COVER PAGE

CDX 19-001
PI: Dr. Una Makris, MD

Improving Outcomes for Older Veterans with Chronic Back Pain and Depression- Aim 3

Protocol, last approved 3/9/2021

The Investigator's Protocol, IRB 18-041

1. Title

Improving Outcomes for Older Veterans with Chronic Back Pain and Depression- Aim 3

2. Principal Investigator and Co-Investigators

Una Makris, MD- Principal Investigator

3. Sponsor of the Study

VACO: VA HSR&D

4. Investigational New Drug (IND) / Investigational Device Exemption (IDE)

Not Applicable

5. Purpose of the Study, Including the Hypothesis to be Tested

The overarching goal of this study is to develop and evaluate a telephone delivered behavioral change intervention for older Veterans with chronic low back pain (cLBP) and comorbid depression, and to ultimately assess its effect on cLBP-related pain, depressive symptoms, and disability. An additional component of this study will include a texting-based intervention to assess the feasibility of a texting program in monitoring Veterans with cLBP and comorbid depression.

Aim 3: Conduct a pilot RCT to assess feasibility for older Veterans with cLBP and depression assigned to receive the behavioral interventions (n=25) versus waitlist control (n=25). For participants assigned to the intervention arm, trained health coaches will deliver the intervention via telephone. All participants, regardless of what group they have been assigned to will undergo several outcome assessments (pre-screening, baseline, mid-point, final assessments) conducted by a blinded research assistant. Subjects randomized to the waitlist control group will be offered the same intervention once the active intervention group has completed the active sessions and assessments.

Annie pilot: Assess the feasibility of a texting-based protocol to assess outcomes (steps, pain, mood) among older Veterans with cLBP and depression among a subset of the larger pilot RCT (n=10-15). This will occur in two phases. The first phase (development) will involve asking up to five veterans who have completed MOTIVATE to give us feedback on usability and understandability of the proposed texting system. The second phase involves answering the texting questions to evaluate feasibility of the texting program (in a sample of 7-10 Veterans); this will be followed by in-depth semi-structured interviews to gather more information about barriers and facilitators of using the texting program.

If referring to the VA CDA-2 Research Plan, please focus only on Aim 3. Aims 1 and 2 have already been IRB approved (#16-024 and #16-069).

6. Background and Results of Previous Related Research

Chronic low back pain (cLBP) in older Veterans is a major public health problem with significant consequences. Up to 70% of the VHA population suffers from chronic pain, of which cLBP is the most common. Annual costs related to back pain exceed $100 billion and will rise with the aging population. While the population of older adults is rapidly rising, we lack evidence-based options in this population because older adults are often

excluded from randomized controlled trials for various reasons including multimorbidity, polypharmacy, frailty and fragmented social support systems.

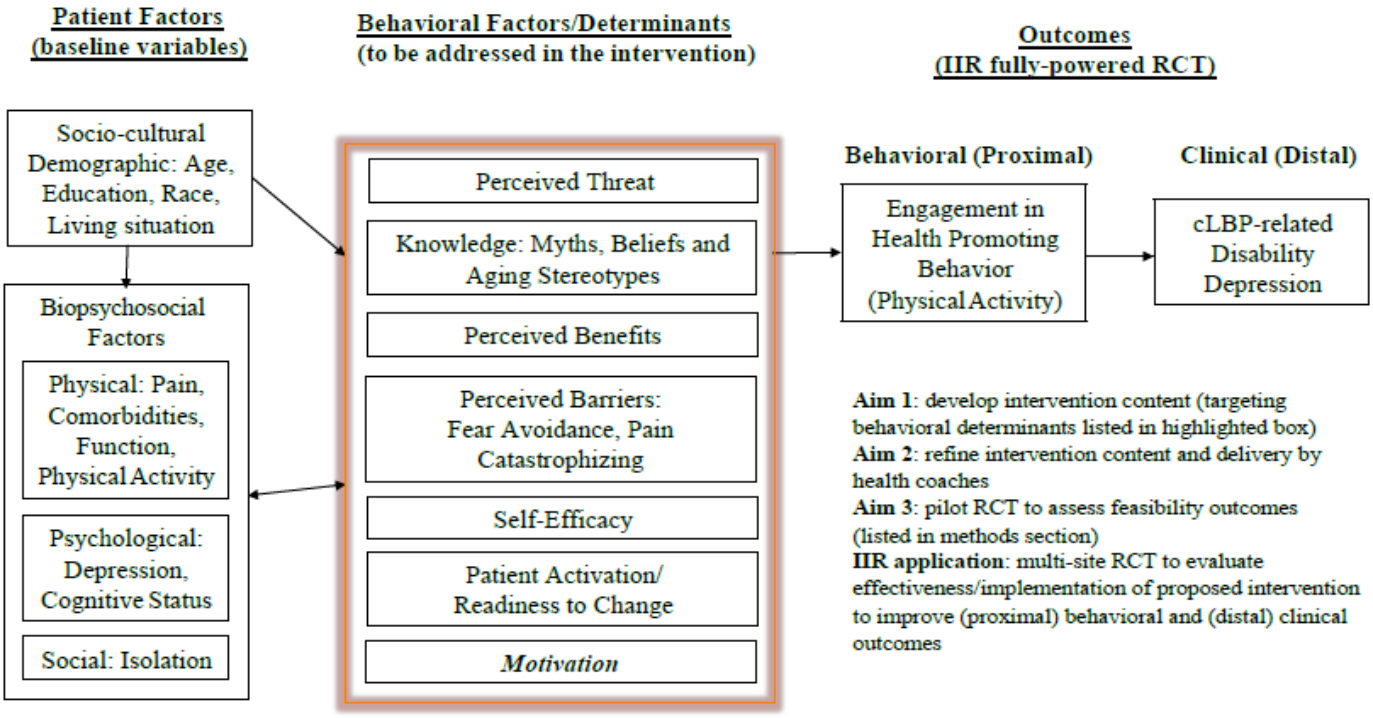
My prior work analyzing 13+ years of data shows that older adults are more likely to develop recurrent back pain if they suffer from depressive symptoms. The relationship between cLBP (≥3 months) and depression is well established: both are risk factors for the others' onset, influence each other's' treatment, and have adverse reciprocal effects on quality of life, disability, and health care costs. Because cLBP and depression are mutually exacerbating, efforts to improve outcomes for both require effective co-management.

Pharmacological management alone has limited effectiveness in older adults. Both cLBP and depression respond well to techniques designed to improve physical/emotional self-management behaviors. Older adults deserve particular attention as there is growing literature that decision making strategies and motivations to change differ from younger populations. Interventions that target age-appropriate motivations, among other behavioral determinants, are ideal for these chronic conditions.

Older Veterans urgently need effective behavioral interventions that simultaneously target cLBP and depression. Multiple studies demonstrate the effectiveness of non-pharmacological therapies in improving chronic pain outcomes, including therapies based on cognitive behavioral principles and/or movement-based strategies (exercise and physical therapy). We know that physical activity is effective (alone or as augmentation therapy) for adults with depression. A recent publication provides evidence that biopsychosocial, multi-component interventions are more effective for patients (average age 45) with cLBP as compared to placebo or physical treatments. However, older adults are consistently excluded from studies for various reasons, mostly having to do with multimorbidity and polypharmacy. There are no multicomponent telephone-based behavioral interventions specifically in older Veterans with cLBP and depression. Because cLBP and depression are mutually perpetuating and exacerbating, a critical piece of this research is to identify and target interrelated behavioral determinants (i.e., beliefs, fear avoidance, self-efficacy, motivation) that play a role in older adult's behavior and subsequent outcomes.

