6-23-2015

A Randomized Controlled Trial of the Feasibility and Preliminary Efficacy of a Texting Intervention on Medication Adherence in Adults Prescribed Oral Anti-Cancer Agents: Study Protocol

Sandra L. Spoelstra
Grand Valley State University, spoelsts@gvsu.edu

Charles W. Given
Michigan State University

Alla Sikorskii
Michigan State University

Constantinos K. Coursaris
Michigan State University

Atreyee Majumder
Michigan State University

See next page for additional authors

JOURNAL: Journal of Advanced Nursing
TITLE PAGE

Full Title A randomized controlled trial of the feasibility and preliminary efficacy of a texting intervention on medication adherence in adults prescribed oral anti-cancer agents: study protocol

Running head TEXT MESSAGE AND MEDICATION ADHERENCE

Authors Sandra L. SPOELSTRA, PhD, RN; Charles W. GIVEN, PhD; Alla SIKORSKII, PhD; Constantinos K. COURSARIS, PhD; Atreyee MAJUMDER, PhDc, BS; Tracy DEKOEKKOEK, RN; Monica SCHUELLER, BA; Barbara A. GIVEN, PhD, RN, FAAN

Author Affiliations Michigan State University, East Lansing, Michigan
College of Nursing (Dr. Spoelstra, DeKoekkoek, Schueller, Dr. BA Given)
Institute for Health Care Studies and Department of Family Medicine (Dr. CW Given)
Department of Statistics and Probability (Dr. Sikorskii, Majumder)
Department of Telecommunication, Information Studies (Dr. Coursaris)

Corresponding Author Sandra L. Spoelstra, PhD, RN
Michigan State University, College of Nursing
1355 Bogue Street, Room C342, East Lansing, MI 48824
Email spoelst5@msu.edu, Phone 517-353-8681

Funding Statement This research was supported by a grant entitled: *Text Messaging to Improve Adherence to Oral Chemotherapy Agents* from the National Cancer Institute (Grant Number 1R15CA176595).

Clinical Trials Registration ClinicalTrials.gov Identifier NCT01889511

Conflict of Interest Statement The authors have no conflicts of interest to disclose.

ABSTRACT

Aim To report a study protocol that examines feasibility, preliminary efficacy, and satisfaction of a text message intervention on the outcome of medication adherence in adult patients prescribed oral anti-cancer agents.

Background Administration of oral anti-cancer agents occurs in the home setting, requiring patients to self-manage the regimen as prescribed. However, many barriers to medication adherence exist: regimens are often complex, with cycling of two or more medications; side effects of treatment; most cancer patients are older with comorbid conditions and competing demands; and cognitive decline and forgetfulness may occur. Research indicates patients miss nearly one-third of the prescribed oral anti-cancer agent dosages. Text message interventions have been shown to improve medication adherence in chronic conditions other than cancer. However, a majority of those patients were less than 50 years of age, and most cancer patients are diagnosed later in life.

Design A two-group randomized controlled trial with repeated measures.

Methods Seventy-five adult patients newly prescribed an oral anti-cancer agent will be recruited (project funded in April 2013) from community cancer centers and a specialty pharmacy. Participants will be randomized to either a control group (n=25; usual care) or an intervention group (n=50; usual care plus text messages timed to medication regimen). Outcome measures include: medication adherence, feasibility, and satisfaction with the intervention. Data will be collected over 8-weeks: baseline, weekly, and exit.

Discussion Standardized text message intervention protocol and detailed study procedures have been developed in this study to improve medication adherence. Trial is registered at ClinicalTrials.gov (Identifier NCT01889511).

Summary Statement: Why is this research needed?

- Patients prescribed oral anti-cancer agents have difficulty with medication adherence due to competing demands with other chronic conditions, forgetfulness, or symptoms from side effects of the cancer or cancer treatment.
- In spite of efforts by clinicians and pharmacists to promote medication adherence, many patients exhibit sub-optimal adherence, which may impact cancer treatment effectiveness.
- Interventions, such as text messaging, are needed to assist patients prescribed oral anti-cancer agents to adhere to treatment regimens to assure a therapeutic dosage of the medication is taken.

Keywords: Text messaging, mHealth, oral anti-cancer agent, cancer, recruitment, randomized controlled trial, medication adherence, intervention

INTRODUCTION

Cancer treatment with oral anti-cancer agents (OAs) is a newer paradigm. More than 50 OAs on the market, 25% of treatment is expected by to delivered in pill form by 2020 (Bestvina *et al.* 2014). Care has moved from supervised cancer centers to the home where responsibility is placed on the patient. Despite clinician efforts to promote medication adherence, a significant problem still exists. Recent reviews on OAs indicate adherence rates are often less than 80% (Bassan *et al.* 2014, Puts *et al*. 2014). Thus, it is important for interventions to promote medication adherence in patients taking OAs to assure a therapeutically effective dosage of the cancer treatment is attained (Soria *et al.* 2011).

Background

Numerous factors influence medication adherence in general; and some information is known regarding factors that influence OA adherence. Factors examined in this study are shown in Figure 1. To address the problem of medication adherence, this protocol focuses on improving self-efficacy and attention. Self-efficacy is the belief about how a person feels, thinks, and motivates themselves and behaves in regard to their capabilities to produce expected levels of performance that influence events that affect their life (Bandura 1977). Evidence shows higher self-efficacy leads to better health behaviors (Champion *et al.* 2007, Gitlin *et al.* 2006); and makes it more likely a patient will adhere to a medication regimen (Puts *et al.* 2014). McCorkle (2011) found empowering patients to care for themselves through improving self-efficacy was a pivotal component of cancer care.

