof-of-concept) into an era of evidence-based interventions that are evaluated with the same rigor as other public health strategies (Labrique, Vasudevan, Chang, & Mehl 2012).

THE REVIEW

Aims

The positive impact of mobile phones in health promotion and management, specifically medication adherence, may be substantial and will be collectively reviewed to guide future research. The major aim of this systematic review is to evaluate the efficacy of mobile phone interventions to improve medication adherence and to describe the characteristics of the interventions. Secondary aims are to explore acceptability and satisfaction of mobile phone interventions as well as evaluate the selected studies in terms of study rigor, impact, cost and resource feasibility, generalizability, and implications for nursing practice and research.

Design

Guidelines from the Centre for Reviews and Dissemination were followed to develop this systematic review (Centre for Reviews and Dissemination 2008).

Search Methods

A comprehensive search was conducted to identify all studies that included the key review question of whether mobile phone interventions can support medication adherence in health promotion and disease management. To this end, a search was performed on PubMed, Web of Science, CINAHL, and PsycInfo to identify research articles related to this topic. All full text manuscripts from January 2002 through January 2013 were identified by the first and second authors (LGP and JHE), including bibliographies of the chosen articles and related reviews. Key terms were used alone and in combination with each other including ‘mobile phone,’ ‘cellular phone,’ ‘text messages,’ ‘text messaging,’ ‘short message service,’ ‘SMS,’ ‘mobile phone application,’ ‘medication,’ and ‘medication adherence.’

Inclusion Criteria

Inclusion criteria for this review were intervention studies that supported medication adherence via a mobile phone [i.e., SMS, application (“app”)] in health prevention or management of acute or chronic conditions. Medication use was measured by objective or subjective data in all studies in order to evaluate the efficacy of the interventions. Studies that used two modalities were included if the primary mode of intervention was mobile phones. All patient populations and languages were considered.

All study designs including randomized controlled trials (RCT) and observational studies were included in this review in order to capture the breadth of research that has been conducted since mHealth is a relatively new field. Pilot studies in mHealth were also included because they have been informative to understand the feasibility and acceptability of using mobile phones in health promotion and management.

Exclusion Criteria

Studies were excluded if the interventions were predominantly conducted via Internet, email, traditional landline telephones or other electronic devices (two-way text-messaging pagers, personal digital assistants, medication alarms) alone or in conjunction with mobile phones. Studies that used co-interventions such as Internet-based communication along with SMS were excluded. Studies that were based on calling patients on their mobile phones were also excluded. Studies using mobile phones to communicate health data to health care providers (e.g., glucose levels) were excluded if medication use was not explicitly addressed. Lastly, more timely studies that were reported in journal abstracts and research conferences such as mHealth Summit and HiMSS were excluded because they were not full-text articles.

Search Outcome

A comprehensive electronic search produced 29 studies: 19 RCTs, 2 quasi-experimental studies, 6 pilot studies with no comparison group, 1 retrospective observational cohort study with matched control, and 1 parallel two-cohort study with randomization (Figure 1). No qualitative studies were found.

Quality Appraisal

The Consolidated Standards for Reporting of Trials (CONSORT) guidelines (Schulz, Altman, & Moher 2010) were used to evaluate the RCTs included in this review (Table 1). The CONSORT checklist of 25 items was used with a score of '1' given to each item reported in the study and an overall score was assigned to each study after independent review of two researchers (LGP and KD). Observational studies were evaluated with the STROBE criteria (von Elm *et al.* 2007) (Table 2). The STROBE checklist was deemed to be appropriate for use in evaluating cohort and case-control studies in this review. The two reviewers discussed any items that were scored discordantly until agreement was reached.

Data Abstraction and Synthesis

Data were abstracted from each eligible study including target condition, length of study, location, sample characteristics, design, intervention, control, measures of medication adherence, and results (Table 3). In addition, frequency, tracking (two-way messaging) and response rate, message content, and satisfaction reports were recorded (Table 4). Supplemental data on methodologies were abstracted such as sample size calculations, effect size calculations, attrition, cost analyses, and application of theory. The eligible studies differed substantially in the medical conditions, patient populations, interventions, and measurement of medication adherence. Therefore, each study was examined in the context of the medication adherence outcomes and patient reported satisfaction.

RESULTS

Efficacy

Overall, 18 of the 29 studies reflected significant improvement in medication adherence rates or biomarkers after receiving SMS while 11 studies reported no difference (Table 3). The interventions differed substantially across studies with a variety of SMS message content and dosing (i.e., frequency, duration). Table 4 describes the studies' tracking, message content and participants' satisfaction with the SMS interventions.

Noteworthy trends were observed between the positive and negative studies. Among the negative studies, SMS tended to have more basic and repetitious content with a simple medication reminder. In contrast, positive studies delivered SMS with a variety of educational and motivational content that may have effectively engaged participants, thus leading to better outcomes. In addition, positive effects on medication adherence occurred in all 8 studies that applied "tailored" or "personalized" SMS.

Characteristics of Studies

Description of Medical Conditions

Among the 29 selected studies, the range of chronic disease processes that were treated varied from diabetes (6), HIV / AIDS (7), asthma (3), schizophrenia (2), hypertension (1), general chronic diseases (1), acne (1), atopic dermatitis (1), systematic lupus erythematosus (1), and immunosuppression after pediatric liver transplant (1). One study addressed antibiotic use for management of acute infections treated in the emergency department. Prevention studies included use of oral contraception (2), Vitamin C to prevent colds (1), and chemoprophylaxis to prevent malaria (1). All of the studies used SMS as the primary intervention. No studies using mobile phone applications ("apps") met the inclusion criteria.

Description of Populations

The majority of investigators recruited a convenience sample from varied sites (e.g., clinics, hospitals, pharmacies, and registries of prescription drug plans). A few used advertisements in local newspapers and magazines as well as university and local websites.

Among the RCTs, the sample sizes ranged from 16 to 962 participants. Seventeen of the 29 studies (59%) had sample sizes of 100 patients or less. The majority of studies included younger populations, although one focused specifically on older adults who were eligible for Medicare benefits (mean age of SMS cohort was 64.8 ± 11.9) (Foreman *et al.* 2012). Five studies included participants with a mean age over 50, which is a positive step forward in establishing the generalizability of mobile phone interventions.

Interventions

Message Content

Thirteen studies sent SMS that were strictly medication reminders. The remaining studies used content other than medication reminders such as education, motivation, prescription-related, disease self-management, generic SMS, or a combination of messages that included medication reminders.

Several studies in this review used SMS to enhance social support and remind patients to take their medication while communicating concern and providing assistance (Cocosila *et al.* 2009; Franklin, Waller, Pagliari, & Greene 2003; Lester *et al.* 2010; Miloh *et al.* 2009; Pop-Eleches *et al.* 2011). One study on prevention of colds with Vitamin C among a young adult population sent interesting and lighthearted messages at random times from a virtual friend named “Tim” (Cocosila *et al.* 2009). In an HIV intervention study, researchers in Kenya typically sent a weekly bulk message to 273 participants asking “Mambo?”

("How are you?"), and research participants responded back either "Sawa" (doing well) or "Shida" (I have a problem) (Lester *et al.* 2010). Health care providers called participants who responded with the latter text and at the end of the study participants reported feeling that someone cared about them because of the protocol (Lester *et al.* 2010). In contrast, other investigators in Kenya who targeted adults with HIV, tested the effect of short versus long messages and found no significant influence on adherence to antiretroviral medications after providing a longer message that offered social support (Pop-Eleches *et al.* 2011).

Tailored or Personalized Messages

Eight studies described their interventions as personalized or tailored. For example, one small pilot study with a younger HIV / AIDS population sent personalized SMS that were developed by the participants at the beginning of the study (e.g., "Superman calling you," "Take it or die") (Dowshen, Kuhns, Johnson, Holoyda, & Garofalo 2012). A visual analog scale and a four day recall of medication administration showed significant changes in scores from baseline (74.7 at baseline to 93.1 at 24 weeks, $P < 0.001$) although the investigators could not document a significant change in CD4 cell count or viral load (Dowshen *et al.* 2012).

Another RCT described 216 asthmatic participants who received tailored SMS that targeted illness and medication beliefs that were assessed at baseline (Petrie *et al.* 2012). A significant improvement in self-reported adherence was noted in the SMS group compared to the control group at 9 months of follow-up after an 18 week intervention (57.8% ± 27.1 vs. 43.2% ± 26 in the intervention and control groups respectively, P = 0.003) (Petrie *et al.* 2012).

The content of SMS using the Mobile Assessment and Treatment for Schizophrenia (MATS) program was tailored in real-time and incorporated the principles of cognitive behavioral therapy (Granholm, Ben-Zeev, Link, Bradshaw, & Holden 2012). The response to the first SMS question ("Did you take your meds today?") triggered a second level of questions that led to a final SMS with encouragement or advice on medication adherence (Granholm *et al.* 2012). In this study, medication adherence improved significantly over 12 weeks, but only for individuals who were living independently (P = 0.018) (Granholm *et al.* 2012).

Dosing of Messages

While the majority of studies delivered SMS once or twice daily, the frequency of delivery was optional (Dick *et al.* 2011; Foreman *et al.* 2012; Shetty, Chamukuttan, Nanditha, Raj, & Ramachandran 2011). Only two studies tapered the frequency of SMS through the duration of the intervention at 4 and 8 weeks (Cocosila *et al.* 2009; Petrie *et al.* 2012). The timing of SMS delivery was commonly tailored to the participants' preferences or coincided with medication dosing.

Frequency of SMS was tailored real-time in a study with diabetic patients via an innovative Real Time Medication Monitoring (RTMM) system that used an electronic medication dispenser. Customized SMS reminders were sent only if the dispenser was not opened (Vervloet *et al.* 2012). Overall, the SMS group took significantly more doses within the agreed time period than the control group

(57% vs. 43%, P = 0.003), however there were no differences in missed doses between the groups (15% vs. 19%, P = 0.065) (Vervloet *et al.* 2012).

Text Responses

The majority of studies delivered one-way messaging while 9 of the 28 studies had participants respond with two-way messaging. Two-way messaging allows for confirmation of SMS with a time-stamped response and is a means of engaging the patients' involvement. The two-way response rates ranged from 35% to 86%. One study used 12 out of 180 messages (0.07%) as two-way for quality control purposes (Castano, Bynum, Andres, Lara, & Westhoff 2012). Along with daily medication reminders, other investigators offered weekly trivia questions that allowed participants to respond; however, the weekly 2-way messaging response rate was only 35% (Arora, Peters, Agy, & Menchine 2012).

Measurement of Medication Adherence

Accurate measurement of medication adherence is imperative when applying an intervention. The discrepancy between self-reported and electronically monitored medication use was evident in some studies (Dowshen *et al.* 2012; Hardy *et al.* 2011). Self-report was the sole measure used to report medication adherence in ten studies, while three studies used pharmacy data solely or in combination with other measurements (Foreman *et al.* 2012; Mbuagbaw *et al.* 2012; Ting *et al.* 2012). Other investigators ranged from exclusively using monitoring systems to reporting adherence with multiple measures (up to five).

In eight studies adherence data were stored through electronic monitoring devices (MEMS, dose counts on inhalers) or used real-time wireless communication to servers (SIMPill, RTMM system). Other objective forms of medication adherence included manual pill counts, biomarkers, and health outcomes (e.g., HbA1C, viral loads, transplant rejection). Less than half of the (13) studies applied multiple methods to measure medication adherence.

Acceptability and Satisfaction

The majority of studies included an evaluation of participant satisfaction that is described (Table 4). A few studies had a brief statement on participant feedback while most studies reported participants' satisfaction using a format of percentages or Likert scales. Overall, the majority of studies reported high participant satisfaction (>80%) in receiving SMS for health management. The lowest satisfaction scores (64%) were seen in the study of Brazilian women with HIV / AIDS that reminded participants to take their medications (da Costa *et al.* 2012). In a study of clinic patients with atopic dermatitis, Boker *et al.* reported that 33% starting ignoring SMS after 2 weeks and 26% found SMS to be "annoying" (2012). The mean age of the SMS group was 22.8 ± 5.6, and they received identical medication reminders that varied only with the patient's name (Boker *et al.* 2012).

DISCUSSION

Efficacy

The majority of interventions (18 out of 29) resulted in improved medication adherence. These data are vital because nonadherence to medication regimens has remained a consistent and well-documented problem in health care. Mobile phones may be a useful adjunct to standard education and counseling about medications and promote the complex behavior required for medication adherence. The groundwork for using mobile phones to improve medication adherence has been explored through these studies, yet the possibilities of mHealth are abundant. The opportunities that exist with applying mobile phones in health interventions is exciting because mobile phones are so commonly used, widely accepted, easily accessible, and affordable. To inform future research on improving medication adherence from mobile phone interventions, the selected studies in this review will be evaluated in the following section in terms of study rigor, impact, cost and resource feasibility, generalizability, and implications for nursing practice and research.

Study Rigor

More rigorous study designs and research methodologies will be important in future studies. The application of reporting guidelines, such as the CONSORT and STROBE criteria used in the Quality Assessment, will help authors clearly report their study processes and allow readers to better evaluate the quality of research. The deficits in reporting criteria as recommended by these guidelines are displayed in Tables 1 and 2 (i.e. harms for RCTs, bias for observational studies). Applying methods such as blinding will reduce bias, as this technique was applied in only 5 studies in this review (Castano *et al.* 2012; da Costa *et al.* 2012; Hou *et al.* 2010; Mbuagbaw *et al.* 2012; Strandbygaard *et al.* 2010). Furthermore, greater generalizability will be a product of community sampling, rather than recruiting primarily from single-center outpatient clinics and from minority groups (Cassimatis & Kavanagh 2012). Recruitment from a convenience sample in most studies may have led to bias in subject selection.

Reporting accurate sample size calculations, effect sizes, measurement, and statistical analyses is essential to move the science of mHealth forward. Among the RCTs, 11 of the 20 studies included a sample size calculation. Some researchers reported that inaccurate and incomplete sample size calculations may have potentially affected their study results (Cocosila *et al.* 2009; Ostojic *et al.* 2005). Effect sizes were reported in only 6 studies. Regarding accurate measurement, a mixed methods approach with electronic devices, biomarkers, and self-report is an important component in strengthening rigor of a study protocol in data collection and corroborating data. In addition, in studies with frequent follow-up visits, more sophisticated statistical models will be valuable to assess change over time without being influenced by missing data. The spectrum of evaluation methods in mHealth research will need to include alternative study designs and methodologies to provide timely information within a rapidly evolving field (Nilsen *et al.* 2012).

It is difficult to generalize the positive findings of the studies to other populations given the differences in study design, group characteristics, comorbidities, and intensity in managing medical conditions. A closer examination of the studies that did not reach statistical significance revealed several study design limitations that may have influenced the results. In addition to inaccurate sample size calculations and measurement issues, the use of additive or interactive effects may have compromised the results. For example, investigators in a study of oral contraceptives realized 88% of their subjects used other co-interventions such as alternative alarm systems (e.g., alarm clocks or mobile phone alarms) (Hou, Hurwitz, Kavanagh, Fortin, & Goldberg 2010). Future studies that consider restricting the use of additional reminder systems to allow the true effect of the mobile phone intervention are required.

Among the studies, the highest attrition rate was 41% at a mean of 4 months in a year-long study of pediatric liver transplant patients (Miloh *et al.* 2009). Although there were no reported risk factor differences for subjects who dropped out, the positive results of receiving SMS to improve adherence to immunosuppressant therapy among the experimental group may have been influenced by the higher adherence characteristics of the remaining subjects overall (Miloh *et al.* 2009). The mean and median rates of attrition in all these studies were both 15%.

The long-term impact of mHealth interventions is needed to document the efficacy and sustainability of these interventions on chronic disease management. The longest study period was 14 months, with the mean and median study durations being 21 and 16 weeks, respectively. A major barrier in using mobile technology may be deterioration of interest as the novelty of the messages decreases over time. Factors that maintain engagement of participants remain unknown and serve as important gaps in research.

Impact

The content of SMS texts may be a determining factor in patients' continued interest and persistence in using mobile phones to improve medication adherence. SMS texts varied widely in content among the studies, with some interventions giving the same daily reminder to take medications and other interventions using a variety of SMS texts that varied in topic.

Although more personable texts might appear to better engage users, the impact of such methods requires further study (Miloh *et al.* 2009; Pop-Eleches *et* al. 2011). The effect of a reward system as simple as an emoticon (i.e., text faces that convey an emotion) (Beal 2013) requires further testing. Tailoring messages with personalized content, building on responses from participants, and delivering SMS in different languages may help to make a more customized program that engages participants.

Future studies that focus on the impact of specific SMS protocols, and are age, gender and culture specific will develop our knowledge about culturally appropriate interventions (Strandbygaard *et al.* 2010). Research should be designed and interpreted in culture-specific contexts. For example, interventions that are targeted at health conditions associated with negative stigma such as HIV require consideration in maintaining confidentiality. In the study in Cameroon, a high proportion of participants disclosed their HIV status to their families during the course of the study (Mbuagbaw *et al.* 2012). In this study, 35% did not want to continue receiving SMS at the end of the trial period, which might indicate the participants' sensitivity in receiving SMS associated with their health status (Mbuagbaw *et* al. 2012).

Importantly, clinical outcomes that are tracked over time to determine efficacy and sustainability of SMS interventions and health-related apps are fundamental to mHealth intervention design. The majority of research studies reviewed here demonstrated feasibility in supporting medication adherence as well as high acceptability and satisfaction among participants. Long-term studies are needed to provide and guide future intervention design so that mHealth can be fully integrated into daily life.

Cost and Resource Feasibility

The cost of implementing a mobile phone intervention needs to be addressed from the providers' and participants' perspectives. Implementing cost-effective programs for long-term participation will continue to be an important factor in achieving positive outcomes. Among the studies reviewed, some participants reported concerns about costs if they continued with the SMS program (Hardy *et al.* 2011). Providing options such as limiting two-way messaging to reduce costs for participants who have limited SMS plans may be a consideration in future studies.

Only five studies reported a cost-analysis of their medication adherence interventions. Cost-analyses will provide important information for policy makers and global funders, particularly in HIV research because reducing viral replication through antiretroviral therapy can decrease transmission of HIV to new partners (Lester *et al.* 2010). Use of mobile phones may offer a major prevention strategy in regions where HIV is endemic and other resources are limited. Another cost-analysis derived by a national pharmacy benefit manager found only a slight increase in pharmacy related costs for the group who received SMS compared to the matched control group, although the differences were not statistically significant (Foreman *et al.* 2012). The total health care costs for these groups were not analyzed but would be beneficial when determining the overall cost benefit of the intervention. Consideration of reimbursement models for medication adherence and mHealth interventions is also needed (Bosworth *et al.* 2011).

Generalizability

Caution is necessary when extrapolating results from different patient populations and conditions such as applying findings established in a study of teenagers with a single condition to older adults who are managing multiple chronic diseases. Likewise, caution is necessary when extrapolating results with chronic disease populations to healthy individuals who are practicing primary prevention behaviors. More studies in areas of health promotion as opposed to chronic disease management are needed as a literature search produced a few studies to date.

Older adults may be perceived as resistant to using mobile technology, however several studies emerged from this review that successfully included older adults. In reality, there are a growing number of technology-savvy older adults. Mobile resources may be offered as a supplement to the care of older adults as they live with chronic diseases. Moreover, older adults often have family members or caregivers who can assist in using mobile technology if technical and physical limitations exist (e.g., poor vision). Although penetration of mobile phones among older adults may be challenging due to their lack of familiarity with current technology, the uptake of mobile phones is likely to change as the population who use SMS or apps grows older (Petrie *et al.* 2012).

Sensitivity to literacy and languages will support mobile phone interventions that reach global populations and increase generalizability. Four studies in this review allowed participants to choose their language preference (Arora *et al.*, 2012; Castano *et al.* 2012; Mbuagbaw *et al.* 2012; Pop-Eleches *et al.* 2011). The global reach of mHealth research is demonstrated in this review with 14 countries being represented, although 13 of the 29 studies were conducted in the United States. Valuable insights into mobile phone interventions in countries with few resources were provided by studies conducted in Kenya, Cameroon, and India. Due to the ubiquitous nature of mobile phones across diverse populations, the modality of mobile technology may be generalizable across many more cultures.

Implications for Nursing Practice and Research

Patients can be empowered to adhere to medication prescriptions through nursing practice. Prescription counseling often comes from nurses in hospital, outpatient, or community settings. Developing strategies with patients and their caregivers to promote medication adherence may be key to successful self-management. Nurses can play an important role in keeping current with the growing number of available mHealth and telemedicine resources for patients. Nurses are encouraged to embrace the potential of mobile technology as a cost-effective and efficacious tool to improve medication adherence.

Many opportunities remain in building mHealth science. Future research may assess the impact on medication adherence and user fatigue from various message contents, frequency of reminders, and text responses (Hardy *et al.* 2011). Nurses can make a significant contribution to understanding the potential of mHealth by applying mixed methods study designs with quantitative and qualitative research, particularly as our search did not find any qualitative studies for inclusion in this review. Moreover, integration of real-time feedback on disease management will be instrumental in designing future interventions (Granholm *et al.* 2012; Vervloet *et al.* 2012).

To date, the research in this area has been relatively atheoretical. Despite the benefits of applying theory to identify potential mediating factors and outcomes (Granger & Bosworth 2011), only 5 out of 29 studies used theory to guide their research. The theories mentioned were Transtheoretical Model (Castano *et al.* 2012), Social Cognitive Theory (Franklin *et al.* 2003), The Health Belief Model of Behavior Change (Mbuagbaw *et al.* 2012), Behavioral Learning Theory (Montes, Medina, Gomez-Beneyto, & Maurino 2012), and Theory of Planned Behavior (Suffoletto, Calabria, Ross, Callaway, & Yealy 2012). It will be important for nurse scientists who design future studies to use a theoretical basis to explain the relationship between study variables. Other health behavioral theories may be developed that take into account the time-intensive, interactive, and adaptive nature of mHealth interventions that demand more intra-individual dynamic regulatory processes (Riley *et al.* 2011).

The efficacy of mobile phone apps versus SMS has yet to be explored in research. As the number of smartphone users continues to grow with 45% of Americans owning a smartphone in 2013 (Brenner 2013), interventions that apply apps as opposed to SMS will inform us about the full potential of mHealth to support medication adherence and disease management. The features that are available from smart phones will likely engage users by allowing more interaction and increased variability.

CONCLUSION

The potential impact of mobile technology in disease prevention and management may be substantial. Research identified in this systematic review has introduced the use of mobile phones to support medication adherence among different patient populations. Future research is required to substantiate these early findings and to provide data on long-term follow-up in a variety of patient populations. Applying appropriate statistical approaches combined with rigorous theory-based interventions may provide important insights into the efficacy and acceptance of mobile technology by patients related to medication use and the factors that mediate its efficacy. Future studies are required to determine the efficacy of different approaches over time as well as to explore topics such as patient acceptance, clinical outcomes, cost-effectiveness, and theory supporting medication adherence behavior. The next decade of research with mobile phones will likely evolve into applying more smart phone apps in place of SMS interventions.

Mobile health will continue to enhance clinical practice and allow for easily accessible and remote solutions, especially for patients with chronic diseases requiring lifelong medication adherence for optimal outcomes. The real possibilities of mHealth in promoting medication adherence await further research and will continue to take shape as the results of pilot studies and rigorous intervention trials continue to inform us in this promising field.