This intervention is grounded in health behavior theories and builds on prior interventions for chronic pain and mental illness in medically complex older adults. Our conceptual model in Figure 1 includes patient characteristics, potential reciprocal relationships between the listed constructs, and emphasizes motivation to change as a key behavioral determinant. One-way arrows show that baseline socio-cultural variables (these are rarely modifiable) influence biopsychosocial factors (i.e. the way an older Veteran may experience pain) and can influence the listed behavioral determinants. The extent and status of specific behavioral determinants (which the proposed intervention will elicit and target) may influence/modify specific baseline biopsychosocial factors as well as both proximal and distal outcomes.

Figure 1: Conceptual Model for Proposed Intervention



Consistent with a recently published model for developing behavioral treatments for chronic diseases, Figure 1 represents a model pathway by which our behavioral intervention is hypothesized to improve behavioral and, ultimately, clinical outcomes. By eliciting and targeting specific behavioral determinants (highlighted box) we will facilitate engagement in a health promoting behavior (physical activity) and ultimately improve cLBP and depression clinical outcomes (disability and depression scores). The behavioral determinants listed in Figure 1 are relevant for both cLBP and depression and include perceived threat, benefits, barriers and self-efficacy (all prominent constructs in the health belief model) as well as readiness to change (from the trans-theoretical model). Consistent with clinical practice, older Veterans with cLBP and depression exhibit variability in the behavioral determinants listed. To increase intervention potency, the intervention targets both cLBP and depression behavioral determinants and seeks to improve outcomes in both conditions.

Older adults (more than younger) appear to be motivated to engage selectively with information that is relevant, positively framed, and fits with their personal goals. For example, when making choices, older adults tend to review and remember relatively more positive than negative information as compared to younger adults. To develop the most robust intervention for older Veterans we must tailor intervention content recognizing that older adults have unique beliefs, [mis]perceptions, as well as different preferred delivery (and wording) of the material as compared to younger individuals. Data suggest that positively-framed messages (emphasizing benefits of walking) are more effective than negatively-framed messages (emphasizing risks associated with not walking) in promoting and activating older adults to walk more. Our intervention content and messaging will target these unique motivations to engage in behavioral change.

Health coach delivered behavioral interventions have been shown to be effective in older adults with chronic pain. A health coach, broadly, is defined as a supportive mentor who motivates, educates and supports clients

to achieve their health goals through lifestyle and behavior adjustments. The health coach for this project, will have experience with chronic [back] pain and depression. The Health coaches will receive extensive training on how to deliver the content to older veterans with depression and chronic back pain. These prerequisites will ensure that the health coach has exposure to principles of motivational interviewing, patient activation, and goal setting. The health coach will receive additional training in motivational interviewing and delivery of the proposed intervention as intended, with the use of an intervention manual. Furthermore, the health coach(es) will complete all required credentialing paperwork and security training. As proposed in Figure 1, the intervention will be delivered via telephone by health coaches using modules that target the listed potential behavioral determinants that specifically focus on how older adults are uniquely motivated to change. The health coaches will educate participants, use motivational interviewing to enhance perceived benefits, reduce barriers to participating in recommended behaviors, and assess motivations and readiness to change. Once a participant is ready for action, health coaches will use motivational coaching as well as goal setting and action planning techniques to facilitate behavioral change.

In Aim 1 of this research we developed a behavioral change intervention, using input and feedback from national experts, other stakeholders, and Veterans. In Aim 2 of this study we recruited a small sample (n=7) of Veterans and pre-tested the roll out of the intervention. We developed study procedures including recruitment procedures, intervention progress tracking, fidelity assessments, outcomes assessments on redcap, and hiring and training of research staff. Using feedback from the health coach, research staff, Veterans, and primary care providers we have modified the intervention manual and procedures, iteratively. This Aim 3 protocol is intended to evaluate the intervention in a larger sample, including a randomized design that includes a waitlist control group.

If referring to the VA CDA-2 Research Plan, please focus only on Aim 2. Aim 1 has already been IRB approved (#16-024). A separate IRB submission will address Aim 3.

7. Definition of the Population to Which the Study is Directed, with Justification

In this study, the sample will be identified and enrolled using a multi-step screening process, very similar to successful recruitment processes that Dr. Makris' mentoring team has used within the VA system. The population of interest for this study is older Veterans (65 years of age and older) with comorbid chronic back pain and depression. Please see Section 6 above for background and justification for why we chose to focus on these chronic conditions in older Veterans. Both are exceedingly prevalent conditions that lead to considerable morbidity in this aging population. Please see Section 8 below for more detail on how cLBP will be defined and subjects selected.

8. Subject Selection, Inclusion and Exclusion Criteria

The eligibility criteria for all Veteran participants are as follows: Veterans who are 65 years or older, with an ICD-10 code for back pain (cLBP) on the problem list who are patients of primary care clinics at the Dallas VA (including community based outpatient clinics). A list of potentially eligible participants will be obtained from the VA corporate data warehouse to verify the presence of a diagnosis of cLBP (by ICD-10 code initially) in the prior 2 years with at least 1 visit for cLBP in the last year.

There will be three potential **recruitment strategies (described in detail in section 12)**, based on what we learned was most effective during Aim 1 and Aim 2 of this study. The *first* method involves: all veterans who meet

criteria for age and cLBP will receive an opt-out letter about the study (included as a supplemental file, will be signed by PRIME or ambulatory care director, as appropriate). The *second* method involves: identifying when potentially eligible participants have appointments in a primary care clinic (including both PRIME and ambulatory care clinics), or specialty clinic such as Rheumatology or PM&R. The provider will introduce the study and research staff to the Veteran in person. The research staff will then describe the study and obtain consent if subject is interested. Additionally, the *third* recruitment strategy involves referral directly from a provider. Dr. Makris will provide a flyer to be posted in PRIME or ambulatory care clinics (see attached to this IRB protocol submission) outlining the eligibility criteria and brief synopsis of the study. If the Veteran is interested in learning more and participating in this study, he or she may call Dr. Makris or the study team at the number provided on the flyer, or, with the HIPAA waiver, the provider may notify Dr. Makris' team to call the Veteran (as additional cosigner on the clinic note). When/if Dr. Makris or her research team speaks with the Veteran (preferably in person but may be over the telephone if more convenient for the Veteran), we will describe the study, risks and potential benefits and obtain consent, also for audio-recording. The eligibility criteria will be assessed and confirmed over the phone or in person (whichever more convenient for Veteran) via self-report and review of CPRS data. If consent is obtained in person, the forms will be signed then. If the discussion occurs over the phone and the Veteran agrees to participate in this study, a consent form, HIPAA authorization and audio-recording consent form will be mailed to the Veterans home. He or she will sign the consent (without social security number) and return via mail or bring the signed forms in person at the time of the in-depth interview.

