Annie for Depression Adherence

PI: Carolyn Turvey
IRB ID #: 201712732

Project Details

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-03 VA Only

I.2 ***Project Title:***
Pilot Study of Technology Assisted Depression Treatment Adherence

I.3 ***Short Title (optional):***
Annie for Depression Adherence

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***

- ***DO NOT include information on studies not proposed in this application.***
- ***Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.***
- ***DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.***

This study will refine and test an intervention designed to improve antidepressant adherence and depression outcomes in Veterans initiating medication to treat depression. Veterans will be assigned to 1 of 2 intervention arms using Annie, VA's mobile short messaging services (SMS) to support self-management of antidepressant medication use or to an attention control condition. Annie is a messaging system similar to a cell phone text messaging service and Veterans do not need to download any application.

If randomized to an intervention arm, Veterans will receive scheduled text messages from "Annie". For example, Annie will ask participants to rate their mood, ask if they have missed nay medication doses, if they are experiencing side effects, if they think the medication is working, etc. These Veterans will also receive a weekly summary of their Annie responses through MyHealtheVet Secure Messaging and 1 of the intervention groups will also receive a weekly supportive phone call. A week before participant's scheduled VA follow-up appointment, Veterans will be reminded to share their most recent weekly summary with their VA provider. Staff will also make the summary available to clinicians as an attachment to a CPRS note. After a follow-up appointment, participants will be invited to complete a recorded interview about their experiences using the Annie text messaging program and to provide any recommendations for changes. VA providers will also be invited to complete a recorded phone interview about their experience with patients using Annie.

For Veterans who are randomized into the attention control condition, research staff will discuss common symptoms of depression , the importance of taking medications as prescribed, and how long it may take for a new medication to work. Staff will contact participants in this arm by phone just prior to scheduled follow up visits to discuss any concerns the patient may be experiencing. A sample of Veterans will be asked to complete a recorded interview about their medication management at the end of the study.

This study will evaluate the use of Annie messages designed specifically to provide Veterans guidance around key reasons for antidepressant self-discontinuation. The intervention combines the use of Annie, information feedback, and My HealtheVet to support depression treatment and therefore it will be referred to as the AIMS intervention and AIMS plus intervention for those who are receiving a weekly phone call.

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***
The proposed study has the following specific aims:
1) Conduct a three-arm pilot randomized controlled trial to assess its acceptability, feasibility, and effectiveness of the AIMS and AIMS plus intervention in improving antidepressant adherence in 75 Veterans receiving an initial prescription of antidepressant therapy, or a change of antidepressant.
2)Conduct a qualitative evaluation of patient and provider barriers to antidepressant treatment and adherence as well as their experience of the AIMS interventions.
3)Refine and finalize the AIMS intervention based on integrated results from Specific Aims 1 and 2.

The primary study hypothesis is that Veterans who receive the AIMS intervention or AIMS plus will have better medication adherence and greater reduction in depressive symptoms at 6 and 12-week post-baseline when compared to Veterans randomized to an attention control condition.

I.6 ***Background and significance and/or Preliminary studies related to this project. (do not indicate "see protocol")***

Depression is a major cause of morbidity and mortality in the Veteran population. According to the Veterans Health Study, the prevalence of significant depressive symptoms among Veterans is 31%, 2- to 5-times higher than among the general US population (27). Depression also greatly increases morbidity, mortality, and cost to VA when combined with other common debilitating illnesses such as heart failure, diabetes, or spinal cord injury. Finally, depression is a significant risk factor for suicide in both civilian and Veteran populations and strategies to improve suicide prevention are a top priority for VA. A recent case control study of completed suicides in Veterans identified improved antidepressant treatment adherence as a key area to improve care for Veterans at risk for suicide.

There are a range of effective pharmacologic and behavioral treatments for depression. However, effective treatment for depression remains elusive for many Veterans. Kales et al. (2016) examined veterans newly prescribed antidepressants and found 29% non-adherence based on self-report, and 53% non-adherence when based on the medication possession ratio using VA pharmacy data. Nationwide, approximately one third of patients discontinue antidepressants within the first month of treatment and 44% discontinue them by the third month of treatment. Samples and Mojtabai (2015) conducted a national survey and found the major reasons reported for discontinuation were side effect burden, patient report of experiencing no benefit from the medication, medication cost, and wanting to resolve depression without using medication.

Another issue is that many patients and providers must work through multiple trials of antidepressants before settling upon the optimal regimen. The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial found only 37% of patients responded to the first antidepressant prescribed, and up to four medication changes were needed to achieve a 67% response rate overall. Successful antidepressant treatment requires attention, patience, and tenacity of both patients and providers.

Dr. Turvey, the principal investigator, has been developing and evaluating patient facing health information technologies in both VA and community settings for the past 10 years. The majority of her work has been exploring the use of My HealtheVet to engage patients in managing their health and care coordination. Dr. Turvey has also developed and implemented interactive voice response depression monitoring technologies. In a community-based study, technology based depression assessment was conducted in the context of a Medicaid disease management program. This technology successfully identified new cases of depression and the protocol for follow-up on patients who endorsed suicidal ideation was successfully implemented.