Attention is the behavioral and cognitive process of selectively concentrating on a discrete aspect of information, whether deemed subjective or objective, while ignoring other perceivable information (Posner & Snyder 2004, Yiend 2010). With OAs, patients are required to engage in behavioral change through attention to self-manage the medication regimen (Insel *et*

al. 2006, Wagner & Ryan 2004). Attention research has also shown that behaviors become effortless through practice, and repetition then leads to habit formation (Insel *et al.* 2006). Thus, focusing on interventions that improve self-efficacy and attention may promote OA adherence.

Mobile health (mHealth) technology, such as Short Message Service (SMS) Text Messages (TM) on cell phones, is evolving as a cost-effective mode of delivering health behavior interventions that can be integrated into daily life, yet tailored to the individuals need (Cole-Lewis & Kershaw 2010, Krishna *et al*. 2009, Riley *et al*. 2011). TMs are known to improve health behaviors across multiple diseases (Cole-Lewis & Kershaw 2010) and evidence exists on TMs as a reminder for prevention (Lakkis *et al.* 2011), smoking cessation (Severi *et al*. 2011), medication adherence in asthma (Johnson *et al.* 2011), and management of diabetes (Riley *et al.* 2011). Evidence is also emerging on the ability of a TM to prompt attention and an automatic response, as the TMs affect different elements of cognition, like working memory (Buehlmann & Deco 2008, Posner & Snyder 2004, Yiend 2010). TMs as an automatic response are thought to motivate behavior change and call people to action (i.e. self-management [adherence to medication regimen]). Using TMs to promote medication adherence in patients prescribed OAs has the potential to improve cancer treatment outcomes.

Theoretical framework guiding the study

To examine the complex problem of OA adherence, this study will use the Social Cognitive Theory to underpin the approach to improving attention and self-efficacy (Bandura 1977). In addition, the Information, Motivation, and Behavioral skills model (IMB) guides the intervention design and testing (see Figure 2) (Fisher *et al.* 2003). A multitude of evidence exists on how self-efficacy supports engaging individuals in behaviors to self-manage (DiMatteo 2004, DiMatteo *et al.* 2007). The IMB model hypothesizes that accurate information, motivation, and

behavioral skills are the critical elements of behavior change; and the relationship between information and behavior are mediated by behavioral skills (Fisher *et al.* 2003, Osborn & Egede 2010, Zarani *et al.* 2010). An informed and motivated person who lacks behavioral skills to self-manage and adhere to a medication may have poorer outcomes, particularly with complex treatments like OAs, where behaviors need to be established and maintained (Fisher *et al.* 2002). Behavioral skills require both objective ability and perceived efficacy to self-manage (Bandura 1977). Thus, the goal of the intervention is threefold: 1) to inform patients; 2) to motivate them by increasing attention to the task; and 3) to increase self-efficacy to complete the task of OA adherence.

THE STUDY

Aim

The aim of this study is to promote medication adherence among adult cancer patients newly prescribed OAs.

Objectives

1. To determine feasibility and satisfaction of a TM intervention among adult cancer patients newly prescribed OAs.
2. To determine preliminary efficacy of TMs on adherence rates for adult cancer patients newly prescribed OAs.
3. To explore the effects of attention, self-efficacy, medication regimen complexity, symptom severity and interference, and comorbid conditions on rate of adherence to OAs.

Hypotheses

- Of those approached to participate in the study, 80% will enroll.

- Of those who are in the intervention group, 80% will complete 21 days of TMs.
- Of those who are in the intervention group, 90% will be satisfied with the TMs.
- The TM group will have significantly higher OA adherence rates than the control group; and the effect size for differences in adherence by group will be moderate to large.
- Adherence will be higher for patients with higher self-efficacy and attention, simpler OA regimens, fewer comorbid conditions and lower reported symptom severity.

Methodology and design

This is a two-group, randomized controlled trial that will examine a TM intervention on adherence of cancer patients to their OAs, funded by the National Cancer Institute in April 2012 (see Figure 3). Patients will be randomly assigned into the control group and receive usual care; or to the intervention group and receive TMs plus usual care. The study will use a single-blind approach, so those collecting data will not be aware of group assignment.

Participants

Patients will be recruited from four community cancer centers and a national specialty pharmacy in the US. Inclusion criteria include: 21 years of age or over; diagnosed with cancer; and prescribed an OA in the past 7-days. Patients must also be able to speak, read, and understand English, own a personal cell phone, and be able to receive phone calls and TMs. Patients who are deaf, blind, or unable to accept phone calls will be excluded. Those with cognitive impairment that limits ability to understand and answer questions will be excluded, as assessed by recruiters. For those who do not know how to TM and want to learn, a manual on how to TM will be provided and the recruiter will provide training.

Sample size determination

Seventy-five patients will be accrued to attain data for 60 patients. Over-sampling to account for a 20% attrition rate, as experienced in an earlier OA study will occur (Spoelstra *et al*.

2013). A 2:1 allocation ratio with 50 assigned to the intervention group and 25 assigned to the control group will occur. This will not maximize power of efficacy determination compared to a 1:1 allocation, however, it will allow for an adequate number of patients to describe feasibility and satisfaction with the TM intervention. For preliminary efficacy determination, it is expected at baseline that 40 in the intervention group and 20 in the control group will be available for analyses post-attrition, out of each group (50 and 25). Given post-attrition sample size estimates, an effect size of 0.78 or greater would be considered statistically significant. The level of significance will be set at 0.05 with a power of 0.80 or greater for a two-tailed test. This means that if the Relative Dose Intensity (RDI), a measure of OA adherence, in the experimental group is 0.78 standard deviation units higher than in the control group, this difference will be detected as statistically significant. If the intervention effect is smaller, statistical significance will not be reached, yet power future studies.