Inclusion Criteria:

- Men and women Veterans aged 65+
- English- speaking
- Self-reported low back pain (+/-radiation) on most days for the past 3 months, that interferes with daily activities. Low back pain interferes with daily activities, assessed with the question "does your back pain limit your ability to do activities around the home or activities that you enjoy?"
- Chronic low back pain with intensity of 4 or higher on 10 point scale
- Depression, PHQ-9$\geq$10 stable (per chart review, no psychotic or suicidal ideation; confirmed over telephone)
- Capable of participating in home-based activity
- Has a smart phone with texting ability to participate in the Annie texting pilot

Exclusion Criteria:

- No telephone
- Not English speaking
- Unwilling to be randomized to either study arm
- Self-reported uncorrected hearing or visual disturbance precluding ability to participate in telephone sessions or read pedometer screen
- Cognitive impairment assessed by Memory Impairment Screen
- Lumbar surgery within the last year

- Self-reported dependence on wheelchair, bed-bound, or severe balance impairment (unable to participate in physical activity intervention)
- Illness requiring hospitalization within the last 3 months that interferes with a home based physical activity intervention. Specific question: Have you been hospitalized for an illness in the past 3 months that would make participating in a physical activity program challenging or unsafe? (Examples include: fall, gout attacks, stroke, heart attack, heart failure, or surgery for blocked arteries)
- Suicidal ideation, prior psychotic episodes requiring hospitalization within the last year

Veterans receiving mental health services at the time of the study recruitment will not be excluded. All mental health treatments and health service-use characteristics will be included in the study analyses as covariates.

9. Number of Subjects in the Study

For Aim 3, we will recruit a total of 50 people to be randomized between two groups of 25 subjects; the waitlist control group (n=25) and the intervention group (n=25).

For the Annie pilot, a subset of the recruited patients will participate in developing and evaluating Annie texting to capture step counts, pain and mood.

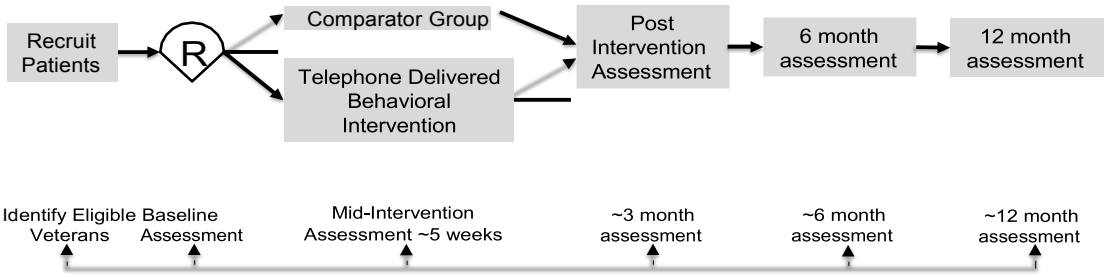
10. Justification for the Use of Vulnerable Populations

Not applicable.

11. Study Design

In Aim 1 of this study, we used input from stakeholder groups to inform development of a theory-based multicomponent behavioral intervention for older Veterans with cLBP and depression—the intervention (Aim 1 in the attached CDA-2 Research Plan). In Aim 2 we conducted preliminary testing of the intervention in a sample of 7 Veterans with the purpose of evaluating procedures for the recruitment process, enrollment, usability of manuals, fidelity ratings, and study procedure. In Aim 3, will we assess the feasibility for older Veterans with cLBP and depression assigned to receive the behavioral intervention (n=25) versus the waitlist control (n=25). Follow-up will also include assessments at 6 months and 12 months post-intervention. In the Annie texting pilot, up to five Veterans who have completed MOTIVATE will be asked to provide feedback on the usability and understandability of the proposed texting system. After this, the feasibility of the texting program will be tested in a small group of Veterans who have completed MOTIVATE (n=7-10). This will be followed by in-depth semi-structured interviews to gather more information about barriers and facilitators of using the texting program to capture data on steps, mood and pain.

Figure 3. Overview of Aim 3 Pilot RCT and Assessment Intervals



Overview of Proposed intervention: The behavioral intervention is designed for older Veterans with cLBP and depression and will include 8 individual telephone sessions delivered by health coaches over a period of 10-20 weeks (up to 5 months total, accounting for additional time between sessions if needed). Based on what we learned from Aim 2, we will allow an additional week or two weeks between sessions (if 1 week scheduled between sessions, we will allow one additional week for scheduling; if 2 weeks allowed we will allow up to 4 weeks); prolonging the time between sessions will be at the discretion of the PI and research team. Exceptions may be made for highly motivated subjects who had unfortunate life circumstances arise.

The content and the order of each session was developed in Aim 1 and then tested and refined in Aim 2 (based on subject and health coach feedback). The behavioral intervention is set-up so that the first session will introduce the participant to the health coach and the program to establish rapport and assess baseline physical activity. The following 6 modules address behavioral determinants (Figure 1 in Research Plan), followed by a final module designed to be a booster session to the overall program. The most recent intervention manual with content for each of the 8 sessions is attached to this IRB submission. We also developed a mirror manual that the coach fills out for each subject (also attached to this IRB submission) that is saved to the secure Makris research folder.

For the physical activity component of the intervention, we will provide an Omron pedometer to subjects, as previously used in VA research studies. The Omron pedometer will be set up by the research team (stride length, setting date/time) and will be mailed to the subject's home in between session 1 and 2. The health coach will remind the subject that this pedometer will arrive via USPS mail to their home and to call the research coordinator when it arrives. The research team will provide technical assistance and instructions to the subject regarding use of the Omron pedometer (to be worn on the waist band, daily, all day aside from showers/baths). The research team will also verbally show the subject how to press the mode and memory buttons to obtain weekly step counts for documentation/tracking physical activity. The subjects will be prompted by the health coach or research staff to report out weekly step counts during subsequent coaching sessions.

In addition to the assessments outlined later in this protocol, specifically at 12 months, we will conduct in-depth semi-structured interviews with ~10-15 participants (8 from both arms of the pilot trial, the health coaches, 2 primary care providers, and 1 mental health provider) using purposive sampling. The health coach/research coordinator will identify Veterans who are at higher risk for drop-out, were less engaged, or were particularly successful at achieving behavioral change. The purpose of this final interview is to learn about the barriers and facilitators to successful intervention delivery and participant retention from the Veteran, health coach, and provider perspective. Interview topics will focus on PARiHS "context" and "facilitation" in Table 1. We will use components of the well-established, VA developed implementation framework, Promoting Action on Research Implementation in Health Services (PARiHS), to inform the interview topics and discussion guide that will yield most useful feedback. Context is about how the microsystem (Dallas VA) impacts likely uptake of the intervention; for example, we will gain a better understanding of potential facilitators to implementation of this intervention. Facilitation is about identifying specific ways to augment the likelihood of implementation.

