A Pragmatic Trial of Brief CBT for Anxiety in VA Primary Care

Funding Agency: Office of Research and Development

Principal Investigator/Study Chair: Terri L. Fletcher, Ph.D., and Jeffrey A. Cully, Ph.D.

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Abstract

Anxiety disorders are common in VA primary care settings and are associated with substantial functional impairment, poor health-related quality of life, suicide, and high rates of comorbid psychiatric and medical disorders. No brief psychotherapy interventions for anxiety currently exist for VA primary care settings - where many Veterans seek care. Cognitive Behavioral Therapy (CBT) is a first line treatment for anxiety but Primary Care Mental Health Integration (PCMHI) providers need an intervention approach for anxiety disorders that is brief, problem-focused, and fits into their system of care.

This 4-year, multisite trial will use a pragmatic randomized trial design to examine the effectiveness and implementation potential of a brief CBT intervention for anxiety delivered either in-person or via VA Video Connect-Home, according to patient preference. CBT will be delivered by existing PCMHI providers at three large VAMCs. Aim 1 will examine the clinical effectiveness of the bCBT intervention vs. EUC for anxiety and quality of life at 4-, 8-, and 12-month follow-ups. Aim 2 will determine factors associated with bCBT response and explore Veteran demographic and clinical factors associated with VVC-H engagement. An exploratory aim will use mixed, qualitative and quantitative methods to better understand implementation successes and challenges related to delivery and impact of bCBT anxiety and VVC-H use in the PCMHI setting.

The project will embed bCBT into PCMHI programs using existing VHA providers. A total of 225 Veterans diagnosed with an anxiety disorder will be recruited from three VAMCs. Eligible Veteran participants will be randomized to a bCBT or to an Enhanced Usual Care (EUC) condition. A professionally diverse set of PCMHI providers will be invited to deliver bCBT. Providers will receive bCBT training and support to embed treatment into their existing practice setting. Veterans randomized to bCBT will receive 4 – 9 sessions based upon treatment response (50% reduction in GAD-7) by session 4. Veterans will also be offered the choice of receiving bCBT in-person or through VVC-H. EUC participants will receive 4 brief monthly check-in calls from study staff and a note placed in their medical record alerting their provider to the presence of significant anxiety symptoms. BCBT treatment and EUC check-in calls will end at 4 months.

The project leverages VA stakeholders at all levels to improve alignment of the work with VA and Veteran initiatives. Clinical outcomes will provide justifications or cautions to inform future evidence-based psychotherapy (EBP) programs. If positive, data will be used to assist VA leadership in the expansion of EBPs and VVC-H in PCMHI. For example, should the project produce robust clinical outcomes - next steps would involve a non-research / demonstration project in one or two VISNs where the project team will train and support a wider group of providers in the delivery of brief CBT for anxiety. The project team will use the training program and clinical intervention materials as well as lessons learned from the proposed HSR&D IIR to support and enhance brief CBT delivery in a non-research context.

List of Abbreviations

Provide a list of all abbreviations used in the protocol and their associated meanings.

ACOS – Associate Chief of Staff
AUDIT-C – Alcohol Use Disorders Identification Test
bCBT – Brief Cognitive Behavioral Therapy
CAPRI – Compensation and Pension Record Interchange
CBT – Cognitive Behavioral Therapy
CCI – Charlson Comorbidity Index
CoE – Center of Excellence
Co I – Co-Investigator
CPRS – Computerized Patient Record System
DSM-5 – Diagnostic and Statistical Manual of Mental Disorders version 5
DSMB – Data Safety Monitoring Board
EBP – Evidence Based Practice
ERS – Expectancy Rating Scale
EUC – Enhanced Usual Care
FE – Formative Evaluation
GAD – Generalized Anxiety Disorder
GAD-7 – General Anxiety Disorder (7-item scale)
HIPAA – Health Insurance Portability and Accountability Act
HSRD – Health Services Research and Development
IE – Independent Evaluator
IIR – Investigator Initiated Research
IQuESt – Center for Innovations in Quality, Effectiveness, and Safety
IRB – Institutional Review Board
LSI – Local Site Investigator
MBC – Measurement Based Care
MCID – Minimally clinically important differences
MCS – Mental Composite Score
MEDVAMC – Michael E. DeBakey Veterans Affairs Medical Center
MINI – Mini-International Neuropsychiatric Interview
OASIS – Overall Anxiety Severity and Impairment Scale
ORD – Office of Research and Development
PCL-5 – PTSD Checklist Civilian Version 5
PCMHI – Primary Care Mental Health Integration
PCP – Primary care physician
PCS – Physical Composite Score
PHI – Protected Health Information
PI – Principal Investigator
PTSD – Post Traumatic Stress Disorder
RA – Research Assistant
R&D – Research and Development
RDC – R&D Committee
RE-AIM QuEST – Reach Effectiveness Adoption Implementation Maintenance Qualitative Evaluation for Systematic Translation
SAE – Serious Adverse Events
SAS – Statistical Analysis System
SC – Site Coordinator
SF-12 – Short Form Health Survey Veteran Version

UAP – Unanticipated serious problems
U-SAE – Unanticipated serious adverse events
VA – Veterans Affairs
VAMC – Veterans Affairs Medical Center
VHA – Veterans Health Administration
VINCI – VA Informatics and Computing Infrastructure
VISN – Veterans Integrated Service Network
VVC-H – VA Video Connect - Home

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1.0 Study Personnel

- Provide name, contact information, facility/organization, and affiliations/employee status for the following:
    - **Principal Investigators/Study Chairs**

Terri L. Fletcher, PhD
Clinical Psychologist
MEDVAMC 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-440-4490
Terri.Fletcher@va.gov

Jeffrey A. Cully, PhD
Clinical Psychologist
MEDVAMC 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-794-8526
Jeffrey.Cully@va.gov

- **Co-Investigators:**

Natalie Hundt, PhD
Clinical Psychologist
MEDVAMC, 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-440-4450
Natalie.Hundt@va.gov

Patricia Chen, PhD.
Research Health Scientist Specialist
MEDVAMC, 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-794-8696
Patricic@bcm.edu

Shubhada Sansgiry, PhD.
Research Health Science Specialist
Methodologist/Biostatistician
MEDVAMC, 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-440-4455
Shubhada.Sansgiry@va.gov

Darius B. Dawson, PhD.
Clinical Psychologist
MEDVAMC, 580
VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Houston
713-791-1414 ext. 10254
Darius.Dawson@va.gov

Veronica McClean, PhD.
PCMHI Director
San Antonio VA Hospital
210-617-5300 ext. 14169
Veronica.McClean@va.gov

Karen Slaton, PhD
PCMHI Director
New Orleans VA Hospital
504-507-2000 x66510
Karen.Slaton@va.gov

- **Collaborators:**

Susan L. Zickmund, PhD.
Research Scientist
Salt Lake City Healthcare System
801-582-1565 x5114
Susan.Zickmund@va.gov

- Indicate the number of potential participating sites (both VA and non-VA) and if there is any graduated start-up plan for the sites

There is a total of 3 participating sites: the Houston, New Orleans, and San Antonio VA Hospitals. Training and recruitment of clinicians and veterans will begin in Houston. Recruitment in New Orleans and San Antonio will take place simultaneously; approximately 3 months after Houston recruitment starts. During the 3-month lag, training and recruitment strategies will be re-evaluated and adapted for efficiency.

2.0 Introduction

- Provide scientific background and rationale for study.
- Include summary of gaps in current knowledge, relevant data, and how the study will add to existing knowledge.

Anxiety disorders are common in VHA primary care and PCMHI settings, but standardized, evidence-based treatment practices for use in these settings are lacking. In FY2017, 657,194 Veterans enrolled in the VHA were diagnosed with an anxiety disorder. Anxiety disorders are associated with substantial functional impairment, poor

health-related quality of life, suicide, and high rates of comorbid psychiatric and medical disorders. Patients with anxiety symptoms are most likely to present in primary care settings, yet rates of treatment are low. In contrast to the advances in treatment of depression and PTSD in VHA, far less attention has been paid to anxiety disorders, despite their high prevalence and associated impairment. For instance, the VHA developed specific practice guidelines for depressive disorders and posttraumatic stress disorder (PTSD), but such guidelines are not available for anxiety disorders. At the same time, the VHA Uniform Mental Health Services handbook requires that Veterans with anxiety disorders have access to EBPs, yet no EBPs for anxiety disorders appropriate for the PCMHI setting have been disseminated. PCMHI providers, who must deliver brief treatments, are left to adapt high intensity EBPs, potentially decreasing the potency of efficacious treatments.

Cognitive behavioral therapy (CBT) is an EBP for all types of anxiety disorders including generalized anxiety disorder (GAD), panic disorder, and social anxiety disorder. However, CBT must be tailored to fit the PCMHI setting, as traditional CBT anxiety interventions were developed for specialty mental health settings, often target specific anxiety diagnoses, and typically require 12-16 sessions of therapy. This intensive model of care is incongruent with the brief intervention approach required for VHA's PCMHI model. Further complicating delivery of CBT for anxiety disorders in PCMHI, repeated exposure to feared cues is considered a critical component of CBT for anxiety but is rarely used in PCMHI and primary care settings[1]. In the absence of EBPs for anxiety tailored to the PCMHI setting, data suggest that most psychotherapy being delivered in PCMHI settings is supportive in nature and not evidence-based care.[2]

Our proposed bCBT treatment for anxiety was specifically designed for use within VA PCMHI settings and uses a patient-centered approach to increase engagement while addressing the mental health needs of anxious Veterans. Emphasis was placed on maximizing intervention potency and minimizing intensity and duration to improve implementation value and alignment with VA PCMHI requirements. The intervention directly addresses challenges to delivery of CBT providing 1) a brief, practical model of care to address multiple anxiety conditions consistent with the PCMHI model (e.g. 4-6 sessions; measurement-based care), and 2) a clinically potent intervention that includes exposure-based skills.

The project also seeks to better understand how Veterans and providers can use VVC-H to improve access to and engagement with EBPs. Video-delivered psychotherapy is as effective as in-person delivery with comparable rates of patient satisfaction[3]. Furthermore, VVC-H delivery has the potential to increase access to care for Veterans facing barriers to in-person care and may improve the efficiency of care in VHA as PCMHI resources are accessed virtually, freeing up costly space at the hospital and freeing hospital support staff to focus on other tasks. Consistent with VHA priorities to modernize the healthcare system and increase access to care, Veterans should be

offered the choice of receiving PCMHI services via telehealth or in-person whenever possible. Although VHA is pioneering implementation of VVC-H technology in specialty mental health clinics, its use in PCMHI settings is rare, and fewer than 1% of Veterans have received mental health care via VVC-H. The current proposal seeks to better understand provider and Veteran attitudes and experiences with VVC-H services to inform future efforts to expand utilization of VVC-H throughout VHA.

The proposed research directly responds to the VHA and HSR&D priority areas of access to care and telehealth and uses a pragmatic trial design and implementation science to support ORD's priority goals of increasing Veterans' access to high quality clinical trials and increasing the real-world impact of research.