Data collection and study procedures

Data will be collected by recruiters on screening and enrollment forms; patient report; medical and pharmacy record review; telephone surveys via trained interviewers at the university for baseline, satisfaction, and exit interviews (and audio recorded); and by TM and AVR. Data from the forms and interviews will be entered and stored in the web-based Patient Reported Outcome Measurement Information System (PROMIS) (www.assessmentcenter.net); and by the company that delivers the TMs and AVRs.

Recruitment, enrollment, and consent

Recruiters will identify eligible patients by monitoring prescription orders. At the clinical sites, the recruiters will talk to patients face-to-face, and if the patient agrees, obtain a signature on the consent and HIPAA form. At the specialty pharmacy, the recruiter will contact

patients by phone, and if the patient agrees, obtain an electronic signature on the consent and HIPAA form via email.

The recruiter will complete the enrollment form (week 0), collecting data from patients by self-report and confirming the information in the medical or pharmacy record when necessary. These data will include name, address, preferred phone number, cancer site and stage at diagnosis, name and phone number of oncologist, preferred interview days and times, and OA regimen information. The OA information will include the medication name, date prescribed, and the date when administration of the OA is to begin. Information obtained on the dose of the OA will include: number of pills to be taken; and the interval for administration and rest periods and when to resume if rest periods are ordered.

In the clinic settings, the recruiter will provide an enrollment folder to the patient which includes written information about the study, a copy of their consent and HIPAA forms, TM procedures (Online Supplemental 1), AVR calling procedures, and a manual (Online Supplemental 2) on how to TM, which was designed by university experts. For those at specialty pharmacy, the university will mail information.

Baseline interview

Trained staff at the university will conduct baseline interviews (week 1) and collect data on measures and items identified in Figure 4. Interviews are expected to take 40-minutes.

Randomization

Following completion of the baseline interview, the university will randomly assign patients to the intervention or control group using a computer minimization procedure programmed by the study statistician. As the sample size is relatively small, a 2:1 ratio was chosen to ensure adequate numbers are exposed to TMs so that conclusions about feasibility and

satisfaction can be reached. Two variables will be used as balancing factors in randomization. The first is OA complexity, which will be divided into two categories: simple or complex, as past research has demonstrated declining adherence as complexity increases. Simple regimens are those that are daily dosing without variation, while complex regimens are twice daily dosing, multiple medications, or cycling with medication dosing starting or stopping. The second is age (<50 and ≥50 years), as certain types of cancer or comorbid conditions may be experienced in those over 50 years of age. In this manner, the design is balanced with respect to dimensions that represent key variables for this protocol. The university will call patients to inform them which group (intervention or control) they are assigned, confirm the times for AVR calls, and the preferred PIN. For those in the TM group, the university will reconfirm the medication schedule.

Control group

The control group will receive usual care, which consists of standard care and materials provided by the oncology office or pharmacy. In general, this includes instructions and information on the OA regimen (e.g. amount of the medication and timing of the doses), common side effects, how to manage symptoms, general ways to remember to take the medication (e.g., calendar or pill box), medication safety (i.e., storage), and how to contact a clinician for problems that arise.

Experimental group

The university will set up delivery of the TMs by programming the electronic software platform to deliver the TMs on the start date of treatment, or if treatment is already started, the next dosage. The TM intervention will be delivered for 21-days (weeks 2 to 4) set to the patient's cycle of treatment and will be tailored to prompt patients to adhere to the OA for the period when they are to take the medication, accounting for when they are to stop the medication and when to

resume. Thus, if a patient is prescribed to begin dosing four days after enrollment, the first TM would be delivered on day 4 in the study. For another patient, they may be prescribed to begin dosing seven days after enrollment, thus, the first TM would be delivered on day 7 of the study.

Online Supplemental 3 shows the TM content for this protocol. Each TM was designed using self-efficacy theory. This includes an introductory TM, six adherence messages to be delivered on a rotating basis, and a TM sent at the conclusion of study. When the intervention starts, the university will send the test TM to confirm the correct cell phone number and receipt of a TM. Patients will be asked to reply to the TM to assure ability to respond. Upon completion of the intervention, a final TM will be sent to each patient. Precautions will be taken to assure that we do not provide a TM on a day when the patient is not to be taking their OA by reconfirming the dosing schedule with the recruiter and the patient. Patients will be asked to inform the university of dose modification or if the OA is stopped at their earliest convenience and instructed to always follow the prescribed dose from their oncologist.

Weekly assessments of medication adherence

Weekly assessments via an AVR call will be made (weeks 2 to 9) to all patients enrolled in the study to assess adherence to OA. In addition, symptom severity from side effects of treatment will be assessed to inform future studies. Calls will be at the desired specified times established by the patients, with responses recorded using the touch-tone pad of a phone. The AVR calls are expected to take five to ten minutes. In prior studies, no patients refused participation because of the interviews or AVR length (Spoelstra *et al*. 2013).

Intervention satisfaction

Satisfaction with the TM intervention will be assessed for all patients in the intervention group by the university during week 5, following completion of all TMs. The intervention group

will be asked about their overall satisfaction with the study, whether they encountered any technical problems, their satisfaction with TMs to remind them to take their medication, and if they would recommend TMs as a medication adherence reminder. Satisfaction with TMs for medication adherence will be measured with a tool using Likert-scaled items, previously developed by this research team and administered in several previous studies (Decker *et al*. 2009, Spoelstra *et al*. 2013). In this protocol, satisfaction will be deemed high if the scores exceed 80%. The interview will be audio-recorded and is expected to last approximately 10 minutes.

Exit interviews

Exit interviews will be conducted at the end of the study (week 10) by phone via trained interviewers at the university. When a patient completes their final AVR call in week 9, an exit interview will be scheduled within seven days. If a patient is unable to complete all AVR contacts, an attempt will still be made to conduct the exit interview. Exit interviews are expected to take 30-minutes.