The initial Annie questions are based on the primary contributors to non-adherence documented in the research literature and have been tested by Dr. Turvey and her team.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***

N/A

II. Research Team

II.1 ***Principal Investigator***

Name	E-mail	College
Carolyn Turvey	carolyn-turvey@uiowa.edu	Carver College of Medicine

II.2 ***Team Members***

VAMC Team Members

Name	E-mail	College	Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Deactivated
Carolyn Turvey, PHD	carolyn-turvey@uiowa.edu	Carver College of Medicine	Yes			No	Yes	No
Bruce Alexander, PharmD, BS	bruce.alexander@va.gov	Carver College of Medicine	No			No	No	No
George Bailey, BS	george.bailey@va.gov	Carver College of Medicine	No			No	No	No
Heidi Ferguson, MBA	heidi-clark@uiowa.edu	Carver College of Medicine	No			No	No	No

Name	E-mail	College	Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Deactivated
Carrie Franciscus, MA	carrie-franciscus@uiowa.edu	Carver College of Medicine	No			No	No	No
Lindsey Fuhrmeister, BA	lindsey-fuhrmeister@uiowa.edu	Carver College of Medicine	Yes			No	Yes	No
Shaliyah Mays, High School	shaliyah-mays@uiowa.edu	College of Liberal Arts and Sciences	No			No	No	No
Kimberly McCoy, MS	kimberly.mccoy2@va.gov	Carver College of Medicine	No			No	No	No
Jane Moeckli, PHD, BA	jane.moeckli@va.gov	Carver College of Medicine	No			No	Yes	No
Raymond Opiola, BA	raymond.opiola@va.gov	Carver College of Medicine	No			No	No	No
Monica Paez, BA	monica.paez@va.gov	Carver College of Medicine	No			No	No	No
Christopher Richards, MA	christopher.richards@va.gov	Carver College of Medicine	No			No	No	No
Samantha Solimeo, MPH, PHD	samantha.solimeo@va.gov	Carver College of Medicine	No			No	Yes	No
Katrina Stadler, High School	katrina-stadler@uiowa.edu	College of Public Health	No			No	No	No
Natalie Suiter, BS	natalie.suiter@va.gov	Carver College of Medicine	No			No	Yes	No
Jennifer Van Tiem, PHD	jennifer.vantiem@va.gov	Carver College of Medicine	No			No	Yes	No
Mary Vaughan Sarrazin, PHD	mary-vaughan-sarrazin@uiowa.edu	Carver College of Medicine	No			No	No	No

Non-VAMC Team Members

Name	Institution	Location	FWA	Role	DHHS Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Email
Nothing found to display.										

II.3 ***The Principal Investigator of this study is:***
Faculty

II.5 ***Select research team member who is the primary contact for study participants.***
Carolyn Turvey

III. Funding/Other Support

III.1 ***Funding Sources***

Type	Source	Grant Title	Name of PI on Grant
Federal Agency	US Department of Veterans Affairs	Pilot Study of Technology Assisted Depression Treatment Adherence	Carolyn Turvey

* new source name

III.2 ***What type of funding agreement would be completed?***
Iowa City VAMC

III.4 ***Does any member of the research team have a personal significant financial interest in the project according to the VA Conflict of Interest Policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest
Carolyn Turvey, PHD	No
Bruce Alexander, PharmD, BS	No
George Bailey, BS	No
Heidi Ferguson, MBA	No
Carrie Franciscus, MA	No
Lindsey Fuhrmeister, BA	No
Shaliyah Mays, High School	No
Kimberly McCoy, MS	No
Jane Moeckli, PHD, BA	No
Raymond Opiola, BA	No
Monica Paez, BA	No
Christopher Richards, MA	No
Samantha Solimeo, MPH, PHD	No
Katrina Stadler, High School	No
Natalie Suiter, BS	No
Jennifer Van Tiem, PHD	No
Mary Vaughan Sarrazin, PHD	No

III.5 ***What is the current status of this funding source?***

Source	Status	Other Status Description
US Department of Veterans Affairs	Awarded	

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project. (If you do not have a specified date, add "upon IRB approval")***
07/01/2018

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***

- ***Do not answer yes, if the involvement includes a device, wire, or instrument***

No

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***

No

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
115

VI.2 ***What is the age of the youngest adult subject?***
18.0

VI.3 ***What is the age of the oldest adult subject?***
99.0

VI.4 ***What is the percentage of adult male subjects?***
80

VI.5 ***What is the percentage of adult female subjects?***
20

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
0

VI.13 ***Describe EACH of your subject populations***

- ***Include description of any control group(s)***
- ***Specify the Inclusion/Exclusion criteria for EACH group***

Veterans (n=75): Veterans will be eligible if they are initiating a new antidepressant medication, or change to a new antidepressant as part of their care. In addition, Veterans need to have 1) a cell phone with text messaging capabilities and 2) have a MyHealtheVet account or be willing to sign up for one and use MyHealtheVet secure messaging.

Exclusion: Veterans who are lacking a cell phone or ability to text message. Comorbid major psychotic disorders (e.g., bipolar disorder), current active substance abuse, high-risk for suicide ideation, or cognitive disorders (e.g., dementia) are ineligible. Patient with comorbid PTSD will be eligible, but only when depression is also indicated in problem list for target visit. If they don't have any MyHeatlheVet account or are not willing to sign up for one, and if they are not willing to use secure messaging.