Table 1. Key Informant Interview Topics Based on PARiHS Framework of Evidence, Context, and Facilitation

PARiHS Dimension: Evidence	PARiHS Dimension: Context	PARiHS Dimension: Facilitation
▪ Perceptions about the strength and motivation for personalized goal-setting ▪ Perceptions about how well goal-setting is accepted by Veterans ▪ Perceptions of how goal-setting affects current practices or can be integrated into routine work flows ▪ Perceptions of how patient activation can be applied to improve outcomes ▪ Perceptions of how motivations to change and identifying meaningful goals can be aligned	▪ Availability of resources to carry out personalized goal-setting ▪ How training and fidelity assessment for personalized goal-setting fit with work demands ▪ Past experiences with collaborating with other VA health care providers (PACT and other) members on self-management or goal-setting ▪ Existing channels of communication for input and feedback among PACT members and other providers regarding goal-setting and self-management	▪ How to align roles in the project with existing responsibilities ▪ Perceptions about what successful implementation will require from staff, patients, and clinicians ▪ Perceptions of skills, attitudes, and beliefs about internal facilitators and study team ▪ Plans for establishing formal communication routines between study team, PACT members and other personnel

For the Annie texting pilot, we will use the VA Annie texting system. A select group of Veterans will be invited to participate in a technology program that involves texting participants to learn more about their health behaviors and status (specifically, step counts, pain and mood). There are two phases to this part of the study. The first phase (development) will involve asking up to five Veterans who completed MOTIVATE to give us feedback on usability and understandability of the proposed texting system. We will elicit opinions on a draft of a discussion guide that will outline the texts Veterans will receive from the Annie texting system. The second phase involves answering the texting questions to evaluate feasibility of the texting program (in a sample of 7-10 Veterans); this will be followed by in-depth semi-structured interviews to gather more information about barriers and facilitators of using the texting program.

12. Description of Procedures to be Performed

We will obtain HIPAA-waiver for screening purposes and will employ ***three separate recruitment techniques*** that have been effective in earlier stages of this study (see section 8 where this was introduced).

The **first** method includes: sending out an IRB-approved opt-out letter signed by Dr. Makris (PI) and the primary care clinic director, Dr. Lilly in PRIME, or Dr. Potu, in Ambulatory Care introducing the study and stating that a research team member may call them if they do not opt-out within 5 days. The research coordinator's phone number will be provided for participants to opt-out or gain more information. If the potential participant does not opt-out, the research coordinator will call the Veteran (making up to 6 attempts to reach the Veteran), introduce them to introduce the study, and obtain verbal consent followed by additional screening for eligibility. Following verbal consent and further screening for eligibility, if patient is eligible and interested, we will mail a consent form, HIPPA Authorization form, and VA Form 10-3203, Consent for Use of Picture and/or Voice to patients. These forms will include pre-paid postage for participants to sign and mail back to the VA (research office). The research team will then sign the consent form and enter a research consent and enrollment note into CPRS. This CPRS note will serve as the notification to the PCP that the patient is enrolled in this study.

The **second** method involves: identifying when potentially eligible participants have appointments in a primary care clinic, ambulatory care (including Polk Street CBOC and/or Fort Worth CBOC), rheumatology or PM&R clinic, having the provider introduce the study and research coordinator to the Veteran in person. The research coordinator will then describe the study and obtain consent if subject is interested.

The **third** recruitment strategy involves referral directly from a provider. Dr. Makris will provide a flyer to be posted in PRIME, ambulatory care, Rheumatology or PM&R clinics (see attached to this IRB protocol submission) outlining the eligibility criteria and brief synopsis of the study. If the Veteran is interested in learning more and participating in this study, he or she may call Dr. Makris or the study team at the number provider on the flyer, or, with the HIPAA waiver, the provider may notify Dr. Makris to call the Veteran (as additional cosigner on the clinic note). When/if Dr. Makris or her research team speaks with the Veteran (preferably in person but may be over the telephone if more convenient for the Veteran), we will describe the study, risks and potential benefits and obtain consent, also for audio-recording. The eligibility criteria will be assessed and confirmed over the phone or in person (whichever more convenient for Veteran) via self-report and review of CPRS data.

The inclusion and exclusion criteria (listed in detail in section 8) that will be assessed via the telephone or in person depending on recruitment method with a combination of self-reported measures, survey, and by review

of electronic medical record data. Veterans receiving mental health services at the time of the study recruitment will not be excluded. All mental health treatments and health service-use characteristics will be included in the study analyses as covariates. Verification of cLBP will be based on the self-report to questions listed in the eligibility screener (provided as supplemental document). Depression criteria will be based on participant self-report of clinically significant depressive symptoms according to the PHQ-9 (in person or via telephone screening). We will use the established cut-off score of ≥10 on the PHQ-9 to signify a clinically meaningful symptom burden. If the Veteran is not already enrolled in mental health clinic and scores ≥10 on PHQ-9, we will send the PCP a message in CPRS notifying him/her and suggesting further discussion about referral to mental health.

A protocol will be in place should the study team identify a potential participant who reports or develops suicidal ideation. For safety purposes, the protocol is as follows: Any patient identified as having suicidal ideation during this screening process will be referred to Dr. Makris and will be referred to the VA suicide hotline that involves warm transfers to mental health professionals. Using a pre-established protocol, Dr. Makris will contact the subject and make arrangements for immediate mental health assessment and treatment based on the subject's symptoms. All suicidal patients will be provided with the VA suicide crisis hotline number, regardless of other immediate clinical interventions. Furthermore, subjects with severe psychiatric diagnoses (as specified among the exclusion criteria) or prior documented inpatient admissions for suicidal ideation will be excluded and not enrolled in the study.

Randomization: Once the baseline assessment has been completed, eligible participants will be randomly assigned to the waitlist control group (n=25) or the intervention (n=25) by applying a set of computer-generated random numbers. Since we are interested in better understanding feasibility of the intervention as compared to the waitlist control, and how behaviors are sustained over time, Aim 3 involves extended follow-up to 12-months. We will use these extended follow-up data to better understand differential attrition as well as preliminary formative implementation evaluation (see below).

At this time, a binder with the intervention manual material will be sent to the subject's home if randomized to the intervention arm. This manual is intended for the patient to follow along with the health coach during phone calls. It will also contain the activity trackers that he/she will use in between session to track activity, step counts, and impact on pain and depression.

We will mail out appointment letters before each intervention visit. Depending on the content of the session, these reminders may also include a list of the subject's values, goals and action plan. The patients will also be called by a research team member or the health coach prior to the scheduled phone calls as a reminder. During Aim 2, we learned that some patients are forgetful about the timing of the phone calls which causes delays-these phone call reminders were helpful.

The health coaches will deliver the 8 (8 modules +3 check-in calls during the goal setting modules) session telephone-based intervention to 25 subjects randomly assigned to the intervention arm. For subjects assigned to the comparator arm (n=25), the "wait-list" control group, they will continue receiving usual care for both cLBP and depression, but not the active intervention.

A research member, not the health coach, will call all subjects regardless of their assigned group to assess outcomes (baseline, mid-intervention and post-intervention). These data will be collected using VA Redcap and the data will be entered behind the VA firewall. Upon completion of the intervention, semi-structured

interviews will elicit stakeholder and participant perceptions of health coaches, use of action plans and responses to coach recommendations (see Table 2 for key informant interview topics).

Feasibility outcomes, including recruitment and fidelity (defined below), will be assessed. Based on previous protocols used at the VA, the phone calls will be audio recorded and 20% of the sessions will be assessed using a fidelity checklist to ensure that the intervention is being delivered as intended. The fidelity checklists (developed based on the most recent intervention manual) will be submitted along with this IRB. The purpose of the fidelity checklists is to verify that the objectives and core concepts for each session are being delivered as intended to the subjects.