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Figure 1. Flow Chart of Study Selection Process

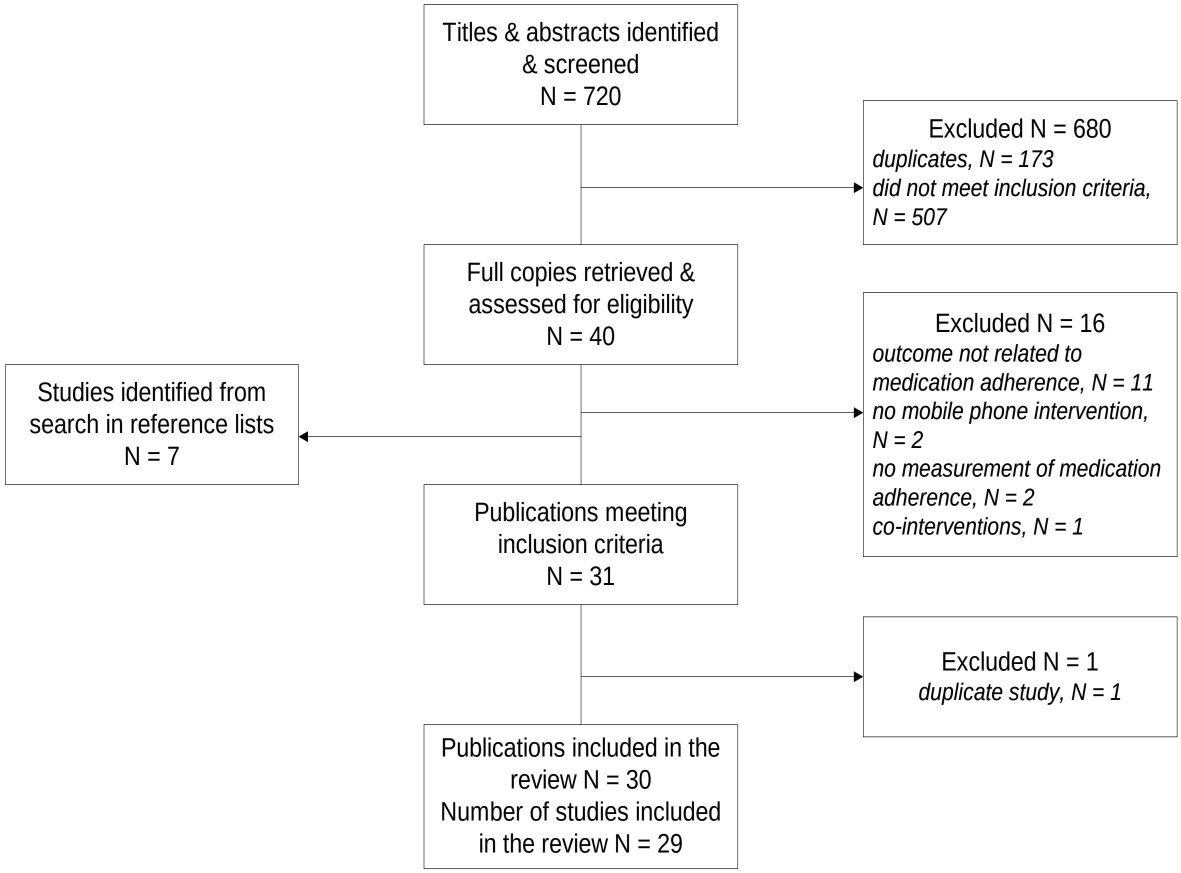

Table 1. Quality Assessment Using CONSORT Guidelines for Randomized Controlled Studi

First Author (year)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	TOTAL
Boker (2012)	✓	✓	✓	✓	✓	✓		✓				✓	✓		✓		✓			✓	✓	✓				14
Castano (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	23
Cocosila (2009)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓			✓	✓	✓			✓	20
da Costa (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓			✓	22
Franklin (2006)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓			✓	21
Hardy (2011)	✓	✓	✓	✓	✓	✓		✓		✓		✓	✓	✓	✓	✓	✓			✓		✓			✓	17
Hou (2010)	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓			20
Lester (2010)	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	24
Marquez Contreras (2008)	✓	✓	✓	✓	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓			✓	✓	✓			✓	18
Mbuagbaw (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	25
Montes (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓				20
Ollivier (2009)	✓	✓		✓	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓			✓	✓	✓				16
Ostojic (2005)	✓	✓	✓	✓	✓	✓	✓					✓	✓		✓	✓	✓			✓	✓	✓				15
Petrie (2012)	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓			✓	✓			✓	✓	✓				16
Pop-Eleches (2011)	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓			✓	✓	✓	✓		✓	20
Shetty (2011)	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓			✓				✓		✓			✓	15
Strandbygaard (2010)	✓	✓	✓	✓	✓	✓		✓				✓	✓		✓	✓	✓			✓	✓	✓				15
Suffoletto (2012)	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	✓	✓	✓	✓			✓		✓				17
Ting (2012)	✓	✓	✓	✓	✓	✓	✓	✓				✓	✓	✓	✓	✓	✓	✓		✓	✓	✓			✓	19
Vervloet(2012)	✓	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓		✓	✓	✓			✓	✓	✓	✓		✓	19

The CONSORT criteria include: (1) Title/abstract. Introduction: (2) background and objectives. Methods: (3) trial design, (4) participants, (5) interventions, (6) outcomes, (7) sample size, (8) sequence generation, (9) allocation concealment, (10) implementation, (11) blinding, (12) statistical methods. Results: (13) participant flow, (14) recruitment, (15) baseline data, (16) numbers analyzed, (17) outcomes and estimation, (18) ancillary analyses, (19) harms. Discussion: (20) limitations, (21) generalizability, (22) interpretation. Other information: (23) registration, (24) protocol, (25) funding (Schulz *et al.*, 2010).

Table 2. Quality Assessment Using STROBE Guidelines for Observational Studies

STROBE criteria	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	TOTAL
Arora (2012)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓		✓	✓	✓			✓	✓	✓	✓	✓	18
Dick (2011)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	20
Dowshen (2012)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	21
Foreman (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	21
Granholm (2012)	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	21
Lewis (2012)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	20
Miloh (2009)	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		18
Pena-Robichaux (2010)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓		19
Zolfaghari (2012)	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	19

The STROBE criteria include: (1) Title/abstract. Introduction: (2) background/rationale, (3) objectives. Methods: (4) study design, (5) setting, (6) participants, (7) variables, (8) data sources/measurement, (9) bias, (10) study size, (11) quantitative variables, (12) statistical methods. Results: (13) participants, (14) descriptive data, (15) outcome data, (16) main results, (17) other analyses. Discussion: (18) key results, (19) limitations, (20) interpretation, (21) generalizability. Other information: (22) funding (von Elm *et al.*, 2007).

Table 3. Studies on Mobile Phones and Medication Adherence

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
Arora (2012) US	Diabetes 3 weeks	Proof-of-concept N = 23 45.4 ± 7.5	SMS with health messages and triggers to promote knowledge, healthy eating, exercise, self-efficacy, and med adherence	Morisky Medication Adherence Scale (MMAS)	Significant improvement on MMAS score (3.5 to 4.75).
Boker (2012) US	Acne 12 weeks	RCT N = 40 22.6	EG: SMS on med reminders for 2 different gels for acne treatment CG: No SMS	Medication tube with MEMS, clinical evaluation of acne	No significant difference in mean adherence rates between EG and CG (33.9% vs. 36.5%, respectively; P = 0.5). Self-reported adherence (responses received) for EG was 74.4%. Both groups had similar clinical improvement of acne.
Castano (2012) US	Oral contraceptive pills (OCP) 6 months	RCT N = 962 EG 20.8 ± 2.5, CG 20.4 ± 2.7	EG: SMS with educational content CG: Routine care	Self-report on continued OCP use, missed pills, interruptions in med use, use at last intercourse	Significant difference in mean adherence rates between EG and CG (75% vs. 54%, respectively; P = 0.003) if follow-up occurred while intervention was ongoing. Adherence was not different between groups after 187 days, 5-8 months or more.
Cocosila (2009) Canada	Prevention of colds: Vitamin C Use 1 month	RCT N = 102 23.8 ± 7	EG: SMS med reminders CG: No SMS	Self-reported pill counts	No significant difference in missed pills during last week of trial between EG and CG (2.5 ± 1.5 vs. 3.3 ± 2.2, respectively). Both groups increased Vitamin C adherence: 1.3 to 4.5 (246%) for EG, 1.6 to 3.7 (131%) for CG.
da Costa (2012) Brazil	HIV/AIDS 4 months	RCT N = 21 34.6 ± 6.9	EC: SMS general health message CG: No SMS	Self-reported adherence, pill counting, and MEMS	No significant differences in adherence between EG and CG. Self-report 100% vs. 84.62%, respectively; P = 0.24. Pill counts 50% vs. 38.46%, respectively; P = 0.60. MEMS 75% vs. 46.15%, respectively; P = 0.19.

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
Dick (2011) US	Diabetes 1 month	Feasibility and usability pilot N = 18 55	"Personalized" SMS on med, blood sugar, foot care, appointment, or administrative	Self-report on number of med doses missed in periods before, during, and 1 month	Significant decrease in number of reported missed med doses from a mean of 1.9 per week at baseline to 0.6 during the study period (P = 0.003) and 0.8 at 1 month follow-up (P < 0.001).
Dowshen (2012) US	HIV/AIDS 24 weeks	Pilot, pre-post design N = 25 23	"Personalized" SMS as med reminder	VAS and AIDS Clinical Trial Group (ACTG) questionnaire 4-day recall Viral load and CD4 cell count at baseline, 12, and 24 weeks	Significant increase in VAS at 12 and 24 weeks (baseline: 74.7; week 12: 93.3, P < 0.001; week 24: 93.1, P < 0.001). Significant improvement in ACTG questionnaire (baseline: 2.33; week 12: 3.24, P = 0.002; week 24: 3.19, P = 0.005). No significant difference in CD4 cell count or viral load between baseline and 12 or 24 week follow-up. Small to moderate effect size (Cohen's d = -0.51 to 0.22).
Foreman (2012) US	Chronic oral med(s) 8 months	Retrospective observational cohort analysis N = 580 EG 64.8 ± 11.9, CG 63.7 ± 13.7	EG: choice of SMS on refill, renewals, transfer, order shipment, general or specific med reminder CG: matched 1:1 on med class then propensity matching score	Proportion of days covered (PDC) Change in PDC from baseline to post-intervention	Significant overall mean PDC higher for EG compared to CG (0.85 vs. 0.77, respectively; P < 0.001). Significant overall mean PDC change higher for EG compared to CG (0.01 vs. -0.07, respectively; P < 0.001).
Franklin (2006) Scotland	Diabetes 12 months	RCT N = 92 13.17	EG: "Personalized" motivational SMS with "Sweet Talk" CG: Standard of care	VAS	Significant difference in VAS between conventional insulin therapy (CIT) patients and CIT with Sweet Talk (P = 0.04). No difference between CIT with Sweet Talk and intensive insulin therapy patients (P = 0.90).
Granholm (2012)	Schizophrenia or schizoaffective disorder	Feasibility and usability pilot	"Personalized" SMS to target med adherence,	Self-report	Significant improvement in adherence but only for individuals who were living

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
US	12 weeks	N = 55 48.7 ± 9.1	socialization, or auditory hallucinations		independently.
Hardy (2011) US	HIV/AIDS 6 weeks	Parallel group RCT N = 25 42.7 ± 6.5	SMS group: "Personalized" SMS with med reminders Beeper group: med reminders	Self-report (7-day recall), pill count, MEMS, and composite adherence score (combining MEMS, pill count, and self report)	Significant differences in mean adherence between groups when measured by MEMS (mean difference: 33.4 ± 9.1, P = 0.002) and composite score (27.1 ± 9.2, P = 0.01). No significant difference by pill count (13.7 ± 9.1, P = 0.15) or self-report (20.2 ± 10.3, P = 0.07).
Hou (2010) US	Contraception 3 months	RCT N = 82 22	EG: SMS med reminders CG: No SMS	Electronic monitoring device to store pills (SIMPill) and paper diary	No significant difference in missed pills per cycle between EG and CG (4.9 ± 3.0 vs. 4.6 ± 3.5, respectively; P = 0.60).
Lester (2010) Kenya	HIV 12 months	RCT N = 538 36.7 ± 8.5	EG: SMS med reminders CG: Standard of care	Self-reported adherence and plasma HIV-1 viral RNA load suppression	Significant difference in adherence rates between EG and CG [RR for non-adherence 0.81, 95% CI 0.69–0.94; P = 0.006). Significant difference in suppressed viral loads between groups (RR for virologic failure 0.85, 95% CI 0.72–0.99; P = 0.04).
Lewis (2012) US	HIV 3 months	Proof-of-concept N = 52 38	"Tailored" frequency of SMS med reminders depending on weekly assessment of adherence	Self-report of missed doses and clinical outcomes (viral load and CD4 count)	Significant difference in number of missed med days for participants from baseline to follow-up (1.90 ± 1.22 vs. 0.94 ± 1.09, Cohen's d = 0.83; t(16) = 2.22, P = 0.04). Significant reduction in viral load from baseline to follow up (P = 0.01; Cohen's d = -0.40), and CD4 counts (P = 0.04; Cohen's d = 0.21).
Márquez Contreras (2008)	Hypertension 6 months	RCT N = 67	EG: SMS med reminders and health info	Pill counts and blood pressure recordings	No significant difference in mean percentage of compliance between EG and CG (91.9% ± 11.5% vs. 88.1% ±

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
Spain		57 ± 10.6	CG: Standard of care		20.8%, respectively; P = NS). No significant difference in blood pressure control between EG and CG (64.7% vs. 51.5%, respectively; P = NS).
Mbuagbaw (2012) Cameroon	HIV 6 months	RCT N = 200 EG: 41.3, CG: 39.0	EG: SMS with motivational and reminder components CG: Standard of care	VAS, self-report, pharmacy refill data (PRD)	No significant difference in VAS between groups (RR 1.06, 95% CI 0.89, 1.29; p = 0.54) or self-reported missed doses (RR 1.01, 95% CI 0.87, 1.16; P = 0.99). No difference in PRD between groups (mean difference 0.1 95% CI 0.23, 0.43; P = 0.62). EG achieved adherence of 90% at 6 months (RR 1.14 95% CI 1.01, 1.29; P = 0.03).
Miloh (2009) US	Immunosuppression post transplant 13 ± 1.5 months	Quasi-experimental N = 41 Median age 15	SMS med reminders	Mean tacrolimus SD, clinical outcomes (rejection)	Significant decrease in tacrolimus level SD before compared to during the study (3.46 to 1.37 mcg/L ($P < 0.005$). Significant reduction of acute cellular rejection before compared to during the study (12 to 2, $\chi^2 = 5.08$; P = 0.02).
Montes (2012) Spain	Schizophrenia 3 month of SMS; month 6 follow-up	RCT N = 254 EG 38.6 ± 10.2, CG 40.6 ± 11.5	EG: SMS med reminders CG: Standard of care	Morisky Green Adherence Questionnaire (MAQ)	Significant change in MAQ total score between EG and CG (25% vs. 17.5%, respectively). Mean changes in MAQ total score from baseline to month 3 were -1.0 (95% CI -1.02, -0.98) for EG and -0.7 (95% CI -0.72, -0.68) for CG (P = 0.02). Significant change remained 3 months after SMS (P = 0.04).
Ollivier (2009) France	Malaria 1 month	RCT N = 424 26.7	EG: SMS med reminders CG: Standard health info	MEMS	No significant difference in med adherence between groups. Decreased adherence rate in both groups (EG 94.6% to 67.6% and CG 95.2% to 65.8%).

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
Ostojic (2005) Croatia	Asthma 16 weeks	RCT N = 16 24.6 ± 6.5	EG: SMS on med therapy and clinic follow-up CG: No SMS	Use of asthma medication; PFT (FEV1% and mean FEV1); daily symptoms; home PEF (peak expiratory flow); clinical records (office visits, hospitalizations, med changes)	No significant difference in med use. EG used 20% higher doses compared to CG. Significant increase in FEV1% predicted in EG (P = 0.01) compared to CG (P = 0.50). No change in mean FEV1 or forced vital capacity. PEF variability significantly different between groups (P = 0.05). Significantly higher symptom scores in CG for cough (P = 0.05) and night symptoms (P = 0.05).
Pena-Robichaux (2010) US	Atopic dermatitis 6 weeks	Pilot, pre-post design N = 25 30.5 ± 13.4	SMS med reminders (3 per week) and educational messages (4 per week)	Self-report	Significant improvement in mean number of days/week of adherence from pre to post-intervention among 72% of participants (3.8 ± 2.4 vs. 6.0 ± 1.7, respectively; P < 0.001).
Petrie (2012) New Zealand	Asthma 18 week SMS intervention; up to 9 months follow-up	RCT N = 216 included 16-45 year olds	EG: “Tailored” SMS based on illness and med beliefs CG: No SMS	Self-report	Significant difference in mean adherence across all time points (6, 12, and 18 weeks; 6 and 9 months) between EG and CG (57.8% ± 27.1 vs. 43.2% ± 26; P = 0.003). Significant difference in proportions of mean adherence of 80% or above between EG and CG (25.9% vs. 15.3%; P = 0.03).
Pop-Eleches (2011) Kenya	HIV 4 months	RCT N = 431 36.2	EG: SMS med reminders: daily vs. weekly, short vs. long CG: No SMS	MEMS	Significant difference in adherence rate between EG and CG receiving weekly SMS (53% vs. 40%, respectively; P = 0.03) and less likely to have treatment interruptions exceeding 48 hours (81% vs. 90%, P = 0.03). No differences between groups receiving daily SMS. No differences between groups receiving short

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
					messages (P = 0.24) or long encouraging messages (P = 0.24).
Shetty (2011) India	Diabetes 1 year	Pilot RCT N = 215 EG 50.1 ± 9.9, CG 50.5 ± 8.3	EG: "Personalized" SMS CG: Standard of care	Fasting plasma glucose (FPG), 2 hour post prandial plasma glucose (2h PG), and HbA1C; adherence to med, diet, and activity prescriptions	Significant decrease in mean FPG (185 + 57 mg/dl to 166 + 54, P < 0.002) and 2h PG (263 + 84 mg/dl to 220 + 67, P < 0.002) in EG. Significant change in 2h PG between EG and CG (14.1 to 34.6% vs. 13.6 to 19.7%; respectively; P < 0.007). Significant change in HbA1C between groups (30.8 to 55.1%, 31.8 to 48.5%, respectively; P < 0.007). Meds "were followed satisfactorily by both groups."
Strandby-gaard (2010) Denmark	Asthma 3 months	RCT N = 26 18.5	EG: SMS med reminders CG: No SMS	Med dose-count on the discos Seretide®, pharmacy reports	Significant absolute difference in mean adherence rate between groups of 17.8% (P = 0.02). Significant increase in mean adherence rate in EG (77.9% to 81.5%, mean change = 3.5%; P = 0.52). Significant decrease in mean adherence rate in CG (84.2% to 70.1%, mean change = -14.2%; P = 0.01).
Suffoletto (2012) US	Oral antibiotic use from emergency department Duration of antibiotic use, up to 2 weeks	RCT N = 200 33 ± 12	EG: SMS query about prescription pickup and dosage taken with educational feedback based on responses CG: Standard of care	Self-report	No significant difference in adherence between EG and CG (57% vs. 45%, respectively; P = 0.16). No difference in proportion of those who had filled prescriptions in first 24 hours between EG and CG (78% vs. 69%, respectively; P = 0.26) or proportion of those who had no pills left (68% vs. 59%, respectively; P = 0.30).
Ting (2012) US	Systematic lupus erythematosus 14 months	RCT N = 41 (subset with medication	EG: SMS on med reminders CG: Standard of care	Self-report, blood levels of HCQ and pharmacy refill reports	No significant difference in self-reported adherence between EG and CG (80% for both). 25% had sufficiently high HCQ blood levels,

First Author, Year, Country	Target Condition and Duration of Study (months)	Design, Sample Size, Mean Age	Experimental and Control	Measures of Med Adherence	Results (med adherence and/or biomarker)
		adherence) 18.6 ± 2.5			29% had undetectable levels. 32% were adherent over 80% of the time by pharmacy refill. Small effect size (Cohen's d < 0.25) on adherence.
Vervloet (2012) Netherlands	Diabetes 6 months	RCT N = 104 55	EG: RTMM system with electronic med dispensers and customized SMS only if dispenser not opened CG: RTMM without SMS	RTMM electronic monitoring system	No significant difference in missed doses between EG and CG (15% vs. 19%, respectively; P = 0.07). No difference in days without dosing between groups (P = 0.28). EG took significantly more doses within agreed time period than CG (57% vs. 43%, respectively; P = 0.003).
Zolfaghari (2012) Iran	Diabetes 3 months	Quasi-experimental N = 77 EG 51.1 CG 53.7	EG: educational SMS CG: telephone contact at least twice a week for first month then weekly	Self-report HbA1C	Significant improvement of med adherence (P = 0.000), diet adherence (P = 0.000), and physical activity (P = 0.000). Significant changes in HbA1C for EG (P < 0.001) and CG (P < 0.001) but no differences between groups (P = 0.19).

2h PG: 2 hour post prandial plasma glucose, CG: control group, EG: experimental group, FPG: fasting plasma glucose, FEV1: forced expiratory volume, HbA1C: Hemoglobin A1C, HCQ: hydroxyl-chloroquine, MAQ: Morisky Green Adherence Questionnaire, med: medication, NS: non-significant, PEF: peak expiratory flow, RCT: randomized controlled trial, SMS: short message service, MEMS: Medication Event Monitoring System, NS: non-significant, PDC: proportion of days covered, PFT: pulmonary function test, PRD: pharmacy refill data, RR: relative risk, RTMM: Real Time Medication Monitoring, SD: standard deviation, VAS: Visual Analog Scale

Table 4. Tracking, Message Content, Satisfaction of SMS Interventions

First Author & Year	Frequency of SMS	Tracking (2-way SMS) & Response	Message Content	Satisfaction
Arora (2012)	Daily (9 am, 12 pm, and 6 pm); frequency of med reminders was 3 per week	Yes, 2-way response was only an option with trivia SMS (one per week) 35% response to trivia SMS	SMS on 5 domains: educational / motivational, med reminders, healthy living challenges, diabetes trivia, and links to free diabetes management tools.	High satisfaction (90-100%) in helpfulness of SMS to take meds, enjoying SMS, wanting to continue SMS, and recommending to others.
Boker (2012)	Twice daily, tailored to participant preference and time of med use	Yes 74% replied they had taken their med (although it did not coincide with MEMS data)	SMS started with participant's name but content identical (med reminder).	33% starting ignoring SMS after 2 weeks. 26% found SMS to be "annoying."
Castano (2012)	Daily; time selected by participant and could be changed on website	Yes, 12 out of 180 (0.07%) of messages were 2-way for quality control purposes Response rate not reported	47 educational messages on 6 domains (risks, benefits, side effects, use, effectiveness, and mechanisms of action) that were repeated up to 4 times, 12 2-way messages for quality control.	Participants satisfied with number (91%), content (91%), and length (91%) of messages.
Cocosila (2009)	Dosing weaned down over 1 month	Yes 44%	Virtual friend named "Tim". SMS divided into reminding-basic, reminding-reinforcing, and reminding-correcting.	Not reported
da Costa (2012)	Every Sat, Sun and alternate working days sent 30 minutes before last required med dose in a day	No	"The UNIFESP informs: take good care of your health."	Timing: 27% - should be closer to time of med intake. Content: 91% - SMS did not need to be changed, 9% - Yes, change the content of SMS daily. Usefulness: 64% - SMS helped them to remember the time to take med. 45% - SMS provided incentive to take care of health or take med; 27% - felt like someone cared about them.
Dick (2011)	Timing and frequency of delivery selected by participant	Possible for participant to respond 80% responses	Recommendations for self-care including med adherence, foot care, and blood sugar monitoring.	94% of participants said SMS helped them to avoid missing medications, 94% strongly agreed that the system was easy to use, and 89% increased the frequency of foot self-examinations.