Providers (n=40): We will ask providers who have Veterans in one of the intervention groups to participate in a recorded phone interview about their experiences with the project.

VI.13.a ***Does this study propose to enroll any subjects who are not Veterans?***
Yes

VI.13.b ***Non-Veterans may be entered into a VA-approved research study that involves VA outpatient or VA hospital treatment (38 CFR 17.45, 17.92), but only when there are insufficient Veteran patients suitable for the study. Provide an explanation for why there are insufficient Veteran patients suitable for the study.***
VA providers

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for inclusion in each of your study populations (include your control population if applicable)***
Using administrative data in preparation for research, we found 2243 unique Veterans seen in either primary care or mental health at the Iowa City VA who received a diagnosis of depression who had no such diagnosis in their medical record for 12 months prior to that diagnosis. In addition, Veterans with existing depression diagnoses who change their antidepressant medication will be eligible for the study. We estimate 30-40% have MHV, and those who do not can sign up as part of the study if interested.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***
The mental health service line and primary care service line leadership have provided support for this proposal and will assist in education clinical teams about the Annie application and this study for patients newly prescribed antidepressants,or a

change in antidepressant medication . Staff may notify their patients of the study and refer to study staff. In addition, to clinic-based recruitment, a study data manager will query CDW pharmacy data daily during the week to identify all instances of new antidepressant prescriptions occurring within the mental health or primary care clinics. A research assistant will then conduct a medical record review of potentially eligible patients to confirm that the antidepressant initiation was intended to treat depression specifically and the patient has not received antidepressants in 6 months prior to the target visit. Patients who meet these criteria will be sent a letter describing the study and a postage paid card where the Veteran can indicate if he or she is interested in the study. Patients who do not return the card will be contacted by phone within one week of the medical visit where the antidepressants were prescribed to determine interest in the study.

VI.16 ***Do you plan to recruit/enroll non-English speaking people?***
No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***

- ***Employee of the PI or employee of a research team member***
- ***Individual supervised by PI or supervised by member of research team***
- ***Individual subordinate to the PI or subordinate to any member of the research team***
- ***Student or trainee under the direction of the PI or under the direction of a member of the research team***

No

VI.20 ***Will subjects provide any information about their relatives?***
No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***
No

VI.26 ***Is this project about pregnant women?***
No

VI.27 ***Will this project involve fetuses?***
No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***
No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***
No

VI.37 ***Does this project involve prisoners as subjects?***
No

VI.46 ***Do you propose to enroll any subjects diagnosed with Posttraumatic stress disorder (PTSD)?***
Yes

VI.47 ***Describe how this protocol will take into consideration the perspectives of individuals with PTSD.***
We will be recruiting participants with a diagnosis of depression, which may be co-morbid with PTSD. If the antidepressant is prescribed for depression, someone with PTSD is eligible and will be treated the same as others in the study.

VI.48 ***Does this study involve a study drug(s)?***
No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***

- VAMC - Iowa City VA HCS
- U.S. off-campus - Patients will complete assessments at a location of their choosing and if randomized to one of the intervention groups, answer texts on their phones. Consents may also occur at subject homes or a CBOC of their choice.

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***
No

VII.B. Project Description (B)

VII.B.1. ***Does this project involve any of the following (Check all that apply):***

- ☑ **Interventional** – Includes **Clinical (or Treatment) trial**, **Physiology intervention/study**, **Behavioral intervention/study**, **Diagnostic Trial**.
  - ☐ **Clinical (or Treatment) trial** – A prospective biomedical or behavioral research study of new treatments, new drug or combinations of drugs, new devices, or new approaches to surgery or radiation therapy. (NIH and ClinicalTrials.gov & FDA)
  - ☐ **Physiology intervention/study** – A pharmacologic or measurement study aimed at understanding basic mechanisms of disease and/or of normal human physiology, often without any therapeutic intent (though a clinical trial could include such components, often labeled as "translational" or "basic science" aims.) Measurements in such studies could include, but are not limited to, a blood draw, EKG, EEG, MRI, auditory or sensory testing, checking vital signs, DEXA scans, eye tracking, specimen collection, exercise, fasting, special diets, etc.
  - ☑ **Behavioral intervention/study** – May be used to refer to studies of individual or group behavior. This option does not include drugs, biologics, or devices but could include psychotherapy, lifestyle counseling, behavior modification, etc.
  - ☐ **Diagnostic trial** – Protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov & FDA)
- ☐ **Observational**
- ☐ **Expanded Access** – A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial. Examples of expanded access include non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access to investigational drug, and parallel track (ClinicalTrials.gov & FDA).
- ☐ **Registry** – The collection and maintenance of data (not including biologic samples) in which: (1) the individuals in the registry have a common or related condition(s), and/or (2) the individuals in the registry are interested in being contacted for future studies by investigators other than those listed in Section II of this project.(UI Guide)
- ☐ **Repository** – The collection, storage, and distribution of human biologic samples and/or data materials for research purposes. Repository activities involve three components: (i) the collection of data and/or specimens such as blood, tissue, saliva, etc.; (ii) the storage of data or specimens, and data management function; and (iii) the sharing of data/specimens with recipient investigators other than the original investigators. (paraphrased from OHRP)
- ☐ **Other**