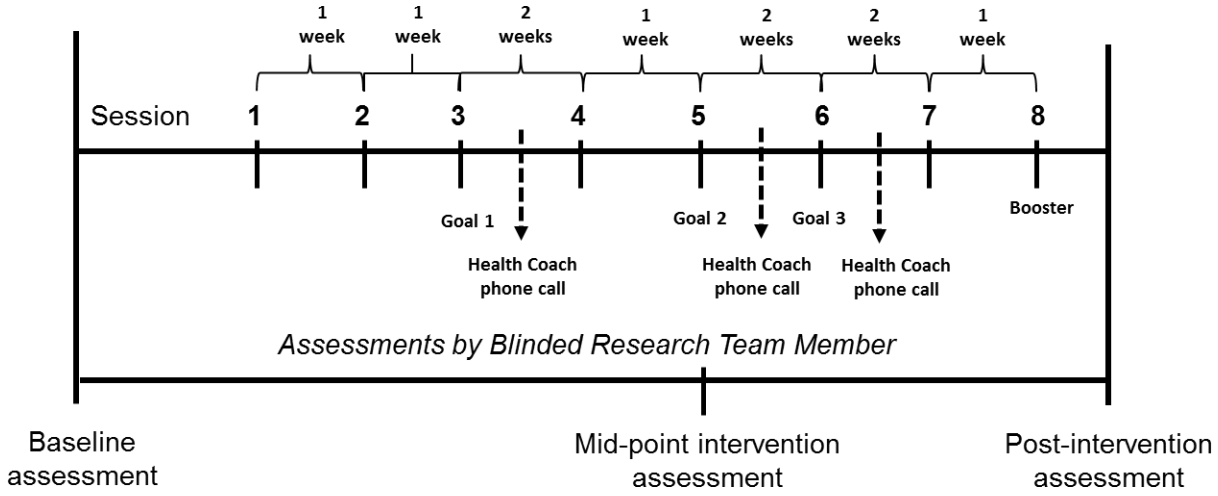
We will use a telephone audio recorder (LRX 40 USB), see previously email correspondence with ISO and PO for IRB 16-024 , Aim 1) to record these sessions. Approval from IT to use LRX 40 USB was obtained already for Aim 1 and Aim 2- we will use the same recording device.

In phase I (development) of the Annie texting-component of the study, we will ask for Veterans' and experts' feedback during telephone calls. Specifically, we will ask select Veterans who completed that MOTIVATE intervention about their experience with cell phone technology, experiences/difficulties of Annie (if used before), content of the proposed Annie texts, and suggestions for improvement regarding the content, frequency, and user-friendliness of the texts. Utilizing this feedback, a texting template and discussion guide for interviews will be finalized. In phase II, the intervention will be delivered via the Annie texting system to a select sample of Veterans in the waitlist control arm who have completed the end assessment, who have been offered the MOTIVATE sessions and who agree to participate in the Annie texting pilot. Veterans will receive a concise, phone-guided training on how to use the Annie texting system. Veterans will receive daily texts regarding step counts and three times weekly texts regarding pain/mood symptoms. Data, including both quantitative and qualitative, will be collected using Annie dashboard (will show response rates to specific text messages), surveys and semi-structured interviews, all conducted via telephone by a research team member. Afterwards, we will conduct semi-structured interviews over the telephone with up to 10 Veterans. Interviews will be audio-recorded (consent obtained upon enrollment in MOTIVATE). These audio-recordings will be securely transferred using a VA encrypted device (Apricorn Aegis Secure Key 3z 256 bit AES XTS Encryption 64 GB USB FIPS Level 3 Validated 140-2) to the UTSW Qualitative Research Committee who will transcribe and code the de-identified transcripts/ data. We will use NVIVO software for data management and coding of the transcripts. The same audio recorder, approved by IRB, from Aims 2 and 3 will be used.

Timing of assessments/ data collection: The research staff will screen, identify eligible Veterans for the study, obtain consent (either in person or verbally (over the phone) initially followed by mailed written consent), and complete further screening for eligibility. If the subject is eligible for this study, the research staff will arrange a separate phone call for a baseline assessment via telephone. The baseline interview must be completed within 2 weeks for the participants to proceed to the intervention. This time frame may be extended at the discretion of the study team. Once the baseline visit is complete then the patient will be informed if randomization allocation.

As seen in the Figure below, the health coaches will conduct the once a week session (or every two weeks depending on the session content) sessions (11 in total), delivered via telephone. A research team member, not the individual conducting the intervention sessions, will complete all assessments via telephone using a structured data collections tool at baseline, 5 weeks (mid-point assessment), at 10 weeks (post intervention

session), 6 months and 12 months post-intervention. Those in the Annie texting-pilot will participate for the duration that the MOTIVATE sessions are typically provide to the waitlist control group (8 sessions over 12-20 weeks). The study team will also conduct interviews as outlined above at 6 months and 12 months to obtain feedback regarding implementation and sustainability of the behaviors learned. The data from these assessments will be entered into a VA Redcap database https://vhacdwweb05.vha.med.va.gov/ that is housed behind the VA firewall on secure research folder on VA servers: \\v17.med.va.gov\v17\NTX\Services\Research\Makris-Research. All data entered into Redcap is de-identified. Following the physical activity session, the health coach or research staff will obtain daily versus weekly step counts that the subject will read out over the phone. Total steps taken will be documented within 1 week, and then at during subsequent health coaching sessions as well as the 10 week assessment by research staff.



Database Management: A project specific spreadsheet has been developed (using word documents) to track subjects within the intervention, plan phone calls, and capture demographics of those who participate. The VA Redcap has been programmed with the specific outcomes assessments for this project, and we will begin to use Redcap to document all electronic data management activities including tracking of screening, recruitment, and progress through the intervention and assessments. The Annie texting data will be collected and stored via the Annie dashboard (https://staff.mobile.va.gov/annie-provider/). All dashboard data is stored on a secure server behind a VA firewall, stored on the VA network, either in the Makris secure research folder or VIREC redcap. The data from health coaching telephone sessions (i.e. goals set by subjects, achievement of goals, barriers to achieving desired goals) will be entered into a parallel health coaching manual (word document) that will be IRB approved and stored behind the VANTHCS firewall in the study secure research folder.

Study data will be stored within password protected data management programs, on password protected computers. No non-study personnel will have access to study data. All research staff will be trained in the appropriate safeguarding of confidential data and in the protection of human subjects. At the end of the study, after analyses are complete, all study data will be de-identified, and the identifying key will be destroyed per VA policies and regulations. The health coach will have restricted access to the study database; he/she will also have access to CPRS as needed.

Audio recordings from the Annie texting pilot, all de-identified, will be transferred off campus for transcribing and coding. Transcription and coding will be completed in collaboration with the UTSW Qualitative Research Core, a group of collaborators with whom Dr. Makris and Dr. Hogan have worked with on other studies. No non-study personnel will have access to study data.