3.0 Objectives

- Describe the study's purpose, specific aims, or objectives.
- State the hypotheses to be tested.
- Indicate the relevance to Veterans and the VA

The primary hypothesis is that anxiety outcomes, as measured by the GAD-7, and quality of life, measured by the SF-12 will be superior at 4-, 8-, and 12-month follow up for patients who are assigned to receive bCBT vs. EUC.

Primary Aim: To determine whether anxiety symptoms (GAD-7) and quality of life (SF-12) differ as a function of the intervention (bCBT for anxiety vs. EUC) at 4-, 8-, and 12-month follow-ups.

Secondary Aims: (Prediction of bCBT response and VVC-H use (bCBT group only)): A) To identify factors associated with bCBT response, namely whether bCBT is effective for specific anxiety disorders (e.g. generalized anxiety, panic, social phobia) and whether number of sessions received, and treatment engagement are critical to outcomes. B) To identify Veteran demographic and clinical factors associated with VVC-H use.

Exploratory Aims: A mixed-methods formative evaluation, informed by RE-AIM QuEST, will collect data related to Reach (#of Veterans receiving bCBT and VVC-H), Effectiveness (bCBT and VVC-H impact), Adoption (# of providers using bCBT and VVC-H), and Implementation (provider bCBT program fidelity and VVC-H potential). Data will be collected from qualitative interviews with Veterans and providers and integrated with quantitative data from provider surveys and chart reviews of bCBT and VVC-H use. With the ORD supplement to the main project, Dr. Dawson will leverage the diverse Veteran populations included in the multisite

parent study (Houston, San Antonio, and New Orleans VA MCs) to understand barriers to treatment and research access for African American and Hispanic Veterans.

The relevance of the research to Veterans is that it will help improve access to mental health services for anxiety problems. The integration of mental health services into primary care has increased access to treatment, but Veterans recently diagnosed with anxiety disorders are still less likely to receive any or as much treatment as other Veterans diagnosed with problems like depression or PTSD. Therefore, effective and time-limited interventions suitable for primary care are needed for this population. In addition, delivering mental health services in a way that matches Veteran preferences and reduces barriers to receiving treatment will further reduce this service gap. The knowledge this project is likely to generate will directly address VHA strategic goals related to improved access to high quality mental health care and increased availability and use of telehealth services (e.g. VA Video Connect-Home; VVC-H).

4.0 Resources and Personnel

- Include a list of personnel, their location, role in the study and their VA affiliation status
- Provide a brief description of each individual's role in the study. Be sure to indicate who will have access to protected health information and who will be involved in recruiting subjects; obtaining informed consent; administering survey/interview procedures; and performing data analysis.
- If applicable provide information on any services that will be performed by contractors including what is being contracted out and with whom.
- If applicable provide information on any Memoranda of Understandings (MOUs), Data Use Agreements (DUAs), and/or CRADAs that are being entered into including with whom and for what reason.

HOUSTON, TX

Terri L. Fletcher, PhD (Principal Investigator): will have responsibility for the overall bCBT training program and lead the bCBT training team including Co-I Hundt. She will lead qualitative efforts and work closely with Dr. Chen. Dr. Fletcher is a clinical psychologist and health services researcher (with a research appointment with the Houston HSR&D Center of Innovation). Dr. Fletcher will also help in recruitment of clinician participants for the project. As part of her role, she will have access to protected health information and be involved with data analysis.

Jeffrey A. Cully, PhD (Multiple Principal Investigator): will have overall responsibility for clinical and scientific aspects of the project. In this role, he will recruit clinician participants, train and supervise research personnel, conduct project meetings, and be responsible for the scientific progress of the research including manuscripts and reporting of study results. Dr. Cully will have access to participants protected health information and work with Dr. Sansgiry on data analysis for the study.

Natalie Hundt, PhD (Co-Investigator): will serve as Co-I and will work directly with Dr. Fletcher as a bCBT trainer. Dr. Hundt will be the primary reviewer of audio recordings to determine fidelity of clinicians. She will attend monthly investigator meetings and will work directly with Dr. Fletcher through weekly training and implementation meetings. In Dr. Hundt's role she will have access participants protected health information and be involved in parts of the data analysis.

Patricia Chen, PhD (Co-Investigator): will work closely with the Dr. Fletcher to implement the project's comprehensive formative evaluation. Dr. Chen works on Dr. Fletcher's ongoing HSR&D IIR and is helping to develop the formative evaluation procedures for study. Dr. Chen will attend the monthly investigator meetings as well as weekly with Dr. Fletcher to discuss formative evaluation procedures and collection of data across the sites. Dr. Chen will work with Dr. Fletcher on the qualitative analysis.

Darius B. Dawson, PhD (Co-Investigator): will work closely with Principal Investigators to carry out the aims of the ORD Diversity Supplement Award. He will attend the monthly investigator meetings as well as meet weekly with Dr. Fletcher and/or Dr. Cully. He will be actively involved in writing manuscripts and reporting of the study results for both the main project and for his diversity, equity, and inclusion supplement to the project. Dr. Dawson's role will require access to protected health information. In addition, he will be involved in parts of the data analysis.

Shubhada Sansgiry, PhD (Methodologist/Biostatistician): will serve as the statistical methodologist and data analyst on the project. She will be actively involved in the planning of statistical analyses and will assist in writing manuscripts. She will also develop the programming for data entry and ensure the accuracy and consistency of data collection. Dr. Sansgiry will attend monthly investigator meetings throughout the project with weekly meetings during year 4 to make rapid progress related to the final study outcomes. Dr. Sansgiry role will require access to protected health information.

Project Coordinator: will assume day-to-day responsibility for project management, including Veteran and clinician recruitment, coordination of all study assessments, coordination of data collection via chart review, entry, and verification. In this role, the coordinator will have access to protected health information and be required to provide informed consent to participants. He/she will attend all project meetings and assist in preparing scientific reports. He/she will also meet weekly with Drs. Cully and Fletcher to

address all project related matters with a specific focus on project administration, project progress, and reporting requirements.

Research Assistant: will assist Dr. Fletcher with coordination of clinician training, as well as coordinate the site and clinician needs assessments. The research assistant will also assist in patient recruitment, which includes consenting for the study and completing surveys with participants. In this role, he/she will have access to protected health information.

Independent Evaluator: will be trained and supervised to conduct all blinded patient outcome assessments for the study. As part of his/her role, the independent evaluator will also recruit and consent Veteran participants for the study. He/she will have access to participants protected health information.

New Orleans, LA

Karen Slaton, PhD (Local Site PI): Dr. Slaton is Director of the PCMHI at the New Orleans VA Hospital. Dr. Slaton will assume site PI responsibilities including regulatory oversight at the site level. All Veteran recruitment will take place by study staff at the Houston VA; but Dr. Slaton will assist with provider recruitment for the study. For this reason, she will have access to participants protected health information. Dr. Slaton is a VA paid clinician and no salary support is requested.

San Antonio, TX

Veronica McClean, PhD (Local Site PI): Dr. McClean serves as the PCMHI Director for the San Antonio VA Hospital. Dr. McClean will serve as the site PI and will be responsible for regulatory oversight of the study at San Antonio. She will also aid in provider recruitment for the site. Dr. McClean's assistance with recruitment will require her to need access to participant protected health information.

5.0 Study Procedures

5.1 Study Design

- Describe experimental design of the study. Include sequential and/or parallel phases of the study, including durations, and delineate which interventions are standard of care and which are research.
- Include a description of how anticipated risk will be minimized and include an analysis of risk vs. potential benefit.

- Provide description of the study population (delineate all categories of subjects – patients, providers, family members, employees, etc.). Include anticipated enrollment numbers
- Include rationale for including or excluding certain populations – in particular vulnerable populations.
- As applicable, provide information on any added protections for vulnerable populations.
- If applicable include information on data and/or specimen banking to include where the bank is located, who will own the data and/or specimens, and who is overseeing the repository.

The proposed 4-year, multisite, randomized pragmatic trial will assess the real-world application of bCBT for Veterans with anxiety, as delivered by frontline VA PCMHI providers at three facilities (Houston, San Antonio, and New Orleans). Veteran participants will be randomized to bCBT or to Enhanced Usual Care (EUC). EUC participants will receive anxiety education materials, a note in their medical record indicating the presence of elevated anxiety symptoms, and 4 brief monthly check-in calls with project staff. Participants randomized to bCBT will have the option to receive bCBT for anxiety delivered either in person, via VVC-H, or both. The primary outcome, anxiety symptoms, will be evaluated at 4-, 8- and 12-month follow-ups.

Evaluation Framework: For this proposal, we chose a randomized pragmatic effectiveness trial to better align the intervention with standard VA clinical practices. To assess feasibility, acceptability, and preliminary implementation outcomes, we chose the mixed methods RE-AIM Qualitative Evaluation for Systematic Translation (RE-AIM QuEST) framework[4] that expands on the original RE-AIM framework by highlighting complementary quantitative and qualitative outcomes for each of RE-AIM's 5 elements: Reach (participation rate of the targeted population), Efficacy/Effectiveness (impact of the intervention on outcomes), Adoption (system-level factors associated with intervention use), Implementation (intervention integrity and quality), and Maintenance (continuance of the intervention). Although this study focuses on effectiveness, we will also collect data from Veterans, providers, and VA clinic and operational leaders about the potential for the intervention to be implemented within VA settings.

All randomized participants will receive a note added to their medical charts. The note will provide information about the patient's anxiety symptoms and any actions being taken by the research team. Notes will provide information about the assessment process and will also indicate that the patient should continue to receive care as usual regardless of their study group assignment.

ARM #1: Brief CBT (bCBT):

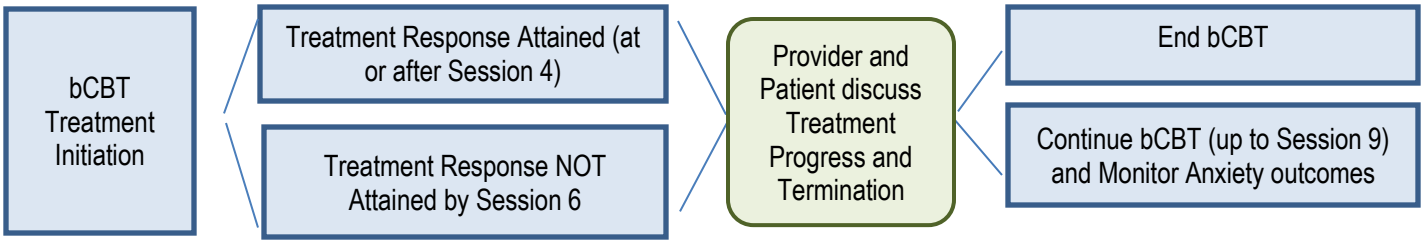
Participants randomized to the bCBT direct referral arm will have their contact information and symptom information obtained from the assessment (e.g. responses from the GAD-7, etc.),

forwarded via encrypted email to a study-consented provider. Provider and clinic personnel will schedule the patient for an initial treatment session. Participants and clinicians will work collaboratively to determine the modality of treatment (i.e., traditional in-person visits, VVC-H, or a mixture). Clinicians will be encouraged to offer 4 weekly treatment sessions but may alter the intensity or "dose" of treatment, based on Veteran anxiety response scores and/or provider/patient decision to discontinue treatment. For completers, the final treatment "dose" may include between 4 and 9 sessions over a course of up to 4 months. Clinicians will be asked to complete the GAD-7 during treatment sessions to assess treatment response (regular GAD-7 administration is consistent with bCBT and measurement-based care). Data on treatment sessions will be documented using template CPRS clinician notes to facilitate clinician documentation, allowing the study team to monitor and extract important treatment information during and after the trial.