First Author & Year	Frequency of SMS	Tracking (2-way SMS) & Response	Message Content	Satisfaction
Dowshen (2012)	Daily at time(s) selected by participant	Yes 48% responses	Participants designed personalized SMS reminder at beginning of study. Examples included: "Don't forget!," "Reminder," "Superman calling you," "Time for fruit cocktail."	81% of participants said they would like to continue to receive SMS after the end of the study, and 95% indicated that SMS helped them "very much" to miss fewer doses of med.
Foreman (2012)	Type and frequency of message selected by participant	No N/A	For those who elected med reminders, the general daily reminder read, "Take your medications today." Option of dosage specific reminders.	Not reported
Franklin (2006)	Daily or twice daily	No, hotline number provided if needed	Tailored SMS from database (examples): "Don't 4get 2 inject!", "Do you have any 'carb counting' questions for the DiaBTs doctors or dieticians?"	97% liked frequency (daily or twice daily), 20% complained about receiving the same message repeatedly.
Granholm (2012)	Monday through Saturday in random order in morning, afternoon, and evening; time within a 2-hour window selected by participant	Yes Question 1: Mean = 86% ± 19%, Median = 93%. Questions 2-3: Mean = 85% ± 21% and 85% ± 30%. Median = 94% and 98%	First question: "Did you take your meds today?" Next 2 questions depending on response, "Do meds help you stay healthy?" or "How can you remember?"	Participant were asked each Friday, ''How helpful were the text messages this week?'' Overall, mean = 3.15 ± 0.84; median = 3.42 (moderately to very helpful). Participants who had more experience with the SMS intervention increased the likelihood of reporting the intervention was helpful.
Hardy (2011)	Daily reminder matching med dosing frequency	Yes Weeks 0-3: median response rate 0.78. Weeks 3–6: response rate 0.62	Choice of following categories: news, weather, celebrity news, humor, jokes, Bible verses, word of the day, baseball, basketball, or football (able to change at weeks 3 and 6).	Qualitative study on 10 participants. 9 of 10 reported that they enjoyed receiving a content-tailored reminder SMS. Only 1 participant, whose content was Bible verses, said that the content helped motivate her in some way to take med.
Hou (2010)	Daily	No	"Please remember to take your birth control pills."	SMS reminder was useful with a median score of 8 on a 0-10 scale. 66% said the SMS reminded them more than 50% of the time to take their meds. 86% of women said they would continue or consider using the reminder system. 97% would recommend or consider

First Author & Year	Frequency of SMS	Tracking (2-way SMS) & Response	Message Content	Satisfaction
				recommending it to others.
Lester (2010)	Weekly	Yes; Response was either: "Sawa" (fine) or "Shida" (problem) fine (65%), problem (3%), no response (32%)	"Mambo?" (How are you?)	98% reported wanting to continue the SMS program. 98% would recommend the program to a friend. In focus groups, patients reported they felt "like someone cares."
Lewis (2012)	Daily for nonadherent; weekly for adherent	Yes Not reported	Nonadherent: "Stop, drop, and pop. Take your meds now." Adherent: "He shoots! He scores! Perfect med adherence. Great job!"	93% reported "always" reading the messages; 76% reported "liking" the messages; and 39% and 29% reported the messages being "very" or "somewhat" helpful, respectively.
Márquez Contreras (2008)	2 SMS per week on random days Mon-Fri between 11 am - 2 pm	No	SMS to encourage adherence and educate on lifestyle. Examples: "Do not stop taking your blood pressure medicine even when you are taking other medicines or have another illness."	Not reported
Mbuagbaw (2012)	Weekly	No, phone number was provided if help needed 48 out of 101 EG patients used feedback option	Motivational messages with a reminder component. Example: "You are important to your family. Please remember to take your medication. You can call us at this number: **+**237 xxxx xxxx."	91% - SMS helped them to remember to take their med, 35% - did not want to continue receiving SMS. 12% - SMS excellent, 30% - very good 30%, 21% - good, 17% - average, 5% - bad, 16% - very bad.
Miloh (2009)	Once or twice daily matching med dosing times	Yes, if patient did not respond within 15-60 min, SMS sent to caregiver Not reported	"Take [name of med] at [set time]. To confirm intake, press REPLY, type CARE 1, and press SEND."	Not reported
Montes (2012)	Daily; participant selected either 11 am or 2 pm	No	"Please remember to take your medication."	Not reported
Ollivier (2009)	Daily	No	"Remember to take your doxycycline pill at midday."	Overall satisfaction with reports that SMS was very useful, generalizable, and was not laborious.
Ostojic (2005)	Weekly	EG sent SMS to researcher (PEF values) daily - 99%	SMS on adjustments of therapy and recommended follow-up with	SMS were convenient and not intrusive.

First Author & Year	Frequency of SMS	Tracking (2-way SMS) & Response	Message Content	Satisfaction
		compliant	monitoring physician.	
Pena-Robichaux (2010)	Daily; time between 7-9 am or 4-6 pm selected by participant	No	SMS with med reminders with alternating educational content and option of additional “fun” SMS or “hook” with choice of forecast, sports scores, or celebrity gossip.	Participants rated the SMS system a mean score of 7.1 ± 2.4 (scale from 1-10). 88% - SMS were helpful, 92% - educational SMS were helpful, 84% - want to continue the system, 84% - would recommend the SMS program to a friend, 72% - willing to pay a small monthly fee for service.
Petrie (2012)	weeks 1-6: 2 daily weeks 7-12: 1 daily weeks 13-18: 3 per week	No	SMS based on baseline scores on Brief Illness Perception Questionnaire and level of medication belief ratings. Example med SMS: “Your preventer medication is not addictive.”	Not reported
Pop-Eleches (2011)	Daily compared to weekly at 12pm	No	Short message: “This is your reminder.” Long message: “This is your reminder. Be strong and courageous, we care about you.”	Not reported
Shetty (2011)	Frequency chosen by participant; median frequency was 2 SMS per week	No	Content chosen by participant. SMS on medical nutrition therapy, physical activity, med reminders, and general healthy living habits.	Not reported
Strand-bygaard (2010)	Daily at 10 am	No	“Remember to take your asthma medication morning and evening. From the Respiratory Unit.”	Perception of receiving daily SMS was positive, although majority found 10am as unsuitable. EG reported SMS became comparable to a simple alarm clock on a mobile phone after some weeks.
Suffoletto (2012)	SMS 1 hour after antibiotic prescribed and 24 hours after participant response	Yes 67% replied to the antibiotic pickup question	Initial SMS: “Welcome to the IMPACT antibiotic study. Text back ‘yes’ when you have picked up your prescription for [Antibiotic].” If no reply, extra SMS. 24 hours after response: ‘‘IMPACT antibiotic study: How many doses of [Antibiotic] did you take between [0:00 PM] yesterday and [0:00 PM] today?’’	91% reported SMS was at least somewhat useful to remind them to pick up their antibiotics. 52% reported it was very useful. 97% reported SMS was at least somewhat useful to remind them to take their antibiotics, with 61% who reported it was very useful.

First Author & Year	Frequency of SMS	Tracking (2-way SMS) & Response	Message Content	Satisfaction
Ting (2012)	Once daily med - 8 am; twice daily med - 8 am and 8 pm	No	Example: “Take ur HCQ now,” “It’s time 4ur meds.”	Participants initially gave informal positive feedback at follow-up clinic visits.
Vervloet (2012)	SMS only if dispenser not opened (reminded for 36% of all prescribed doses)	No	“Have you taken your medication yet? Please take your medication as prescribed by your health care provider.”	EG reported more awareness of med use compared to CG (P = 0.04). Accuracy in taking med was not significant (P = 0.10). 83% - “It is good to know I am reminded if needed,” 75% - “SMS reminders support me in med use,” 18% - “I do not react to the SMS reminders,” 21% - “SMS reminders are disturbing,” 66% - “SMS reminders are useful.”
Zolfaghari (2012)	6 SMS every week (except holidays)	No	Messages set in 3 priorities: diet adherence, med adherence, and stress management.	Not reported

CG: control group, EG: experimental group, med: medication, N/A: not applicable, PEF: peak expiratory flow, SMS: short message service

Chapter 3

Self-Efficacy Theory: Using Mobile Technology to Improve Medication Adherence

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Self-Efficacy Theory: Using Mobile Technology to Improve Medication Adherence

Medication adherence is a subject of interest for behavioral scientists, psychologists, clinicians, and theorists alike. Medication adherence is a complex process that cannot be simplified to the mechanics of individuals understanding the need to take medications and adhering to their prescribed regimens. Previous research has shown that knowledge and competency in medication use alone do not lead to behavior change in taking prescribed medications (Bandura, 1982; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Schedlbauer, Schroeder, Peters, & Fahey, 2004). Numerous precipitating factors and barriers affect medication adherence, and this complex process can be better understood when examining theoretical relationships and processes. Perceived self-efficacy is cited as a powerful mechanism in determining behavior change (Bandura, 1987) and was explored as the theoretical framework for an intervention to improve medication adherence.

Self-efficacy is defined as the belief in one's own capabilities to perform certain actions that have influence in his or her life (Bandura, 1987). Self-Efficacy Theory (SET) was chosen from a number of other theories pertaining to adherence (e.g., Health Belief Model, Health Promotion Model, Theory of Reasoned Action, Stages of Change Theory) because it seemed most appropriate when considering an intervention study designed to test the efficacy of mobile technology using text messaging to improve adherence to cardiac medications (i.e., antiplatelet and statin) among patients with a history of myocardial infarction (MI) and/or percutaneous coronary intervention (PCI). In the pilot randomized controlled trial (RCT), use of mobile phone text messages (TM) that provided daily medication reminders and/or health education was hypothesized to increase self-efficacy related to adhering to cardiac medications. The hypothesis was that TM would aid in mastery of medication use and thereby build self-confidence and self-management skills in medication self-administration. The aims of this chapter are to: a) provide an overview of SET beginning with its roots in Social Cognitive Theory (SCT); b) examine the impact, sources, and measurement of self-efficacy; c) present a revised theoretical model using SET as the framework for the intervention study; and d) discuss each of the components and relationships of the revised model including mobile technology, self-efficacy, medication adherence, personal factors, and social support.

Social Cognitive Theory

Albert Bandura is often linked to his work in SET, which was derived from SCT. Bandura developed SCT in the 1970's after he conceptualized the role of self-beliefs in relation to the original components of observational learning and vicarious reinforcement that were the foundational elements of social learning theories (Pajares, 2010). In SCT, Bandura (1986) further described a view of human functioning that emphasizes the importance of cognitive, vicarious, self-regulatory, and self-reflective processes in human adaptation and change. Individuals are viewed as self-organizing, proactive, self-reflecting and selfregulating rather than as reactive beings who are driven by environmental forces or concealed inner impulses (Bandura, 1986). From this theoretical perspective, human functioning is viewed as the product of a dynamic interplay of personal, behavioral, and environmental influences (Pajares, 2010). These three elements will be further described in relationship to self-efficacy.

Another tenet of SCT is the view of human agency, or intention to act, in which individuals are agents proactively engaged in their own development and capable of making things happen by their actions (Pajares, 2010). Within human agency, individuals possess self-beliefs that enable them to exercise a measure of control over their thoughts, feelings, and actions (Bandura, 1986). Bandura (1986) provided a view of human behavior in which the beliefs that people have about themselves, including perceived self-efficacy, are critical elements in the exercise of control and personal agency. Social Cognitive Theory is comprised of a large set of factors that operate as regulators and motivators of established cognitive, social, and behavioral skills (Bandura, 1986). Compared to other theories, SCT is a comprehensive theory of health behavior change and includes concepts identified in the Health Belief Model, Protection Motivation Theory, Theory of Reasoned Action, and Theory of Planned Behavior, as well as concepts missing from other theories (Sirur, Richardson, Wishart, & Hanna, 2009).

Self-Efficacy Theory

Self-Efficacy Theory offered a link from SCT that focused on self-beliefs to individual action. Of all the thoughts that affect human functioning, perceived self-efficacy is considered to be at the very core of SCT (Pajares, 2010). The majority of Bandura's work transitioned from SCT to a career of exploring self-efficacy and its effect on behavior. According to SET, individuals strive to control events that affect their lives, and this need influences all individual action (Bandura, 1986). Perceived self-efficacy influences how people feel, think, behave, and motivate themselves (Pajares, 2010). Self-efficacy not only determines the effort an individual will expend in the activity but also how long the individual will persist in the activity in the face of obstacles or negative consequences (Buchmann, 1997).

Sources of Self-Efficacy

Self-efficacy is derived from four principal sources of information: enactive experience (performance accomplishments), vicarious experience, verbal persuasion, and physiological state (emotional arousal). Figure 1 outlines the major sources of efficacy information and the principal sources through which diverse modes of influence can alter behavior (Bandura, 1977). This discussion will be centered around the basic sources of efficacy without detail given to the various modes of induction as it is beyond the scope of this dissertation.

The first source of self-efficacy is enactive attainments, or performance accomplishments, and is the most influential source of efficacy information because it is based on mastery experiences (Bandura, 1982). Self-efficacy is increased by mastery, or expert skills, and diminished by lack of experiences or past failures. Users of mobile technology who have experience and confidence in their adeptness with technology may have increased self-efficacy with mobile technology. In contrast, individuals who have not used their mobile phone beyond the telephone feature may not report increased self-efficacy from receiving TM for medication reminders and/or health education. Increased self-efficacy through enactive attainments can transfer to other similar or different situations (Bandura, 1977).

The second source of self-efficacy is vicarious experiences, or observing others successfully model behaviors that they believe they can master (Bandura, 1982). Similarly, witnessing others fail in tasks can be discouraging and lead to lowered perceived self-efficacy. In the context of using a mobile phone, individuals who witness the successful use of a mobile phone to promote health behavior change may feel more confident in their own abilities to use the same technology. Unstated social pressures often encourage individuals to perform on a similar level and motivate them to improve performance on any given task such as using mobile phone technology to improve their health maintenance behaviors.

Thirdly, verbal persuasion often influences self-efficacy because of its ease and availability and involves people using strategies such as suggestion, exhortation, and instruction to sway others into certain behaviors (Bandura, 1977). Verbal persuasion is considered a weak method for increasing self-efficacy unless previously established belief in one's abilities is present (Bandura, 1977). However, the influence of verbal persuasion is not well established because previous studies have examined the effect of verbal persuasion on outcomes expectations rather than on enhancing self-efficacy (Bandura, 1977).

In this RCT, TM with personalized reminders to take medications and health education served as “verbal persuasion” for patients to take their medications.

The final source of self-efficacy is a physiological state from which individuals partly judge their capability, strength, and vulnerability (Bandura, 1982). In Bandura’s 1997 explanation of this concept, he previously labeled physiological state as emotional arousal, which refers to the benefit of stressful and threatening situations in informing personal competency (Bandura, 1977). When there is high arousal, it is expected that individuals would not expect success if they are tense and viscerally agitated (Bandura, 1982). As the population of interest in the RCT has recently experienced a MI and/or PCI, their general state may be anxious, thereby diminishing perceived self-efficacy to use mobile technology and adherence to medications. In contrast, anxiety might induce enhanced medication self-administration to avoid the recurrence of a cardiac event.

In his early work, Bandura sought to prove the explanatory and predictive power of his theory through a series of experiments for severe snake phobics who received treatment based on enactive, vicarious, cognitive, and emotional modes of influence (Bandura, Adams, Hardy, & Howells, 1980). The results of the studies confirmed that the various modes of influence all increase self-perceptions of efficacy. Behavior change was directly related to self-efficacy change, independent of the four modes by which self-efficacy was enhanced (Bandura et al., 1980). The four sources of self-efficacy can have a dynamic, synergistic effect on behavior and can influence different types of behavior depending on the expected outcome. An individual's response to the exposure of self-efficacy sources is individualized, and is a result of the dynamic relationship of behavior, personal factors, and environmental factors that will be explored further.

Impact of Self-Efficacy

Self-efficacy has been studied in many dimensions of health behavior change such as health promotion activities, self-management of chronic diseases, and health-maintenance behaviors. A wide variety of populations have been studied in many contexts. Prior research on self-efficacy showed that it is indeed a high predictor of health-related behavior and has been well studied in the areas of exercise, smoking cessation, and heart failure. Given the potential of self-efficacy to change behavior, research interventions have been implemented to increase perceived self-efficacy. Beyond the spheres of health behavior and psychology, self-efficacy has also been studied extensively in the contexts of organizations and education.

According to Jeng & Braun (1994), SET and the Health Belief Model have been the most frequently employed theories in cardiac rehabilitation research. Research studies measuring self-efficacy emerged in the early 1980s. In a study of post-MI patients, self-efficacy scores were more effective than peak treadmill heart rate in predicting the intensity and duration of subsequent physical activity (Ewart, Taylor, Reese, & DeBusk, 1983). Researchers concluded that self-efficacy to perform moderately intense activities of daily living at the time of hospital discharge was the best predictor of functional and social status in patients who had coronary artery bypass grafting (Allen, Beck, & Swank, 1990).

The impact of self-efficacy has been studied in regards to medication use, smoking, healthy eating, exercise, weight control, and controlling disease (Sol, van der Graaf, van Petersen, & Visseren, 2010). Participants were treated for one year through office visits and telephone calls on cardiovascular risk factor reduction and received support in self-management of healthy living based on SET (Sol et al., 2010). Improved self-efficacy was associated with more physical activity, healthy food choices, and general control of cardiovascular disease although there was no improvement in smoking or alcohol intake (Sol et al., 2010). Medication adherence scores were very high at baseline and did not change based on the intervention (Sol et al., 2010).

Beyond studying self-efficacy in the context of self-management of chronic disease and health status, researchers have also established the link between self-efficacy and long-term clinical outcomes such as hospital admissions and all-cause mortality. In a prospective cohort study called the Heart and Soul Study, the association of self-efficacy with objective measures of cardiac function (i.e., exercise treadmill test, echocardiogram, and stress echocardiogram) was evaluated (Sarkar, Ali, & Whooley, 2009). Low self-efficacy was associated with worse baseline cardiac function and with increased risk of HF hospitalizations in 1,024 ambulatory patients with coronary heart disease (CHD) over 4.3 years (Sarkar, Ali, & Whooley, 2009). This suggests that self-reported cardiac self-efficacy provides a rapid, potentially useful assessment of cardiac function for ambulatory CHD patients (Sarkar, Ali, & Whooley, 2009). The authors concluded that self-reported self-efficacy may add additional insight beyond the standard data in the ambulatory setting about risk for hospitalization, and perhaps mortality.

According to Bandura (1986), perceived self-efficacy can impact outcomes such as chosen course of action, effort, perseverance through obstacles and failures, resilience to adversity, self-hindering or self-aiding thought patterns, coping skills with environmental demands, and the level of accomplishments that are realized. The development of an individual's perception of self-efficacy comes from previously perceived efficacy, symbolic meaning attached to the behavior and its expected outcome, affective states, motivation for action, and selection of attention and environment (Bandura, 1997). Bandura (1982) describes factors that diminish the effect of self-efficacy on behavior including faulty self-knowledge, misjudgment of task requirements, unforeseen situational constraints on actions, disincentives to act on one's self-perceptions of efficacy, ill-defined global measures of perceived self-efficacy or performance, and new experiences that result in reappraisals of self-efficacy.

Measurement of Self-Efficacy

Bandura (1997) states that self-efficacy should be measured specifically to a defined activity in a particular context and environment with consideration of barriers and behavioral challenges (Clark & Dodge, 1999). For example, post-MI patients can feel confident about their ability to eat a healthy diet but have no confidence in their ability to lose weight. Self-efficacy should not be considered as generalizable to all behaviors. This is partly because the four sources of self-efficacy are considered to vary across different activities and also possess a dynamic, synergistic effect. The specialization of self-efficacy is supported by the development of specific self-efficacy tools to measure specific behaviors. In the context of the present RCT, self-efficacy will be measured with a general self-efficacy tool (Generalized Self-Efficacy Scale) and also one that is specific for medication adherence (Self-Efficacy for Appropriate Medication Use Scale), to determine whether using mobile technology will increase self-efficacy (Risser, Jacobsen, & Kripalani, 2007; Scherer & Maddux, 1982).

Self-Efficacy and Mobile Technology

Mobile technology continues to grow in potential when considering its impact on self-efficacy. As discussed earlier, technology can be a means of self-efficacy through several different sources such as performance accomplishments, vicarious experiences, verbal persuasion, and emotional arousal. Although there are many studies that have examined the use of mobile phone interventions in behavioral change, four studies have specifically examined the effect of mobile phones on self-efficacy.

In one RCT, a significant mediating effect of self-efficacy in smoking cessation was found by showing differences in self-efficacy scores between HIV/AIDS patients who received proactive counseling sessions with pre-recorded messages via their mobile phones compared to patients who received recommended standard of care (p = 0.02) (Vidrine, Arduino, & Gritz, 2006). Another RCT targeting smoking cessation included the use of multi-media with

54 weeks of e-mail, web pages, interactive voice response, and text messaging and showed a significant difference in adherence to nicotine replacement therapy and a higher level of post-cessation self-efficacy in the treatment group compared with the control group ($p < 0.001$) (Brendryen & Kraft, 2008).

A pilot study demonstrated positive changes in diabetes management self-efficacy along with improved levels of glycosylated hemoglobin and diabetes self-care activities among patients who received daily coaching using patients' clinical data via their mobile phones (Katz & Nordwall, 2008). Another diabetes intervention using Sweet Talk, a text-messaging support system designed to enhance self-efficacy, facilitated uptake of intensive insulin therapy and improved glycemic control in pediatric patients with Type 1 diabetes (Franklin, Waller, Pagliari, & Greene, 2006). The intervention was associated with improvement in diabetes self-efficacy ($p < 0.005$), self-reported adherence ($p < 0.05$), and diabetes social support ($p < 0.001$) although it did not have a positive influence on glycemic control (Franklin et al., 2006).

These four studies demonstrate the potential for mobile phone technology to increase self-efficacy leading to behavior change. As described above, SET has been examined in studies related to behavioral change such as smoking cessation and the management of chronic conditions such as diabetes. In the next section, the potential for mobile technology to influence self-efficacy to enhance medication adherence in the RCT will be discussed beginning with the theoretical model that was constructed using SET.

Theoretical Model

Self-Efficacy Theory postulates that human agency (or intention) is developed and maintained on the basis of three interactions: a) personal factors in the form of cognition, affect, and biological events; b) behavior; and c) environmental influences (Bandura 1986; Pajares, 2010). This transactional view of self and society results in a triadic reciprocity, which he describes as the concept of reciprocal determinism (Bandura, 1986).

The SET includes three interacting determinants influence each other bidirectionally, as reflected in Figure 2, but the idea of reciprocity does not equate to equal strength among the determinants. The influence of each of these factors varies for different activities and circumstances, as it takes time for a causal factor to exert its influence (Bandura, 1986). The triadic model in Figure 2 is commonly cited as the theoretical model that explains SET, although self-efficacy was added by the author to add clarity to the theoretical model. As noted previously by Pajares (2010), self-efficacy is at the core of this theory.

A revised theoretical model was developed for the current study based on SET and shows the dynamic interaction of self-efficacy and three major corresponding components addressed in the proposal: medication adherence, personal factors, and social support. For this study, behavior from the SET will be considered a proxy for medication adherence; personal factors will refer to sociodemographic and clinical characteristics; and environment will be operationalized as social support (Figure 3). The RCT was designed to study the potential relationships between mobile phone use, self-efficacy, and the three components identified in the model.