Instruments and measures

Factors examined in this protocol are shown in Figure 4. Medication adherence is defined as the degree or extent of conformity to the recommendations regarding day-to-day treatment prescribed by the provider with respect to the timing, dosage, and frequency for the duration of time from the initiation of the medication to discontinuation of therapy (Cramer *et al*. 2008). Adherence rates will be calculated two ways: 1) proportion of pills prescribed will be compared to pills taken; and 2) relative dose intensity (RDI).

Medication adherence will be measured by self-report, by recall of the number of OA pills taken in the past seven days. This will occur during the weekly automated voice response system (AVR) calls; and during the exit interview. The proportion of OA pills taken compared to what

was prescribed will be calculated to determine a rate of adherence. RDI, the amount of OAs taken over a specific time in relation to what was ordered, will be based on pharmacy dispensing records and self-reported pill counts (AMGEN 2008). The RDI will be calculated by examining the dose taken divided by standard dose intensity (prescribed number of pills) multiplied by 100 over the study period. A cumulative determination of adherence for the period between baseline and exit will be examined as an indicator of how adherence rates are related to persistence of the medication regimen over the 10 weeks.

Data that is collected via self-report will include: patient characteristics such as age, race, and sex; cancer site and stage; OA type and regimen complexity; presence of any of the 10 most commonly occurring comorbidities (yes/no) (cardiac disease, hypertension, emphysema, asthma, renal disease, diabetes mellitus, alcohol abuse, depression, arthritis, and anemia); and if taking a medication for the comorbidity (yes/no).

Cognition was assessed using the Cimprich Attentional Function Inventory, which is scored from not at all to extremely well across three elements (Cimprich *et al.* 2011). Three constructs of cognition were examined via subscales in the instrument: effective action, attentional lapses, and interpersonal effectiveness; with internal consistency reliability of 0.95.

Self-efficacy will be assessed using the Medication Adherence Self-efficacy Scale (MASES-R), Cronbach α 0.92 (Ogedegbe *et al.* 2003); the Medication Adherence Rating Scale (MARS), Cronbach α 0.66 (acceptable for a short 5-item scale) (Thompson *et al.* 2000); and the Brief Medication Questionnaire (BMQ-Specific), Cronbach α 0.77 (Horne *et al.* 1999).

Social support will be assessed using the Medication Specific Social Support (MSSS) tool, Cronbach α 0.79 (Lehavot *et al.* 2011). A PROMIS tool will be used to assess depressive

symptoms (8a-form) and physical function (4a), both with Cronbach α above .85 (Pilkonis *et al.* 2011).

Severity of 19 prevalent symptoms associated with side effects or OAs will be examined using the Symptom Inventory (Given *et al.* 2008). This includes: weakness, pain, headache, fatigue, skin rash/skin sores, numbness or tingling in the hands/feet, redness peeling or pain in the hands and or feet, swelling of the hands or feet, joint swelling and pain, sores in mouth, lack of appetite, nausea or vomiting, diarrhea, constipation, sleep disturbance, cough, shortness of breath, anxiety, and fever of 101.0 or higher. Patients will be asked if, within the past seven days, they have experienced each symptom (yes/no), and, if yes, to rate the severity on a 10-point scale; and scores will be summed (0 to 190). Alpha coefficients are 0.72 and 0.78 for the number and severity sub-scales, respectively.

The feasibility of providing TMs will be measured by the number of TMs delivered; and by any discontinuation of TMs during the course of the study. Acceptability of TMs will be measured by the number of patients who accept enrollment compared to the number who were offered to participate; and by the percent of patients who complete the study. Feasibility will be further assessed by examining the reasons for attrition in the intervention group from satisfaction survey questions.

Data analysis

SAS 9.4 will be used for analysis. As an initial step, basic descriptive statistics will be computed for variables of interest, frequency distributions, and measures of central tendency, skewness, and variability. The primary outcome for intervention efficacy determination is adherence. Age, sex, and race, comorbid conditions, site of cancer, symptom severity, and self-efficacy will be compared between groups at baseline to verify the success of randomization. If

systematic differences are discovered, then these variables will be included as covariates in the statistical models described below.

Primary analyses of each of the hypotheses will be as follows. Regarding percentage enrolled, the proportion of patients who were offered to participate in the study compared to those who actually enrolled will be summarized with a point estimate and a confidence interval. For intervention completion, the proportion of TMs received by the patient over the three week time period will be estimated, and the test of significance will be performed. Regarding satisfaction, the proportion of patients who report high satisfaction with the TM intervention will be summarized, and a test of significance will be performed. For patients in the intervention group, regression modeling will be used to describe how binary variables of use of the tailored TMs (e.g., continuing versus stopping the TMs or not returning TMs) are related to satisfaction.

To determine preliminary efficacy of the intervention, for the approximately continuous outcome variable of adherence expressed as RDI, general linear modeling will be used if the dependent variable is approximately normally distributed. If not, normalizing transformations will be applied and, if they are not successful, generalized linear modeling with appropriately distributed errors (e.g., Beta) will be employed. Patient characteristics and any variables not balanced at baseline will be entered as covariates in addition to the study group variable.

Since the protocol for this exploratory study is not powered for a formal hypothesis test, estimates of the effect sizes will be obtained and the confidence intervals will be used to inform future work. The effects of self-efficacy, OA regimen complexity, comorbid conditions, and symptom severity on adherence will be explored by adding these to the general or generalized linear model described above. As in the preliminary efficacy analyses, formal tests of statistical significance will be supplemented with estimates of the effect sizes to inform future work.