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***
No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***
No

VII.B.18 ***Does this project involve testing the safety and/or efficacy of a medical device?***
No

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***

- Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records - We will use administrative data sources (e.g. Corporate Data Warehouse (CDW) and CPRS) to identify patients with a new antidepressant and use ICD10 codes to screen for inclusion/exclusion. In addition, we will chart screen for inclusion/exclusion criteria and abstract information about their antidepressant (for example, name, dose, etc.).
- Letter -
- Referral from colleague - Veterans will be referred from their primary care or mental health care providers.
- E-mail -

VII.D.2 ***List the individual data elements you will need to access/use from the patient or clinic records to identify potential subjects for recruitment***

We will use administrative data sources (e.g. Corporate Data Warehouse (CDW) and CPRS to access pharmacy record information to identify patients who were newly prescribed an antidepressant and will then chart screen subjects for inclusion (e.g. confirm depression diagnosis) and exclusion criteria (e.g. comorbid significant mental health diagnoses). SSN will be used as an unique identifier and name and contact information will be accessed for recruitment (i.e. address, phone number).

VII.D.3 ***Describe why you could not practicably recruit subjects without access to and use of the information described above***

Without this information, we would not be able to tailor recruitment to Veterans who were newly prescribed antidepressant medications or have had a change in antidepressant medication.

VII.D.4 ***Describe why you could not practicably obtain authorization from potential subjects to review their patient or clinic records for recruitment purposes.***

Using the methods described above we will minimize contacting many Veterans who may not be eligible for the study. It is impractical to obtain authorization to review their records for recruitment purposes.

VII.D.5 ***Describe plans to protect the identifiers from improper use or disclosure***

Only IRB approved, VA approved research team members will have access to the subject information and database. All VA approved research team members must complete required annual training for patient security and confidentiality. The database will be stored on a secure VA server behind the VA firewall. Patients will be assigned a study identification number.

VII.D.6 ***Describe your plan to retain research records until disposition instructions are approved by the National Archives and Records Administration and are published in VHA's Records Control Schedule (RCS 10-1)***

All research documents/data(and/or audio/video recording) will be retained until disposition instructions are approved by the National Archives and Records Administration (NARA) protocol published in VHA's Record Control Schedule (RCS 10-1). Data will remain on a secure VA server in accordance with NARA requirements. Should NARA requirements recommend disposition, at that time the data will be destroyed per the Office of Information & Technology (OI&T) and the latest VA Data Security Protocols for secure file deletion.

VII.D.7 ***Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule***

Yes

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***

Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***

At a clinic visit or at the patient's home.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***

Yes

VII.D.11 ***Describe:***

A member of the research team may discuss the study by phone after referral from clinician or to follow up on mailed recuitment materials to assess study interest and screen for the study as needed.

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Carolyn Turvey, PHD	Yes
Bruce Alexander, PharmD, BS	No
George Bailey, BS	No
Heidi Ferguson, MBA	No
Carrie Franciscus, MA	No
Lindsey Fuhrmeister, BA	Yes
Shaliyah Mays, High School	No
Kimberly McCoy, MS	No
Jane Moeckli, PHD, BA	Yes
Raymond Opiola, BA	No
Monica Paez, BA	No
Christopher Richards, MA	No
Samantha Solimeo, MPH, PHD	Yes

Name	Consent Process Involvement
Katrina Stadler, High School	No
Natalie Suiter, BS	Yes
Jennifer Van Tiem, PHD	Yes
Mary Vaughan Sarrazin, PHD	No

VII.D.14 ***The PI has formally delegated the responsibility of conducting the consent process and obtaining consent to the individuals listed above. The individuals delegated this responsibility have received appropriate training to perform these activities.***
Yes

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***
- Letter or Information sheet containing elements of consent
- Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***
Yes

VII.D.17 ***Choose one of the following to indicate why you are requesting that the IRB waive the requirement to obtain a subject signature as documentation of consent:***
A. The research presents no more than minimal risk (minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests)

AND

The study involves no procedures for which consent is normally required ouside of a research context. *(This type of waiver is often permitted for a minimal risk mail-out survey that includes a cover letter with all elements of consent, and returning the survey indicates consent. You cannot request this waiver if the study also involves the use of any protected health information (PHI).)*

VII.D.18 ***Explain why this meets the chosen criteria in A. or B. above:***
The waiver of documentation of consent is only for VA providers. A letter informing the provider of the study will be provided with the questionnaire providers are asked to complete. The questionnaire will ask their feedback about their experiences with patients enrolled in the study. There is no more than minimal risk to the provider in completing this voluntary questionnaire. By completing the questionnaire the provider is verifying their consent to participate in the study.