Treatment completion will be defined as 4 or more sessions over the 4-month treatment period. A 50% reduction in baseline GAD-7 scores will indicate treatment response[5,6]. Providers and patients will collaboratively determine whether additional bCBT skill sessions are needed based on treatment response. A 50% reduction in anxiety symptoms was chosen, based on prior work and evidence from other studies[7,8,9]. This response criterion also appropriately classifies responders with variable baseline anxiety levels.

During active treatment, clinicians will be asked to discuss anxiety symptoms and response with participants as part of the treatment process. Providers will be encouraged to deliver bCBT as long as it remains appropriate for any given patient. If a patient is discovered to have additional needs that make the use of bCBT inappropriate, the clinician can opt to seek additional or alternative care for the patient. The presence of severe depression, substance abuse, and comorbid PTSD could all require the clinician to change or add treatments. At the end of the 4-month treatment period, clinicians will be encouraged but not required to discontinue treatment. For patients who reach the response criterion, clinicians will introduce the potential for treatment discontinuation. For patients who do not reach the targeted anxiety goal by the final session (4th session), clinicians will work with the patient to determine whether additional sessions would be helpful. The provider will have the option to continue care or refer the patient to other therapies that are not a part of the research study based on their clinical judgment.

Figure 1. Response to bCBT and Determination of Treatment Ending



The proposed bCBT intervention (See Appendix 5G) uses a patient-centered approach to increase engagement while addressing the mental health needs of anxious Veterans. A bCBT provider manual and a patient workbook provide structure and increase Veteran participation. The patient workbook will be made available both in hard copy and in an electronic version. The workbook includes intervention session information and worksheets, along with homework assignments to engage Veterans during VVC-H sessions and facilitate between-session activities. The bCBT intervention skill modules use CBT-based techniques established in our prior trials[10, 11] and flexibly apply these skills to improve anxiety symptoms and overall quality of life (see Table 1). All participants take part in an initial session where they receive psychoeducation on anxiety and the bCBT treatment approach, set goals, and begin self-monitoring. Three core skill sessions focused on relaxation, cognitive, and exposure techniques follow. Participants who do not show treatment response at session 4 will be offered up to 4 additional cognitive and/or exposure skill sessions. All participants receive a final wrap-up session to review gains and plan for maintenance of skills.

Table 1. bCBT Intervention Overview

Session Type	Modules	Content / Description
Session 1	Adapt and Overcome Treatment Overview	Assessment of Veteran concerns, anxiety, worry, and stress; psychoeducation about core symptoms of anxiety; treatment module overview; setting initial goals; self-monitoring
Session 2	Relaxation Skill	Learning How to Relax: Controlling emotional/physical sensations using deep breathing
Session 3	Cognitive Skill	Increasing Helpful Thoughts: Understanding how thoughts affect anxiety; practicing adaptive statements or calming thoughts
Session 4	Exposure Skill	Facing Your Struggles 101: Psychoeducation - avoidance in anxiety; understanding how exposure exercises reduce anxiety; building an exposure hierarchy;
Optional Sessions	Advanced Cognitive Skill	Managing Unhelpful Thoughts: Monitoring and modifying unhelpful thoughts
	Exposure Practice	Facing Your Struggles - Practice: Graduated in-session exposure may include in vivo exposure (for specific fears/worries), interoceptive exposure (for fear of bodily sensations), and/or imaginal exposure (for worry/fears about future outcomes)
Final Session	Wrap-up Session	Review of progress/skills; maintaining changes; addressing barriers

ARM #2: Enhanced Usual Care:

Following randomization, EUC participants will receive educational materials about managing anxiety (see Appendix 9A). These material will be made available to the participant both by mail

and through a weblink. They will also receive a letter encouraging them to discuss treatment options with their VA care providers (see Appendix 9). We will place a note in the participant's electronic medical record notifying his/her PCP and most recent PCMHI provider (if applicable) of the presence of anxiety symptoms. Additionally, EUC participants will receive 4 brief monthly check-in calls from study staff to review the resource list and assess current anxiety symptoms and serve as an attention control (see Appendix 9B for resource list, and Appendix 5H for EUC manual). EUC participants will receive the same study reimbursement as bCBT participants and will be asked to complete the same assessments at 4-, 8-, and 12-month follow-ups. Due to ethical concerns of withholding needed treatment, EUC participants will NOT be restricted from receiving mental health services including psychotherapy during the study period. We fully expect that EUC participants may receive anxiety treatments (e.g., antianxiety and antidepressant medications or psychotherapy).

bCBT Providers:

PCMHI providers who conduct psychotherapy as part of their VA scope of practice will be targeted for recruitment. Providers will not be restricted based on profession. PCMHI clinic directors at all three sites have agreed to support the project and will be the primary points of contact for provider recruitment. PCMHI directors will identify a local champion to further enhance recruitment and communication between the clinical site and study team. Based on the staffing at these sites and rates of provider participation in our prior trials, we expect to enroll 25 providers across the sites.[10] Providers from our recently completed trial included social workers, psychologists, physician assistants, as well as psychology and social work interns and postdoctoral fellows.

bCBT Training:

A tailored training program (See Appendix 5I) will be assigned to each provider based on an initial needs assessment (See Appendix 4A). Tailored training improves relevance, meaning, and motivation while reducing inefficiencies[12]. Working with a bCBT trainer (Fletcher or Hundt), each provider will be assigned tailored training elements to complete. All providers will be required to complete the exposure training module. Although the full training program takes 8 hours to complete, providers with prior CBT training and experience will need far less time to complete their program. Most providers in our earlier studies required 3-4 hours to complete training. Providers will be eligible to receive bCBT referrals from the study after completing the training.

Intervention Fidelity:

With the patient's written permission, bCBT sessions will be audio-recorded. Consent for audio recording is not required for participation. Recordings will be uploaded to and maintained on a VA shared drive. These audio-recorded sessions are to be used for training purposes only and will not be placed in the Veteran's medical record. BCBT trainers will assess providers'

adherence and competence using a previously developed standardized rating measure[13]. Rating scores range from 0-8, where 6 is considered "good"[11,13]. All sessions for each provider's first bCBT patient will be reviewed by a bCBT trainer who will provide feedback to the provider after sessions 2 and 5 (or at the end of treatment). Following review of a provider's first patient, bCBT trainers will review the provider's next 2 exposure sessions as well as 2 randomly selected sessions and will provide feedback to providers on these sessions 2 more times during the first 6 months. If a provider receives a rating of 5 or less on any session, the bCBT provider will review an additional session covering the same skill and provide feedback on this "developmental area". Regardless of ratings, providers will not be removed from the trial, but will receive feedback to address needs. This approach closely resembles that followed in current VA training initiatives.

Minimization of Risk

Veteran Participants:

To maximize confidentiality, participants will receive a unique study number that is attached to study related data. Data will be kept in locked file cabinet housed in a data storage room that has a security keypad as entry. All electronic data files will be maintained within the VA setting and behind the VA firewall. In addition, all electronic data files will be password protected for additional security.

In the event of a participant who reports suicidal ideation during the assessment or treatment process, a specific protocol will be used to triage the participant to the appropriate source of VA care. As part of all baseline and follow-up assessments, study staff will closely monitor and explore all indications of suicidal thinking. The PHQ-9 item #9 asks for responses about thoughts of being "better off dead or hurting yourself in some way". Study staff will follow up on any positive response to this item using a structured crisis assessment protocol (see Appendix 5, Suicidal Ideation Assessment.) The structured assessment will distinguish between passive vs. active suicidal thinking, identify any intent or plans for self-harm, and inquire into family, health care, or community supports (see Appendix 5 for detailed listing of the structured assessment). Participants who express suicidal ideation will be discussed with a study investigator (licensed VA provider) who will triage and refer for care as appropriate. If it is an emergent situation the research assistant will page an on-call licensed practitioner (study PI or co-investigator). The PIs, and other study staff (Dr. Hundt) are licensed mental health practitioners and will serve as the on-call staff.

Provider Participants:

Prior to any provider recruitment efforts, union representatives at the national level will be notified of the study proposal. Potential therapists will be referred by their clinic director and/or VISN mental health leadership and subsequently screened for appropriateness by the study investigators. The study team will be careful to ensure that VISN leadership or clinic directors do

not require clinicians to engage in this work. Any clinician who does not wish to participate will be excluded. Clinician participants final decision to participate or not will not be made known to their supervisor or VISN leadership. Clinicians who wish to participate (receive the training and provide care) will be enrolled. Therapist information related to performance and feedback will be coded within the study so that no therapist specific information will be identifiable outside of the study itself.

No participants provider nor veteran will be identified in any reports that may be published. Study participants are not required to take any study medication or undergo any invasive procedures; therefore, we do not foresee any study-related adverse events.

Potential Benefits

Veteran Participants:

Participants randomized to the treatment arm will be provided with bCBT while participants randomized to the enhanced usual care arm will receive educational products designed to increase their ability to manage their emotional health issues. Additionally, EUC participants will be encouraged to seek services for their anxiety symptoms. Participants may feel less anxiety, worry, and associated symptoms and may experience an improved ability to perform normal activities of daily life.

Provider Participants:

All clinicians will receive expert bCBT training and ongoing consultation to learn how to apply bCBT in their daily practice.

Analysis of Risk vs. Potential Benefit

The risk-benefit ratio of the study suggests that the proposal is reasonable given the potential direct benefits to participants via the intervention and education provided as well as the potential for this research to benefit other Veterans and the larger research and clinical community by providing detailed information on the use of brief cognitive-behavioral therapy for Veterans.

The potential benefits of the study are numerous, with many involving the provision of care to participants but also including information related to how the VA can improve its ability to train and implement psychotherapies in the primary care setting. Data to be obtained from this study will provide important information on the use of brief cognitive-behavioral therapy for Veterans with anxiety as provided by frontline VA practitioners. Should the intervention prove effective, the study team will target clinical and research initiatives designed to further increase the implementation of these procedures within VA. Risks of the study are minimal and many research participants will be provided with care that may not be available within existing care settings.

Description of study population

Age range of participants:

Young adults (18-21)
Adults (22-65)
Seniors (Over 65)

Veteran Participants:

Veterans with clinically significant symptoms of anxiety defined as GAD-7 total scores of 10 or more at two screening occasions to ensure consistency of anxiety symptoms. The GAD-7 is the current anxiety measure used by VA PCMHI clinics and is appropriate for monitoring change in anxiety symptoms over time[5]. Veterans will be excluded only for factors that would render bCBT inappropriate for the PCMHI setting: 1) cognitive impairment, 2) presence of bipolar, psychotic or substance use disorders. Veterans currently receiving psychotherapy for anxiety at the time of enrollment WILL be excluded so as not to duplicate services. Veterans receiving antidepressant medications or psychotherapy for conditions other than anxiety at the time of enrollment WILL NOT be excluded.