Ethical considerations

University and hospital human subject committee approvals were obtained in 2013 (IRB# 12-1258M). Recruiters will approach eligible patients, present the study, and obtain written consent to participate. Patients will be provided an enrollment folder which contains a brochure and a copy of the signed consent and HIPAA forms. Patients will be notified that data collected will be kept confidential, that they are able to withdraw from the study at any time, if desired, and that their participation will not affect their usual care. To assure privacy and confidentiality, the recruiter will help the patient to set up a password on their cell phone for TMs, and to select an AVR personal identification number (PIN) for the weekly calls.

Validity and reliability

Assuring protocol fidelity and integrity will occur by monitoring provision of TMs. This design will allow us to carefully document the intervention and its integrity. Bellg *et al.* (2004) argue that fidelity is represented by how delivery, receipt, and enactment lead to outcomes. In this study, the delivery (interviews and TMs), receipt (contacts), and enactment (adherence) will be documented as measures for each component of the protocol. All data will be checked immediately after data collection and any errors identified will be corrected by the university.

DISCUSSION

"Regardless of oncologists' best efforts in diagnosis and treatment; optimal outcomes are possible only through patient behavior. The key is structuring solutions that encourage optimal behavior on the part of the patient" (Express Scripts, 2010). Currently, adherence to OAs is sub-optimal for many patients (Spoelstra *et al.* 2013, Spoelstra *et al.* 2015). In general, interventions to promote medication adherence have had minimal effect (Conn *et al.* 2009). In response, this protocol is potentially transformative, as it is among the first to examine whether cancer patients

will accept tailored TMs to promote adherence to their OAs and if these messages are sufficiently robust to be associated with adherence to the OA.

TMs are a technology-driven, easy-to-use intervention that will encourage optimal adherence among cancer patients on OAs. TMs can easily be tailored to a specific patient's oral agent regimen, thus making this intervention usable for simple or more complex OAs. Further, delivering the TMs on cell phones makes this intervention readily accessible. Likewise, it is the first study to enroll a cohort of patients who are newly prescribed OAs. Past research has demonstrated that adherence levels begin to decline two months after the initiation of therapy (Streeter *et al.* 2011). Thus, this protocol could help inform initiation of care, where patterns of behavior are established and carried out through the entire oral agent treatment regimen. This research also begins to explore how non-adherence is related to contextual characteristics such as comorbid conditions or self-efficacy, thus informing future research. This type of intervention can transform care for cancer patients who have treatment in pill form by improving adherence to oral agents and improving their clinical outcomes, while- at the same time conserving health care resources.

Few studies have examined the feasibility of TMs in older patients, nor in those with cancer. This protocol sets a means of testing acceptability and preliminary efficacy in cancer patients prescribed OAs. This proposed study will enhance the state of the science as little is known regarding acceptability of TMs in cancer patients, the majority of whom are older. This proposed study has the potential to transform care for cancer patients newly prescribed OAs, supporting adherence to the treatment regimen to assure the dosage of the medication required to treat the cancer can be delivered as prescribed.

Limitations

A major limitation in this protocol is the ability to measure medication adherence. This is related to the state of the science and a lack of reliable and practical measures of medication adherence. Measuring medication adherence presents several potential problems with reliability as not all dose changes are documented in pharmacy records and patient self-report may contain response bias or not be reported accurately.

CONCLUSION

This innovative intervention involves a readily available technology that can be used to interact with patients on a regular, consistent basis that would otherwise not be possible, feasible, or cost effective if done in a one-by-one interaction with a health care provider. The number of cancer patients who receive chemotherapy in pill form is increasing and TMs may enable them to adhere and complete their cancer treatment. Thus, TMs have high generalizability and the potential to transform care.

Figures

Figure 1. Schematic of relationships among factors influencing medication adherence in this protocol

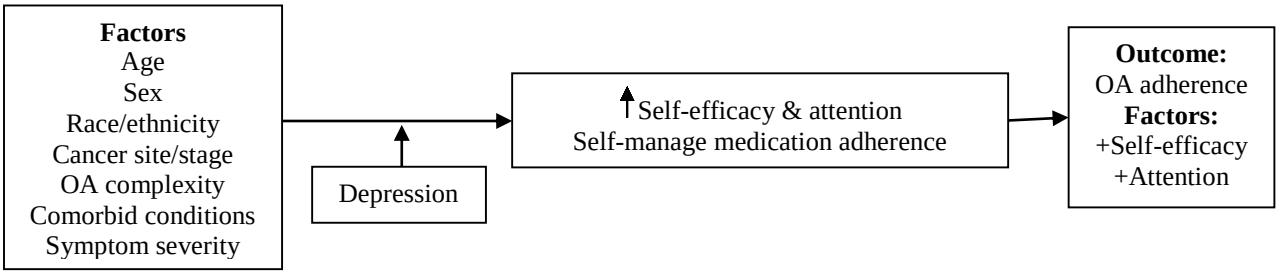

Figure 2. Synthesized social cognitive and Information Motivation Behavioral Skill model guiding the intervention in this protocol