VII.D.18.a ***Does the information you are collecting from subjects involve health information (either oral or written)? NOTE: The VHA considers all identifiable information collected from researcher's individually identifiable information based upon the 18 HIPAA identifiers. (See VHA Handbook 1605.1, Appendix B for explanation of Individually-identifiable Health Information and De-identification).***
Yes

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***
Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***
1. Were you recently prescribed or start taking a new medication to treat depression?
2. Some participants in this study will be asked to use text messaging on their cell phone. You would be responsible for any costs related to receiving, or sending these text messages. Are you willing to use text messaging if needed for the study?
3. Do you expect to have a VA follow-up appointment for your depression treatment in the next 3 months?
4. Do you have MyHealthevet, VA's patient portal?
a. For some participants, one aspect of the study will be receiving secure messages in MyHealtheVet from the research team. Are you willing to use MyHealtheVet in the study?
b. With MyHealtheVet you can do things like refill a prescription, message with your care team, check appointment times, or view your VA health record information lab results. For some participants, one aspect of the study will be receiving secure messages in MyHealtheVet fro the research team. Would you be willing to register and use MyHealtheVet in the study? See (Recruitment_Screen_Ques_AnnieIRB)

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***

Yes

VII.D.22 ***Describe the information being collected and the purpose for keeping this information.***
We will keep screening results, either negative or positive, or response/non-response in order to track ineligibility reasons and calculate overall response rates. It is necessary to determine differences between participants vs. non-participants to understand if there are differences that might reflect response bias and consequently influence generalizability of our findings.

VII.D.23 ***Will this information be shared with anyone outside the VA research team members?***
No

VII.D.25 ***<u>After</u> the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
No

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.***
The goal is to enroll and randomize participants within 4 weeks of initiating their treatment for antidepressant medications, thus we will ask participants to decide as soon as possible about their interest in participating once contacted.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***
After consent, he/she will be randomized and study procedures will begin.

VII.D.29 ***Provide a description of the enrollment and consent process for adult subjects***

- ***Describe each study population separately including control population***
- ***Include when recruitment and consent materials are used***
- ***Use 3rd person active voice "The Principal Investigator will identify subjects. For example, the principal investigator will identify potential subjects, the study coordinator will discuss the study with subjects over the telephone and schedule the first study visit, etc..."***
- ***Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process***

Veterans: Potential participants will be identified in two ways.

Clinic Based Referral: Patients can be referred to the study directly by their prescribing VA provider/care team. When the research assistant is contacted, he/she will review the medical record to verify a diagnosis of depression and screen for exclusion criteria. If eligible, the RA will meet with the patient after their clinic visit if feasible. If we are unable to meet the patient at the clinic, staff will follow-up by phone to review the study and schedule an in-person consent visit.

Mailed Invitation: In addition to clinic based recruitment, a study data manager will query CDW pharmacy data daily to identify instances of new antidepressant prescriptions occurring within the mental health and primary care clinics. A research assistant will then conduct a medical record review of potentially eligible patients to confirm inclusion and exclusion criteria. Eligible Veterans will be sent a recruitment letter introducing the study (Veteran recruitment letter.doc) and will include study contact information for Veteran to call to report interest/no interest in the study. Patients who do not contact staff will be called a minimum of 10-days after mailing the recruitment letter to assess study interest (Recruitment phone script.doc). We will wait a minimum of 3 days before making 2nd phone call. If we do not speak in person, we will leave messages as outlined in the phone script document. Only two attempted recruitment calls will be made.

Interested Veterans will also be asked screening questions to determine eligibility (Recruitment screening questions.doc). If eligible for the study, we will schedule an in-person visit at the nearest VA outpatient clinic or the patient's home to complete consent, randomization, and baseline assessments.

VA Providers: We will ask the Veteran to take the provider consent letter, provider questionnaire, and postage paid envelope in a sealed envelope to their appointment with their VA provider. To facilitate participation, a waiver of signature of consent will apply to providers. We will send the questionnaire to the provider more than once, if they have an appointment with another participant in the project. Providers may fill out multiple questionnaire's if they see more than one participant in the study. In addition, the research staff will send an email to the VA provider 1 week prior to the appointment using this template (VA provider_emailnotify_appt_1_29_20.docx). The purpose of the email is to send the patient's cumulative graph directly to the provider and to let them know the Veteran will be bringing a provider packet with a consent letter and questionnaire for them to fill out and return in the postage paid envelope, if they agree to participate in the study.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:

- ***Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.***
- ***Participants will be provided with false information regarding the particular behaviors of interest in the research.***
- ***Procedures include a confederate pretending to be another participant in the study.***

- ***Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.***
- ***Study is designed to introduce a new procedure (or task) that participants are not initially told about.***
- ***If yes, a waiver of informed consent must be requested under question IV.3.***

No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
Yes

VII.E.1.a ***Will any subjects be blinded to which study arm they have been assigned?***
No

VII.E.2 ***Describe randomization scheme/assignment including ratio such as 1:1, 2:1 etc.***
After consent, patients will be randomized to one of the three study arms (AIMS intervention, AIMS intervention plus or attention control condition) and the respective protocols described below. Randomization will be blocked by service line(primary care/mental health) and if the patient is new to antidepressant therapy or changing to a new antidepressant. We aim to recruit approximately half of the participants from primary care and half from mental health and to have equal representation of those new to antidepressant therapy or changing to a new antidepressant. Prior to consent the study assistant will identify the randomization envelope and take it to the home visit. It will be opened after consent to determine treatment assignment.