The theoretical model in Figure 4 shows a bidirectional relationship between each of the three determinants of human behavior and overlaps with self-efficacy because of the interplay that exists between each of these components. As depicted in Figure 4, self-efficacy is central in the model because of its relationship to each of the components. The varying relationships between the variables will now be examined beginning with the outcome variable of the research study, medication adherence, and its association with self-efficacy. Personal factors and social support will then be examined in the context of medication adherence as it is the outcome variable of the study.

Self-Efficacy Theory and Medication Adherence

Several studies have validated the association between self-efficacy and medication adherence. The direct relationship between these two constructs was not examined in this research study, however the mediating effect of self-efficacy to influence medication adherence will be analyzed. The close association between increased self-efficacy leading to improved medication adherence has been previously established by the following studies. Self-efficacy predicted disease management behavior such as medication and dietary adherence, exercise, and managing stress (Clark & Dodge, 1999). Self-efficacy has also been associated with increased rates of adherence to blood pressure medications among African-American women (Warren-Findlow, Seymour, & Brunner, 2011).

Personal Factors and Medication Adherence

Bandura's (1986) original concept of personal factors included cognitive, affective, and biological events. In this RCT, personal factors referred to select sociodemographic and clinical characteristics. Among the select personal factors, many have been shown to have a significant impact on medication adherence such as older age, marital status, level of education, employment, presence of comorbidities, and polypharmacy (Chiou et al., 2009; Dunbar-Jacob, Bohachick, Mortinmer, Sereika, & Foley, 2003; Gatti, Jacobson, Gazmararian, Schmotzer, & Kripalani, 2009; Ho et al., 2006; Maddox & Ho, 2009; Mann, Allegrante, Natarajan, Halm, & Charlson, 2007). However, conflicting data and views may exist about certain factors that put individuals at risk for poor adherence. For example, older adults have been identified as having better adherence for many reasons including that they consider their condition seriously, have less hectic or busy schedules, and have a routine for taking their medications (Billups, Malone, & Carter, 2000). At the same time, older adults face challenges in adhering to medications because they can have financial difficulty and cognitive deficits that affect memory. This represents the complexity of studying medication adherence and the importance of assessing individuals' risk based on collective data in different aspects such as their health belief of taking medications, use of reminder systems, and ability to afford medications.

One of the clinical characteristics that is associated with medication adherence includes depression. Depression is often presented in the literature as a risk factor for nonadherence. Depression is commonly associated with CHD and can have significant effects on medication adherence (Garner, 2010). One third of patients with recent MI, acute coronary syndrome, or congestive heart failure will meet criteria for minor or major depression, and even mild depression can dramatically alter adherence to medical therapy (Jiang, Glassman, Krishnan, O'Connor, & Califf, 2005; Garner, 2010).

Improving our understanding of the modifiable patient characteristics that predict poor adherence has been limited to date and will be a key step in planning effective interventions (Mann et al., 2007; Swanlund, Scherck, Metcalfe, & Jesek-Hale, 2008). Factors leading to medication adherence may be extremely complicated and interventions should be tailored to each individual. One of the first steps to identify individuals who are at high risk for nonadherence is to recognize the physical, psychosocial, and practical challenges of medication adherence. This RCT identified the personal factors and social support factors that correlate with medication adherence in patients with CHD using SET to help inform this research.

Social Support and Medication Adherence

Social support was examined as a surrogate for environment from Bandura's original model. As described earlier, environment is one of the three major determinants of human agency, or acts done intentionally, thus social support is thought to be a predictor of behavior. Extensive research and literature has supported the power of involving family members and caregivers in patient care with acute and chronic illness. Bandura also outlined social support as a major source of self-efficacy.

A systematic review and meta-analysis of 25 studies in the etiology and prognosis of CHD provided insight into the significance of two different forms of social support in the post-MI population (Barth, Schneider, and von Kanel, 2010). The first form is functional support, which describes the help and encouragement by a social network (e.g., helping with tasks, providing information, helping evaluate situations, and feeling loved), while structural support refers to individuals' interaction with the network (e.g., number of contacts, frequency of communication, membership in groups, and marital status) (Barth et al., 2010). Among the etiologic studies, evidence showed that low functional social support may influence the prevalence of CHD with a relative risk range of 1.00-2.23 (Barth et al., 2010). In prognostic studies, results consistently showed that low functional support affects cardiac and all-cause mortality with a relative risk range of 1.59-1.71 (Barth et al., 2010). The influence of structural support was less clear in this meta-analysis. The authors concluded that interventions to increase perceived functional social support in patients with CHD are important to improve cardiovascular and all-cause mortality (Barth et al., 2010).

Other studies specifically addressed the impact of social support on medication adherence. A recent study demonstrated that strong social support was a predictor of adherence to antihypertensive medications (Criswell, Weber, Xu, & Carter, 2010). Along with examining self-efficacy as previously described, researchers performed a post-hoc analysis of two RCTs of a physician-pharmacist collaborative intervention to provide intensified hypertension management and counseling (Criswell et al., 2010). The investigators found a significant improvement in social support scores ($p < 0.05$) in the intervention group who involved family members and educated the patient regarding treatment decisions and options (Criswell et al., 2010).

One study among post-acute coronary syndrome patients demonstrated a significant interaction between higher partner stress (perhaps a surrogate for low social support) and nonadherence (Molloy, Perkins-Porras, Stroke, & Steptoe, 2008). This study examined whether social network size (structural social support) and partner stress predicted medication adherence, cardiac rehabilitation attendance, and quality of life 12 months following hospitalization. Among the 193 patients, partner stress predicted medication nonadherence (odds ratio: 2.89, 95% CI = 1.21, 6.95). Patients with large social networks were more likely to attend rehabilitation (odds ratio: 3.42, 95% CI = 1.42, 8.25). Both partner stress and smaller social network size were associated with poorer quality of life and may partly influence cardiovascular morbidity and mortality through recovery behaviors and maintenance of quality of life.

The meta-analysis of social support and CHD-related studies as well as those related to medication adherence demonstrated the close link between social support and health outcomes and behavior. Effective interventions to enhance existing relationships or promote other social networks (e.g., cardiac rehabilitation or technology-based support groups) can improve medication adherence or other health-related behaviors.

Self-Efficacy as a Mediator

The present RCT examined the impact of TM with medication reminders and health education to influence self-efficacy by comparing self-efficacy scores at baseline and after 30 days. Self-efficacy was examined as a mediator of medication adherence. The role of self-efficacy as a mediator to behavior is outlined in one of Bandura's (1977) earliest writings, "Self-Efficacy: Toward a Unifying Theory of Behavioral Change." Self-Efficacy Theory includes two types of expectations that have strong influences on behavior and outcomes: efficacy expectations and outcome expectations. Figure 5 is illustrated from Bandura's work in 1977 and shows the difference between efficacy expectations and outcome expectations.

Bandura (1977) describes efficacy expectation as a conviction that one will successfully execute the behavior that is required to produce the outcome, whereas outcome expectation is an individual's estimate that a given behavior will lead to certain outcomes. Bandura (1977) differentiates efficacy and outcome expectations because individuals can believe a particular behavior will produce an outcome, but an outcome can be compromised if they have serious doubts about their ability to perform the behavior (low perceived self-efficacy). Efficacy expectation is multi-faceted and includes the decision to perform an activity, effort expended in performing the activity, and persistence in the behavior despite possible barriers (Jeng & Braun, 1994). Efficacy expectations appear to have greater relevance in predicting behaviors and are often the focus of behavior interventions (Jeng & Braun, 1994). In this RCT, self-efficacy is believed to mediate the process by which a person behaves in taking their prescribed cardiac medications.

Summary

An overview of SET along with a review of self-efficacy in behavioral change interventions with specific applicability to the dissertation study has been presented. In review, Bandura (1986) describes human agency, or intention to act, as the product of a dynamic interplay of personal, behavioral, and environmental influences. Self-Efficacy Theory incorporates the core role of self-efficacy in these bidirectional relationships that determine behavior. According to Bandura (1997), self-efficacy is part of a self-regulatory process through which individuals transform intrapersonal resources, behavior, and environmental resources toward a desired goal. The pilot RCT evaluated the influence of receiving mobile phone TM for medication reminders to increase self-efficacy. The mediating effect of self-efficacy on medication adherence was evaluated.

Self-Efficacy Theory is believed to be a relevant theory in the context of this research intervention because it is one of the most powerful determinants of behavioral change. Bandura (1997) reported that a shift was required from scaring people into positive health behaviors to providing them with tools to have personal control over their health habits. By providing a medication reminder intervention for patients with CHD, it was expected that the TM reminders would increase self-efficacy, or personal control and confidence, in their medication adherence behaviors. Building self-efficacy that leads to successful medication adherence is expected to ultimately lead to optimal health outcomes for patients who live with chronic disease.

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Figure 1. Sources of Self-Efficacy (Bandura, 1997)

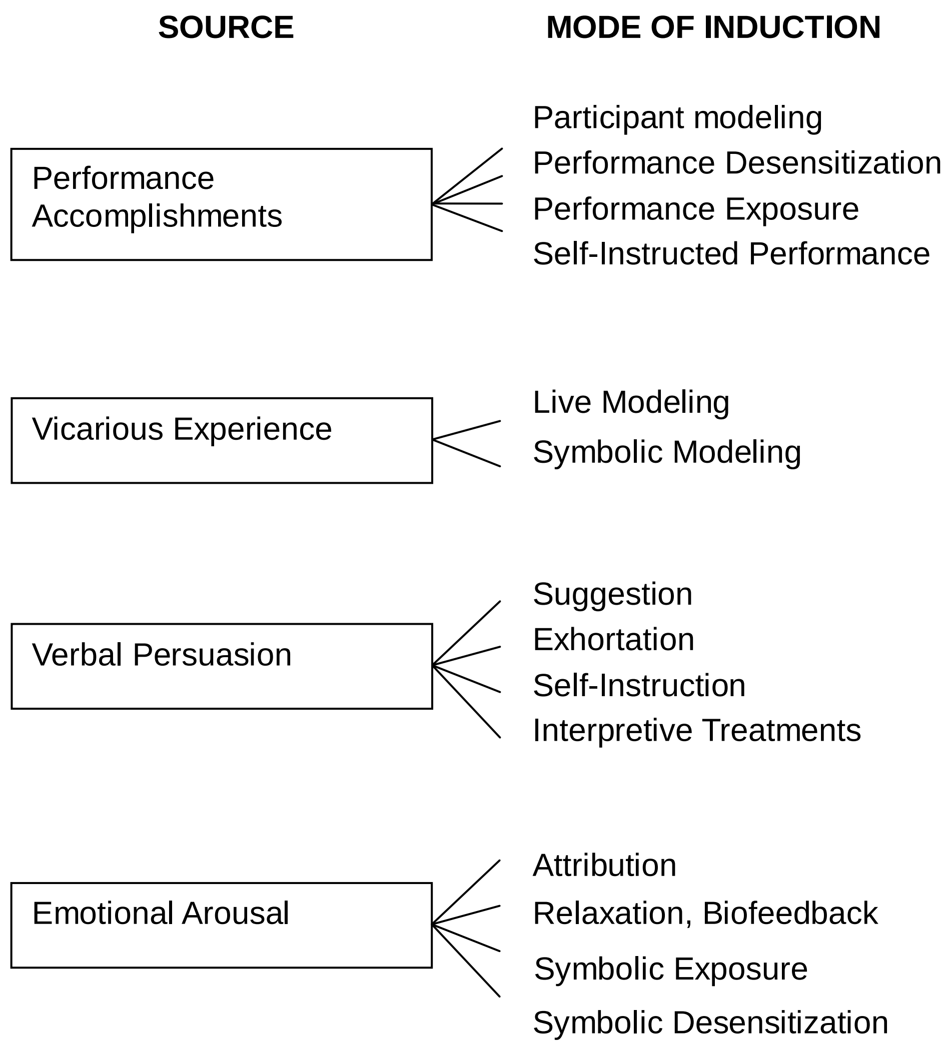


Figure 2: Revised Self-Efficacy Theory (*Self-Efficacy not in original model)

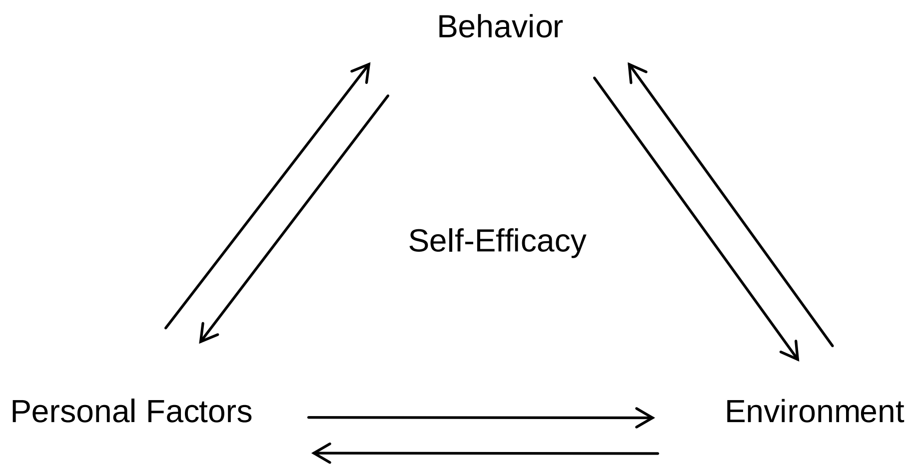


Figure 3. Corresponding Components of Self-Efficacy Theory and Text Messaging Intervention

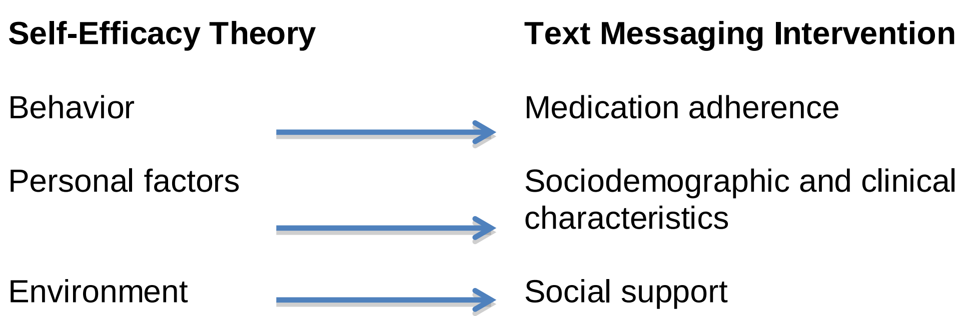


Figure 4: Theoretical Model for Mobile Technology to Promote Medication Adherence Applying the Revised Self-Efficacy Theory

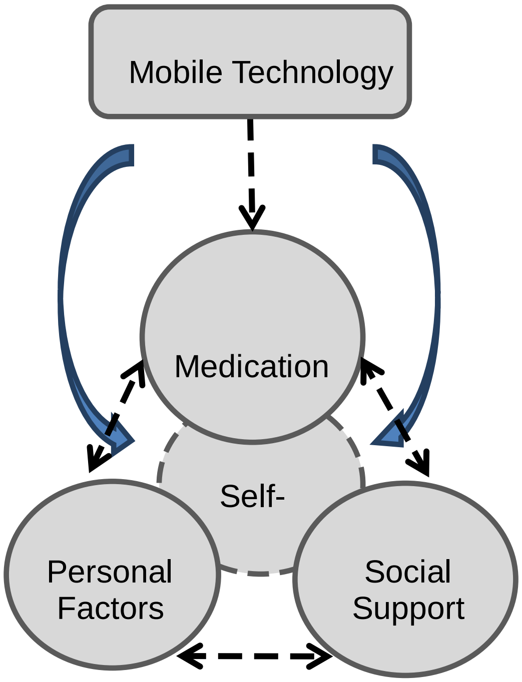
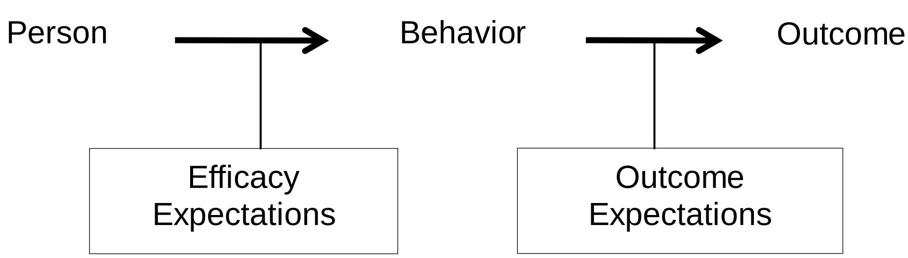


Figure 5: Self-Efficacy as a Mediator to Behavior (Bandura, 1977)



Chapter 4

Electronic Measurement of Medication Adherence in Older Adults

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Electronic Measurement of Medication Adherence in Older Adults

Abstract

Background: The measurement of medication adherence is important in both clinical practice and research settings. Accurate measurement of medication includes acquiring data on patterns of medication use and is prerequisite to offering effective medical therapy, improving clinical outcomes, and determining the efficacy of the therapy.

Objectives: The aims of this paper are to: 1) present a brief overview of current electronic methods of medication measurement; 2) explore the advantages and disadvantages to each approach; 3) discuss future trends in medication adherence assessment; 4) and promote the role of nurses in measurement of medication adherence.

Method: A comprehensive review of electronic forms of medication measurement was performed. A description of each method along with the advantages and disadvantages is presented including oral and inhaled electronic monitors, personal electronic devices, mobile phones, electronic blisters, electronic health records, and video and photo-assisted observation.

Discussion: Electronic monitoring of medication self-administration is under rapid development. Nurses can play an integral role in promoting medication adherence by adopting electronic forms of medication measurement. Advances in technology will continue to develop and influence the future of electronic medication measurement to enhance patient care.

Key Words:
Medication, medication adherence, measurement, electronic

1. Introduction

Medication nonadherence is a major global challenge as more than half of individuals with chronic diseases do not take any or all of their medications correctly [1, 2]. In developing countries with limited resources and access to health care, medication nonadherence is assumed to have even greater magnitude and impact [2]. Medication adherence is an important phenomenon for all individuals, but particularly for older adults and those with chronic illness. On average, patients over 65 years old take five medications and experience issues with polypharmacy, cost, cognitive impairment, and frailty [3, 4]. Among patients with chronic diseases, the complexity of medication regimens is magnified when considering dosage frequency and special instructions for use [5-7]. Medication nonadherence is a major barrier to achieving optimal health as demonstrated by increased rates of emergency department visits, hospitalizations, morbidity, and mortality that are attributed to intentional or nonintentional medication nonadherence [8, 9].

The measurement of medication adherence is important in both clinical practice and research settings. In clinical practice, accurate measurement of patient medication administration is a prerequisite to medication adherence, in addition to offering effective medical therapy that optimizes clinical outcomes. In research settings, accurate assessment of medication adherence will lead to conclusive data about the efficacy of the therapy or intervention being tested. Nurses can address the barriers for medication adherence and can be integral change agents in promoting innovative medication measurement in clinical practice and research that is tailored to specific interventions and individual patient groups.

2. Background of Medication Adherence Measurement

Measurement of medication adherence has traditionally included acquiring data on patterns of medication use from sources such as patient self-report (i.e., interviews, diaries, questionnaires). Direct observation and pill counts have been other popular and inexpensive methods to record adherence. Clinical signs can be followed to track improvement of certain medical conditions (i.e., blood pressure as a biomarker for hypertension or pedal edema as a sign of hypervolemia). Biomarkers provide vital clinical information about medication adherence, and they are defined as characteristics that are objectively measured as indicators of normal biologic, pathogenic, or pharmacologic processes to therapeutic intervention [10]. Biomarkers include laboratory tests that assess clinical status and management of chronic disease (e.g., cholesterol levels and viral loads) or other physical samples that test for direct concentration levels of medications (e.g., in blood, urine or hair). Hair analysis has become a more popular form of measurement and may offer an appropriate alternative to blood and urine testing by providing information on the quantity of drug administered over a longer period of time (weeks to months) [11]. A rarely used form of medication adherence measurement is the addition of metabolites to medications in order to prove ingestion of medications (e.g., low doses of digoxin, phenobarbital, bromide, and riboflavin) [12, 13]. A preferred approach to achieve accurate measurement is to use multiple direct and indirect sources including use of biomarkers and self-report [1].

Electronic monitoring of medication self-administration is under rapid development. Electronic devices have been available for use in clinical and research settings in the form of electronic pill containers [Medication Events Monitoring System (MEMS)] and metered dose inhalers (MDI's) and continue to be a popular form of measurement. Future measurement methods that are under investigation and development include use of the mobile phone, other forms of home-based electronic devices, electronic medication blisters, video and photo-assisted observation, and electronic health records. The current methods of electronic measurement are summarized in Table 1. The aims of this paper are to: 1) present a brief overview of current electronic methods of medication measurement; 2) explore the advantages and disadvantages of each approach; 3) discuss future trends in medication adherence assessment; 4) and promote the role of nurses in measurement of medication adherence.

3. Electronic Monitoring Modalities

3.1 Oral Medication Monitors - The MEMS is a computerized monitoring system that includes a computer chip located inside a standard pill bottle cap. The MEMS allows data, including the date and time of bottle opening, to be downloaded to a computer [14]. The MEMS is a common objective method of measuring medication adherence, and it is generally well accepted by patients [15, 16]. The MEMS can identify patterns of nonadherence such as the "toothbrush effect" or "white-coat adherence", which pertain to patients improving their medication taking behavior in the ten days preceding an appointment with their health care provider [16].

Another electronic medication monitor is MedSignals, which is an organizer that consists of four plastic containers to monitor patients taking multiple medications. It stores data from every lid opening, creating a record that is time-stamped and documented in real time [17]. Data are uploaded automatically on an immediate, daily or weekly basis to a host server on the Internet [17]. Since 2008, data have been transferred through a telephone line, but a new model allows mobile phones with Bluetooth technology to monitor individuals remotely and immediately transfer the data to patient records [17]. MedSignals reminds patients and caregivers about medication schedules through personalized alerts via email, text, fax, customized electronic medical records connections, or automated phone calls in various languages [17]. Settings are displayed for each plastic container so clinicians and researchers are able to remotely monitor medication use [17]. MedSignals is tailored for health care providers, researchers, home health agencies, and caregivers and is available for consumer purchase unlike MEMS, which is unavailable for personal use.

The benefits of the electronic oral medication monitors cannot be discounted as they document drug holidays (missing doses for at least two consecutive days) or overuse of medication [16]. However, disadvantages of the electronic oral medication monitors include the inability to confirm how many pills were removed from the bottles and containers or if the pills were actually consumed. Electronic oral medications monitors also have potential mechanical problems. For example, problems reported with the MEMS device include equipment, battery, or actuator switch failure, as well as patients damaging the cap or placing it near a microwave oven [15]. Other issues with MEMS devices include the need to carry the pill bottle for medications that require more than once daily dosing, which poses a problem for men who do not carry a purse [15]. In addition, patients may resist using the MEMS device because it is necessary to use individual bottles instead of the convenience of their pill organizer. Another consideration is the time and ability to download the data from electronic sensors to the computer. Overall, the clinical benefit of the MEMS and MedSignals is limited by the high cost of the monitors and software.