Provider Participants:

PCMHI providers who conduct psychotherapy as part of their VA scope of practice will be targeted for recruitment. Providers will not be restricted based on profession and may include psychologists, social workers, counselors, physician assistants, as well as psychology and social work interns and postdoctoral fellows.

Added protections for vulnerable populations:

No vulnerable populations will be targeted for enrollment, except for VA employees who provide mental health treatment to Veterans. No added protections are planned outside those described above.

5.2 Recruitment Methods

- State how many subjects will be needed.
- Describe when, where, how and by whom potential subjects will be identified and recruited.

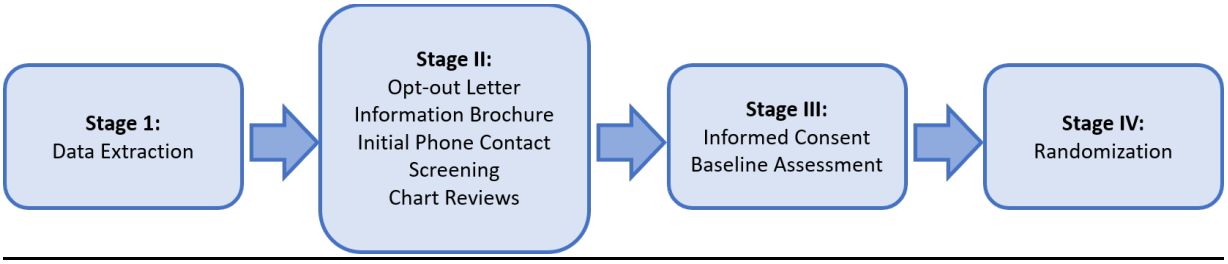
- Describe materials that will be used to recruit subjects, e.g., advertisements. Include materials as an appendix or separate attachment.
- Describe any payments to subjects, including the amount, timing (at the end of the study or pro-rated for partial study participation), method (e.g., cash, check, gift card), and whether subjects will experience a delay in receiving the payment.

Veteran Participant Recruitment:

All Veteran participants will be current recipients of services at the Houston, New Orleans, or San Antonio VAMCs. Veterans with clinically significant symptoms of anxiety will be included after screening on two occasions to ensure consistency of anxiety symptoms (GAD-7 score of 10 or greater; telephone screen and baseline appointment). Participants will be excluded only for factors that would render bCBT inappropriate for the PCMHI setting, including: 1) cognitive impairment, 2) presence of bipolar, psychotic or substance-abuse disorders, 3) Veterans currently receiving psychotherapy for anxiety at the time of enrollment WILL be excluded so as not to duplicate services. For participants who have received a psychotherapy appointment within the last 3 months, we will confirm the treatment provided will not conflict with the study's intervention. The study team will also review information with participating clinicians to confirm they feel the treatments would not conflict with each other. Veterans receiving antidepressant medications at the time of enrollment WILL NOT be excluded.

Based upon sample-size calculations (including attrition over time), the total sample to be randomized is 225. Participants are not randomized until after confirmation of anxiety after the baseline. Because final determination of study inclusion cannot be determined until the baseline appointment, we anticipate needing to provide consent to approximately 425 Veterans total. Approaching Veterans who are not necessarily treatment seeking is a critical component of the project and allows for increased reach to Veterans who might otherwise go unrecognized by the healthcare system. The recruitment procedures comprise four stages designed to maximize reach while minimizing participant burden and confusion about study procedures.

Figure 2. Veteran Recruitment Flow Chart



Stage I:
The first stage will consist of a data extraction from national VA databases to identify the pool of potential study participants. This data extraction will target patients who received care at the Houston, New Orleans and San Antonio VA hospitals. Facility categorization will be based on the location of the patient's current primary care provider. Initial database extraction will request information on Veterans who receive care at one of the three sites, who are diagnosed with an anxiety disorder, do not have a documented diagnosis of cognitive impairment, and who are eligible for PCMHI services.

Stage II:

Recruitment by opt-out letter
In stage two, study personnel at the Houston VAMC will mail potential participants an opt-out letter and a study brochure to their home address as listed in CAPRI. The letter will state that study staff will call within two weeks unless the patient requests not to be contacted. The patient may make a no-contact request via a telephone number listed in the letter. The RA will follow a script for the initial telephone contact (see Appendix 5B, screening telephone script), and will acquire additional contact information in case the call should get disconnected (e.g. participant hangs up, phone dies, etc.) or the participant has a crisis during the call. Participants will be asked questions to screen for anxiety (see Appendix 8A, GAD-7) during the initial phone contact. A chart review will then be conducted for Veterans to confirm the patient is not currently receiving any other psychotherapy treatment for anxiety. For participants who have received a psychotherapy appointment within the last 3 months, we will confirm the treatment provided will not conflict with the study's intervention. Chart reviews will be conducted by staff in Houston. Staff in Houston will utilize the Compensation and Pension Record Interchange (CAPRI) and Joint Legacy Viewer (JLV) to review the charts of New Orleans and San Antonio participants.

Recruitment by Provider referral
Local Site Investigators will contact mental health providers at their respective facilities and CBOCs to explain the study and provide study brochures (see Appendix 5A, Informational Brochure) with study information that can be given to potential participants. Providers will have the option to discuss study participation with Veterans with anxiety in their clinics. If a patient is interested in being contacted for the study, the provider will either: 1) have the patient complete Form 10-5345 -- *Request for and Authorization to Release Health Information*, or 2) refer the patient to the study team via cosigned progress notes or VA encrypted email. The study team will either call the Veteran directly (see ORD approval for proactive calling) or the Veteran may be mailed an opt-out letter. Potential study participants will be contacted by a main site RA (See Appendix 5B, Script for Screening Phone Contact) to provide more information about the study, determine interest in participation, and confirm eligibility. If eligibility criteria appear to be met during the screening call, study staff will complete chart review utilizing VA CAPRI/JLV to verify that initial inclusion/exclusion criteria has been met.

Stage III:
Eligible participants (those who screen positive for anxiety on the GAD-7) will be sent a consent form and HIPPA medical records release form for review and signatures either by mail or VA-approved encrypted email (e.g.: Azure RMS, MyHealtheVet, DocuSign) according to participant preference. The potential participant will be called within two weeks to discuss the informed consent documents (Appendix 5D, Veteran ICF and Appendix 5L, HIPAA) and to have any questions answered. A full baseline assessment will be scheduled within two weeks of receiving the signed informed consent form and HIPPA form. (Note: No baseline will be completed until the signed study consent and HIPPA form have been returned.) The independent evaluator or RA assigned to complete the baseline will administer assessments to confirm the presence of anxiety (Appendix 8A, GAD-7) and non-presence of cognitive impairment (see Appendix 6A, Cognitive Screen), of bipolar and psychotic disorders and substance use (Appendix 6B, MINI), and of alcohol use (Appendix 6C, AUDIT-C). The independent evaluator or RA will also administer the Diversity Supplement assessments (Appendix 6E, Diversity Supplement) to evaluate whether sociocultural factors are associated with the severity and type of anxiety symptoms among Veterans of different race/ethnicity groups.

Stage IV:
Participants still eligible following the baseline assessment will be randomized to the direct referral or EUC groups.

Provider Participants:

Provider participants will be recruited from the Houston, San Antonio, and New Orleans sites. PCMHI clinic leads have endorsed the project and national union representatives will be informed of the study prior to initiation of the project. PCMHI staffing levels at the three facilities are robust - Houston has 12 psychologists and 4 social workers; San Antonio has 15 psychologists, 7 social workers, and 2 master's level counselors. New Orleans has 2 psychologists, and 2 social workers and is in the process of expanding their PCMHI program. In addition, PCMHI social work and psychology interns and fellows are eligible to participate. Target recruitment of 32 providers is conservative given staffing levels, new mental health hiring initiatives, trainee participation, and staff turnover.

All Providers will be asked to complete interviews post-implementation. These exit interviews with providers will assess perceived bCBT effectiveness and explore factors that impeded or facilitated bCBT use and delivery via VVC-H, including provider-initiated modifications and workarounds, and maintenance potential. The interviews will last approximately 30-45 minutes and will be conducted by Co-I Chen. Providers will not be compensated for the interviews.

5.3 Informed Consent Procedures

- Indicate if informed consent will be obtained and/or if you are requesting a waiver of informed consent or waiver of documentation of informed consent. If the research involves multiple phases, specify for which phases of the research the waiver(s) is being requested and/or the informed consent will be sought.

- Describe who will be obtaining informed consent, if applicable, and any circumstances that may need to be addressed (e.g. subjects with impaired decision-making ability and the use of a legally authorized representative, etc.)

- If applicable, indicate how local site study personnel will be trained regarding human subjects protections requirements and how to obtain and document informed consent.

Veteran Participants:

This intervention has a specific focus on increasing Veterans' access to mental health services via strategies such as VVC-H and telephone-based assessments. Determining the effectiveness of these strategies requires a sample of Veterans that represents the Veteran community at-large and does not include only highly selected, motivated, or resourceful individuals. The proposed recruitment strategies represent the study team's attempt to reduce the research burden on our Veteran participants and to reach a wider audience of Veterans, many of whom do not get the care they need.

The informed consent process for all sites will be completed by the Houston research staff. This study does not involve subjects with impaired decision-making ability.

All potential participants will be mailed a study introductory letter informing of the opportunity to participate (see Appendix 5F, Patient Recruitment Letter). They will be provided with a number they can use to verify the project is VA research. Potential participants will be able to opt-out by using the provided telephone number.

Anyone who does not opt-out within two weeks from the date of the mailing will be called and provided with an explanation of the study. This initial phone contact will begin with reference to the recruitment letter and will explain the purpose of the research. Potential participants will be given an opportunity to ask questions about the study. After questions have been answered to their satisfaction and inquiries made about the participant's interest, they will be asked if they give their verbal permission to proceed with the screening questions. Interested participants will be screened for the presence of anxiety symptoms. These brief screening questions are

expected to take no more than 10-15 minutes. Participants who screen positive for anxiety on the GAD-7 will be sent a Veteran Informed Consent Form (see Appendix 5D, Veteran Informed Consent Form) and a HIPPA medical records release form by mail or VA-approved transmission source (DocuSign). The potential participant will be contacted within two weeks of sending the ICF/HIPPA to discuss the documents and be given an opportunity to ask additional questions about the study.

Once a valid, signed informed consent form has been returned, the participant's name will be added to a master study enrollment list. The consented participant will be contacted and scheduled for a baseline assessment to occur within two weeks. A telephone script (see Appendix 5C) will be utilized by the RA to complete the baseline interview. As part of the script, the RA will review the procedures involved in the project, as well as their rights as a participant in a research study. Participants will, again, be provided an opportunity to ask questions. After the baseline interview is completed, the RA will complete a chart review to confirm the Veteran is not receiving any other psychotherapy treatment that would potentially conflict with the treatment.

Permission to text message and/or email participants is requested in the written informed consent document as an optional matter, and is not required for study participation. With the Veterans' consent, text messaging and email will be used for appointment reminders, for links to study materials and blank assessment packets, and for links to study results when available. These communications will be sent only from VA-approved devices, which are password protected and encrypted, and the communications will not contain PHI.