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
Yes

VII.E.4 ***List all questionnaires, surveys, written assessments and ATTACH each one to the application. (NOTE: You are NOT prohibited from attaching copyrighted materials to this application)***
Demographics, technology use, and eHealth
Medication Adherence Rating Scale (MARS) (Generic, Antidepressant, or Mental Health)
Patient Health Questionnaire (PHQ-9)
The Frequency, Intensity, and Burden of Side Effects Ratings (FIBSER)
Treatment Self-Regulation Questionnaire (TSRQ)
Health Care Climate Questionnaire (HCCQ)
Patient Activation Measure-Mental Health (PAM-MH)
Perceived Competence
Qualitative Questionnaire - Patients
Annie_ProviderQuestionnaire_1_29_20.docx
WeeklyCall_Outline

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
Yes

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if applicable.

DESCRIBE:

- ***What subjects will be asked to do/what happens in the study (in sequential order)***
- ***The time period over which procedures will occur***
- ***The time commitment for the subject for individual visits/procedures***
- ***Long-term followup and how it occurs***

Action Plan-REF-Expired Consents Used 2/18/2020: The project coordinator will review the shared drive folder containing consent documents and project attachments to ensure all documents are updated, as needed, after each modification and continuing review. In addition, the project coordinator will monitor the file folders once a month to ensure the files are up-to-date.

After consenting paperwork is complete (including HIPAA authorization), the patient will complete the baseline questionnaires about their mood, medication adherence and side effects, technology use, patient activation, and self-efficacy (see VIIE.4 for list of possible assessments). We estimate it will take approximately 20-30 minutes to complete. The patient will then be randomized to the AIMS Intervention, AIMS intervention plus or Attention Control Condition. As needed, staff will assist Veterans with My HealtheVet registration and authentication for a Premium account. For those assigned to AIMS or AIMS plus, enrollment and education will proceed as outlined below.

AIMS Intervention (Group 1): Study staff will review the Depression Education materials (Annie Depression Education.doc), the Annie text messaging program (Annie Quick Guide.doc) and complete verbal consent with the Veteran for Annie enrollment. For example, staff will review that their provider will not regularly review or read their responses to Annie prompts between medical visits as Annie is a self-management tool. Staff will collect information to assign the Annie protocol and to customize a goal for the protocol (e.g. I want to work on sleep) (Annie enrollment log.doc). The Veteran will be instructed during the consent visit to text “start” to Annie's phone number (75338/ or an alternate number depending on their cell phone carrier) to begin using Annie. Staff will review how he or she may use My HealtheVet to send secure messages to VA staff, as well as to research staff. A study specific secure messaging group will be used. After the participant has been assigned to the Annie protocol, staff will verify that s/he texted start and will follow up with the participant as needed if s/he does not text start. We will also send a MyHealtheVet secure message welcome message for training and follow up with a brief phone call to answer any questions about secure messaging or Annie.

Participants will be sent a weekly summary of their messaging. After the first week, participants will also be sent a cumulative summary of their total responses to Annie via MHV secure messaging. We will monitor and collect process data on if and when they open the secure message.

The standard practice in both the Mental Health and Primary Care clinic at the Iowa City VA is to schedule a four to six-week follow-up visit with patients after initiating a new antidepressant to evaluate effectiveness and a 12-week follow-up to ensure continued benefit. Though there is some variability in the degree to which clinics and patients can accommodate two visits within the 12-week post antidepressant initiation period, at least one follow-up visit will be scheduled within the proposed study period. Antidepressants are typically prescribed in 30-day supplies unless there are concerns about potential for overdose.

10 days prior to the follow-up visit for antidepressant evaluation, study staff will mail the most recent summary report of their responses to Annie (AnnieWeeklyForm-Weekly.docx) and the provider packet to the Veteran. The team will also call or send a Secure Message to remind participants to share the information mailed, at their appointment. The most recent summary report will also be added to VISTA Imaging with a CPRS note for access by their provider in the medical record for follow-up visits to evaluate antidepressant treatment response in the 12-week time period. At the end of study participation, patients will be invited to complete a 15-30 minute recorded qualitative telephone interview to understand their experience and satisfaction using the Annie application and their experience using information with their provider (Veteran qualitative interview.doc). Data collected through the Annie messaging application does not assess suicidal ideation, however, if a Veteran reports a low mood as indicated by a rating of 1-4, they will be presented with an Annie response that also includes the Veteran's crisis line. The Annie Dialogue and questions are provided as an attachment (Annie Text Messaging Dialogue).

AIMS Intervention Plus (Group 2): If randomized to this group they will receive the AIMS Intervention as outlined above in addition to a weekly phone call from study staff to review their progress.

Attention Control Condition (Group 3): Patients in the attention control condition will also meet with study staff in person for consent and randomization. During this visit, study staff will review the Depression Education materials with the Veteran (Annie Depression Education.doc) Veterans in this arm will be contacted if needed, to assess Suicidal Ideation based on indication of Suicidal Ideation accessed on the PHQ9 in the 6 and 12 week assessment. A sample of Veterans (n=10) will also be asked to complete a 15-30 minute recorded qualitative interview about their antidepressant medication management at the end of 12 weeks(AttentionControlInterviewGuide.doc)

All participants: Within 1 week of consenting the Veteran, study staff will notify the prescribing provider of their patient’s research study enrollment and randomization to AIMS, AIMS plus, or the attention control condition (Provider notification letter.doc).