3.2 Inhaled Medication Monitors - Several electronic monitoring mechanisms are available for MDI's and nebulizers. Examples of electronic MDI's include the DOSER, MDI Chronolog, MDILog, and Smartinhaler while the Nebulizer Chronolog is an example of a nebulizer that electronically monitors use. The DOSER is an electronic MDI with a microchip that displays the number of inhalations taken within a 30 day period [18]. The SmartInhaler contains a microprocessor to record adherence with optional audiovisual reminders (i.e., emitting different levels of light and sound) [18]. The MDI-Log and DPI-Log are more sophisticated devices than can monitor more than one thousand actuations and are downloadable by the patient, caregiver, and clinician for viewing [18]. The microchip monitors both actuation and inhalation from aerosol and dry powder devices, and downloaded information allows clinicians to make more informed treatment decisions relative to inhaler adherence [18].

Electronic inhaled medication monitors are able to detect the major limitation of “dumping” that may occur with inhaled medications [19]. “Dumping” is the act of discarding unused medications before they are checked for adherence and is a phenomenon noted by several investigators who reported 15% of the control group dumped over 100 actuations of the inhaler’s contents in a three hour period, whereas no dumping was found among the treatment group [20]. Similar to other electronic monitors, equipment failure and inability to confirm ingestion of medications are disadvantages associated with inhaled monitors [19]. Other disadvantages are similar to oral medication monitors such as additional costs and time with using the equipment, software, and personnel along with potential mechanical failures.

3.3 Personal Electronic Devices - Advancements in technology are allowing patients, caregivers, and clinicians to make strides with adherence to self-administration of medication. Several patient-friendly electronic alarm systems are available commercially for pill organizers, watches, and pagers. Personal home monitors are becoming available for consumer use. For example, GlowCaps is a digital pill bottle that sends messages via lights, sounds, music, and automated phone calls and is an excellent alternative to traditional pill containers and reminder systems for home use [21]. An electronic chip on the pill cap monitors when the bottle is opened and wirelessly sends alerts through a mobile network to individuals or their caregivers. GlowCaps also have a button that uses mobile connectivity to contact the patient's pharmacy for refills then triggers an automatic callback to confirm the request [21]. The use of GlowCaps generates a weekly email summary with personalized information that can be shared with a "health buddy" and compliance reports are mailed to designated health care providers monthly [21]. Thus, these devices help build a network of social support from caregivers and health care providers.

Testing is currently underway to introduce another form of a personal electronic pill device referred to as a GlowPack. The GlowPack is a resealable pouch that holds blister packs, inhalers, injectable solutions, liquid medication, and topical ointments that works similarly to the GlowCap [21].

Since GlowCaps have only been available since early 2013, it is premature to discuss the willingness of consumers to purchase and use the medication devices. At the current time, GlowCaps are only available for purchase through one pharmacy chain and are not covered by insurance, which militate against their widespread use. However, the personal investment may help engage patients and caregivers in using the device to promote medication adherence. In addition, monthly service plans allows for connectivity to an assigned wireless network but incurs additional costs to using the device. With the rapid development of technology and research, it is likely that personal electronic devices will gain greater acceptance and popularity as our society becomes more adept related to electronic and wireless forms of self-monitoring.

3.4 Mobile Phones - Researchers are currently investigating the use of mobile phones to promote adherence to medications. Given the popularity of mobile phones, intervention studies support that this modality may be feasible and effective in promoting adherence and managing acute and chronic disease [22-24]. Text messaging interventions using short message service (SMS) have been most widely applied, while few investigators have tested interventions using a mobile phone application. Once a patient has responded to a reminder alert to take medications or an application is used, two-way messaging can verify intake of medications. This electronic medication diary may be a viable way to promote medication adherence, particularly when strict adherence is required (e.g., in high risk populations such as HIV patients and patients following organ transplant).

Research using mobile phones to improve medication adherence has demonstrated conflicting results. The potential for mobile phone use in health care has not been well defined and remains a tremendous opportunity for future research, especially for patients with chronic diseases requiring lifelong medication adherence for optimal outcomes. In the future, further integration of mobile phones with electronic health records (EHR) can support communication between patients and their health care providers.

Disadvantages of using mobile phones may be deterioration of interest as the novelty of monitoring adherence wanes over time. Factors that maintain engagement of participants remain unknown and serve as important gaps in research. The long-term impact of mobile health interventions is needed to document the efficacy and sustainability of these interventions on medication management. Individuals who are less technically inclined, such as older adults may have difficulty with using mobile phones for medication monitoring due to unfamiliarity with text messaging or using applications, difficulty with fine motor skills, and resistance to using mobile phones for the purpose of monitoring.

3.5 Electronic Blisters – Medication paper blisters have been used by pharmacists in the past to monitor medication use, however this technique has been unreliable given the patient has the ability to "dump" medications. Smart Blisters are radio-frequency enabled self-adhesive labels that can be affixed to existing standard medication blister packages and have been tested by researchers with promising results [25]. This medication monitoring system uses wireless data transmission and Internet server storage capabilities to maintain data [25]. Although Smart Blisters are still in an early development phase, the concept of using this type of electronic technology adds another option for monitoring.

High cost and an inability to confirm ingestion of medications are pertinent disadvantages to this method of adherence assessment. In addition, using blisters may be challenging for patients who have a complex medication regimen and use pill organizers. Mechanical failures are also potential disadvantages to accurate medication monitoring.

3.6 Electronic Health Records - Maximizing the potential of EHR and pharmacy records can be a valuable way to measure medication adherence and maintain a permanent history of medication use. The expanded development of EHR such as electronic prescribing [26] can promote communication on medication information between health care providers, hospital systems, pharmacies, and patients. Improving interdisciplinary communication through an integrated EHR will be a critical step in improving the current state of adherence and optimizing the clinical value it can bring to patients.

The current system must transition from an organization-specific EHR that stores health records to one that can seamlessly transfer valuable medication information to a broader network of providers and patients. Data that are available through pharmacy records are limited to the dates the medication was dispensed, which may not reflect actual medication administered [27]. Historically, refill records have been restricted to health care providers in closed clinical settings such as large health organizations (e.g., the Veteran's Administration and Kaiser Permanente), although some large pharmaceutical companies are reporting patterns of medication refills to providers. Open communication between health care providers and pharmaceutical companies needs to be developed and strengthened in order to use pharmacy records as a viable source of measuring medication use. Dependency on the health care team to accurately input data and for patients to communicate any changes that have been made outside the system is also a potential disadvantage to this mode of adherence measurement.

3.7 Video and Photo Assisted Observation - Researchers have piloted the use of mobile direct observation of treatment by having tuberculosis patients in Kenya transmit daily video recordings via mobile phones of medication self-administration [28]. Using mobile health technology may be a substitute for face-to-face visits with health care workers in remote areas where the incidence of tuberculosis and autoimmune deficiency is high and medication adherence levels are suboptimal. Video assisted methods to measure adherence may be most valuable in regions where patients would be required to travel long distances to meet with health care providers for a short period of time for the purpose of monitoring treatment.

Another innovative way to measure adherence is to have patients take pictures of medications prior to self-administration with mobile phones [29]. Mobile technology such as the mobile phone is likely to influence medication adherence measurement in the future due to its ubiquitous use.

Video and photo assisted observation can significantly reduce costs of personnel resources, however this mode of adherence measurement requires regular surveillance and communication with patients. This method requires dependable wireless services and more significant patient participation than other forms of adherence measurement.

4. Discussion and Implications for Nurses

Electronic methods for measuring medication adherence are developing rapidly. Most electronic methods are more costly than traditional methods of self-report and may limit their use in both clinical practice and research. Development of more clinician- and patient-friendly methods of monitoring and evaluating adherence are necessary to bring the issue of medication adherence measurement to the forefront of clinical encounters as opposed to restricting it to research settings. Another prerequisite to successful measurement of medication adherence is patient participation with electronic devices. The rapid integration of technology with daily living such as smartphones will continue to change monitoring and measurement techniques.

Examining medication adherence from a wider scope, a radical transformation is needed within the nursing, medical, and pharmacy communities to support surveillance and remedy barriers to medication adherence such as making a connection to clinical outcomes after distribution of prescriptions. Furthermore, changes in health policies may be required to keep prescribers and pharmacies more accountable to monitor adherence.

Future trends in medication measurement include use of electronic devices with remote monitoring that allow instant feedback on medication adherence for patients, caregivers, clinicians, and researchers. Although a variety of electronic methods of medication measurement are currently available and even more are in development, other methods of measuring medication adherence will remain important in both nursing research and clinical practice. Multiple methods of measurement can corroborate adherence behaviors. The importance of maintaining effective communication with patients cannot be underscored when using electronic devices and other traditional methods of measurement. The availability and development of technology will continue to reshape the measurement of medication adherence.

The electronic methods that have been described can provide resources for nurse clinicians and researchers to monitor patients by innovative and multifaceted methods. Nurses are in a unique position to enhance medication adherence by implementing best clinical and research practices. Nurse practitioners, in particular, have specialized education and training to assess, prescribe, and monitor medication adherence [4]. In clinical practice, all nurses can promote medication adherence by coordinating interdisciplinary collaboration with a team of physicians, pharmacists, and nurses to ensure accurate medication use through effective communication with patients and caregivers.

Although the focus of this review has been on electronic measurement of medication adherence, we recognize that nurses' responsibilities go beyond assessment of patients' medication behaviors. Nurses teach self-management skills and have successfully used case-management, education, behavioral counseling, and social support to improve adherence and health outcomes [2, 29, 30]. Nurses have significantly contributed to improvement of medication adherence through tailored, multifaceted interventions, as well as through persistent and long-term follow-up [31]. Nurses can be strong patient advocates by providing individualized counseling on medication adherence such as using memory aids, pill organizers, and minimizing the complexity of the medication regimen.

Nurses can also lead interventions to promote medication adherence with their research training and further translate effective interventions to clinical practice. Initiating comparative effectiveness studies among medication measurements can also add a significant contribution to the adherence literature. The booming growth of the older population and increased prevalence of co-morbidities make medication non-adherence a critical problem to address in clinical and research settings [6, 22]. Nurses can be a vital force in an interdisciplinary effort to improve medication adherence for all populations by applying innovative methods to promote and measure adherence.

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Table 1. Electronic Measurement Methods of Medication Adherence

Future Methods	Description	Advantages	Disadvantages
Oral and inhaled monitors	Electronic system that digitally records	Patterns of use are provided; Well accepted by patients	Costly; Requires software and analysis; Potential equipment problems with battery, actuator, switch, or damage to the cap; Each pill bottle contains one medication type; Activation does not necessarily reflect ingestion of medication
Personal electronic devices	Devices that monitor medication use (pill bottles, mobile phones)	Patient friendly; Reminds patients to take medications	Potentially costly; Potential technical difficulties; Efficacy not established
Mobile phones	Text messaging and applications using personal mobile phones	Mobile phones are used ubiquitously; easily accessible for patients	Potential to produce “alarm effect” after long term use; Older patients may be resistant; Efficacy not established
Electronic blisters	Radio-frequency enabled labels affixed to standard paper blister packages	Uses wireless technology and allows real-time data transmission	Potentially costly; Potential technical difficulties; May be challenging to use with complex medication regimen
Electronic health records	Medication records available for universal use	Does not require patient participation; produces a history of medication use	Privacy may be compromised; May not include most updated information
Video and photo assisted observation	Patients record themselves taking meds via video or mobile phone	Cost-saving compared to direct observation (travel costs, labor from health care or research personnel); More convenient	Requires maintenance of video or other equipment; Requires frequent recording by patient and monitoring by health care or research personnel

Chapter 5

A Text Messaging Intervention to Promote Medication Adherence for Patients with Coronary Heart Disease: A Randomized Controlled Trial

Chapter 5

A Text Messaging Intervention to Promote Medication Adherence for Patients with Coronary Heart Disease: A Randomized Controlled Trial

Abstract

Introduction: More than half of individuals with chronic diseases do not take medications as prescribed. Pharmacologic treatment for secondary prevention of coronary heart disease (CHD) is critical to prevent adverse clinical outcomes. The primary aim of this randomized controlled trial was to compare adherence to antiplatelet and statin therapy among patients after myocardial infarction and/or coronary stent procedure who: 1) received text messages (TM) for medication reminders and health education (TM Reminders + TM Education), 2) received TM for health education (TM Education Alone), and 3) did not receive TM (No TM). We hypothesized that the two intervention groups would have better adherence as compared to the No TM group.

Methods: A mobile health intervention was designed to deliver customized TM for 30 days. We assessed and analyzed medication adherence with electronic monitoring devices [Medication Event Monitoring System (MEMS)] by One-Way ANOVA and Welch tests, two-way TM response rates by *t*-tests, and self-reported adherence (Morisky Medication Adherence Scale) by Repeated Measures ANOVA.

Results: Among 90 patients (76% male, mean age 59.2 years), MEMS revealed a significant difference in adherence among groups for antiplatelets only ($p < .05$). Specifically, the TM Reminders + TM Education group had a higher percentage of correct doses taken (88.0 ± 14.0 vs. 72.4 ± 27.6; $p = .016$) and a higher percentage of prescribed doses taken on schedule compared to the No TM group (86.2 ± 15.4 vs. 69.0 ± 29.2; $p = .01$). The TM Education Alone group had a higher percentage number of doses taken compared to the No TM group (95.8 ± 9.5 vs. 79.1 ± 27.7; $p = .01$). Two-way TM response rates were higher for antiplatelets than statins (90.2 ± 9 vs. 83.4 ±15.8; $p = .01$). Self-reported adherence improved for all groups over time, but did not differ among groups.

Conclusions: TM increased adherence to antiplatelet therapy demonstrated by MEMS and TM responses. This text messaging intervention shows promise in promoting medication adherence in patients with CHD; however, more research is needed to explore the full potential of mobile health.

1. Introduction

Coronary heart disease (CHD) is the leading cause of death and loss of disability-adjusted life years worldwide [1]. Yet among patients who have experienced a myocardial infarction (MI), rates of medication nonadherence range from 13 to 61% [2]. The adherence rate among individuals who live with chronic diseases in the developed world is 50% [3]. The reasons for medication nonadherence are multifaceted and include challenges related to the health system, health condition, and patient characteristics including socioeconomic status and therapeutic regimen [1].

Numerous observational studies have documented a strong association between medication nonadherence among patients with CHD and adverse clinical outcomes such as rehospitalization, morbidity, and mortality [1,4-6]. A study on adherence to medications for secondary prevention of CHD showed nonadherence was associated with 50-80% increased hazard of mortality and 10-40% increased hazard of cardiovascular-related hospitalization [6]. Specifically, premature discontinuation of antiplatelet medications (i.e., clopidogrel) has been associated with a 2-fold increase in rehospitalization and a 9-fold increase in annual mortality [7-8]. Morever, sustained use of statins has been associated with at least a 45% risk reduction in mortality among patients with and without history of CHD, thereby demonstrating their cardioprotective properties [9-10].

As outlined in the secondary prevention guidelines, it is imperative for patients who have experienced a MI or percutaneous coronary intervention (PCI) to adhere to the recommended medication regimen including antiplatelets and statins [10]. Failure to adhere to antiplatelet therapy may cause in-stent thrombosis and death; however, 1 in 5 Medicare patients do not fill their prescriptions by 7 days after PCI with a drug-eluting stent and 1 in 7 fail to do so by 3 months [11]. Furthermore, the rate of adherence with statins is poor, with less than half of patients continuing their medication after 1 year of initiation [12].

Using technology to promote behavioral strategies such as self-monitoring, positive reinforcement, and coaching can facilitate adoption and integration of medication taking into daily life patterns [13]. The use of technology may provide an innovative, practical, and inexpensive means to promote medication adherence when compared to other behavioral and educational strategies that have had disappointing results [14]. Over the past decade, mobile health (mHealth) interventions have been applied to promote management of acute and chronic disease, although their efficacy is still being established. Research specifically focusing on medication adherence has demonstrated a trend toward positive results; however, the data are inconsistent [15-20].

No studies have been reported to date on the use of mobile technology exclusively for patients with CHD. The potential for mobile phone use in health care is currently being defined and remains a significant opportunity for future research.

1.1. Aims

We examined the efficacy of a mHealth intervention using text messaging, also referred to as short message service (SMS), to improve adherence to antiplatelet and statin medications among patients with a history of MI and/or PCI. The primary aim was to compare medication adherence among three groups: 1) patients who received text messages (TM) for medication reminders and health education (TM Reminders + TM Education), 2) patients who received TM for health education (TM Education Alone), and 3) patients who did not receive TM (No TM). The secondary aim was to explore feasibility and patient satisfaction with mobile phone use to improve medication adherence among patients who received TM. The hypothesis was that patients who received TM for medication reminders and/or education would have better adherence to their medication regimen as compared to patients who did not receive TM. In addition, patients who received TM for medication reminders and/or health education would consider mobile phones to be positive and effective in improving medication self-administration.

2. Methods

2.1. Research design

The research design of this study was a prospective, randomized controlled trial (RCT) that used a quantitative approach to collect and analyze data. This longitudinal study included two experimental groups (TM Reminders + TM Education and TM Education Alone) and a control (No TM) group with follow-up conducted at 30 days.

2.2. Sample

A convenience sample of 90 patients with CHD was enrolled. Inclusion criteria were: a) $\geq$ 21 years of age, b) hospitalized for non-ST elevation MI, ST elevation MI, or PCI, c) prescribed an antiplatelet medication [thienopyridine class of ADP receptor inhibitors and/or a cyclooxygenase inhibitor (i.e., aspirin)], d) prescribed a statin medication (HMG-CoA reductase inhibitors), e) owned a mobile phone with text messaging capability, and f) were able to speak, read, and understand English. Exclusion criteria included: a) cognitive impairment that limited ability to understand and complete questionnaires, and b) inability to operate a mobile phone.

2.3. Procedure

The study was approved by the Institutional Review Board at the designated medical center for recruitment as well as the academic institution that sponsored the study. The recruitment center was a non-profit, community hospital in Northern California. Recruitment took place between April 2012 and March 2013 until the final sample size was obtained. Eligible patients were first introduced to the research study by other health care providers (cardiologists or nurses) then interested patients were provided details of the study and enrolled by the principal investigator (PI).

After written consents were obtained in the hospital, patients completed the Mini-Cog Test to assess cognitive function [21] and demonstrated fine motor skills to verify eligibility. Eligible patients opened sealed opaque envelopes that contained the assignment to one of three groups (TM Reminders + TM Education, TM Education Alone, or No TM). Group assignment was generated by random allocation sequence using blocks of six that was prepared by a biostatistician. The PI assigned patients to their groups by distributing envelopes in consecutive, numbered order. Due to the nature of the study design, the PI and patients could not be blinded to the intervention once group assignment was determined.

Clinical data were collected from medical record review, and patients completed the following questionnaires: 1) sociodemographic survey, 2) Morisky Medication Adherence Survey (MMAS-8), 3) Manage Disease in General Scale (MDGS), 4) Self-Efficacy for Appropriate Medication Use Scale (SEAMS), 5) Social Support Survey, and 6) Beck Depression Inventory [22-26]. All questionnaires had good reliability with Cronbach's alpha value of greater than 0.80 in this sample. The Medication Event Monitoring System (MEMS) was used to objectively monitor adherence as the opening of the two electronic pill bottles provided a time-stamp corresponding with medication self-administration. All patients were given two electronic pill bottles since the majority of patients took their antiplatelet medications in the morning hours and statin medications in the evening as prescribed by their cardiologist. Patients were instructed to take their other medications using their usual regimen (i.e., pill organizer, pill bottles).

The primary intervention for this research study was based on Self-Efficacy Theory by Bandura. Briefly, this theory postulates that belief in one's capability to successfully perform certain behaviors influences level of motivation, affective states, and action [27].

The intervention included TM reminders to take antiplatelet and statin medications. During the 30 days of participation, both experimental groups received TM from a customizable program through CareSpeak Communications “mobile Health manager” platform (New Jersey). The TM Reminders + TM Education group received personalized TM reminders that were delivered at times selected by patients that correlated with their medication schedule (i.e., daily or twice daily). The medication reminders were two-way, requiring patients to respond back to confirm receipt. An example of a medication reminder was, “John, take Plavix 75 mg at 9:00 AM. Respond with 1.”

Both of the experimental groups received one-way educational health messages on cardiovascular risk reduction on Monday, Wednesday, and Friday at 2 pm. The purpose of the health TM was to determine whether patient education, delivered three times a week, would enhance medication adherence as opposed to direct medication reminders, delivered twice daily. An example of a health education message was, “Remember to see your cardiologist and/or primary physician 1-2 weeks after your hospitalization.”

Patients were called close to the end of their 30 day participation to schedule a follow up visit at which time three questionnaires related to medication adherence and self-efficacy were repeated. In addition, MEMS bottles were collected and data downloaded. All patients were given a $20 gift card as well as additional reimbursement if their wireless package did not include text messaging.

2.4. Outcome measures

First, data from the MEMS provided four different indicators of adherence including: 1) total number of doses taken, 2) percentage of prescribed doses taken, 3) percentage of days correct number of doses were taken, and 4) percentage of doses taken on schedule. Second, the response rate to the TM medication reminders by the TM Reminders + TM Education group was to correspond to adherence. Third, medication adherence was assessed using the MMAS-8, a self-report measure completed at baseline and at follow-up. The MMAS-8 is a well-validated tool and correlates with other adherence measures such as medication refill rates and electronic monitoring devices (e.g., MEMS) [23,29-31].

For the secondary aim, feasibility and patient satisfaction were assessed by successful execution of the intervention, patient participation, and by the Mobile Phone Use Questionnaire. The latter questionnaire was developed for the purpose of the study and sought to obtain patients' experience with using mobile phones for medication reminders and/or education.

Due to the early stages of research using mHealth interventions, there is no standard effect size that is widely accepted for medication adherence studies. This RCT helped to establish an appropriate effect size to support future research.

2.5. Statistical analysis

Descriptive statistics, means and standard deviations (SD) for quantitative variables, and frequencies and percentages for categorical variables were provided for all sociodemographic, clinical, and psychosocial variables. Study group differences of all characteristics were examined with one-way ANOVA and chi-square analyses. All data were analyzed with intention to treat. Missing data were assumed to be missing completely at random. The criterion for significance was set a priori as α = .05. SPSS 21.0 was used for all analyses.

A one-way ANOVA was used to examine the difference in objectively measured adherence values from MEMS data among groups at follow-up; however, the assumption of homogeneity of variances was not satisfied with the exception of one of the variables, therefore, the Welch test was used. Post-hoc pairwise comparisons with the Bonferroni correction were conducted to adjust for significance across pairwise contrasts (i.e., $p < .017$ for $k = 3$). A matched paired *t*-test was performed to compare response rates to TM for the TM Reminders + TM Education group between the antiplatelet and statin medication reminders. In order to determine if there were differences among groups in the change in self-reported (MMAS-8) between baseline and follow-up at 30 days, a Repeated Measures Analysis of Variance (RMANOVA) analysis was conducted. Lastly, patient satisfaction scores among the TM Reminders + TM Education and TM Education Alone groups were analyzed with *t*-tests.

3. Results

3.1. Characteristics of study participants

Ninety patients were recruited to participate and completed baseline questionnaires; however, six patients withdrew or were lost to follow-up. Figure 1 displays patient screening and recruitment according to the CONSORT guidelines [28]. No differences in sociodemographic, clinical, or psychosocial characteristics were found among groups (Table 1). Overall, the sample characteristics included a mean age of 59.2 years (SD 9.4, range 35-83), 24%

female, 22% non-White, 29% Medicare-insured, and 70% employed. Clinical characteristics included 37% with a history of CHD, 30% with prior coronary revascularization, and mean body mass index of 29.3. Psychosocial characteristics demonstrated very mild to mild depression and moderately high social support.