Consent to audio record bCBT sessions is also included in the written informed consent document and explained as an optional matter, not required for participation. Participants who decline being audio recorded will have a note placed in the research master record indicating such. Providers will be notified via encrypted email of participants randomized to the direct referral group who declined being audio recorded. Providers will ask bCBT participants who consented to audio recording for their verbal consent prior to audio recording bCBT sessions.

Veteran Qualitative Interview:

A subset of Veteran participants randomized to the treatment group will be invited to complete a one-time qualitative interview focused on their experiences receiving bCBT for anxiety through video-to-home and/or in person (see Appendix 5E, Veteran Qualitative Interview ICF). The study will recruit a total of 28 participants that fall into 3 categories: 1) 4 Veterans with no bCBT engagement (0 sessions), 2) 4 Veterans with little engagement in bCBT (1-3 sessions), and 3) 20 Veterans who fully engaged in treatment (4 or more sessions). The third group will be further stratified to include 10 who opted for and 10 who declined VVC-H.

To determine their interest in completing the interviews, participants will be contacted at the 4-month time period or immediately following their decision to end treatment. Veterans that agree to complete the interview will be sent the written informed consent form by mail or VA-approved transmission source. The potential participant will be contacted within two weeks of the mailout to discuss the document and be given an opportunity to ask questions about the interview. Upon receipt of a valid, signed study informed consent form the participant will be contacted and scheduled for the qualitative interview to occur within 2 weeks.

Qualitative interviews with Veterans and providers may be conducted and recorded using a VA-approved web conferencing platform (e.g., Microsoft Teams) on a secured VA laptop. Interviewers will contact Veterans at their preferred phone number using the platform's call-out feature. VA providers can be contacted and interviewed through their employee accounts on the platform. At the beginning of the interview, the interviewer will ask for verbal consent to record the interview. Recording will occur through a secured VA laptop behind the VA firewall. The platform will produce an audio file and auto-generated transcript file. These files are automatically stored behind the VA firewall and on a password-protected cloud storage (SharePoint) accessible only to the qualitative interviewer. Once available, a copy of the interview audio file will be downloaded and stored in a secured drive (M:Drive) that is accessible only to designated research team members, and sent to the VA Centralized Transcription Service. Interviews, at the option of the interviewer, may be recorded with Audacity software behind the VA firewall. In both cases, the audio file will be immediately saved to the project folder on the secure VA drive. If neither of these technologies is available, a study team member may serve as notetaker or scribe while the qualitative interview is being conducted.

Diversity Supplement Qualitative Interview:

The diversity supplement to the main study will also recruit a subset of 24 randomized Veterans to complete a one-time qualitative interview to understand barriers to treatment and research access for African American and Hispanic Veterans (see Appendix 7B). The Veterans selected will be stratified by race/ethnicity (12 African American; 12 Hispanic) based on self-reported racial/ethnic identity, which will be confirmed using the Multigroup Ethnic Identity Measure (MEIM2). Dr. Dawson or another staff member will contact them to describe the goals of the supplement project and gauge the Veteran's interest in completing an interview. Dr. Dawson or another study team member will interview interested participants by telephone. Interviews will last approximately 60 minutes. Interviews will be audio recorded, using the same methods described above in the Veteran Qualitative Interview, and professionally transcribed.

Clinician Participants:

Clinicians will be recruited from the Houston, San Antonio, and New Orleans sites and included as study participants. National union representatives will be informed of the study. Currently,

Houston has 12 psychologists and 4 social workers; San Antonio has 15 psychologists, 7 social workers, and 2 master's level counselors. New Orleans has 2 psychologists, and 2 social workers and is in the process of expanding their PCMHI program. In addition, PCMHI social work and psychology interns and fellows are eligible to participate.

Potential risks faced by Clinician participants are expected to be minimal and relate to psychological discomfort that may be associated with completing the training and applying the intervention. Clinicians may also experience pressure with time in meeting the training and consultation requirements. To minimize burden, clinicians can complete the training at their own pace. These procedures are similar to other trainings clinicians receive as part of their continued training practice.

Potential therapists will be referred by their clinic director and/or VISN mental health leadership and subsequently screened for appropriateness by the study investigators. Clinicians identified as interested will be contacted via email by study staff to confirm interest. A follow-up call will be made if there is no email response from the clinician. When interest is confirmed, a consent form will be sent by a VA-approved transmission source or mailed to clinicians prior to the meeting. A time will be set up to review the consent form (see Appendix 4, Clinician Consent Form) with the clinician by phone or in person. During the meeting, the study team member will review the document and explain all procedures requested of a participating clinician and address any questions posed. Providers will be informed of the qualitative interview during the initial consent process. Clinicians will have the option to return the signed consent via a VA-approved transmission source, email or mail. A digital electronic VA signature from clinicians will be considered as valid as a handwritten signature. Those providers signing a written informed consent document will be scheduled for bCBT training and their name will be added to the master list of enrolled participants. At post-implementation, when they are contacted to schedule and complete the qualitative interview, clinicians will have another opportunity to decline if they wish.

All project staff are required to undergo significant training on the protection of human subjects, research methods, and the importance of integrity in the research process. Study team members who are authorized to recruit participants and/or obtain informed consent will be trained on specific study consent procedures by the study PIs (Cully and Fletcher), the Project Coordinator, or the main site RA. Each person will be required to administer a mock consent where they will receive hands on experience on possible questions and proper ways to address. All recruitment of Veteran participants will be done by research staff at the Houston VA. There are no paid research staff at the other facilities. Ongoing, weekly team meetings will be conducted in-person or via conference calls with local site study team members together with the main site project team to ensure study protocols continue to be followed consistently throughout the study.

5.4 Inclusion/Exclusion Criteria

- Describe the criteria that determine who will be included in or excluded from the study.

Veteran Participant Criteria:

Eligible Veteran participants are those who: 1) have received Primary Care Mental Health Integration services, or who are eligible for PCMHI services (They are not receiving specialty mental health services) services at the Houston, New Orleans, or San Antonio VAMCs, 2) have a documented diagnosis of an anxiety disorder, and 3) endorse clinically significant symptoms of anxiety on two occasions to ensure consistency of anxiety symptoms (GAD-7 score of 10 or greater; telephone screen and baseline appointment). The GAD-7 is the current anxiety measure used by VA PCMHI clinics and is appropriate for monitoring change in anxiety symptoms over time[5].

Exclusion criteria are 1) cognitive impairment (documented diagnosis of a cognitive disorder in chart review or 3 or more errors on a 6-item cognitive screener), 2) bipolar or psychotic disorder (documented diagnosis in chart review or as assessed by the MINI 3) substance use disorders (document substance use disorder in chart review or assessed by the MINI or a score of 4 or more on the AUDIT-C), and 4) current receipt of psychotherapy for anxiety. For participants with a psychotherapy appointment within the last 3 months, we will confirm the treatment provided will not conflict with the study's intervention. Veterans receiving antidepressant medications at the time of enrollment WILL NOT be excluded.

Provider Criteria:

PCMHI providers who conduct psychotherapy as part of their VA scope of practice will be targeted for recruitment. Clinicians will <u>not</u> be restricted based on discipline or prior CBT experiences but will be expected to have an interest in obtaining training and willingness to use bCBT in their practice. Providers will not be restricted based on profession. The only exclusion criteria for clinicians will be for those clinicians who are not appropriately authorized to provide psychotherapy as part of their scope of practice at the VA.

5.5 Study Evaluations

- Describe all evaluations to be conducted (including screening; tests/questionnaires that will be administered; any procedures that

subjects will be required to complete) and data collection methods. Include materials as an appendix or separate attachment.

Aims 1 & 2 Quantitative Measures: Measures were selected for their strong psychometric properties, ability to detect patient-centered change, and feasibility for adoption/implementation within VA PCMHI clinics.

Anxiety: We chose the Generalized Anxiety Disorder Screener (GAD-7[14]) as our primary anxiety measure because of its brevity, psychometrics and, most importantly, because it has been adopted by VHA's national PCMHI program. The GAD-7 is a seven-item self-report instrument that is psychometrically strong and valid for use in the primary care setting[5,14]. A GAD-7 score of 10 or higher will be required for study inclusion. Treatment response will be defined as a 50% reduction in baseline GAD-7 scores. Note: Study staff will administer the GAD-7 as part of all outcome assessments; bCBT providers will also administer it as part of their MBC practices when delivering bCBT.

The Overall Anxiety Severity and Impairment Scale (OASIS[15]) will be a secondary measure of anxiety. Unlike the GAD-7, which will be administered by both research staff and PCMHI providers, the OASIS will only be administered by research staff, thereby avoiding response bias that may occur in the clinical setting. The OASIS is a widely used five-item measure of anxiety for primary care settings[5,16] assessing anxiety frequency, anxiety severity, avoidance behaviors, social interference, and interference at work, school, or home[15]. The OASIS has demonstrated good internal consistency, and convergent and divergent discriminative validity in primary care[16,17]. A 50% reduction in symptoms on the OASIS is indicative of treatment response[5,6].

Quality of Life and Functional Status: We will assess quality of life using the 12-item Short Form Health Survey for Veterans (SF-12V[18]), an instrument adopted by VHA as a measure of functional status. SF-12V responses can be summarized in component scores for physical (PCS) and mental (MCS) functioning. Minimally clinically important differences (MCIDs) for PCS and MCS scores are a change of 5.0 or more[19,20].

Other Demographic and Clinical Data: Demographic data will include age, gender, ethnicity, income, marital status, education, employment, and distance from the VA and/or CBOC[10]. Diagnosis of anxiety disorders, PTSD, and depression will be based on the MINI structured interview[21]. Each diagnosis will be dichotomized and coded as present/absent. PTSD severity will be assessed using the PTSD Checklist-Civilian Version (PCL-5[22]), a standardized self-report rating scale that corresponds to DSM-5 symptoms of PTSD and possess strong psychometric properties. Medical complexity will be calculated using the Charlson Comorbidity Index (CCI) as defined by VA database extractions for the 12 months prior to the baseline date. The Charlson score has been widely used in the literature for assessing morbidity and mortality[23,24]. Psychotropic medications will be collected through VINCI databases following procedures used

in the team's prior work[10,11,25]. Medication tracking will include information on start date of medication, dose, and days-supply. Medication use will be coded for presence or absence and changes in type or dosage. We will monitor medications use in both bCBT and EUC groups through database extraction after the 12-month assessments to allow us to determine whether assignment to bCBT affected receipt of medications. Mental health service use: Mental health service use will be monitored for each participant to allow us to control for non-bCBT mental health service use. We will collect data via review of VA medical records as well as from a self-report non-VA service-use questionnaire (Appendix 6G). We will use CDW to capture data on emergency room visits and hospitalizations and will compare the frequency and types of such visits between arms (and between in-person and VVC-H bCBT encounters) quarterly. We will involve clinical leadership and the IRB if there are between-group differences in these safety measures.

bCBT Treatment Variables: Treatment delivery variables will include Intensity/Dose, Session Delivery Format: Intensity/dose of bCBT will be defined as the total number of sessions attended. Delivery format (VVC-H vs. in-person) will be documented for each session to allow us to examine the impact of VVC-H use on outcomes. These data will be collected via note templates and chart review procedures. ***Working Alliance*** will be assessed using patient and therapist report forms of the Working Alliance Inventory - Short Form (WAI-S).[26] The WAI-S (Appendix 8I) consists of 12 items and yields an overall score. VVC-H variables of interest including Veteran comfort receiving in-person VHA care, confidence using video technology, and logistic access to video technology will also be assessed at baseline.