Veteran participants will be sent a packet of questionnaires to complete at 6 weeks and 12 weeks post baseline assessments. The questions will take approximately 30 minutes to complete. The questions will ask them about their mood, medication adherence and side effects, patient activation, and self-efficacy (see VII E.4 for list of assessments). These will be mailed shortly before these time frames with postage paid return envelopes. If the questionnaires are not returned within two weeks, study staff will call the Veteran to check on completion and offer to complete verbally by phone. Subjects will receive $25.00 for their time when they complete the study.

As the PHQ-9 measure is assessing depression and includes a question on suicidal ideation, any endorsement of ideation will be referred to Dr. Turvey and the clinical team for further evaluation. The suicide prevention case managers may also be called. Subjects will be informed in the consent process of any safety measures that may be taken in response to concern on suicidal ideation. A CPRS note will be added to document the outcomes of question 9 on the PHQ-9.

Participants will receive $25.00 for their time when they complete the study.

VA Providers: We will ask the Veteran to take the provider consent letter, questionnaire and postage paid envelope in a sealed envelope to their appointment with their VA provider. Completing the questionnaire is voluntary. By completing the questionnaire the VA provider is providing their consent to participate in the study. The estimated time to complete the questionnaire is 5 minutes. The questionnaire content includes: did the patient share the graphs, did the provider and patient discuss the graphs, did the information shared influence the depression treatment, rating of helpfulness of graphs shared, and provider feedback on how to improve Annie protocol and graph document for future use.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***

Yes

VII.E.8 ***Describe - any procedures need to be included in the consent:***
We will make multiple attempts to reach the patient by phone. If after 4 attempts there is no contact, we will send an unable to reach letter.

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
Yes

VII.E.10 ***Cash***
No

VII.E.11 ***Gift Card***
No

VII.E.12 ***Check***
No

VII.E.16 ***Other***
Yes

VII.E.17 ***Describe:***
Direct deposit through the VA research office.

VII.E.19 ***Describe the compensation plan including***

- ***Compensation amount and type per visit***
- ***Total compensation***
- ***Pro-rating for early withdrawal from study***

Veterans may be compensated $25 for their time upon completing the study.

Payments will be processed through the VA Research Office. We will ask all subjects to complete a vendor form to comply with VA regulation that research subjects to be paid by direct deposit to their bank account.

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
Possible risks to Veterans include disclosure of personal health information while participating in the Annie messaging system and frustration or fatigue completing study intervention assessments. There may also be some frustration with the Annie system if there is difficulty responding to the system or an expectation that providers will be checking the information submitted through Annie. As we are working with patients with a diagnosis of depression, there is a risk of suicidal ideation being identified during the study and a plan for addressing this risk is outlined below.

VIII.2 ***What have you done to minimize the risks?***

- ***If applicable to this study ALSO include:***
  - ***How you (members of your research team at Iowa) will monitor the safety of individual subjects.***
  - ***Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)***

All participants will be informed that at any time they can refuse to answer any questions or end their study participation. If a patient randomized to the intervention asks to stop text messaging, Annie messages will be discontinued and we will ask these Veterans if they are willing to continue with the study assessments or if they want to stop all study activities. Data collected through the Annie messaging application does not assess suicidal ideation, however, if a Veteran reports a low mood as indicated by a rating of 1-4, they will be presented with an Annie response that also includes the Veteran's crisis line. The PHQ-9 does have a question about suicidal thoughts. If there is any indication of ideation the Veteran will be contacted to assess their response and asked questions according to a risk assessment protocol (Suicide Risk Assessment Guide.docx). Dr. Turvey is a clinical psychologist and will be notified of all cases where there is ideation. We will also work with the suicide prevention case manager at the VA and their mental health or primary care providers as needed.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***

No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
We don't know if participants will benefit from being in this study. However, all Veteran participants in this study will be provided with information about using My HealtheVet to communicate with their team and to access information about their recent clinical notes if they are a Premium account user. The information we learn will help us to better inform potential solutions to improve medication adherence for Veterans.

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***
According to the Veterans Health Study, the prevalence of significant depressive symptoms among Veterans is 31%. While there are number of effective pharmacologic and behavioral treatments for depression, effective treatment for depression remains elusive for many Veterans. If effective, this study will contribute to understanding of how to help engage patients in the shared decision making for management of medications for their depression medication based on objective information tracked during the initiation of the medication and by promoting communication with their care team about any issues experienced.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***
Only data necessary to answer the research questions will be collected in a way the subject's privacy is protected. Study interviews will be conducted privately and the information provided will only be available to approved personnel. Participants are informed they can refrain from answering any questions they do not want to answer and can end their participation at any time. To protect confidentiality study research materials are identified by a study ID and stored in locked file cabinets. Electronic data are maintained on a secure VA server behind the VA firewall. Only IRB approved research team members have access to study data.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***
Yes

X.3 ***Provide the intended usage of SSN:***

- To provide compensation to subjects
- Other - Real SSN is required for the CAPRI system, which is needed for access to the clinician Annie application.