3.2. Medication adherence

Comparison of medication adherence data with MEMS among groups revealed a significant difference among groups for antiplatelet medications only in the percentage of prescribed number of doses taken, percentage of correct doses taken and percentage of prescribed doses taken on schedule [$F(2, 42) = 3.84$, $p = .03$; $F(2, 41) = 3.29$, $p = .047$; $F(2, 41) = 3.53$, $p = .04$, respectively] (Table 2). Additionally, the mean number of doses of antiplatelets taken approached significance [$F(2, 40) = 3.17$, $p = .053$]. Further analyses showed the TM Reminders + TM Education group had a higher percentage of correct doses taken and percentage of prescribed doses taken on schedule compared to the No TM group [$t(36) = 2.5$, $p = .02$; $t(37) = 2.6$, $p = .01$, respectively]. In addition, the TM Education Alone group had a higher percentage number of doses taken compared to the No TM group [$t(31) = 2.8$, $p = .01$]. The analysis of MEMS data was limited to 68 patients for antiplatelets (76%) and 64 patients for statins (71%) due to loss of bottles (n = 3), lack of use (n = 16 for antiplatelets, n = 20 for statins), inability to contact patient (n = 1), and technical difficulties (n = 2).

Patients in the TM Reminders + TM Education group were asked to respond to each text message to indicate receipt. The mean response rate to two-way text messaging showed a significantly higher mean response rate to antiplatelet medications (M = 90.2%, SD = 9) compared to statin medications (M = 83.4%, SD = 15.8) ($t(26) = 3.1$, p = .01).

Total mean scores of the self-reported MMAS-8 revealed no significant differences among groups at either baseline or 30 days ($F(2, 0.44) = 0.10$, $p = 0.91$) (Table 3). Total medication adherence scores changed over time ($F(1, 18.38) = 19.25$, $p < 0.001$); however, no significant differences were found among groups over time ($F(2, 1.76) = 1.76$, $p = 0.16$).

The effect size of the intervention was calculated on antiplatelet prescribed doses on schedule by comparing the TM Reminders + TM Education and No TM groups. There was a medium to large effect size with Cohen's $d = .69$.

3.3. Feasibility and patient satisfaction

Of the 53 patients in the experimental groups who completed the Mobile Phone Use Questionnaire at the 30 day follow up, both experimental groups reported high satisfaction with receiving TM. The majority of patients reported moderate to strong agreement in their responses to: "Satisfied with receiving TM for health," "Receiving TM helped me to take medications," and "Felt someone cared by receiving TM" (Figures 2-4). Only 6.7% of patients reported technical difficulties with receiving TM while 78.4% strongly or moderately agreed that the text messaging feature on their mobile phone was easy to use.

4. Discussion and Conclusion

4.1. Discussion

The MEMS data showed better medication adherence in the two experimental groups who received TM for antiplatelet medications compared to those who did not. The lack of difference in adherence among groups for statins may be consistent with the poor adherence that is generally seen with statin medications as well as the challenge of taking medications more than once daily, particularly statins that are generally prescribed for the evening [12].

Two-way messaging with the TM Reminders + TM Education group revealed a high response rate to the medication reminders with a significantly higher response to antiplatelet medications compared to statins. The higher adherence to antiplatelets may have been related to their perceived importance of taking antiplatelet medications following MI and/or PCI. Less frequent TM responses to statin reminders may be a reflection of mobile phone use patterns because individuals took statins in the evening rather than the morning.

Self-reported medication adherence did not differ among patients who received or did not receive TM for medication reminders and/or education. All patients' self-reported adherence improved over time, which was a positive change after experiencing a major cardiac event.

Feasibility and patient satisfaction was established in the high satisfaction scores following the study. Overall, there was a relatively low attrition rate of 6.7%.

In terms of measurement of medication adherence, a disadvantage to interpreting the MEMS data was the lower frequency of analyzable data (76% of antiplatelet and 71% of statin medications, respectively). Poor usage by patients was the main reason for unanalyzable data among other previously reported difficulties. The majority of patients were recruited for the study on the day of hospital discharge. Given the anxiety that they may have experienced related to a new diagnosis of CHD and hospital discharge, they may have been experiencing higher levels of stress with using MEMS as opposed to other patients who have been recruited to use MEMS in non-acute settings. In addition, many patients were resistant to changing their habit of using pill organizers or did not want to carry the MEMS bottles with them while traveling. Despite these challenges, this sample of CHD patients had higher mean adherence of secondary prevention medications as compared to adherence reported in other studies [2].

In addition to the challenge of obtaining complete MEMS data, other limitations may apply. First, the relatively small convenience sample may have undermined the external validity of the findings. The sample was predominately male, white, and employed. The results may be quite different in populations reflecting greater diversity. Second, the sample may have underrepresented patients who were uncomfortable using mobile phones as these patients may have declined to participate in the study leading to unintentional sample selection bias. Third, the follow up period of 30 days was relatively short and did not provide long-term adherence trends or clinical outcomes, particularly given the setting of a chronic disease such as CHD. However, we were able to assess the risk of early in-stent thrombosis following PCI since the majority occurs in the first month following PCI [32]. Fourth, self-report and MEMS data collection have their own inherent limitations [31]. MEMS and TM two-way responses may not have reflected actual medication taking since patients could have responded to the TM and unscrewed the MEMS cap without actually ingesting the medication. Finally, use of MEMS may have added unintentional attention to regular medication-taking habits for all groups. The Hawthorne effect of using MEMS should be considered, although a comparison of other studies concluded that the use of MEMS to measure medication adherence does not suffer from this type of bias [33]. In other studies, adherence data from MEMS have yielded the lowest adherence rates compared with other adherence measures [33].

Despite the potential limitations, several positive attributes of this study are notable. No research to date regarding the use of mobile phones in the population of MI and/or PCI patients has been previously reported. Although there was a large range in age (35-83 years) of enrolled patients, the mean age of 59.2 years (SD 9.4) demonstrated feasibility of applying mHealth for an older population. Numerous patients were unfamiliar with using the text messaging feature prior to participating in this study; however, they were successful in their participation with a limited number of patients reporting technical difficulties. The feasibility of a mobile phone intervention may be generalizable to a wider population affected by chronic disease as well as those who initiate participation in an intervention aimed to improve medication adherence after experiencing a significant acute medical event.

Another strength of this study was the use of multiple measures of medication adherence to understand the patterns and barriers to medication self-administration. The MEMS MMAS-8 were used in this study to corroborate medication adherence since both types of measures offer important information that is complementary yet different from each other [34]. Although responses to TM by the TM Reminders + TM Education group do not prove patients took their medications, the high response rates indicated engagement with the intervention. Lastly, there may be underestimated benefits of the TM such as providing a source of social support.

Future research in mHealth will help determine the appropriate dosing and content of TM through long-term studies. As 97% of the patients underwent PCI in this study with 85 % receiving a drug-eluting stent that requires at least one year of dual-antiplatelet therapy, long-term adherence levels and clinical outcomes should be monitored for definitive benefit in the future. As our population ages, text messaging and use of mobile phone applications will be more familiar and routine. Further research is required to determine the individual and group characteristics that are more likely to benefit from mobile phone interventions in order to create engaging, sustainable, and long-term programs. Along with individual and group characteristics, other considerations when designing and implementing technology-related interventions include type of illness/condition, setting (acute, non-acute), timing of intervention following diagnosis, and duration of intervention. Although there was no harm or unintended effects as a result of this intervention, the risk of mHealth interventions requires further investigation [35]. Cost analysis of interventions is also an important step in evaluating mHealth [35]. Finally, more advanced health behavior theories and models that account for the interactive and adaptive nature of mHealth interventions will need to be developed and tested [36].

4.2. Conclusions

The majority of effective interventions for medication adherence has been complex and has not lead to large improvements in adherence and clinical outcomes [36]. Thus, there has been a movement to apply innovative strategies to assist patients in medication adherence for chronic disease management [37]. Integrating technology to interface with patients through mHealth, eHealth, and telehealth is currently a major initiative of medical and research communities and may be relevant for patients to enhance self-management of chronic disease.

This study supports the efficacy of using mobile phones in promoting adherence to antiplatelet therapy during the vulnerable time period of 30 days following MI and/or PCI. Nonadherence to cardiac medications may result in increased morbidity and mortality, thus multiple modalities including receiving TM reminders may enhance adherence. Although influencing patients' adherence behavior may be a challenge, particularly for older adults, persistent efforts in applying nontraditional modalities such as mHealth will provide a substantial contribution to efforts to improve medication adherence.

4.3. Practice Implications

This RCT has established feasibility and high satisfaction with a text messaging intervention among patients with CHD. Text reminders and health education messages improved adherence in antiplatelet medications, which are critical in the time period following stent deployment. This study may help launch further research in the rapidly growing field of mHealth in order to provide a potential solution to the challenges in medication nonadherence.

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Table 1. Sociodemographic, Clinical, and Psychosocial Characteristics

	TM Reminders + TM Education	TM Education Alone	No TM	*p*
Sociodemographic Characteristics				
Age, y (range 35-83)	58.2 ± 10.6	58.3 ± 8.5	61.1 ± 9.1	0.40
Gender				0.32
Female	7 (23.3)	10 (33.3)	5 (16.7)	
Male	23 (76.7)	20 (66.7)	25 (83.3)	
Race				.06
Non-white	11 (36.7)	5(16.7)	4 (13.3)	
White	19 (63.3)	25 (83.3)	26 (86.7)	
Level of education				0.86
<12 years	3 (10)	5 (16.7)	2 (6.9)	
High school	4 (13.3)	3 (10)	5 (17.2)	
College	13 (43.3)	15 (50)	13 (44.8)	
Graduate	10 (33.3)	7 (23.3)	9 (31)	
Employment				0.77
Non-employed	10 (33.3)	8 (26.7)	12 (40)	
Employed	30 (66.7)	22 (73.3)	18 (60)	
Annual salary[a]				0.22
<20,000	7 (24.1)	7 (25.9)	9 (32.1)	
20,000-60,000	3 (10.3)	6 (22.2)	9 (32.1)	
60,000-150,000	14 (48.3)	7 (25.9)	7 (25)	
>150,000	5 (17.2)	7 (25.9)	3 (10.7)	
Insurance				0.74
None	1 (3.3)	3 (10)	1 (3.3)	
Private	14 (46.7)	14 (46.7)	17 (56.7)	
Medicare	11 (36.7)	6 (20)	9 (30)	
Other	4 (13.3)	7 (23.3)	3 (10)	
Relationship status				0.42
Single	6 (20)	10 (33.3)	10 (33.3)	
With partner	24 (80)	20 (66.7)	20 (66.7)	
Clinical Characteristics				
Coronary risk factors				
Hypertension	18 (60)	16 (53.3)	18 (60)	0.83
Dyslipidemia	20 (66.7)	22 (73.3)	24 (80)	0.51
Diabetes	8 (26.7)	6 (20)	9 (30)	0.66
Family history	13 (43.3)	8 (26.7)	6 (20)	0.13
Prior CAD or MI	10 (33.3)	8 (26.7)	15 (50)	0.16

Prior revascularization	9 (33.3)	5 (17.2)	13 (43.3)	0.08
MI during admission	15 (50)	13 (43.3)	13 (43.3)	0.87
Ejection fraction[b]	56.5 ± 10.3	55.5 ± 9.6	56.9 ± 13.2	0.90
Body mass index	29.7 ± 6.8	29.5 ± 5.4	28.5 ± 5.9	0.73
Hemoglobin A1C[c]	6.3 ± 1.3	5.6 ± 0.9	6.8 ± 2.3	0.20
Psychosocial Characteristics				
Depression[d*]	4.45 ± 3.38	7.18 ± 6.64	6.59 ± 6.00	0.14
Social support[e**]	84.37 ± 9.05	81.79 ± 17.41	79.83 ± 13.29	0.44

Data are presented as mean ± SD, n (%)
CAD, coronary artery disease; MI, myocardial infarction
N = 90 total; n = 30 each group
Missing data: a: n = 84, b: n = 77, c: n = 42, d: n = 88, e: n = 89
*Based on Beck Depression Inventory (range 0-63)
**Based on MOS Social Support Survey (range 19-95)

Table 2: Medication Adherence Based on MEMS

Antiplatelets				
	TM Reminders + TM Education (n = 24)	TM Education Alone (n = 19)	No TM (n = 25)	*p*
Mean Doses Taken	28.2 ± 3.6	28.2 ± 4.1	23.7 ± 8.3	0.05
Percent Doses Taken	93.7 ± 11.9	95.8 ± 9.5	79.1 ± 27.7	0.03
Percent Correct Number Doses	88.0 ± 14.0	87.2 ± 16.5	72.4 ± 27.4	0.047
Percent Doses Taken on Schedule	86.2 ± 15.4	85.7 ± 18.2	69.0 ± 29.2	0.04
Statins				
	TM Reminders + TM Education (n = 24)	TM Education Alone (n = 20)	No TM (n = 20)	*p*
Mean Doses Taken	27.7 ± 4.2	27.1 ± 4.9	25.0 ± 6.4	0.28
Percent Doses Taken	92.4 ± 14.0	90.1 ± 16.2	83.3 ± 21.3	0.28
Percent Correct Number Doses	85.4 ± 16.6	81.3 ± 16.4	73.4 ± 23.8	0.18
Percent Doses Taken on Schedule	84.1 ± 19.4	79.7 ± 19.3	74.4 ± 21.1	0.31

Table 3: Self-Reported Medication Adherence Scores (MMAS-8)

	TM Reminders + TM Education (n = 28)	TM Education Alone (n = 28)	No TM (n = 28)	*p*
Baseline	6.20 ± 1.66	5.85 ± 2.10	6.01 ± 1.84	0.77
Follow-up at 30 days	6.43 ± 1.22	6.73 ± 1.49	6.96 ± 1.44	0.37

Data are presented as mean ± SD
*Group by time effect p = 0.16

Figure 1. Patient Screening and Recruitment

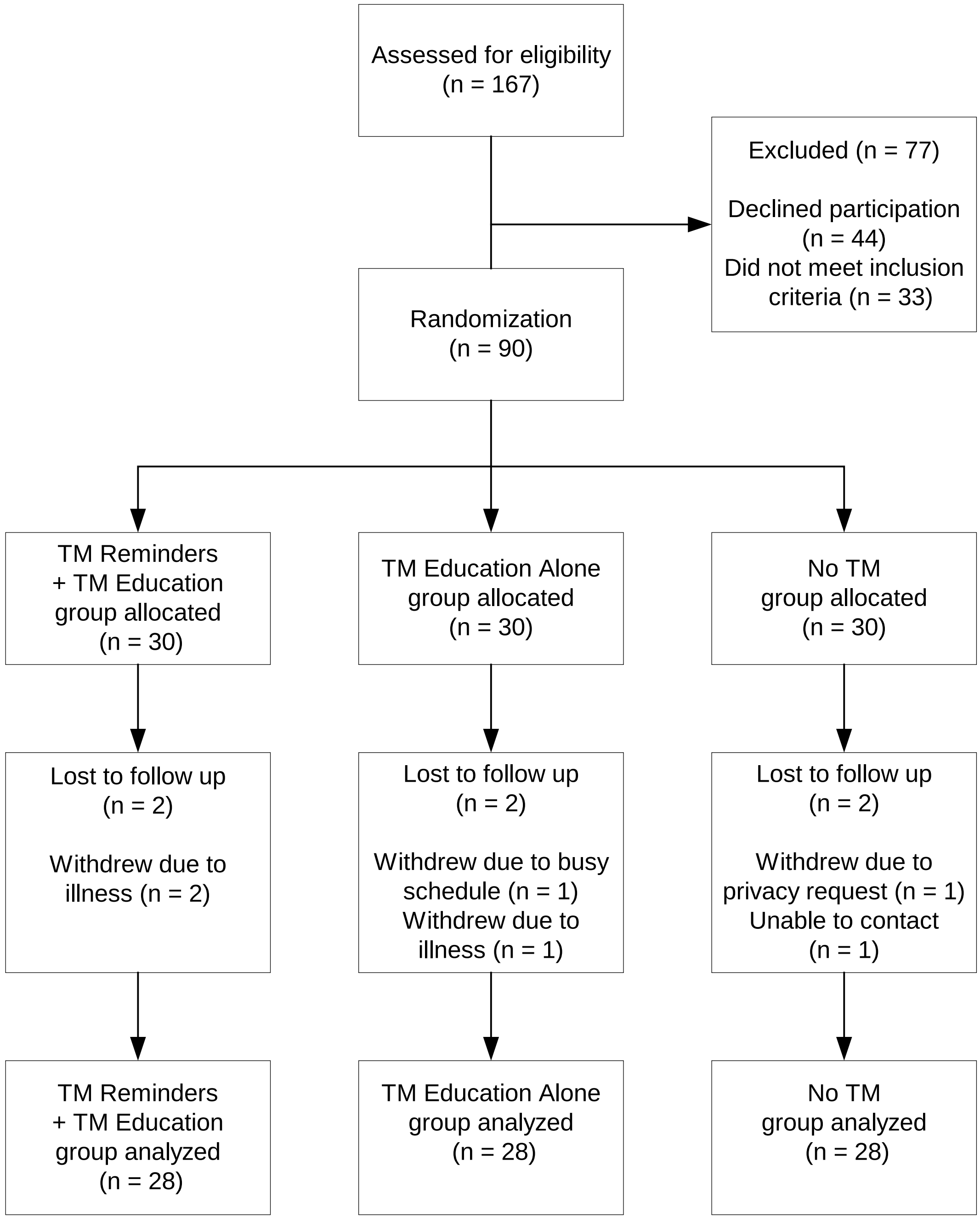
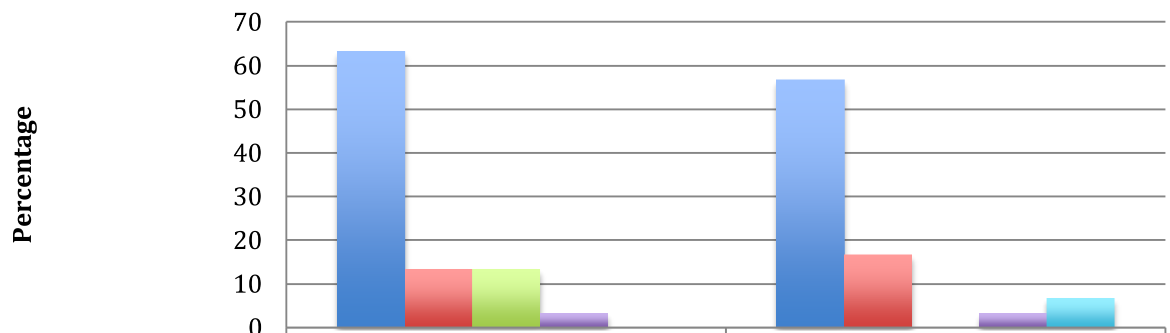
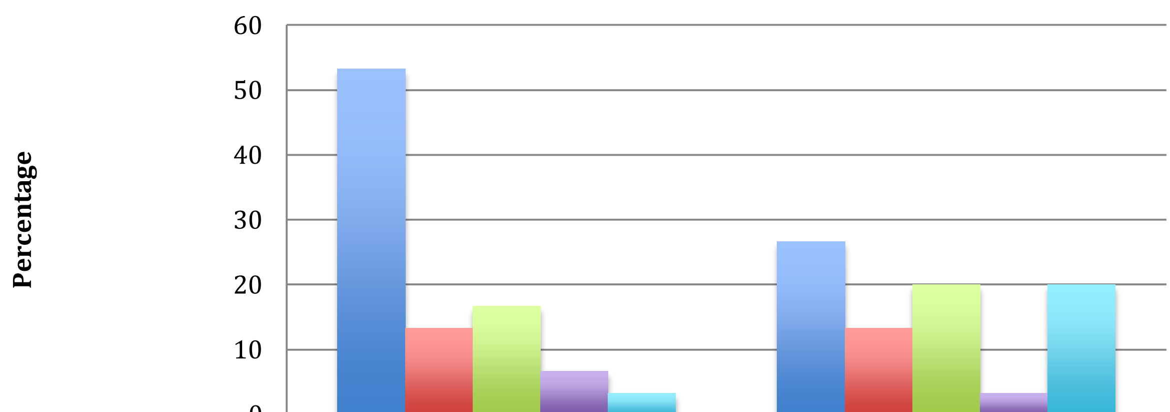


Figure 2: Responses to “Satisfied with Receiving Text Messages for Health”



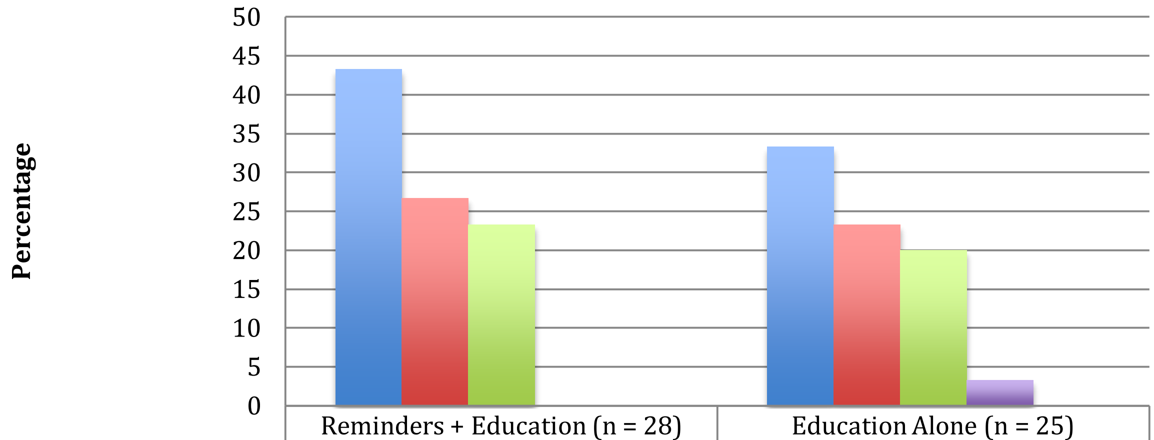
	Reminders + Education (n = 28)	Education Alone (n = 25)
Strongly Agree	63.3	56.7
Moderately Agree	13.3	16.7
Neutral	13.3	0
Moderately disagree	3.3	3.3
Strongly disagree	0	6.7

Figure 3: Responses to “Receiving Text Messages Helped Me to Take Medications”



	Reminders + Education (n = 28)	Education Alone (n = 25)
Strongly Agree	53.3	26.7
Moderately Agree	13.3	13.3
Neutral	16.7	20
Moderately disagree	6.7	3.3
Strongly disagree	3.3	20

Figure 4: Responses to “Felt Someone Cared by Receiving Text Messages”



	Reminders + Education (n = 28)	Education Alone (n = 25)
Strongly Agree	43.3	33.3
Moderately Agree	26.7	23.3
Neutral	23.3	20
Moderately disagree	0	3.3
Strongly disagree	0	0

Chapter 6

Predictors of Medication Adherence Using Text Messaging:

A Randomized Controlled Trial

Chapter 6

Predictors of Medication Adherence Using Text Messaging: A Randomized Controlled Trial

Abstract

Introduction: Medication nonadherence is closely linked with increased morbidity and mortality in patients with coronary heart disease (CHD). The complex behavior of medication adherence is influenced by numerous factors and may be a key modifiable risk factor for CHD. We sought to identify sociodemographic, clinical, and psychosocial factors that would predict medication adherence among patients 30 days following myocardial infarction and/or coronary stent placement. We hypothesized that older age, living with a partner, higher level of education, lower depression, and higher social support would predict medication adherence.

Methods: In a prospective, randomized controlled trial, a customized mobile health intervention was designed to deliver: 1) text messages (TM) for medication reminders and education, 2) TM for education alone, or 3) no TM. The Morisky Medication Adherence Scale was used to determine the outcome variable of medication adherence. Electronic chart review and questionnaires acquired data on sociodemographics, depression, social support, and clinical history. A multiple regression analysis was performed to identify variables that would predict self-reported medication adherence.