Secondary Measures: To better understand factors that may contribute to participant treatment response, the protocol includes brief assessments for the following: social support (Appendix 8E and Appendix 8F) and attachment style (Appendix 8K). Careful consideration has been taken into selection of the measures, as not to add any undue burden on participants.

ORD Supplement Measures: In addition to baseline measures included in the parent study, Veteran participants will be asked to complete additional quantitative measures at baseline (see Appendix 6F, Diversity Supplement). Racial/Ethnic Identification will be measured using the first open-answer item of The Multigroup Ethnic Identity Measure (MEIM)[27], created to distinguish between particular ethnic groups, using 1 item. Perceived Discrimination will be assessed using the 9-item Perceived Discrimination Scale (PDS)[28] daily discrimination subscale. The measure evaluates daily discrimination experiences based on the participant's race, ethnicity, religion, physical appearance, or other characteristic. Anxiety Disorder Phenotype will be assessed using the 18-item Anxiety Sensitivity Inventory (ASI)[29]. The measure has 3 subscales: physical concerns, cognitive concerns and social concerns. It is valid and reliable in clinical samples, and the subscales have empirical construct validity.[3] Perceptions of Mental Health Treatment Access will be assessed using the 32-item Barriers to Access to Care Evaluation scale (BACE)[30]. It has demonstrated good reliability and validity in measuring key barriers to access to mental health care for adults.

Initial Telephone Screening Assessment:

Anxiety Assessment #1: Veterans who score 10 or greater on the GAD-7 will be considered eligible for inclusion and receive further evaluation for conditions that require specialty mental health services that would render care in PCMHI inappropriate.

Baseline Assessment:

Veterans who screen eligible during the telephone assessment will be invited to complete a full baseline after signed consent has been obtained to determine final eligibility. During the baseline, we will collect demographic information on age, gender, ethnicity, household income, marital status, education, and employment status (Appendix 6F). We will assess symptoms of anxiety (Anxiety Assessment #2) using the GAD-7[14] and a second established measure, the OASIS[15]. Other baseline measures will include: 1) a 6-item cognitive screening exam, where a cutoff of 3 or more errors will be used to exclude participants[31], 2) a diagnostic interview to document specific anxiety, depression, and/or PTSD diagnoses[21,32], quality of life (Appendix 8D, SF-12V[18]), depression (Appendix 8C, PHQ-9[33]), attachment styles (Appendix 8K), social support (Appendix 8E & 8F) and PTSD symptoms (PCL-5[22]), 3) the AUDIT-C[34] and MINI to obtain information related to bipolar, psychotic, and substance use disorders. In addition, during the baseline, participants will be asked to complete the Diversity Supplement measures (Appendix 6D) to evaluate whether sociocultural factors are associated with the severity and type of anxiety symptoms among Veterans of different race/ethnicity groups.

After the baseline assessment, a medical-record review will be completed and, regardless of eligibility status, we will place a note in participants medical records indicating the presence or absence of elevated anxiety symptoms.

Study Procedures for Handling Participant Suicidal Ideation: As part of all baseline and follow-up assessments, study staff will monitor and explore indications of suicidal thinking. Study staff will use a structured crisis-assessment protocol (see Appendix 5) to follow up on positive responses to items involving suicidal thinking. Participants who express suicidal ideation will be forwarded to a study investigator who will triage and refer for care as appropriate.

Data-Collection Schedule

Quantitative data will be collected for 12 months following baseline to allow us to examine the long-term effects of the intervention (see Table 4). An initial telephone assessment will screen for exclusion criteria, with final eligibility determined at the baseline appointment. Four-, eight-, and twelve-month follow-up assessments will be conducted by blinded independent evaluators. Upon completion of the follow-up assessment period, the Veteran will be mailed a Thank You

note (See Appendix 10B) notifying them that their participation in the study is complete and acknowledging their contribution to this research.

Table 4. Assessment Schedule – Effectiveness Aims

	Screen	Baseline	4 mo (post tx)	8 mo F/ U	12 mo F/U
GAD-7	X				
Cog Screen, Demographics, Diversity Supplement, Charlson Index, Attachment, Social Support, Chart Review		X			
MINI – Anxiety, Depression, Mania, Psychosis, Substance use and PTSD modules, Audit-C		X			
GAD-7, OASIS, SF-12V, PCL-5, PHQ-9,		X	X	X	X
Working Alliance Inventory (Patient and Clinician)			X		
Charlson Comorbidity Index – Database Extraction					X
Medication and Health Service Use -- Database Extraction					X

Mixed Methods Exploratory Aim:

We will conduct a mixed-methods formative evaluation (FE), informed by Stetler et al.,[35] to evaluate the implementation of the bCBT clinical intervention and VVC-H. The RE-AIM QuEST[4] framework will inform qualitative and quantitative data collection related to reach, effectiveness, adoption, implementation, and maintenance (see Table 5). We will collect FE data during the study's pre-implementation (Y1 Q1-Q2), implementation (Y1 Q3 – Y3 Q4) and post-implementation (Y4 Q1-4) phases.

Pre-implementation: During pre-implementation, we will conduct semi-structured interviews with the PCMHI clinical director and bCBT champion at each site. Directors and clinical champions will review and provide feedback on the bCBT materials, training materials, provider bCBT delivery procedures, and provider preparedness to deliver exposure in PCMHI. Pre-implementation findings will allow us to refine the bCBT delivery approach, address barriers, and tailor provider support procedures. Consenting of the staff for the pre-implementation interviews will not be warranted as no identifiers will be collected during the interviews.

Implementation: During implementation, using stratified purposive sampling,[36] we will recruit 24 bCBT-arm Veteran participants to take part in the formative evaluation. We will inquire regarding interest in particiapating in the FE interview at the end of the 4 month follow up assessment, and a time to complete the informed consent process will be scheduled for interested participants. A separate FE consent process will avoid confusion during the initial consent process. The FE subsample will include three groups of Veterans: 1) 4 Veterans with no engagement in bCBT (0 sessions), 2) 4 Veterans with little engagement (1-3 sessions), and 3) 20 Veterans who fully engaged in treatment (4 or more sessions). The third group will be further stratified to include 10 who opted for and 10 who declined VVC-H. Given the exploratory nature of this aim, data saturation is not our primary goal. Rather, we seek to gather diverse Veteran experiences to inform future implementation of bCBT and VVC-H in PCMHI. Veterans will complete semi-structured interviews focused on reach (e.g. to prepare for future bCBT outreach efforts) and

effectiveness (e.g. personal impact) of bCBT and bCBT delivered via VVC-H, including experiences with exposure skills. We will augment these data with descriptive chart-review data on bCBT and VVC-H delivery (e.g. number of bCBT sessions, number of VVC-H sessions, measurement-based care and note template use, Veteran bCBT engagement, and provider bCBT fidelity ratings). Veterans will be compensated $30 for completing interviews.

Post-implementation: We will conduct exit interviews with study providers to assess perceived bCBT effectiveness and explore factors that impeded or facilitated bCBT use and delivery via VVC-H, including provider-initiated modifications and workarounds, and maintenance potential. We will augment these data with summary descriptive data on constructs described in the implementation phase. Veteran and provider semi-structured interviews will last approximately 30-45 minutes and will be conducted by Co-I Chen. Detailed interview notes will be taken at all interviews; implementation and post-implementation interviews will be audio-recorded; recordings will be transcribed. Draft interview guides for each project phase are included in Appendix 7.

Table 5: Application of RE-AIM QuEST (adapted from Forman et al. 2017)

Dimension	Quantitative	Qualitative
Reach	# of Veterans receiving bCBT, VVC-H	Veterans perspectives on barriers/facilitators receiving bCBT only and bCBT + VVC-H
Effectiveness	Measurement-based care data - weekly GAD-7 (chart reviews)	Veterans' and providers' perspectives of the impact of bCBT on anxiety; impact of VVC-H as a delivery modality
Adoption	# of providers using bCBT, VVC-H	Providers' reasons for using bCBT and VVC-H
Implementation	Provider fidelity to bCBT as rated by experts from audio recordings; clinical coding accuracy of VVC use	Providers' perceptions on using bCBT and VVC-H in practice; modifications/workarounds; contextual barriers and facilitators related to bCBT and VVC-H use
Maintenance	Not evaluated in the current proposal	Providers' perceptions on continued use of bCBT materials; continued use of VVC-H technology

5.6 Data Analysis

- Provide sample size determination and analysis (include anticipated rate of screen failures, study discontinuations, lost to follow-up etc.).
- Describe how, where and by whom the data will be analyzed.

Primary aim: Anxiety and Quality of Life differ as a function of bCBT for anxiety vs. EUC:

All analyses will be done on an intention-to-treat basis, and participants will be analyzed in the group to which they were randomized. We will first determine whether participants randomized

to the two study arms differed on baseline characteristics, age, race, gender, medical or mental health comorbidities, and anxiety. Chi-square tests will be used for categorical variables and t-test for continuous and ordinal variables.

We will examine the normality of the distributions of both primary outcomes and will consider transformations such as the log or the inverse. Because we are using an unequal randomization (see sample size section), it is especially important to test the assumption about the homogeneity of the variance of the residuals across the levels of the independent variables[37]. For analyses of our primary outcomes, we will test the homogeneity assumption before testing for differences between the bCBT and EUC groups. If the assumption of equal variances is violated, we will use statistical tests such as the approximate t-test, which uses individual sample variances instead of the pooled variance. In addition, we will obtain Satterthwaite's approximation of the degrees of freedom. For the regression models, we will test whether the residual variances are equal and, if necessary, we will fit unequal variance models to obtain better estimates of the standard errors of the difference between groups. We will calculate the absolute differences in outcome measures between baseline and 12-month follow-up and the effect sizes of the bCBT group compared with EUC. We will also examine effect sizes for the bCBT group baseline vs. post-treatment and 8-month follow-up.

To compare changes in anxiety symptoms between the two groups over time, we will use a longitudinal, mixed-model analysis containing terms for the intercept, treatment, time, and interaction between time and treatment. In separate analyses, we will compare changes in quality-of-life between the two groups over time using a similar mixed-model approach. The mixed-model analysis will allow us to nest patients by site. Any baseline characteristics found to be significantly different between bCBT and EUC will be included in the model, as will any differences in mental health service use. The four time points (baseline, 4-, 8-, and 12-month) will allow us to assess the immediate impact of treatment and the longer-term retention, improvement, or decay in outcomes. The treatment effect will measure differences between the intervention and control groups at baseline, and the time effect will measure whether there was an overall change over time in the outcome. The term of most interest will be the interaction between time and treatment, which will indicate whether there is a difference over time between the two groups. The use of the random-coefficient model will allow us to fit a line for each participant using his/her available data, including participants with missing values, and maximize the power to detect differences.