13. Anticipated Data and Data Analysis

Study variables collected at pre-screen, baseline, mid and/or end- assessment measures: The research staff will collect data, listed below:

- Demographics (age, gender, ethnicity, education, marital and living situation from CPRS initially, then confirmed during the baseline assessment);
- Distance (in miles) from nearest VA facility, from address available in CPRS, confirmed by subject;
- Comorbidities will be obtained from CPRS, prior to baseline, using the previously validated self-report version of the Charlson index;
- Substance use will evaluate for alcohol abuse (Short Michigan Alcoholism Screening Test), and illicit substance use (Drug Use Questionnaire [DAST-10] that was found previously to negatively impact outcomes;
- Mild cognitive impairment (MCI) - subjects not excluded based on the telephone Memory Impairment Screen will be screened for the presence of MCI with a Six-Item Screener. Prior research demonstrates that cognitive function mediates the relationship between pain and physical performance in older adults with cLBP. This may also impact adherence to behavioral interventions;
- Future Time Perspective scale consists of 10 statements about the subjective perceptions of time and is most commonly used to assess time horizons;
- Medications (see below for more details);
- Body mass index will be obtained from CPRS; Self-report of pain, physical/psychological/social function, quality of life (see primary/secondary outcomes).
- Sleep: PROMIS SF 6-item questionnaire to assess sleep
- Resilience: Connor Davidson Resilience Short Form: CDRISC 10 item that assesses resilience
- Patient Satisfaction Survey – six questions about the subject's experience in the study that will be asked at the end assessment
- Texting response rates of Veterans via Annie dashboard.
- Trends of step counts, pain scores, and mood scores overtime via the Annie texting dashboard
- Patient satisfaction survey among Annie texting pilot - questions on the about the subject's experience will be asked at the end of the assessment

Primary Feasibility Outcome Measures in Aim 3: Feasibility outcomes will be useful for the planning a hybrid effectiveness/implementation merit IIR award. These outcomes include: enrollment rates across different primary care clinics at Dallas VAMC; intervention adherence (measured as number of sessions the subject engaged in) and retention; use trends of Annie texting over time.

Upon completion of the intervention, a member of the research team (not the individual conducting the intervention sessions) will conduct in-depth semi-structured interviews and will also seek ratings of the helpfulness of skills taught (Likert scale), overall satisfaction, and whether the information presented provided appropriate motivation to continue practicing learned skills. The data collected from these

interviews will help with formative evaluation of the program to better identified which Veterans are at higher risk for drop-out, were less engaged, or were particularly successful at achieving behavioral change. The interviews will also help identify what barriers and facilitators are in place to delivering a successful intervention and retained participants from the Veteran, health coach and provider perspective. Interview topics will use the PARiHS framework. Among Annie pilot participants, in-depth structured interviews will be done to assess opinions regarding Annie texting system. A draft discussion guide has been included.

Fidelity: The health coach will receive additional training in Motivational Interviewing from Dr. Saxon. Following a manual driven approach, the health coach will be evaluated on fidelity to the content of each coaching session. All intervention sessions will be audiotaped using a digital phone recording system (LRX 40USB http://www.veccorp.com/pdf/lrx-40usb.pdf) that records both sides of the telephone conversation and will be saved to a secure server behind the VA firewall. We will obtain written consent to audiotape these conversations. Twenty percent of the audiotapes following a detailed checklist to assess fidelity. The health coaches will receive feedback and additional training during scheduled weekly research "trouble-shooting" meetings

Primary Outcomes for Future Effectiveness Trial

- Physical function/ self-reported disability will be measured by the Roland Morris Disability Questionnaire (RMDQ). The RMDQ is valid, reliable and responsive to change in community dwelling patients with cLBP. Pain disability is important because this is a major treatment target in patients with chronic pain
- Depression will be measured using the previously validated PHQ-9. A PHQ-9 cutoff score of >10 will signify clinically meaningful symptom burden (sensitivity and specificity =88% for major depressive disorder).

Secondary Outcomes include physical, psychosocial consequences associated with cLBP and depression:

- Pain interference and pain behavior will be measured using NIH PROMIS instruments.
- Pain intensity will be measured with the PEG Three-Item Scale, which assesses average pain intensity, interference with enjoyment of life, and interference with general activity on a scale from 0 to 10)";
- Quality of life will be measured with the well-validated PROMIS Global Health scale (physical and mental health);
- Social functioning is an important contributor to disability in those with depression and chronic pain. We will measure social isolation using PROMIS measures, based on our preliminary data, by older Veterans with cLBP;
- Current medications (regularly scheduled and as-needed) will be collected at baseline and subsequent assessments from CPRS and then confirmed with the subject over the telephone. Subjects are also asked if they are taking additional medications. As described, we will create four " yes/no" variables reflecting medication use: acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), opioids (including tramadol), and other agents such as anti-depressants used specifically for pain (versus depression), gabapentin, other anticonvulsants, corticosteroids, topical anesthetic

and capsaicin preparations.

- Variables abstracted from the electronic medical record include (baseline, 3, 6): opioid use, psychotropic medications, hospitalizations, and clinic visits (including mental health appointments). These are important health utilization outcomes that will be explored in future studies.

Proximal/Behavioral Outcomes

- Physical activity: We will evaluate overall physical activity level using a portable, lightweight, Omron HJ-320 pedometer. Participants will wear the pedometer clipped to their right lateral waistband for 24 hours per day for 7 consecutive days (except during shower or water activities) to obtain 5 complete days of physical activity data. This will be explained in detail at the time of recruitment call. More details about the device are provided in a separate attachment. Instructions to Veterans on how to safely enhance physical activity using this device are also provided in a separate attachment.

Other measures associated with achieving behavioral and clinical outcomes

- Patient Activation Measure (PAM) assesses patients' skill, confidence, and knowledge in managing issues related to their healthcare.
- Arthritis Self-efficacy scale is a 10-point Likert scale that measures the belief or confidence the subject has to perform 8 specific activities or tasks, based on arthritis.
- Physical activity contemplation ladder;
- Expectations of the intervention are asked with the following three questions: 1) How likely is this program to improve my ability to walk? 2) How likely is this program to improve my back pain? 3) How likely is this program to improve my depression/mood?
- Global impression of change will be assessed using the Patient Global Impression of Change Scale, a 7-point scale (1 = No change (or condition has gotten worse) to 7 = great deal better and a considerable improvement that has made all the difference) asking participants to rate their change (if any) in pain since starting the study.
- Pain Stages of Change Questionnaire (PSOCQ) evaluates attitudes, intentions, and behaviors consistent with stages of change for pain self-management.
- Therapeutic alliance will be assessed using the Working Alliance Inventory Short-Form will measure therapeutic relationship between patients and therapist (health coach in our study). To allow the therapeutic relationship to develop, subjects will complete this assessment starting at5 weeks.
- Sleep: PROMIS SF 6-item questionnaire to assess sleep
- Resilience: Connor Davidson Resilience Short Form: CDRISC 10 item that assesses resilience
- Annie texting system: A select group of subjects will receive text messages to collect their step counts, pain scores, and mood levels

Analyses for Aim 3: Feasibility outcomes will be measured by recruitment rates, adherence, retention and intervention fidelity. For Aim 3 we will add prompts during the semi-structured interviews that focus on

how subjects, if applicable, achieved an increase in physical activity. For example, did they build more walking- based activities in their daily routine (walking to the store rather than driving) or did they add new activities to accumulate more steps? We will also inquire about whether goals achieved were congruent with motivations to change behavior and how these motivations may influence sustained behavior. Fidelity assessment, as described above, will result in feedback to the health coaches and will ensure that the health coaches deliver the intervention as intended.

For the Annie pilot, feasibility will be tested in phase I and phase II. In phase I, a small group of Veterans and experts will be asked open-ended questions on their thoughts of the Annie system. The Annie texting protocol will be modified so it best serves the needs of veterans. In phase II, feasibility will be assessed by looking at response rates through the Annie dashboard. At the end of phase II, structured interviews will take place among the participants regarding their opinions, barriers, and thoughts for improvement of the Annie texting system as tool to assist in pain management.