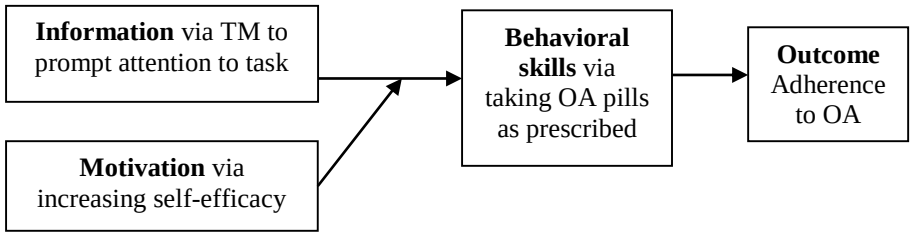

Figure 3. CONSORT schematic of steps in this protocol

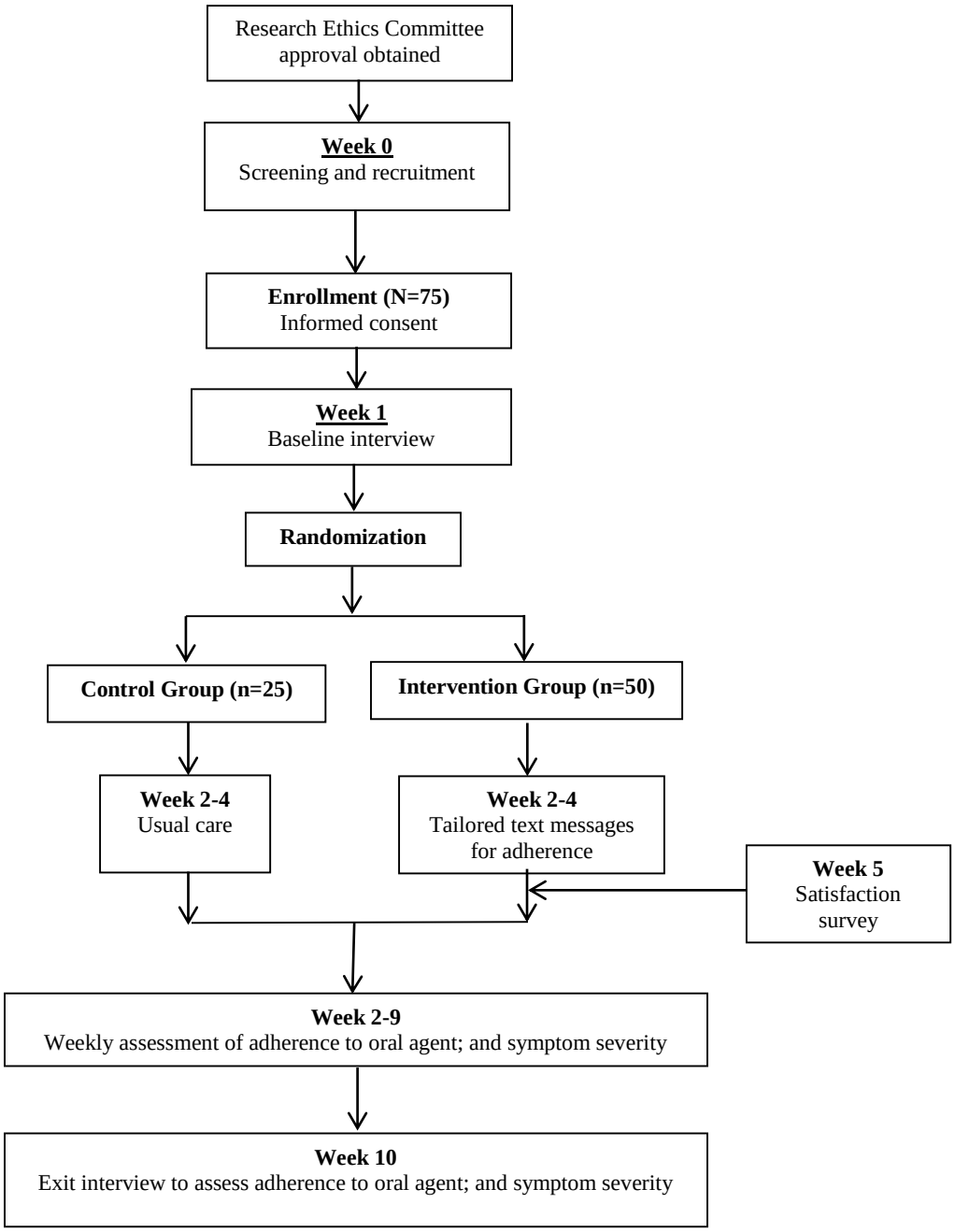

Figure 4. Measures and instruments in this protocol

Main Concepts, Measures, Collection Schedule, and Measurement Objective for This Study			
Concept	**Measure**	**Schedule**	**Measurement Objective**
Characteristics	Self-report and confirmed by recruiter	Baseline	Age, race, sex
Cancer	Diagnosed by oncologist and confirmed by recruiter	Baseline	Cancer site/stage
Cancer treatment	Oral agent/regimen and confirmed by recruiter	Baseline	Prescribed regimen dosage
Social Support	Medication Specific Social Support (MSSS)	Exit	Level of social support received while taking the medication
Self-efficacy	Medication Adherence Self-efficacy Scale (MASES-R), Self-Efficacy Adherence Medication (MARS-M), Brief Medication Questionnaire (BMQ-Specific)	Baseline, exit	Level of self-efficacy
Depressive symptoms	Patient Reported Outcome Measurement Information System (PROMIS) 8a short-form	Baseline, exit	Absence or presence of depression
Physical Function	Patient Reported Outcome Measurement Information System (PROMIS) 6a short-form	Baseline, exit	Level of physical function
Cognition	Cimprich Attentional Function Inventory	Baseline, exit	Level of cognition
Comorbidity and SCM for conditions	Comorbidity (yes/no); Self-Care Management (SCM) of each (yes/no)	Baseline	Existence of comorbid conditions and SCM
Symptoms	Symptom Experience Inventory (yes/no) and rate the severity on a 10-point scale	Baseline, weekly, exit	Presence of and level of symptom severity
Adherence	Patient recall, number of pills taken in the past week compared to prescribed dose; and Relative Dose Intensity (RDI)	Weekly and exit	Adherence rate
Feasibility, and satisfaction	Messages delivered and discontinuation; number offered and enrolled; and satisfaction tool	Calculated at exit	Acceptability and satisfaction

References

AMGEN. (2008) Increasing awareness of relative dose intensity in an evidence-based practice. Retrieved from http://www.onsedge.com/pdf/amgenEBP.pdf on 1 May 2015.