Secondary Analyses: Prediction of bCBT response and VVC-H use:

We will run two logistic regression analyses using only data from participants who received bCBT. In analysis 1, we will identify characteristics that predict response to treatment as defined as a reduction of 50% on the GAD-7. Predictor variables will include: baseline anxiety severity (GAD-7 score), presence of specific anxiety diagnoses (GAD, Panic, Social Anxiety, Other), medical comorbidities, and brief CBT-related factors (number sessions received and treatment engagement). In analysis 2, we will identify characteristics associated with VVC-H use. VVC-H

use will be classified as any (one or more VVC-H sessions) or none. Predictor variables will include: age, distance to VA facility in miles, medical comorbidities, depression and PTSD (presence or absence), and Veteran self-reported comfort receiving in-person VHA care and confidence using video-based services and technology.

Implementation Analyses (Exploratory):

Analyses will use data from the mixed-method formative evaluation described above. Qualitative pre-implementation data will be analyzed using rapid qualitative analysis, a systematic and rigorous process, to provide data in real-time to tailor the intervention, and identify contextual barriers prior to rollout[38,39,40]. Implementation and post-implementation interviews with providers and Veterans will be analyzed using directed content analysis[41] consisting of deductive (a priori) codes from the RE-AIM QuEST framework. Inductive (a posteriori) codes that emerge from providers' and Veterans' experiences with the intervention and VVC-H delivery will also be identified. We will utilize Atlas.ti software to facilitate analysis and management of qualitative data. Quantitative data will be collected and analyzed as descriptive data.

Sample Size and Power Calculations

Primary Aim: To determine whether anxiety symptoms (GAD-7) and quality of life (SF-12) differ as a function of the intervention (bCBT for anxiety vs. EUC) at 4-, 8-, and 12-month follow-ups. A three-step sample-size calculation indicates that 225 anxiety patients will need to be randomized to draw conclusions regarding the primary hypothesis that bCBT will be superior to EUC at 4-, 8, and 12-month assessments.

Step 1: Power to detect GAD-7 differences. A sample size of 138 anxiety patients is needed to detect an effect size = 0.38 for the differences between bCBT and EUC GAD-7 outcomes using a two-sided t-test with 80% power at the .05 significance level, adjusted for repeated measures[37]. The formula for the sample size, adjusting for repeated measures, is $N = \frac{2*(Z_{(1-\alpha/2)} + Z_{(1-\beta)})^2\ [1+(T-1)\rho]}{d^2\ T}$, where N is the sample size per group, $Z_{(1-\alpha/2)}$ and $Z_{(1-\beta)}$ are the (1-α/2) and (1-β) percentiles of the normal distribution, T is the number of follow-up measures, ρ is the correlation coefficient of the repeated measurements, and d is the effect size[42]. Solving this with T = three follow-up measurements after baseline, d = 0.38, and ρ = .7 yields a sample size per group of 69, and total sample N^t =138.

Quality of Life Outcomes. Our prior study of patients with anxiety or depression[10] resulted in mean, standard deviations, and effect size of 7, 11, and 0.3 respectively for the SF12V mental component score (MCS). SAS® proc power indicated that a two-sided t-test with 80% power at the .05 significance level requires a sample of 40 patients per group (80 total). Because the sample required for the anxiety measure (GAD-7; n=138) is greater than that needed for the

quality-of-life measure (SF12V; n=80), adjusting for repeated measures, unequal sample, and clustering on provider is presented below for the anxiety measure.

Step 2: Unequal Randomization. To increase power for the project's secondary and implementation outcomes and to reduce unnecessary recruitment, unequal allocation will be used where approximately 60% of Veterans will be randomized to bBCT. As noted by Dumville et al.[37], an unequal number of participants per group is an under-used technique that offers advantages for randomized trials, most notably, reduction in unnecessary recruitment. Revised total sample size $N'=N(1+k)^2/4k$, where N=138 and k=1.5, which gives revised total sample N'= 145. The individual sample size in each of the two groups are $N'/(1+k)$ and $kN'/(1+k)$; giving n=58 in the EUC group and n=87 in the bCBT group.

Step 3: Provider Inflation Factor. The bCBT sample size was then inflated to account for the intraclass correlation due to clustering of patients within providers[43]. We also will adjust the sample sizes for both the bCBT and EUC groups to account for attrition. Because only participants receiving bCBT are assigned to a provider, we first determined the average number of bCBT patients per provider (87 bCBT patients/25 providers = 3.5 patients per provider). To account for clustering in the bCBT group, the number of bCBT patients is inflated by the factor $[1 + (\overline{m} - 1)\, c]$, where $\overline{m}$ is the average number of bCBT patients per provider and c is the correlation among patients seen by the same provider. Based on the sample size of 87 bCBT patients and an assumed correlation among patients of .10[43], our inflation factor is 1.25 (87 x 1.25 = 109). Finally, to account for attrition, we assumed an attrition rate at 1 year of 25% (109*(1/ 0.75) = 145) gives 145 bCBT patients. A similar clustering inflation factor was not used for the EUC group, as no providers are assigned. Attrition rate of 25% was assigned to the EUC group (58*(1/ 0.75) = 78), rounded to 80 for randomization. The final number of randomized patients equates to 225 (145 bCBT and 80 EUC).

Secondary Aims:
Prediction of bCBT response and VVC-H use (bCBT group only). To assess predictors of bCBT response and VVC-H use, at least 10 events per variable in the logistic-regression models are needed to have unbiased estimates of the sample variance of the regression coefficients[44]. No sample-size calculations were conducted for secondary aim, but SAS® proc power (version 9.4)[45] indicated a sample of 145 is adequate for 80% power to test odds ratio of 2.5, and conservative estimates for sample size and assumptions necessary to run the analyses suggest the project will be appropriately powered for 10 variables[46]. Secondary analyses will include 8 variables for aim 2A (bCBT response; model #1) and 8 variables for aim 2B (VVC-H prediction; model #2).

Provider Sample. No formal sample size calculations were used for the implementation-focused elements of this project. Rather, the team will invite all CBOC providers at the sites within the Houston, New Orleans, and San Antonio VAMCs to participate and subsequently evaluate how many providers opted to engage in the bCBT project. These procedures are common for implementation-focused trials that often have a smaller pool of "subjects". Designs of this nature

often look less at statistical significance and instead focus more on descriptive quantitative data and depth interviewing and qualitative analyses to determine impact and “lessons learned”.

Data and Quality Assurance:

Independent Evaluation: Outcome data will be collected by independent evaluators (IEs) who will be blinded to randomization. All IEs will be based in Houston, with direct oversight by Dr. Cully. IEs will undergo training and calibration on all study measures and be regularly reassessed for quality.

Missing Data: We anticipate that most missing data will be due to attrition (see below). We will examine missing data for bias and conduct sensitivity testing using longitudinal hierarchical mixed models. We will conduct sensitivity analyses using tests for missing completely at random[41] to evaluate whether the reasons for loss to follow-up at the various times are related to observed values of the outcome variables.

Minimization of Attrition: A 25% attrition rate was used for sample size calculations, based on our prior and ongoing psychotherapy trials with Veterans[10]. Dropouts will include any participants who indicate a desire to withdraw or are lost to follow-up after randomization. The flexible delivery approach aims to decrease attrition and increase bCBT engagement and adherence. We will also minimize attrition by reducing our “research presence" using telephone assessments, limiting research contact, compensating participants, and allowing bCBT participants who drop out of treatment to continue with research follow-up assessments.

All analyses for the study will occur exclusively at the Houston HSR&D CoE under the direction of the study PIs (Fletcher and Cully) and study data analyst (Sansgiry).

5.7 Withdrawal of Subjects

- Describe any anticipated circumstances under which subjects will be withdrawn from the research without their consent.
- Describe the consequences of a subject's decision to withdraw from the research and the procedures for orderly termination of participation by the subject (e.g., the subject contacting the investigator for an end-of-study visit).
- Describe procedures if a subject is withdrawn or withdraws from the intervention portion of the study but agrees to continue in the follow-up phases or for safety outcome purposes.

There is no foreseeable circumstance for which research participants will be withdrawn from the study without their consent. If a participant chooses to withdraw from the study, there will be no consequences. The subject will not lose any rights or permissions s/he currently receives. To

withdraw from the study, an individual will be asked to contact the study staff to inform of the decision and remove their participation status in the project databases.

bCBT patients who drop out of treatment will be allowed to continue with research follow-up assessments. The provider will be notified in one of two ways: 1) via the Veteran during the session; 2) the research staff will notify the provider that the Veteran no longer wishes to receive treatment. The Veteran's research file will be notated with withdrawal and that he/she is still willing to complete the follow-up assessments.

5.8 Subject Compensation

Veteran Participant Compensation:

Only Veteran participants will be compensated in the study. Study clinicians are not eligible for compensation given their VA appointment. Veteran participants will be compensated $30 for each study assessment completed which will be at baseline, 4-month assessment, 8-month assessment, and 12-month assessment. There is a total of 4 study assessments which will allow a Veteran to be compensated up to a total of $120.00 if all study assessments are completed. If a participant has electronic funds transfer set up with the VA or agrees to sign up, then they will be eligible to have the money deposited directly into their account. Veterans not interested in signing up for electronic funds transfer will receive compensation via debit card. The debit card process can take up to 8 weeks to be received and an electronic fund transfer takes approximately 10 days to appear in the account. We will also offer the option of being compensated with Veterans Canteen Service coupons (Canteen Bucks).

A subset of Veterans randomized to the direct referral arm will be invited to complete a one-time qualitative interview regarding their experiences in the brief CBT program. We will recruit a total of 28 participants that fall into 3 categories: 1) 4 Veterans with no bCBT engagement (0 sessions), 2) 4 Veterans with little engagement in bCBT (1-3 sessions), and 3) 20 Veterans who fully engaged in treatment (4 or more sessions). The third group will be further stratified to include 10 who opted for and 10 who declined VVC-H. The interview will last 30-45 minutes, and Veterans will be compensated $30 for their time completing the interview.

A second subset of 24 randomized Veterans will be invited to complete a one-time qualitative interview (see Appendix 7B) regarding barriers to treatment and research access for African American and Hispanic Veterans. These Veterans will be stratified by race/ethnicity (12 African American; 12 Hispanic) based on self-reported racial/ethnic identity, which will be confirmed using the Multigroup Ethnic Identity Measure (MEIM2). Interviews will last approximately 60 minutes, and will be audio recorded and professionally transcribed. Participants will be compensated $75 if they complete this qualitative interview. Veterans may be compensated up

to a maximum of $225.00 if they complete all study follow-up assessments and both qualitative interviews.

6.0 Reporting

- Include procedures for reporting unanticipated problems, serious adverse events, and protocol deviations.
- Include information about whether the study has a Data Monitoring Committee and if so, how often it will meet.

All unanticipated serious adverse events (U-SAEs) and unanticipated serious problems (UAPs) will be reported to the VA Central IRB within five business days. U-SAEs will be reported to VA Central IRB regardless of their relationship to the research. All protocol deviations, violations, and/or noncompliance will be reported to the VA Central IRB within five business days of the reporting individual becoming aware of the occurrence.

Safety information, including SAEs/UAPs, that will be collected:

During completion of the study assessment timepoints the participants mental health will be accessed via questions administered. Participants demonstrating increased mental health distress, based upon responses to the assessment, will be evaluated and referred for additional assessment and intervention as needed. Participants in need of immediate treatment (e.g., active psychosis or suicidal intent) will be referred for appropriate services with VA upon identification. Study staff will follow up on any positive responses to items involving suicidal thinking, using a structured crisis-assessment protocol (see Appendix 5). Participants who express suicidal ideation will be forwarded to a study investigator who will triage and refer for care as appropriate.