Proposed Analyses: Exact binomial method will be used to estimate rates of recruitment, intervention adherence, retention, and drop-out along with the corresponding 95% confidence intervals. Multiple levels of treatment retention will be defined, including partial intervention completion (% who do not complete all sessions), intervention dropout (% who dropout of intervention but continue to do assessments), research dropouts (% who remain in intervention, but do not complete assessments), and intervention + research dropouts (% who do not complete intervention or assessments). We will further break down the enrollment and retention calculations by examining enrollment/retention differences by treatment group, health coach, gender, age, race/ethnicity, and initial cLBP and depression severity using cross-classification tables.

As exploratory analyses, pre-post improvement in disability (RMDQ) and depression (PHQ-9) scores, as well as secondary and intermediate outcomes, from baseline to 3 months will be compared based on a two-sample t-test or Wilcoxon rank-sum tests between the two groups. The difference in improvement will be estimated and the 95% confidence interval will be reported. We will estimate the preliminary effect size and variance of effect for the above outcomes. Linear mixed models will be used to assess whether there is a difference in the above outcomes over time within and between the two groups. We will include distance (in miles) from a VA facility as a covariate in the exploratory outcome analyses, as suggested by reviewer.

We will describe, for the subset of subjects receiving the intervention, whether physical activity (proximal outcome) and clinical outcomes (disability and depression scores) change over time based on the 1) proportion of the total sessions completed, and 2) the proportion of individual sessions completed. This will help us estimate optimal dose of the intervention (for example, whether completion of 4 vs. 7 vs. 8 of 10 sessions produces similar outcomes) and may inform which specific sessions are absolutely critical. SAS (version 9.3, Cary, NC) statistical software will be used.

Our formative evaluation may help to identify parts of the process that need refinement to maximize the feasibility and extension of the project to different sites (in anticipation of the IIR proposals). Also, part of the formative evaluation process will be to understand how implementation factors influence the optimal dose of our intervention. This evaluation may highlight which intervention components (or active ingredients) resulted in a change in behavior or other outcome result and potentially why (barriers/facilitators of change from an implementation standpoint).

Analyses for the Annie-texting pilot: Phase 1: these qualitative and interview data will be used to inform

consent and procedure development for Phase 2. No formal analytic methods will be used.
Phase 2: feasibility will be assessed by looking at response rates through the Annie dashboard. At the end of phase 2, semi-structured interviews will take place among the participants regarding their opinions, barriers, and thoughts for improvement of the Annie texting system as tool to assist in pain management.

14. Provisions for Managing Adverse Reactions

We do not anticipate any adverse reactions as this study only involves interviews; hence, there is minimal risk of physical injury.

As part of the Annie texting pilot, we will develop orientation materials introducing the VA Annie texting system, which includes statements regarding safety and who to contact for questions or concerns. The Annie dashboard will be monitored twice/ week by the MOTIVATE research team for any concerning texts that may prompt a phone call for escalating symptoms. Similarly, if a subject persistently does not respond to any of the Annie text prompts, the research team will call the Veteran for a check-in and to trouble shoot any issues with technology.

15. Risk/Benefit Assessment

The research involves a telephone-based program by a health coach over 10-20 weeks followed by an interview and in some, the Annie texting pilot; hence, there is minimal risk of physical injury. Participants will be asked to be more physically active and track their steps with a pedometer. As they become more active there is a risk of fall and injury. However, the health coach will focus on safely increasing walking and fall prevention strategies. The amount of activity we are asking participants to do is considered standard of practice and not strenuous activity that could result in injury. Another possible risk to patients is loss of time and potential breach of confidentiality. Risks include participant burden and resulting fatigue. There is no economic or legal risk in this study. To prevent or minimize any potential risks, patients may stop the interview at any point during this study if they feel any distress.

Discussing pain or psycho-social factors including comorbid depression may result in further psychological distress. There is no economic or legal risk in this study. To prevent or minimize any potential risks, the participant may stop the health coaching, assessments, or interview process at any time.

Since we will be recruiting older Veterans with comorbid depression, we have a plan in place should a Veteran be found to have worsening mental health conditions(s). If the Veteran develops worsening depressive symptoms during this study, the PCP will be notified to make appropriate follow-up or evaluation with Mental Health. In the case of suicidality endorsed over the telephone, as standard measures at the VA, we will provide the VA suicide hotline, warm transfer to mental health specialist, follow up with mental health services, and communication with the PCP. If the Veteran endorses suicidal or homicidal ideation during an in-person interview, the Veteran will be escorted to the Emergency Department for in-person psychiatric evaluation. The PI will be immediately notified of any de-escalation of mental health conditions.

All risks will be discussed in the consent form.

What is the overall risk classification for the research: minimal

Describe procedures that will be utilized to prevent/minimize any potential risks or discomfort? The subject will be told that they can stop participating in this study at any time if he or she becomes uncomfortable with

the questions being asked.

The other potential risk is a breach in confidentiality. All electronic data will be stored within password protected data management programs, on password protected computers. No non-study personnel will have access to study data. All research staff will be trained in the appropriate safeguarding of confidential data and in the protection of human subjects. At the end of the study, after analyses are complete, all study data will be de-identified, and the identifying key will be destroyed per VA policies and regulations.

We anticipate that our procedures to minimize risk of confidentiality will be highly effective. In the unlikely event of loss of patient confidentiality, we will have a procedure in place for responding in timely and appropriate manner. The study participant who experiences loss of confidentiality will be informed by the Principal Investigators (Una Makris, MD) in writing and by phone of the loss of confidentiality. VA clinical leadership, the IRB and participant will be informed in the case of such an event.

16. Data Safety Monitoring

Does this study require a Data Safety Monitoring Plan (DSMP)? NO

Does this study have a Data Safety Monitoring Board (DSMB)? NO

17. Process for Obtaining Informed Consent and Protecting Patient Privacy

This study will be approved by the VA North Texas Health Care System Institutional Review Board (IRB). We will ask the IRB for a Waiver of HIPAA Authorization to identify Veterans who are eligible to be approached with requests to participate in the study. Such a waiver is justified because: minimal risk is anticipated; the waiver will not adversely affect the rights and welfare of subjects; and this aspect of the project cannot be practically conducted without waiver.

The study sample will be identified and enrolled using a multi-step screening process, very similar to successful processes that Drs. Fraenkel and Naik use within the VA system. Through use of a HIPPA waiver, a list of Veterans 65 years old or older, with an ICD –10 code for back pain on the problem list in the last two years, will be generated from the VA corporate data warehouse. Eligible participants will have had at least one visit for cLBP in the last year.

We will obtain HIPAA-waiver for screening purposes and will employ ***three separate recruitment techniques*** that have been effective in earlier stages of this study (see sections 8 and 12).

The **first** method includes: sending out an IRB-approved opt-out letter signed by Dr. Makris (PI) and the primary care clinic director, Dr. Lilly in PRIME, or Dr. Potu, in Ambulatory Care introducing the study and stating that a research team member may call them if they do not opt-out within 5 days. The research coordinator's phone number will be provided for participants to opt-out or gain more information. If the potential participant does not opt-out, the research coordinator will call the Veteran (making up to 6 attempts to reach the Veteran), introduce them to introduce the study, and obtain verbal consent followed by additional screening for eligibility. Following verbal consent and further screening for eligibility, if patient is eligible and interested, we will mail a consent form, HIPPA Authorization form, and VA Form 10-3203, Consent for Use of Picture and/or Voice to patients. These forms will include pre-paid postage for participants to sign and mail back to the VA (research office). The research team will then sign the consent form and enter a research consent and enrollment note into CPRS. This CPRS note will serve as the notification to the PCP that the patient is enrolled in this study.