Results: The sample included 90 patients with a mean age of 59.2 years (SD 9.4, range 35-83). Age, years of education, depression, and social support

explained 26% of the total variance in medication adherence ($R^2 = .26$, $p < .001$). In the final model, less depression ($p = .004$) and higher social support ($p = .02$) positively predicted higher medication adherence, controlling for the other variables in the model.

Conclusions: Future research is needed to better understand the potential mediators and moderators of medication adherence as well as the potential of mobile health interventions to influence adherence and psychosocial factors. Addressing depression and social support in research and clinical practice should be a priority to improve medication adherence in patients with CHD. Psychosocial factors cannot be underestimated in their impact to motivate, sustain, and succeed in behavioral change and self-management of chronic disease.

Introduction

Coronary heart disease (CHD) is the leading cause of death and loss of disability-adjusted life years worldwide [World Health Organization (WHO), 2004]. Medication nonadherence in patients with CHD is closely linked to adverse clinical outcomes such as rehospitalization, morbidity, and mortality (Dunbar-Jacob, Bohachick, Mortinmer, Sereika, & Foley, 2003; Ho, Bryson, & Rumsfeld, 2009; Ho et al., 2008). Extensive research and clinical guidelines in the management of myocardial infarction (MI) and CHD support the role of pharmacologic treatment for secondary prevention of CHD (Jneid et al., 2012; O'Gara et al., 2013; Smith et al., 2006).

Medication adherence is a complex phenomenon with multifaceted reasons for nonadherence and numerous interventions that have been tried over many decades (Bosworth et al., 2011; Brown & Bussell, 2011; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008). The complex behavior of medication adherence can be better understood when examining theoretical relationships and processes. Understanding the variables and mechanisms that influence medication adherence is important when designing and implementing effective strategies.

Self-efficacy

Self-efficacy is defined as the belief in one’s own capabilities to perform certain actions that have influence in an individual’s life (Bandura, 1987). The Self-Efficacy Theory by Bandura (1997) was selected to guide this research study and postulates that self-efficacy influences level of motivation, affective states, and action. Perceived self-efficacy is cited as the most powerful mechanism in determining behavior change (Bandura, 1987) and has been studied in many dimensions of health behavior change such as health promotion activities, self-management of chronic diseases, and health-maintenance behaviors. Given the potential of self-efficacy to change behavior, research interventions have been implemented to increase perceived self-efficacy.

Self-efficacy has been examined in areas of health related behavior with conflicting results in relation to medication adherence (Clark & Dodge, 1999; Sol, van der Graaf, van Petersen, & Visseren, 1999). Previous research has shown that knowledge and competency in medication use alone do not lead to medication adherence (Bandura, 1982; Haynes et al., 2008; Schedlbauer, Schroeder, Peters, & Fahey, 2004). Educational and behavioral interventions have been linked to increased self-efficacy and improved medication adherence (Clark & Dodge, 1999; Warren-Findlow, Seymour, & Brunner, 2011), although other interventions have led to increased self-efficacy and social support without an improvement in medication adherence (Criswell, Weber, Xu, & Carter, 2010).

Predictors of medication adherence

Numerous factors support and create barriers that affect medication adherence. Personal factors such as gender, ethnicity, employment, polypharmacy, education, and income have been inconsistent predictors in the literature (Dunbar-Jacob, Bohachick, Mortinmer, Sereika, & Foley, 2003; Gatti, Jacobson, Gazmararian, Schmotzer, & Kripalani, 2009; Ho et al., 2006; Maddox & Ho, 2009; Mann, Allegrante, Natarajan, Halm, & Charlson, 2007).

Compared to other psychosocial factors, poor social support has been more consistently associated with medication nonadherence (Ho, Bryson, & Rumsfeld, 2009). Interventions to enhance social support in patients with chronic diseases have shown positive outcomes in increasing medication adherence (Criswell et al., 2010; Franklin, Waller, Pagliari, & Greene, 2006; Gallager, Luttik, & Jaarsma, 2011; Lester et al., 2006).

Depression and medication nonadherence have also been closely associated with patients who have CHD (Bane, Hughes, & McElnay, 2006; Dempe et al., 2003; Gehi, Haas, Pipkin, & Whooley, 2005). Although it is identified as a modifiable risk factor for CHD (Yusuf et al., 2004), depression is often under-diagnosed and under-treated among patients with CHD (Bane et al., 2006).

Aims

In the recent decade, novel behavioral interventions in the form of mobile health (mHealth) technologies have been introduced in order to address the problem of medication adherence. The aims of this randomized controlled trial (RCT) were to determine the impact of a mobile phone text messaging intervention designed to improve medication adherence by comparing self-efficacy among three CHD groups who: 1) received medication reminders and health education (“TM Reminders + TM Education” group); 2) received health education (“TM Education Alone” group); and 3) did not receive text messaging (No TM). The second aim was to identify the personal (sociodemographic and clinical characteristics) and psychosocial factors that are associated with and predict medication adherence. The first hypothesis was that text messages (TM), in which daily medication reminders and/or health education were provided, would increase self-efficacy for adherence to cardiac medications by building self-confidence and self-management skills in medication self-administration. For the second aim, older age (>65 years), living with a spouse/partner, higher level of education, less depression, and higher social support were hypothesized to be associated with and predict medication adherence.

Methods

Research Design and Sample

The research design of this study is a prospective RCT that used a quantitative approach to collect and analyze data. Inclusion criteria were: a) ≥ 21 years of age, b) hospitalized for non-ST elevation MI, ST elevation MI, or PCI, c) prescribed an antiplatelet medication [thienopyridine class of ADP receptor inhibitors and/or a cyclooxygenase inhibitor (i.e., aspirin)], d) prescribed a statin medication (HMG-CoA reductase inhibitors), e) owned a mobile phone with text messaging capability, and f) were able to speak, read, and understand English. Exclusion criteria included: a) cognitive impairment that limited ability to understand and complete questionnaires, and b) inability to operate a mobile phone.

Procedure

The study was approved by the Institutional Review Board at the designated medical center for recruitment as well as the academic institution that sponsored the study. The recruitment center was a non-profit, community hospital in Northern California. Patient recruitment took place between April 2012 and March 2013 until the final sample size was obtained. Eligible patients were first introduced to the research study by other health care providers (cardiologists and nurses) and then interested patients were given details of the study by the principal investigator (PI).

Patients who provided written informed consent opened sealed opaque envelopes that contained the assignment to one of three groups (TM Reminders + TM Education, TM Education Alone, or No TM). Group assignment was generated by random allocation sequence using blocks of six that was prepared by a biostatistician. The PI assigned patients to their groups by distributing envelopes in consecutive, numbered order. Due to the nature of the study design, the PI and patients could not be blinded to the intervention once group assignment was determined. All subjects were given a $20 gift card as well as additional reimbursement if their wireless package did not include text messaging.

Data Collection

The questionnaire for self-efficacy was administered at baseline and at the end of the patient’s study period of 30 days. The Self-Efficacy for Appropriate Medication Use (SEAMS) scale was developed to assess one's ability adhere to medications in chronic disease management (Risser, Jacobsen, & Kripalani, 2007).

Psychosocial variables of social support and depression were evaluated at baseline from the Social Support Survey of the Medical Outcomes Study and the

Beck Depression Inventory (Beck, Ward, Mendelson, Mock & Erbaugh, 1961; Sherbourne & Stewart, 1991). The self-reported Morisky 8-Item Medication Adherence Scale (MMAS-8) was administered at baseline and 30 days to assess medication adherence (Morisky, Ang, Krousel-Wood, & Ward, 2008). The Medication Event Monitoring System (MEMS) was used to objectively monitor adherence as the opening of the two electronic pill bottles provided a time-stamp to correspond with medication self-administration.

Intervention and Outcomes

The primary intervention for this research study included TM reminders to take antiplatelet and statin medications for 30 days after hospitalization. Both experimental groups received TM from a customizable program through CareSpeak Communications mobile Health manager platform (New Jersey). The TM Reminders + TM Education group received personalized, two-way TM reminders corresponding with the dosing regimen of their medications (i.e., daily or twice daily). Two-way messages required patients to respond back to confirm receipt. An example of a medication reminder was, “John, take Plavix 75 mg at 9:00 AM. Respond with 1.”

Both of the experimental groups also (TM Reminders + TM Education and TM Education Alone only) received one-way health messages (i.e., not requiring response) on cardiac risk reduction on Monday, Wednesday, and Friday at 2 pm. The purpose of the cardiovascular risk reduction messages was to determine whether patient education would enhance self-efficacy. An example of a health education message was, “Remember to see your cardiologist and/or primary physician 1-2 weeks after your hospitalization." The outcome measures included general and medication self-efficacy as well as variables related to medication adherence.

Statistical Analyses

In order to compare self-efficacy among groups, a repeated measures analysis of variance (RMANOVA) analysis was conducted to detect a change in self-efficacy between baseline and 30 days among the three groups. A RMANOVA was also conducted to compare medication adherence over time. Missing data were assumed to be missing completely at random. The criterion for significance was set a priori as $\alpha = .05$. SPSS 21.0 was used for all analyses.

To identify the variables that were associated with medication adherence, individual relationships were analyzed between each personal (sociodemographic and clinical characteristics) and psychosocial factor with medication adherence. Correlations were obtained for continuous and dichotomous variables while one-way ANOVAs were performed for categorical independent variables with more than two levels. Variables that showed at least a moderate correlation and had a significant relationship to medication adherence with a *p*-value less than 0.10 were included in a multiple regression analysis. The multiple regression analysis provided the optimum combination of the variables that explained the total percent of variance in medication adherence as well as indicating the unique contribution of each variable to the regression model.

Results

Characteristics of Study Participants

A convenience sample of 90 patients was recruited and completed baseline questionnaires. Six patients withdrew or were lost to follow-up. Figure 1 displays patient screening and recruitment according to the CONSORT guidelines (Schulz, Altman, Moher, 2010). No differences in sociodemographic or clinical characteristics were found among groups (Table 1). Overall, the sample characteristics included patients with a mean age of 59.2 years (SD 9.4, range 35-83), 24% female, and 22% non-White. Clinical characteristics included 37% with a history of CHD, 30% with prior coronary revascularization, and mean body mass index of 29.3.

Medication self-efficacy

Total scores of the SEAMS to examine self-efficacy among the three groups did not detect significant differences at either baseline or 30 days ($F(2, 31.31) = .73$, $p = .49$) (n = 82) (Table 3). Over time, all groups improved in total scores for self-efficacy ($F(1, 114.62) = 8.32$, $p = .01$); however, no significant difference was found in self-efficacy scores among groups over time ($F(2, 6.24) = .45$, $p = .64$).

Association with Medication Adherence

Baseline self-reported medication adherence was used to determine associated factors of medication adherence prior to the text messaging intervention. Analysis of each personal and psychosocial factor in relationship to medication adherence revealed age, male gender, education, depression, and social support as potential variables that were included in a multiple regression analysis in which baseline medication adherence was the dependent variable (n = 87). A total variance of 33% in medication adherence was found, which was explained by the optimally weighted combination of the five independent variables (R^2 = .33, F(5, 81) = 7.99, p < .001). In the multivariate analysis, males (β = -.924, p = .02), less depression (β = -.101, p = .03), and higher social support (β = .042, p = .002) were significantly associated with medication adherence, after controlling for other variables in the model. Age and education were not significant contributors to the final multiple regression model.

Predictors of Medication Adherence

Follow-up medication adherence scores were then analyzed in order to determine the variables that predicted medication adherence after 30 days of the text messaging intervention (n = 82). The same personal and psychosocial factors identified as associated factors at baseline were significantly correlated at p < 0.10 with the exception of gender at follow-up. Group assignment was not significantly correlated with medication adherence and was not added to the model. The multiple regression analysis at 30 days with medication adherence as the dependent variable showed age, years of education, depression, and social support explained 26% of the total variance in medication adherence (R^2 = .26, F(5, 76) = 5.25, p < .001). Less depression (β = -0.080, p = .004) and higher social support (β = .026, p = .02) positively predicted higher medication adherence in the final model, after controlling for the other variables.

Discussion

To our knowledge, this is the first mHealth intervention promoting medication adherence among patients following MI and/or PCI as well as the first to report the connection between self-efficacy and medication adherence based on an mHealth study. In summary, self-efficacy was not different among patients with CHD following a 30 day text messaging intervention with medication reminders and health education. Self-efficacy improved for all groups over time, but did not differ between groups based on the intervention. Both self-efficacy and medication adherence scores increased for all groups from baseline to follow-up, which were expected since the variables were highly correlated.

Male gender, less depression, and higher social support were positively associated with higher medication adherence at baseline, while less depression and higher social support predicted higher medication adherence after the intervention. Since there was a variance of 5 patients who were compared at baseline and follow-up, a separate baseline regression analysis was conducted with the same patients performed at follow-up. No differences were found, confirming that the patients who withdrew or were lost to follow-up did not influence the results.

Strengths and Limitations

Through this RCT, feasibility of applying mHealth to an older population with chronic disease was established (mean age of 59.2 years, SD 9.4, range 35-83). More specifically, patients were recruited from an acute care setting following a major coronary event and had a low attrition rate of 6.7%.

In addition, although other text messaging interventions have been reported across a wide variety of acute and chronic illnesses in medication adherence, research in this area has been relatively atheoretical. Theories that have been mentioned in other text messaging interventions to improve medication adherence are the Transtheoretical Model (Castano, Bynum, Andres, Lara, & Westhoff, 2012), Social Cognitive Theory (Franklin et al., 2003), Health Belief Model of Behavior Change (Mbuagbaw et al. 2012), Behavioral Learning Theory (Montes, Medina, Gomez-Beneyto, & Maurino 2012), and Theory of Planned Behavior (Suffoletto, Calabria, Ross, Callaway, & Yealy 2012). The current intervention tested the Self-Efficacy Theory with a questionnaire that was related to medication-related self-efficacy.

Several limitations may apply in this RCT. First, the relatively small convenience sample may have limited the external validity of the findings and made it challenging to detect differences among groups. Furthermore, missing data occurred due to patient withdrawal or being lost to follow-up (n = 6), patient preference not to complete questionnaires (n = 2), and unintentional failure to administer the MDGS (n = 8). Second, the sample may have underrepresented patients who were uncomfortable using mobile phones as they declined to participate in the study leading to unintentional sample selection bias. Third, the follow-up period of 30 days may not have allowed ample time to distinguish changes in self-efficacy, particularly with managing a chronic disease such as CHD. Fourth, the SEAMS may not have been sensitive to assess change in self-efficacy although the Cronbach alpha was 0.89 (Risser et al., 2007). Finally, self-reported medication adherence was used as the dependent variable for the multiple regression. Although objective data were obtained, analyzing variables at baseline and follow-up were only possible with self-reported data, whereas MEMS data was obtained at a single point (i.e., follow-up).

Depression

Research over six decades supports the impact of psychosocial risk factors that contribute to both the risk of developing CHD and the worsening of clinical course and prognosis (Albus, 2010). Depression has been linked to neuroendocrine pathways leading to increased platelet activation, cortisol, and catecholamine excess along with an altered autonomic nervous system function that influence the pathogenesis and progression of coronary atherosclerosis and subsequent CHD (Vieweg et al., 2006). Although biological factors have been attributed to depression, poor adherence to medications may be a key mechanism by which depression contributes to the increased risk of coronary events among patients with depression.

Our research supports prior studies that identified depression as a powerful predictor of medication nonadherence among patients with CHD (Bane et al., 2005; Dempe et al., 2013; Gehi et al., 2005; May et al., 2010; Rieckmann et al., 2006). In one study among patients with CHD, the odds of medication nonadherence were 3.6 times greater among patients with depression compared to patients without depression (Dempe et al., 2013). Despite the undisputed association between depression and medication nonadherence, other important questions remain. The causal role of depression in adverse clinical outcomes has been difficult to determine as well as the biobehavioral pathways that link depression to cardiac morbidity and mortality (Freedland & Carney, 2013). In addition, it has been a challenge to determine whether treatment of depression can improve cardiac outcomes including event free survival (Berkman et al., 2003; Freedland & Carney, 2013)

Social Support

Similar to depression, low social support has been linked to etiologic studies of CHD as well as cardiac and non-cardiac mortality in prognostic studies (Barth, Schneider, & von Kanel, 2010; Lett et al., 2007). Investigators have reported the association between social support and clinical outcomes with important conclusions. In an observational study following patients after MI for one year, low social support was associated with more depression and anginal symptoms along with poorer quality of life and mental function compared with patients with high social support (Leifheit-Limson…, 2010). In the ENRICHD trial, higher perceived social support was found in the experimental group compared to the usual care group after six months of therapy; however, there were no differences in the composite primary end point of death or recurrent MI between groups after 29 months (Berkman et al., 2003). Reporting clinical outcomes is important in understanding effective strategies, accurately measuring variables, and interpreting the results of social support.

Some physiological mechanisms have been suggested to explain how social support influences health outcomes (i.e., stress-buffering effect) (Uchino, 2006); however, it can also be proposed that providing accountability and encouragement (i.e., social support) can help patients' adherence to medications, thus leading to improved health outcomes. In an observational study that included patients with acute coronary syndrome, practical but not emotional support predicted greater than two-fold increase in medication adherence among patients who had two or more sources of practical support after one year (Molloy et al., 2008). From this study, it was suggested that the impact of practical support on CHD outcomes may be mediated through key secondary prevention behaviors such as receiving more prompts and reminders about medications and health behaviors as well as help with filling prescriptions (Molloy et al., 2008). In application to our mHealth intervention, TM reminders could similarly be considered as a practical source of support and perhaps a mediator to improved adherence.

Implications

These research findings substantiate the need for an interdisciplinary effort to address depression and social support during patients' hospitalization and follow-up. Increasing awareness of the detrimental effects of depression to patients and caregivers may encourage patients to seek clinical support for therapeutic interventions. Assessing depression at subsequent outpatient visits will be equally valuable.

Efforts to improve social support may reduce CHD risk in patients with depression given that low social support influences the development and outcome of depression (Barth et al., 2010; Lett et al., 2007) and depression has consistently been shown to be an important predictor of CHD. Specifically, patients with a recent coronary event can be encouraged to join group cardiac rehabilitation and support groups focused on patients with CHD (e.g., Mended Hearts). Social support may be a potential benefit of mHealth interventions and another opportunity to reach patients in a consistent, nonintrusive, and nonthreatening manner. In summary, text messaging interventions can enhance self-efficacy through reminders and feedback on treatment success, provide a form of social support, and establish social networks in addressing psychosocial factors in this high risk population (de Jongh, Gurol-Urganci, Vodopivec-Jamsek, Car, & Atun, 2008). In turn, increased self-efficacy and support systems may influence health behaviors and improve self-management of chronic diseases (de Jongh et al., 2008).

Future Research

Future research is needed to better understand factors that support and create barriers to self-efficacy, as well as medication adherence in patients who experience a major acute medical event such as MI and/or PCI. In addition, testing novel secondary prevention strategies to promote self-efficacy can be considered. For example, researchers are currently investigating a theory-based Internet and mobile phone based intervention to support maintenance of self-management behaviors as an extension of cardiac rehabilitation (Antypas & Wangberg, 2012). Long-term interventions that help build self-efficacy will need to be analyzed over longer intervals of time to test sustainability and efficacy.

Lastly, theory testing of current models is required to understand relationships between potential mediators and moderators of self-efficacy as well as medication adherence. Moreover, new advanced health behavior theories and models that account for the interactive and adaptive nature of mHealth interventions are current gaps in the literature and opportunities for development and testing (Riley et al., 2011). The efficacy of technology-related interventions will continue to be defined as the science of mHealth research develops through an interdisciplinary effort (Nilsen et al., 2012).

Conclusion

This study tested a novel, theory based approach to enhance self-efficacy in patients who experienced a MI and/or PCI. Self-efficacy did not change over a 30 day period as a result of the TM intervention; however, this RCT confirmed that psychosocial factors such as depression and social support were powerful associated factors and predictors of medication adherence. Psychosocial factors cannot be underestimated in their impact to motivate, sustain, and succeed in behavioral change and self-management of chronic disease. Addressing psychosocial factors is an essential area of focus for an interdisciplinary effort to increase secondary prevention efforts such as medication adherence in patients with CHD.