Bandura A. (1977) Self-efficacy: Toward a unifying theory of behavioral change. *Psychological Review* **84**(2), 191-215. doi: 10.1037/0033-295X.84.2.191.

Bassan F., Peter F., Houbre B., Brennstuhl M.J., Costantini M., Speyer E. & Tarquinio C. (2014) Adherence to oral antineoplastic agents by cancer patients: definition and literature review. *European Journal of Cancer Care* **23(**1), 22-35. doi: 10.1111/ecc.12124.

Bellg A.J., Borrelli B., Resnick B., Hecht J., Minicucci D.S., Ory M., Ogedegbe G., Orwig D., Ernst D., Czajkowski S. (2004) Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. *Health Psychology* **5**, 443-451. doi: 10.1037/0278-6133.23.5.443.

Bestvina C.M., Zullig L. L., Rushing C., Chino F., Samsa G.P., Altomare I., Tulsky J., Ubel P., Schrag D., Nicolla J., Abernethy A.P., Peppercorn J. & Zafar S.Y. (2014) Patient-oncologist cost communication, financial distress, and medication adherence. *Journal of Oncology Practice* **10**(3), 162-167. doi: 10.1200/jop.2014.001406.

Buehlmann A. & Deco G. (2008) The neuronal basis of attention: rate versus synchronization modulation. *The Journal of Neuroscience* **28**(30), 7679-7686. doi: 10.1523/JNEUROSCI.5640-07.2008.

Champion V., Skinner C.S., Hui S., Monahan P., Juliar B., Daggy J. & Menon U. (2007) The effect of telephone versus print tailoring for mammography adherence. *Patient Education and Counseling* **65**(3), 416-423. doi: 10.1016/j.pec.2006.09.014.

Cimprich B., Visovatti M., Ronis D. L. (2011) The Attentional Function Index—a self-report cognitive measure. *Psycho-Oncol* **20**(2), 194-202. doi: 10.1523/JNEUROSCI.5640-07.2008.

Cole-Lewis H. & Kershaw T. (2010) Text messaging as a tool for behavior change in disease prevention and management. *Epidemiologic Reviews* **32**(1), 56-69. doi: 10.1093/epirev/mxq004.

Conn V. S., Hafdahl A. R., Cooper P. S., Ruppar T. M., Mehr D. R., Russell C. L.. (2009) Interventions to improve medication adherence among older adults: meta-analysis of adherence outcomes among randomized controlled trials. *Gerontologist* **49**(4), 447-62. doi: 10.1093/geront/gnp037

Cramer K.A., Roy A., Burrell A., Fairchild C.J., Fuldeore M.J., Ollendorf D.A. & Wong P.K. (2008) Medication compliance and persistence: terminology and definitions. *Value Health* **11**(1), 44-47. doi: 10.1111/j.1524-4733.2007.00213.x.

Decker V., Spoelstra S., Miezo E., Bremer R., You M., Given C. & Given B. (2009) A pilot study of an automated voice response system and nursing intervention to monitor adherence to oral chemotherapy agents. *Cancer Nursing* **32**(6), E20-E29. doi: 10.1097/NCC.0b013e3181b31114.

DiMatteo M. R. (2004) Variations in patients' adherence to medical recommendations: A quantitative review of 50 years of research. *Medical Care* **42**(3), 200-209. doi: 10.1097/01.mlr.0000114908.90348.f9.

DiMatteo M.R., Haskard K.B. & Williams S.L. (2007) Health beliefs, disease severity, and patient adherence: A meta-analysis. *Medical Care* **45**(6), 521-528. doi: 10.1097/MLR.0b013e318032937e.

Elliot A.J., Mooney C.J., Douthit K.Z. & Lynch M.F. (2014) Predictors of older adults' technology use and its relationship to depressive symptoms and well-being. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences* **69**(5), 667-677. doi: 10.1093/geronb/gbt109.

Express Scripts. 2010 drug trend report, complex challenges, new solutions. Retreived on May 1, 2015 from www.express-scripts.com/research/studies/drugtrendreport/2010.

Fisher J., Fisher W.A., Bryan A.D. & Misovich S.J. (2002) Information-motivation-behavioral skills model-based HIV risk behavior change intervention for inner-city high school youth. *Health Psychology* **21**(2), 177-186. doi: 10.1037/0278-6133.21.2.177.

Fisher W.A., Fisher J.D. & Harman J. (2003) The information-motivation-behavioral skills model: a general social psychological approach to understanding and promoting health behavior. In *Social Psychological Foundations of Health and Illness* (Suls, J. & Wallston, K. A. ed.), Wiley-Blackwell, Hoboken, NJ, pp. 82-106. doi: 10.1002/9780470753552.ch4

Gitlin L.N., Hauck W.W., Winter L., Dennis M.P. & Schulz R. (2006) Effect of an in-home occupational and physical therapy intervention on reducing mortality in functionally vulnerable older people: preliminary findings. *Journal of the American Geriatrics Society* **54**(6), 950-955. doi: 10.1111/j.1532-5415.2006.00733.x.

Given B.A., Given C.W., Sikorskii A., Jeon S., McCorkle R., Champion V. & Decker D. (2008) Establishing mild, moderate, and severe scores for cancer related symptoms: how consistent and clinically meaningful are interference based severity cut points? *Journal of Pain and Symptom Management* **35**(2), 126-135. doi: 10.1016/j.jpainsymman.2007.03.012.