The **second** method involves: identifying when potentially eligible participants have appointments in a primary care clinic, ambulatory care (including Polk Street CBOC and/or Fort Worth CBOC), rheumatology or PM&R clinic, having the provider introduce the study and research coordinator to the Veteran in person. The research coordinator will then describe the study and obtain consent if subject is interested.

The **third** recruitment strategy involves referral directly from a provider. Dr. Makris will provide a flyer to be posted in PRIME, ambulatory care, Rheumatology or PM&R clinics (see attached to this IRB protocol submission) outlining the eligibility criteria and brief synopsis of the study. If the Veteran is interested in learning more and participating in this study, he or she may call Dr. Makris or the study team at the number provider on the flyer, or, with the HIPAA waiver, the provider may notify Dr. Makris to call the Veteran (as additional cosigner on the clinic note). When/if Dr. Makris or her research team speaks with the Veteran (preferably in person but may be over the telephone if more convenient for the Veteran), we will describe the study, risks and potential benefits and obtain consent, also for audio-recording. The eligibility criteria will be assessed and confirmed over the phone or in person (whichever more convenient for Veteran) via self-report and review of CPRS data.

Following verbal consent and further screening for eligibility, if patient is eligible and interested, we will mail a consent form, HIPPA Authorization form, and VA Form 10-3203, Consent for Use of Picture and/or Voice to patients. These forms will include pre-paid postage for participants to sign and mail back to the VA (research office). The research team will then sign the consent form and enter a research consent and enrollment note into CPRS. This CPRS note will serve as the notification to the PCP that the patient is enrolled in this study. At this time, a binder with the intervention manual material will be sent to the subject's home. This manual is intended for the patient to follow along with the health coach during phone calls. It will also contain the activity trackers that he/she will use in between session to track activity, step counts, and impact on pain and depression. We will mail out appointment letters before each intervention visit. The patients will also be called prior to the scheduled phone calls as a reminder. During Aim 2, we learned that some patients are forgetful about the timing of the phone calls which causes delays- these phone call reminders were helpful.

Prior to audio recording sessions and conducting the telephone based behavioral intervention, study staff will obtain consent and HIPPA authorization from all subjects. All data will only be accessible to authorized study personnel and will be stored on password protected and secure networks.

For the Annie texting pilot, upon IRB approval, existing MOTIVATE patients among the waitlist control group will be contacted. We will discuss the Annie-texting pilot, answer questions and if interested, we will ask for verbal consent (including consent for audio-recording of telephone interviews and de-identified interview material to be analyzed by the UTSW Qualitative Research committee).

All measures will be taken to protect patient privacy and reduce risk of a breach in confidentiality. The data will be de-identified and will be stored in a locked office with a locked file cabinet to ensure patient safety. Any data entered into the computer system will be located in a secure file folder behind the VA firewall and will meet VA security precautions. Only the study personnel will have access to these. For the Annie texting pilot, texting data will be collected and stored on the Annie dashboard. The Annie dashboard is located on a secure server behind a VA firewall. Only researchers will have access to this data. All other qualitative and quantitative data will be de-identified and stored as above. For analysis purposes, the de-identified interview data will be analyzed at UTSW by the Qualitative Research Committee.

18. Documentation of Informed Consent

Please see sections 12 and 17 about recruitment and consenting process. As potential participants indicate their interest in participating in the study during the initial recruitment call, verbal consent will be recorded in the study database. During the verbal consent process, research staff will review the study objectives, what is required of the participant, review eligibility criteria, and answer any questions the participant may have. Once verbal consent has been confirmed, research staff will mail a hard copy of the consent form with a pre-paid postage for the participant to sign and mail back to research staff. Participants will be instructed to not document their social security number on the consent form. Once the signed consent has been received, study staff will sign and date the consent and the participant will be officially enrolled in study. Study staff will enter a note in CPRS if patient consents and enrolls in this study.

As outlined in sections 12 and 17, the second method involves meeting with a potentially eligible participant in person. In this situation, the research staff will describe the study and obtain consent if subject is interested, in person. The third method involves a provider referring a patient directly to the study team via poster flyers.

Once the Veteran is consented and enrolled in the study, the research staff will enter a CPRS note to notify the PCP that the patient is participating in this study.

19. Payment to Subjects for Their Participation

For this study, we will provide incentives to all the Veterans who will be recruited (n=50). Each subject will receive a modest incentive after completion of each data collection assessment. Subjects will be paid $15 after completion of each assessment of baseline and outcome variables (not the intervention sessions). This will include assessment at baseline, mid-intervention ~ 5 weeks, post intervention at ~10 weeks, 6-month assessment and 12-month interview (if selected) for a total of potentially $75 if they complete all assessments of the study. Those in the Annie texting pilot will receive an additional $15.

20. Provisions for Data Storage and Confidentiality

A study database will be built to securely capture study data and activities and will be behind the VA firewall The study data (word documents and VA redcap) will be accessible by VA credentialed research personnel only. All surveys, call logs, recruitment efforts, selected CPRS data, and generated reports will be housed behind the VA firewall. The database will be designed to alert research staff when subjects are due for assessments, allowing for the assessment data to be seamlessly captured in the database. For the Annie texting pilot, texting data will be collected and stored on the Annie dashboard. The Annie dashboard is located on a secure server behind a VA firewall. Other study data, including qualitative/quantitative data will be housed behind a VA firewall, and only accessible to VA credentialed research personnel. The de-identified audio-recordings form the Annie pilot (phase 2) will be securely transferred outside of the VA for transcription and analysis.

Database access will be restricted to authorized study staff only, with full capacity limited to individual roles of study staff. For further details on database security, please see section Database development and management.

Audio-recordings will be transferred to UTSW for transcription and coding. Recordings will be de-

identified, with each recording assigned a unique number that does not correspond to patient identifiable information. It will be transferred via a VA approved encrypted device (Apricorn Aegis Secure Key 3z 256 bit AES XTS Encryption 64 GB USB FIPS Level 3 Validated 140-2).

The most salient risk to patients is the potential for a loss of confidentiality. Confidentiality will be strictly maintained throughout the study. Patient names and addresses will not be known to anyone except for Dr. Makris and research team. Study datasets will be located on a secure, limited-access server in accordance with the VA's data security policy and secure workstations. Audio-recordings will be stored in the VA Makris secure research folder and/or on an encrypted device that will be used to transfer the de-identified data off-site to UTSW for coding and analysis prior to returning to the VA shared folder.

In accordance with HIPAA, only the study team will have access to protected health information (PHI). All paper records, if needed (we anticipate majority of data will be electronic), will be maintained in a locked cabinet in the research team's locked office. Computerized data, once feasible and necessary for analysis portions of this project, will be de-identified and stored on a password protected computer in a locked office of the research team.

21. Provisions for storage/analysis of research specimens

Not applicable.

22. Dissemination of Research Results

Results of the study will be submitted for publication to peer-review medical journals and presented at research conferences. Dr. Makris will lead all efforts for the dissemination of these results.

23. Multi-Center Research

Not applicable.

> *If referring to the VA CDA-2 Research Plan, please focus only on Aim 3. Aims 1 and 2 have already been IRB approved (#16-024 and #16-069).*