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

- Electronic records (computer files, electronic databases, etc.) - All electronic records will be maintained in a study folder located on a server behind the VA firewall. The study folder and all contents are only accessible to IRB approved research team members with authentication credentials to the VA network and access to the specific data folder. Project data will be stored on a VA HSR&D server, which is maintained, backed-up, and secured in a locked server room by the Iowa City VA's Office of Information and Technology (OI&T) department. Hard copy records will be kept in a locked file cabinet in the research coordinator's office at the Iowa City VA CADRE research offices. Qualitative interviews will be recorded on HIPAA Compliant digital recording device. Qualitative data will be de-identified so that any presentation of specific quotes or problems discussed will not be easily attributed to Veteran or provider. A system of study ID numbers will be used to identify data, rather than patients' names or other personal identifiers. All research team members will complete appropriate VA training and credentialing to participate in the study. De-identified data for Insignia Health per licensing requirements will be sent using the standard VA protocol for sharing de-identified data. The Privacy Officer will be notified when data is to be shared with Insignia for review prior to providing.
  - Name - Carrie Franciscus
  - Title - Database Manager
  - University/VA Job Classification - Database Manager
- Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - Hard copy study forms will be kept in a locked file cabinet in the research offices in CADRE Research Offices. Authorizations to transport will be in place for transport of information from VA to consent visits and back to VA.

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
No

X.6 ***Describe***
Per licensing agreements, de-identified data will be provided to Insignia Health for the Patient Activation Measure . Insignia compares this data with its normative data set to continually identify opportunities to refine PAM. All HIPAA 18 identifiers will be removed, and a Data Manager and Privacy Officer will review the data to ensure that all identifiable elements have been removed.

X.7 ***Does your study meet the NIH criteria for a Certificate of Confidentiality or will you be applying for Certificate of Confidentiality?***
No

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
Quantitative: This is a three-arm RCT with equal randomization between groups using blocked randomization to ensure equal enrollment in intervention arms. The primary hypothesis is that patients in the AIMS intervention will have better antidepressant treatment adherence as indicated by both the MARS and Proportion of Days Covered Metric. These outcomes are continuous measures assessed at 6-week and 12-week post-baseline. Initial exploratory analyses will determine assumptions of normality apply. If violations are found, variables will undergo appropriate transformation (e.g. logarithmic) to produce a more normal distribution. A simple two-sample t-test for difference in means will be conducted separately for both 6-week and 12-week outcomes to test the primary and secondary study outcomes. We expect the Proportion of Days Covered Metric will be more informative at 12-weeks post baseline, but we will test at 6-weeks also. The MARS measure will be informative at both 6 and 12 weeks post baseline.

To estimate treatment effect on PHQ-9 total score a linear mixed effects (LME) model will be conducted, with initial models including only treatment group and time period with a random effect that accounts for repeated measures over the same subject. We will inspect the data for differences in baseline patient characteristics to confirm that randomization resulted in balanced characteristics between patients in the control and treatment arms. If imbalance exists, we may opt to use a regression approach to control for possible differences. We will not have adequate power to conduct complex multivariate analyses. However, as this is a pilot study, exploration of associations between potential covariates and primary outcomes will provide a general understanding of key variables to include in a future RCT. We will also conduct exploratory analyses of the relation between the intervention, core concepts within Self-Determination Theory, and treatment outcomes.

If attrition occurs, recruitment will continue until all intervention arms include 25 patients but final analyses will include all patients who enrolled and completed two or more study assessments. Post-hoc exploratory analyses will inform the overall interpretation of these results. If a Veteran indicates he or she wishes to stop the study, we will respect the request and emphasize that participation is voluntary, but ask for a brief explanation for why they are stopping and if it coincides with them discontinuing their antidepressant medication, or if it reflects a negative experience with the Annie application. We will conduct exploratory analyses to test if baseline variables predict termination of the Annie application, antidepressants, or both.

Qualitative: Quantitative assessment of Veterans will be complemented by a qualitative interview. The qualitative assessment is designed to understand whether AIMS is helpful in addressing the problem of depression medication nonadherence. We will interview Veterans from both study arms and a sample of their associated VA providers as outlined earlier.

Interview data analysis will be conducted using a rapid abstracting approach, facilitated using a structured interview format. First, study team members will independently review the interview audio (or notes), recording participant's responses as a series of key phrases or concepts by question, using a template document. Second, team members will review these responses at a subject- and question-level to identify and reconcile points of divergence. Responses will be further aggregated into binary or categorical concepts with accompanying exemplars in subject's own words. Finally, the team will prepare a summary report of: barriers to integration of Annie into clinical practice; barriers to patient use of Annie in self-management; and potential points of refinement to AIMS for further testing.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***
This is a pilot study and the primary aim is to determine acceptability and feasibility and to estimate effect size. The proposed trial will allow us to estimate intervention-attention control differences, variance, and intra class correlations need to plan for a larger trial. The primary outcome, the Medication Adherence Rating Scale has a published mean of 6.0 and standard deviation of 2(47). If attrition occurs, recruitment will continue until both intervention arms include 20 patients but final analyses will include all patients who enrolled and completed two or more study assessments. We will also include providers in our study, and will aim to recruit 35 subjects. We expect to enroll 115 adult subjects for this pilot, this number includes Veterans and providers. We have set the number to 115 in case of attrition.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
No

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***
No