Horne R., Weinman J. & Hankins M. (1999) The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health* **14**(1), 1-24. doi: 10.1080/08870449908407311.

Insel K., Morrow D., Brewer B. & Figueredo A. (2006) Executive function, working memory, and medication adherence among older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences* **61**(2), 102-107. doi: 10.1093/geronb/61.2.P102.

Johnson K.B., Culpepper D., Scott P., Gordon J.S. & Harris C. (2011) The utility of providing automated medication dose reminders to young children on chronic medication. *Journal of Telemedicine & Telecare* **17**(7), 387-391. doi: 10.1258/jtt.2011.110314.

Krishna S., Boren S.A. & Balas E.A. (2009) Healthcare via cell phones: a systematic review. *Telemedicine Journal and e-Health*, **15**(3), 231-240. doi: 10.1089/tmj.2008.0099.

Lakkis N. A., Atfeh A.M., El-Zein Y.R., Mahmassani D.M. & Hamadeh G.N. (2011) The effect of two types of sms-texts on the uptake of screening mammogram: A randomized controlled trial. *Preventive Medicine* **53**(4-5), 325-327. doi: 10.1016/j.ypmed.2011.08.013.

Lehavot K., Huh D., Walters K.L., King K.M., Andrasik M.P. & Simoni J.M. (2011) Buffering effects of general and medication-specific social support on the association between substance use and HIV medication adherence. *AIDS Patient Care and STDs* **25**(3), 181-189. doi: 10.1089/apc.2010.0314.

McCorkle R., Ercolano E., Lazenby M., Schulman-Green D., Schilling L.S., Lorig K. & Wagner E.H. (2011) Self-management: Enabling and empowering patients living with cancer as a chronic illness. *CA: A Cancer Journal for Clinicians* **61**(1), 50-62. doi: 10.3322/caac.20093.

Ogedegbe G., Mancuso C.A., Allegrante J.P. & Charlson M.E. (2003) Development and evaluation of a medication adherence self-efficacy scale in hypertensive African-American patients. *Journal of Clinical Epidemiology* **56**(6), 520-529. doi: 10.1016/s0895-4356(03)00053-2.

Osborn C.Y. & Egede L.E. (2010) Validation of an information-motivation-behavioral skills model of diabetes self-care (IMB-DSC). *Patient Education and Counseling* **79**(1), 49-54. doi: 10.1016/j.pec.2009.07.016.

Pilkonis P. A, Choi S. W., Reise S. P. (2011) Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS): Depression, anxiety, and anger. *Assessment* **18**(3):263-283. doi: 10.1177/1073191111411667

Posner M.I. & Snyder C.R. (2004) *Attention and cognitive control (D. A. Balota & E. J. Marsh ed.).* Psychology Press, New York, pp. 205-223.

Puts M.T., Tu H.A., Tourangeau A., Howell D., Fitch M., Springall E. & Alibhai S.M. (2014) Factors influencing adherence to cancer treatment in older adults with cancer: a systematic review. *Annals of Oncology* **25**(3), 564-577. doi: 10.1093/annonc/mdt433.

Riley W.T., Rivera D.E., Atienza A.A., Nilson W., Allison S.M. & Mermelstein R. (2011) Health behavior models in the age of mobile interventions: are our theories up to the task? *Translational Behavioral Medicine* **1**, 53-71. doi: 10.1007/s13142-011-0021-7.

Severi E., Free C., Knight R., Robertson S., Edwards P. & Hoile E. (2011) Two controlled trials to increase patient retention in a randomized controlled trial of mobile phone-based smoking cessation support in the United Kingdom. *Clinical Trials* **8**(5), 654-660. doi: 10.1177/1740774511416524.

Soria J.C., Blay J.Y., Spano J.P., Pivot X., Coscas Y. & Khayat D. (2011) Added value of molecular targeted agents in oncology. *Annals of Oncology* **22**(8), 1703-1716. doi: 10.1093/annonc/mdq675.

Spoelstra S.L., Given B.A., Given C.W., Grant M., Sikorskii A., You M. & Decker V. (2013) An intervention to improve adherence and management of symptoms for patients prescribed oral chemotherapy agents: an exploratory study. *Cancer Nursing* **36**(1), 18-28. doi: 10.1097/NCC.0b013e3182551587.

Spoelstra S.L., Given C.W., Sikorskii A., Majumder A., Schueller M. & Given B.A. (2015) Treatment with oral anticancer agents: symptom severity and attribution, and interference with comorbidity management. *Oncology Nursing Forum* **42**(1), 80-88. doi: 10.1188/15.ONF.42-01P.

Streeter S. B., Schwartzberg L., Husain N., Johnsrud M. (2011) Patient and Plan Characteristics Affecting Abandonment of Oral Oncolytic Prescriptions. *Journal of Oncology Practice* **7**(3S): 46s-51s. doi: 10.1200/JOP.2011.000316

Thompson K., Kulkarni J. & Sergejew A.A. (2000) Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophrenia Research* **42**(3), 241-247. doi: 10.1016/S0920-9964(99)00130-9.

Wagner G.J. & Ryan G.W. (2004) Relationship between routinization of daily behaviors and medication adherence in HIV-positive drug users. *AIDS Patient Care and STDs* **18**(7), 385-393. doi: 10.1089/1087291041518238.

Yiend J. (2010) The effects of emotion on attention: A review of attentional processing of emotional information. *Cognition & Emotion* **24**(1), 3-47. doi: 10.1080/02699930903205698.

Zarani F., Besharat M.A., Sadeghian S. & Sarami G. (2010) The effectiveness of the information-motivation-behavioral skills model in promoting adherence in CABG patients. *Journal of Health Psychology* **15**(6), 828-837. doi: 10.1177/1359105309357092.