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Figure 1. Patient Screening and Recruitment

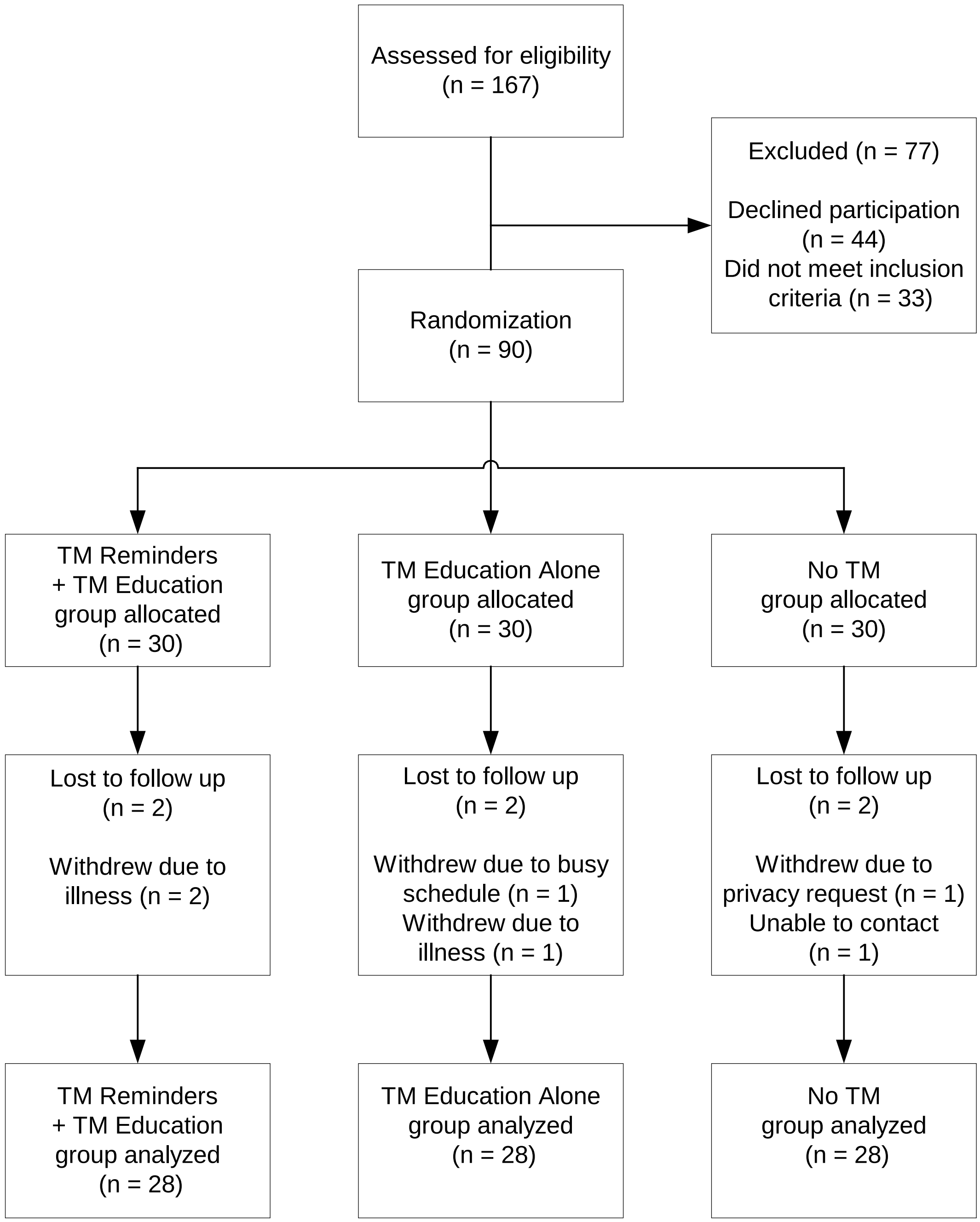

Table 1. Sociodemographic, Clinical, and Psychosocial Characteristics

	TM Reminders + TM Education	TM Education Alone	No TM	*p*
Sociodemographic Characteristics				
Age, y (range 35-83)	58.2 ± 10.6	58.3 ± 8.5	61.1 ± 9.1	0.40
Gender				0.32
Female	7 (23.3)	10 (33.3)	5 (16.7)	
Male	23 (76.7)	20 (66.7)	25 (83.3)	
Race				.06
Non-white	11 (36.7)	5(16.7)	4 (13.3)	
White	19 (63.3)	25 (83.3)	26 (86.7)	
Level of education				0.86
<12 years	3 (10)	5 (16.7)	2 (6.9)	
High school	4 (13.3)	3 (10)	5 (17.2)	
College	13 (43.3)	15 (50)	13 (44.8)	
Graduate	10 (33.3)	7 (23.3)	9 (31)	
Employment				0.77
Non-employed	10 (33.3)	8 (26.7)	12 (40)	
Employed	30 (66.7)	22 (73.3)	18 (60)	
Annual salary[a]				0.22
<20,000	7 (24.1)	7 (25.9)	9 (32.1)	
20,000-60,000	3 (10.3)	6 (22.2)	9 (32.1)	
60,000-150,000	14 (48.3)	7 (25.9)	7 (25)	
>150,000	5 (17.2)	7 (25.9)	3 (10.7)	
Insurance				0.74
None	1 (3.3)	3 (10)	1 (3.3)	
Private	14 (46.7)	14 (46.7)	17 (56.7)	
Medicare	11 (36.7)	6 (20)	9 (30)	
Other	4 (13.3)	7 (23.3)	3 (10)	
Relationship status				0.42
Single	6 (20)	10 (33.3)	10 (33.3)	
With partner	24 (80)	20 (66.7)	20 (66.7)	
Clinical Characteristics				
Coronary risk factors				
Hypertension	18 (60)	16 (53.3)	18 (60)	0.83
Dyslipidemia	20 (66.7)	22 (73.3)	24 (80)	0.51
Diabetes	8 (26.7)	6 (20)	9 (30)	0.66
Family history	13 (43.3)	8 (26.7)	6 (20)	0.13
Prior CAD or MI	10 (33.3)	8 (26.7)	15 (50)	0.16

Prior revascularization	9 (33.3)	5 (17.2)	13 (43.3)	0.08
MI during admission	15 (50)	13 (43.3)	13 (43.3)	0.87
Ejection fraction[b]	56.5 ± 10.3	55.5 ± 9.6	56.9 ± 13.2	0.9
Body mass index	29.7 ± 6.8	29.5 ± 5.4	28.5 ± 5.9	0.73
Hemoglobin A1C[c]	6.3 ± 1.3	5.6 ± 0.9	6.8 ± 2.3	0.20
Psychosocial Characteristics				
Depression[d*]	4.45 ± 3.38	7.18 ± 6.64	6.59 ± 6.00	0.14
Social support[e**]	84.37 ± 9.05	81.79 ± 17.41	79.83 ± 13.29	0.44

Data are presented as mean ± SD, n (%)
CAD, coronary artery disease; MI, myocardial infarction
N = 90 total; n = 30 each group
Missing data: a: n = 84, b: n = 77, c: n = 42, d: n = 88, e: n = 89
*Based on Beck Depression Inventory (range 0-63)
**Based on MOS Social Support Survey (range 19-95)

Table 2: Medication Self-Efficacy Scores

Medication Self-Efficacy				
	TM Reminders + TM Education (n = 27)	TM Education Alone (n = 27)	No TM (n = 28)	*p*
Baseline	32.29 ± 6.82	32.98 ± 5.99	33.32 ± 6.04	0.81
Follow-up at 30 days	35.37 ± 3.77	34.23 ± 4.92	33.92 ± 4.04	0.72

Data are presented as mean ± SD
Based on the Self-Efficacy for Appropriate Medication Use Scale (range 13-39)
Group by time effect: $p = 0.49$

Chapter 7

Conclusions

Chapter 7

Conclusions

Objective of Dissertation

The overall objective of this dissertation was to determine the efficacy of mobile technology to promote medication adherence. The beginning chapters presented the significance of medication adherence, a systematic review of mobile phone interventions to promote medication adherence, a proposed theoretical model applicable to this study, and an overview of electronic methods to measure medication adherence. The results of the randomized controlled trial (RCT) using a mobile phone intervention to promote medication adherence among patients with coronary heart disease (CHD) was then presented. The previous chapter reviewed self-efficacy and other predictors of medication adherence as determined by the pilot RCT.

Purpose of Intervention

More specifically, the primary purpose of the intervention was to establish the efficacy of text messaging to improve adherence to antiplatelet and statin medications among patients with myocardial infarction (MI) and/or percutaneous coronary intervention (PCI). Given the generally older population of CHD patients, feasibility and satisfaction with a text messaging intervention is important to establish for future research. The results of this pilot study aid our understanding of the factors that influence medication adherence in patients with CHD and can be applied to future research.

Review of Findings

In Chapter 5, data from the Medication Event Monitoring System (MEMS) showed better medication adherence in the two experimental groups who received text messages (TM) for antiplatelet medications compared to those who did not, although no significant differences in adherence were found among groups for statins. In contrast, self-reported medication adherence did not differ among patients who received or did not receive TM for medication reminders and/or education. Interestingly, all patients' self-reported adherence after experiencing a major cardiac event improved over time, which was a positive change. The discrepancy between adherence data may reflect the incongruity between true and perceived medication adherence, challenges in proper MEMS use, or the Hawthorne effect. Limitations of the intervention have been discussed in previous chapters, including a limited sample of 90 patients, which could have led to a Type II error, thereby weakening the results and interpretation of findings.

Nevertheless, two-way messaging with the TM Reminders + TM Education group revealed a significantly higher response by patients about taking antiplatelet medications compared to statins. This finding also supports better adherence to antiplatelet therapy, as replying to TM was meant to represent confirmation of medication self-administration. High adherence to antiplatelet therapy was likely due to perceived importance of taking antiplatelet medication following teaching in the hospital about its role in preventing life-threatening complications such as in-stent thrombosis.

Other important findings were highlighted in Chapter 6. Consistent with self-reported findings of medication adherence in the previous chapter, medication self-efficacy improved for all groups over time, but did not differ among groups based on the intervention. By chance, the control group had higher general self-efficacy scores compared to the TM Education Alone group at baseline and 30 days, but the groups did not differ based on the intervention.

More importantly, Chapter 6 identified variables that were associated with and predict medication adherence. Male sex, less depression, and higher social support were positively associated with higher medication adherence at baseline, while less depression and higher social support predicted higher medication adherence after the intervention. A subgroup analysis showed males significantly improved in self-reported adherence as a result of the intervention, but males in the control group had significantly higher change scores in self-reported medication adherence compared to the TM Reminders + TM Education group. The results of higher self-efficacy in the control group and lack of difference in self-reported medication adherence were unexpected, and further supports the null findings of the intervention related to self-report.

Implications of Research

The 2020 Impact Goals of the American Heart Association are: “By 2020, to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular diseases and stroke by 20%” (Lloyd-Jones et al., 2010). Improving cardiovascular morbidity and mortality can be achieved in part by increasing medication adherence to improve health promotion as well as disease prevention and management. As the late former General Surgeon C. Everett Koop once stated, “Drugs don’t work in patients who don’t take them” (Osterberg & Blaschke, 2005).

The viability of applying mHealth among patients with acute and chronic diseases has been established over the past decade through feasibility studies and more rigorous studies such as RCTs. This study has confirmed the feasibility and satisfaction of a mobile phone intervention among patients with a diverse age range (35-83 years) who were recruited during their hospitalization for MI and/or PCI.

The research findings contribute to clinical, social, and policy implications that will be discussed in the next section. Relevant implications to mHealth are briefly reviewed in these categories and future directions suggested.

Clinical Implications

Prior interventions to improve medication adherence have included combinations of providing increased information, reminders, self-monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care, as well as making the medication schedule simpler. However, even the most effective interventions did not lead to large improvements in adherence and treatment outcomes (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008), confirming how difficult it is to change human behavior and the challenge of conducting and testing behavioral interventions. In reviewing this list, it is clear that mHealth interventions can substitute or supplement many efforts that have been tried in the past. mHealth can offer more tailored, convenient, and regular contact with patients to help sustain medication adherence. Future technology-based interventions will likely be a combination of mHealth, eHealth, and telehealth to provide health education, monitor health status, enhance self-management, offer social support and social networking opportunities, and facilitate communication between patients, caregivers, and health care providers.

Important clinical lessons can be gained from the current study. Encouraging medication adherence following a coronary event is vital and can be fostered in many different forms. This text messaging intervention provided one modality that stressed the importance of antiplatelet and statin therapy in the medical management of CHD. This study also demonstrated the value of providing health education three times a week as evidenced by the significant difference in objective adherence to antiplatelet therapy by the TM Education Alone group compared to control group.

Next, patients may benefit from the provision of personal tools for medication adherence such as mobile applications or use of a similar text messaging program such as CareSpeak mobile Health manager that was used for the current study. Participating in this research study by tracking medication use with an electronic medical device may have motivated patients and can be a model for future interventions by providing high risk patients with consumer products such as GlowCaps to build a sense of accountability.

Finally, asking patients about barriers to medication adherence during their hospitalization and follow-up outpatient visits may prevent morbidity and rehospitalization. In addition, understanding and addressing the predictors of medication nonadherence such as depression and low social support are important steps to help patients and caregivers. Options to encourage social support may include mobile interactivity or face-to-face interactions at group cardiac rehabilitation or other supportive settings.

Social Implications

Unlike other research interventions to promote adherence that have been tried in the past, mHealth is a field that has stimulated immense interest from numerous stakeholders. mHealth is a revolution that has significantly affected health researchers and has motivated new partnerships with engineers, computer scientists, systems and data analysts, health insurance payers, regulators and policy makers, and business organizations (e.g., pharmaceutical and life-sciences). National governments, global health agencies, and the telecommunications sector have recognized the potential inherent in these technologies and are also important players in the mHealth movement (Labrique, Vasudevan, Chang, & Mehl, 2012). As mHealth science continues to develop, health care providers and consumers may be deeply impacted.

One of the superior benefits to mHealth is the potential ability to improve health services, access, and health outcomes for underserved populations in developing countries. In fact, the mHealth Working Group was created in 2009 by a conglomerate of global health organizations to foster collaboration on mHealth implementation in achieving global health strategies, standards and practices (mHealth Working Group, 2013).

mHealth will continue to influence our society and the way we communicate with patients and deliver care. Mobile technologies allow for "fine-grained tailoring of communication with the user," real-time data collection and analysis, and person-level ecosystems of sensors that collect and analyze data from multiple sources (Atienza & Patrick, 2011).

Policy Implications

Public health and advocacy programs will play an important role in achieving goals for cardiovascular health promotion and disease prevention in the next decade and beyond (Lloyd-Jones et al., 2010). Cost-effectiveness research is also a major consideration when considering health promotion interventions such as medication adherence. For example, the key impetus to design an intervention using TM instead of a mobile phone application in this study was the cost of designing, implementing, and maintaining an application that would only be available to smartphone users. Text messaging is a cost-effective means to communicate with large populations in developed and undeveloped countries.

More generally, policy implications also consist of security and privacy issues surrounding health information that is collected and shared in the mobile space. For example, policy makers have required that shared medical data be compliant with the Health Insurance Portability and Accountability Act (HIPAA) requirements (Atienza & Patrick, 2011). Furthermore, recent attention has been given to wireless medical device regulatory requirements by the Federal Communications Commission (FCC) and the U.S. Food and Drug Administration

(FDA) to protect consumers of mobile phone applications that may pose harm and risk if they do not work as intended (Atienza & Patrick, 2011; Foreman, 2013).

Future Directions

The future of mHealth will depend on solid evidence of efficacy, effectiveness, and population-level reach and impact (Atienza & Patrick, 2011). Although stakeholders may be anxious to propagate mHealth solutions, the "science" of mHealth is still in the early stages. This study highlighted some research opportunities and gaps, which will be briefly discussed.

Although this study only tracked differences in adverse clinical outcomes over 30 days, long-term quality outcomes will be important to monitor in the future. Cholesterol levels were originally included as objective data in this study, however the timing of the analyses were not sufficient to obtain an adequate sample since only 35% of patients had accessible cholesterol levels completed within 3-6 months of hospital discharge. Biomarkers will provide important data for future studies to assess the clinical value of mHealth interventions. Potential risks will need to be clearly reported in the literature through ongoing quantitative and qualitative research.

Next, future researchers will need to define the content, frequency, and duration of communication that will sustain the attention of users long-term. This intervention attempted to examine two different aspects: content and frequency. The TM Reminders + TM Education group received TM twice daily in most cases as medication reminders along with educational TM three times a day. The TM

Education Alone group received educational TM three times a week in order to maintain consistent contact with the patient to determine if the TM would prompt them to take their medications. In future studies, the frequency of reminders and educational TM will need to be better defined to alert and inform patients, yet avoid being mundane, intrusive, and producing an “alarm effect”.

In addition, comparative effectiveness research may be appropriate in the setting of technology based interventions in the area of medication adherence. As the next generation of mHealth interventions is conducted using smart phone applications, these can be compared to text messaging interventions. Researchers using comparative effectiveness designs can also compare mHealth and eHealth interventions as well as traditional voice communication and text messaging interventions for promoting medication adherence.

Furthermore, as previously mentioned in Chapter 3, health behavior theories and models are needed to guide the development of complex interventions that are adaptable over time in response to various inputs (Riley et al., 2011). A multivariate theoretical model with potential predictors of medication adherence will allow for systematic investigation of the most relevant variables (Wu, Moser, Chung, & Lennie, 2008). Although the Theory of Self-Efficacy provided a basic theoretical model for this study, a more advanced model outlining key variables of medication adherence should be considered in future research.

Lastly, further development of objective medication adherence measurement tools are needed such as electronic medication organizers as an alternative to the very popular form of individual MEMS bottles that posed problems with accurate data collection in the current study. Having multiple forms of measurement appears to be beneficial as self-report and MEMS results were dissimilar in this study.

Summary

This intervention was aimed to promote medication adherence and achieved feasibility, high patient satisfaction, improved objective medication adherence through electronic monitoring, higher subjective adherence in TM responses for antiplatelets compared to statins, and supported our understanding of psychosocial factors that impact medication adherence. This pilot RCT helped to strengthen the groundwork for future mHealth interventions and can be easily applied to a wider population of patients, particularly for adherence to long-term medications for chronic disease management.

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Appendix

Appendix: Study Questionnaires

The Eight-Item Morisky Medication Adherence Scale (MMAS-8) – Revised
1. Do you sometimes forget to take your pills? Yes No
2. Over the past two weeks, were there any days when you did not take your medications? Yes No
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it? Yes No
4. When you travel or leave home, do you sometimes forget to bring along your medications? Yes No
5. Did you take your medicine yesterday? Yes No
6. When you feel like your health condition is under control, do you sometimes stop taking your medicine? Yes No
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your medication treatment plan? Yes No
8. How often do you have difficulty remembering to take all your medication? 1 Rarely/Never 2 Once in a while 3 Sometimes 4 Usually 5 Always

Self-Efficacy for Appropriate Medication Use (SEAMS) (Risser, Jacobson, & Kripalani, 2007)		
How confident are you that you can take your medicines correctly…		
1. When you take several different medications each day?		
1 Not confident	2 Somewhat confident	3 Very confident
2. When you take medicines more than once a day?		
1 Not confident	2 Somewhat confident	3 Very confident
3. When you are away from home?		
1 Not confident	2 Somewhat confident	3 Very confident
4. When you have a busy day planned?		
1 Not confident	2 Somewhat confident	3 Very confident
5. When they cause some side effects?		
1 Not confident	2 Somewhat confident	3 Very confident
6. When no one reminds you to take medicine?		
1 Not confident	2 Somewhat confident	3 Very confident
7. When the schedule to take the medicine is not convenient?		
1 Not confident	2 Somewhat confident	3 Very confident
8. When your normal routine gets messed up?		
1 Not confident	2 Somewhat confident	3 Very confident
9. When you are not sure how to take the medicine?		
1 Not confident	2 Somewhat confident	3 Very confident
10. When you are not sure what time of the day to take your medicine?		
1 Not confident	2 Somewhat confident	3 Very confident
11. When you are feeling sick (like having a cold or the flu)?		
1 Not confident	2 Somewhat confident	3 Very confident
12. When you get a refill of your old medicines and some of the pills look different than usual?		
1 Not confident	2 Somewhat confident	3 Very confident
13. When a doctor changes your medicine?		
1 Not confident	2 Somewhat confident	3 Very confident

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MOS Social Support Survey (Sherbourne & Stewart, 1991)				
1. About how many close friends and close relatives do you have (people you feel at ease with and can talk to about what is on your mind)?				
Write in number of close friends and close relatives: ☐				
People sometimes look to others for companionship, assistance, or other types of support. How often is each of the following kinds of support available to you if you need it?				
2. Someone to help you if you were confined to bed…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
3. Someone you can count on to listen to you when you need to talk…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
4. Someone to give you good advice about a crisis…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
5. Someone to take you to the doctor if you needed it…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
6. Someone who shows you love and affection…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
7. Someone to have a good time with…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
8. Someone to give you information to help you understand a situation…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
9. Someone to confide in or talk to about yourself or your problems…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
10. Someone who hugs you…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
11. Someone to get together with for relaxation…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
12. Someone to prepare your meals if you were unable to do it yourself…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
13. Someone whose advice you really want…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time
14. Someone to do things with to help you get your mind off things…				
1 None	2 Little of the Time	3 Some of the Time	4 Most of the Time	5 All of the Time

15. Someone to help with daily chores if you were sick…

1	2	3	4	5
None	Little of the Time	Some of the Time	Most of the Time	All of the Time

16. Someone to share your most private worries and fears with…

1	2	3	4	5
None	Little of the Time	Some of the Time	Most of the Time	All of the Time

17. Someone to turn to for suggestions about how to deal with a personal problem…

1	2	3	4	5
None	Little of the Time	Some of the Time	Most of the Time	All of the Time

18. Someone to do something enjoyable with…

1	2	3	4	5
None of the time	A Little of the Time	Some of the Time	Most of the Time	All of the Time

19. Someone who understands your problems…

1	2	3	4	5
None	Little of the Time	Some of the Time	Most of the Time	All of the Time

20. Someone to love and make you feel wanted…

1	2	3	4	5
None	Little of the Time	Some of the Time	Most of the Time	All of the Time

Permission not required

Beck's Depression Inventory (Beck, 1961)
1. 0 I do not feel sad. 1 I feel sad. 2 I am sad all the time and I can't snap out of it. 3 I am so sad and unhappy that I can't stand it.
2. 0 I am not particularly discouraged about the future. 1 I feel discouraged about the future. 2 I feel I have nothing to look forward to. 3 I feel the future is hopeless and that things cannot improve.
3. 0 I do not feel like a failure. 1 I feel I have failed more than the average person. 2 As I look back on my life, all I can see is a lot of failures. 3 I feel I am a complete failure as a person.
4. 0 I get as much satisfaction out of things as I used to. 1 I don't enjoy things the way I used to. 2 I don't get real satisfaction out of anything anymore. 3 I am dissatisfied or bored with everything.
5. 0 I don't feel particularly guilty 1 I feel guilty a good part of the time. 2 I feel quite guilty most of the time. 3 I feel guilty all of the time.
6. 0 I don't feel I am being punished. 1 I feel I may be punished. 2 I expect to be punished. 3 I feel I am being punished.
7. 0 I don't feel disappointed in myself. 1 I am disappointed in myself. 2 I am disgusted with myself. 3 I hate myself
8. 0 I don't feel I am any worse than anybody else. 1 I am critical of myself for my weaknesses or mistakes. 2 I blame myself all the time for my faults. 3 I blame myself for everything bad that happens.
9. 0 I don't have any thoughts of killing myself. 1 I have thoughts of killing myself, but I would not carry them out. 2 I would like to kill myself. 3 I would kill myself if I had a chance.

10.	
0	I don't cry any more than usual.
1	I cry more now than I used to.
2	I cry all the time now.
3	I used to be able to cry, but now I can't cry even though I want to.
11.	
0	I am no more irritated by things than I ever was.
1	I am slightly more irritated now than usual.
2	I am quite annoyed or irritated a good deal of the time.
3	I feel irritated all the time.
12.	
0	I have not lost interest in other people.
1	I am less interested in other people than I used to be.
2	I have lost most of my interest in other people.
3	I have lost all of my interest in other people.
13.	
0	I make decisions about as well as I ever could.
1	I put off making decisions more than I used to.
2	I have greater difficulty in making decisions more than I used to.
3	I can't make decisions at all anymore.
14.	
0	I don't feel that I look any worse than I used to.
1	I am worried that I am looking old or unattractive.
2	I feel there are permanent changes in my appearance that make me look unattractive.
3	I believe that I look ugly.
15.	
0	I can work about as well as before.
1	It takes an extra effort to get started at doing something.
2	I have to push myself very hard to do anything.
3	I can't do any work at all.
16.	
0	I can sleep as well as usual.
1	I don't sleep as well as I used to.
2	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3	I wake up several hours earlier than I used to and cannot get back to sleep.
17.	
0	I don't get more tired than usual.
1	I get tired more easily than I used to.
2	I get tired from doing almost anything.
3	I am too tired to do anything.
18.0	My appetite is no worse than usual.
1	My appetite is not as good as it used to be.
2	My appetite is much worse now.
3	I have no appetite at all anymore.

19.

0 I haven’t lost any weight, if any, recently.
1 I have lost more than five pounds.
2 I have lost more than ten pounds.
3 I have lost more than fifteen pounds.

20.

0 I am no more worried about my health than usual.
1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think of anything else.

21.

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I have almost no interest in sex.
3 I have lost interest in sex completely.

Permission not required

Questionnaire on Mobile Phone Use

Please describe your experience using a mobile phone to receive text messages. Did you receive…? (please check one)

_____ medication reminders and health information
_____ health information

1) It was easy to use the text messaging feature on my mobile phone.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

2) I liked using my mobile phone to receive text messages with health information.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

3) I had technical difficulties while using my mobile phone over the past 30 days.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

Please describe any technical difficulties and frequency:

____

4) Overall, I was satisfied with receiving text messages to help me with my health.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

5) I believe using my mobile phone helped me remember to take my medications.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

6) The frequency and timing of text messages was NOT convenient.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

I would prefer to change the frequency of text messages to <u>remind me to take medications</u> I take TWICE A DAY:

____ once a day
____ twice a day
____ 3 times per week
____ once a week

I would prefer to change the frequency of text messages <u>on health information:</u>

____ once a day
____ twice a day
____ 3 times per week
____ once a week

7) I felt like someone cared about me and my health by receiving text messages following my heart attack.

1	2	3	4	5
Strongly Disagree	Moderately Disagree	Neutral	Moderately Agree	Strongly Agree

8) Please list 2 or more recommendations for using mobile phones for future research.

____

____

____

____

____

Thank you for completing this questionnaire!

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