All occurrences of events resulting in a participants' death, life threatening experience, hospitalization, prolonged hospitalization, or persistent or significant disability will be documented. Any occurrence of an event that results in the need for medical or other interventions to prevent any of the above listed outcomes will be documented as well. As such, any participants identified as having an immediate mental or physical health issue will be referred to care as appropriate.

Frequency/methods of safety-related data collection:

Collection of safety information will commence when the first participant is enrolled in the study. Safety information may be collected either 1) during baseline and follow up assessments, 2) during bCBT sessions, or 3) during telephone contacts with participants made for purposes of

scheduling assessments and/or treatment sessions. All participants will complete comprehensive assessments via telephone at baseline and at 4-, 8-, and 12-month follow-ups. Symptoms of anxiety, depression, and suicidal ideation will be assessed at these time points. Secondly, the Research Coordinator or RA will periodically contact patients to schedule study-related appointments. The participants or other informants may report information related to their safety at those times.

Conditions that would trigger an immediate suspension of the research:

This intervention will compare a brief, structured cognitive-behavioral intervention with usual care practices in VA PCMHI. The active treatment, bCBT, utilizes well-established psychotherapeutic techniques to enhance patients' self-management of anxiety. No medications, invasive procedures, or untested techniques will be used. We do not anticipate the occurrence of events that would necessitate the immediate suspension of research because of 1) the low probability of adverse events from the intervention in either arm of the study, 2) all participants will continue to receive usual care services within the VA, and 3) no treatment will be withheld from any participants.

Specify procedures to determine when and how to notify individual participants or their health care providers of findings that may affect the participant's health or welfare:

The decision to contact a patient and/or their health care provider regarding patient welfare can be made in two ways. First, the Project Coordinator, RA, or independent evaluators will conduct routine checks on participants' safety and well-being, including an assessment of suicidal ideation, during baseline and follow up assessments. These study personnel will notify the patient and/or their healthcare provider as necessary.

Second, data and safety monitoring is expected to be conducted at both the local and national levels. At the local level, data and safety monitoring will occur for any identified adverse events. Any participants identified as having an immediate mental or physical health issue will be referred to care as appropriate. Participants will also be accessed for suicidality if a positive response is given to item 9 on the PHQ-9 measure. Responses to the suicide assessment will be reviewed with a licensed psychologist (Fletcher, Cully, Hundt, McClean, or Slaton) to determine the level of severity and if additional intervention is warranted.

At the national level, the study is under review by the VA's Data and Safety Monitoring Board (DSMB). We will continue to provide the national DSMB with comprehensive annual and semi-annual reports for formal independent review of study safety and recruitment practices.

7.0 Privacy and Confidentiality

- Describe whether the study will use or disclose subjects' Protected Health Information (PHI).
- Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, Certificates of Confidentiality, and separation of identifiers and data)
- If data and biological specimens will be banked, specify

The use of de-identified, identified, and coded data will be utilized for participants in this study. Protected health information (PHI) obtained from patient participants will include: name, age, date of birth, home address, contact phone number, last 4 digits of their social security number (which allows us access to their medical record). PHI requested from enrolled clinicians will be restricted to their name. Information obtained about participants (clinician and veteran) will be kept strictly confidential and not disclosed.

Each participant (clinician and veteran) in the study will receive a unique ID number to increase confidentiality. Data obtained from participants will be maintained in a password protected electronic database. Data and audio recordings will be limited to the study team and stored on VA computers (behind the VA firewall) under Drive:M. As another level of security, access to study folders will be restricted to study team members listed on the delegation of authority. In addition, all electronic data files will be password protected for additional security. To maintain privacy, assessments and interviews will be conducted in one of several private interview rooms available or in the study staffs' office. Private interview rooms will be scheduled for use at the time the assessment is scheduled. All electronic data files will be maintained within the VA setting and behind the VA firewall. Access to research records will be restricted to the Co-PIs and project staff.

Although data from bCBT sessions and interviews from the exploratory aim are being recorded, only data from qualitative interviews conducted for the exploratory aim will be transmitted for transcribing purposes. Approved staff from the VA Salt City (VASLC) will transcribe the Pragmatic Trial of brief CBT for Anxiety in Primary Care audio files. The VASLC has a Professional Transcription Service available to VA sites and monitored by their own IRB. The audio recordings to be transcribed by VASLC staff will be labeled by the subject's unique alphanumeric code and saved behind the VA Firewall in Dr. Fletcher's secure shared project folder on the M drive. The VASLC transcription staff will be given access to a sub-folder within Dr. Fletcher's secure project folder. Approved study staff will place a copy of the audio files in this folder for an approved VASLC transcriptionist to access for the purposes of transcription. The VASLC transcriptionist will transcribe each interview verbatim and save the completed transcript in the sub-folder using the same alphanumeric code. No data (audio files, in process transcripts, or completed transcripts) will leave the Michael E. DeBakey VAMC secure research server.

As completed transcripts become available, approved study staff will move these files from the transcriptions sub-folder into another sub-folder that is only accessible to study staff, where they will be stored and accessed for qualitative analyses.

All project staff are required to have undergone focused training on privacy, the protection of human subjects, research methods and the importance of integrity in the research process. Houston VA HSR&D IQuESt Computing Center also requires all project staff to review the Data Security Compliance Agreement which describes the center's data security protocol. Each project staff member must sign an acknowledgement that they have reviewed the policy and agree to follow the policy before accessing data. The Houston VA HSR&D IQuESt Computing Center data security policy conforms with current VA policies and has been reviewed and approved by the MEDVAMC Chief Information Officer, Information Security Officer, and Privacy Officer.

8.0 Communication Plan

- Include plan for ensuring all required local site approvals are obtained and notifying the Director of any facility where the research in being conducted but the facility is not engaged.
- Include plan for keeping all engaged sites informed of changes to the protocol, informed consent, and HIPAA authorization
- Include plan for informing local sites of any Serious Adverse Events, Unanticipated Problems, or interim results that may impact conduct of the study.
- Include plan for ensuring the study is conducted according to the IRB-approved protocol.
- Include plan for notifying all local facility directors and LSIs when a multi-site study reaches the point that it no longer requires engagement of the local facility (e.g., all subsequent follow-up of subjects will be performed by the PI from another facility).

Plan for engaged facilities:

- Upon approval of the PI/SC application Form 108, each local site will submit VA Central IRB Form 104 (Local Site Investigator Application), which must be signed by the Local Site Investigator, his/her supervisor, and the local site ACOS/R&D or Chief of Staff.

- Upon VA Central IRB approval of the Form 104 Local Site Investigator Application, the local site R&D Committee must provide written approval for the research to be conducted at the local site before the research begins.
- The Project Coordinator will maintain copies of the local site R&D Committee approvals in the main site regulatory binder.
- Local site Investigators or their designated study team member Research Assistants (RAs) will maintain copies of the main site approval, as well as the local site R&D Committee approvals in their respective local site regulatory binders

Plan for non-engaged facilities:

This research study will not take place at any facility not engaged in the research (i.e., without a Local Site Investigator Project Application approval).

Plan for notifying and obtaining local site approval of amendments and other administrative changes:

- Upon VA Central IRB approval of all PI/SC Amendments and Local Site Amendments (including modifications to the protocol, the procedures for verbal informed consent and HIPAA authorization, and any administrative change approvals), the Project Coordinator will send an electronic copy of the approval and all attachments via email to the Local Site Investigator to submit to the local site R&D Committee for approval (when required by the local site RDC).
- The Project Coordinator will maintain copies of all approval documents, including local site R&D Committee approvals (when required by the local RDC) in the main site study binder.
- The local site Investigator or local site RA will maintain copies of all PI/SC Amendments and Local Site Amendments (including modifications to the protocol, the procedures for verbal informed consent and HIPAA authorization, and any administrative change approvals) that pertain to their respective site in the local site regulatory study binders.
- The local site Investigator or local site RA will maintain copies of their respective local site R&D Committee approvals (when required by the local site RDC) in their local site study binder.
- When the local site R&D Committee requires approval of amendments and/or administrative changes, no change will be implemented prior to receiving documentation of the approval of the local site R&D Committee.

Plan for keeping all engaged sites informed of changes to the protocol, informed consent, and HIPAA authorization:

A. *Regular meetings and conference calls:* The Co-PIs will lead regular conference calls and meetings that will include discussions of changes to the protocol, informed consent process and the HIPAA authorization. Study team members will be notified through

these conference calls and meetings of upcoming changes, as well as when the PI receives notification from the VA Central IRB of final approval of such changes.

- The PI will lead weekly meetings to discuss the study status with the study leadership team (select co-Investigators, Project Coordinator, and other study team members)
- The PI will lead weekly conference call discussions with the Local Site Investigator and her study team.
- The PI will lead monthly meetings in person and via conference calls to provide status update/discussions with all Co-Investigators, Local Site Investigator, and all local site study team members

B. *Shared drive:* The Project Coordinator will maintain a shared drive on the Houston VA HSR&D IQuESt secure server (that resides behind the VA firewall) that is accessible to local site study team members**.** The Project Coordinator will maintain the most current version of all IRB approved documents on this shared drive.
   - When new or revised documents are submitted for approval, the Project Coordinator will notify the Local Site Investigator and her study team that changes have been submitted for approval and are under review by the VA Central IRB.
   - Upon VA Central IRB approval of a new or revised form, the Project Coordinator will notify the Local Site Investigator and her study team that the new form has been approved. The PI or the Project Coordinator will provide training on newly approved procedures to all local site study team members.
   - All local site personnel will be asked to do the following:
     - File a printed copy of the VA Central IRB approval, and all newly approved documents, in the local site study binder.
     - Destroy all blank supply copies of previously approved versions of any newly approved study forms.
     - Begin using the new form, or applying the newly approved procedure, immediately.

Plan for informing local sites of any Serious Adverse Events, Unanticipated Problems, or interim results that may impact conduct of the study:

- The Project Coordinator will notify all participating sites immediately of any SAEs, Unanticipated problems, or interim results that have the potential to affect implementation of the study. A copy of the SAE report or Protocol Deviation report that is submitted to the VA Central IRB will be sent to the Local Site Investigator, as well as their local site study team members via encrypted email. Additional copies will be sent to the local site R&D Committees.
- The PI will discuss SAEs, Unanticipated Problems, Protocol Deviations, and interim results that may affect the conduct of the study during the weekly and monthly, meetings.

Plan for ensuring the study is conducted according to the IRB-approved protocol:

- The importance of conducting the study according to the IRB-approved protocol is emphasized by the PI to all study team members on a regular basis. In particular, all research team members are required to read the IRB-approved protocol (and any subsequent amendments), and research staff will receive specific training from the PI or Project Coordinator regarding protocol elements relevant to their study role before their involvement in the study begins. This study-specific training is over and above the mandatory trainings that all research staff receives.
- During weekly and monthly meetings, the PI will follow-up with the LSI to ensure that she continues to adhere to the protocol and to standard research compliance procedures as required by the VA.
- The PI will require the LSI to hold weekly or bi-weekly meetings with their respective local site study teams.

Plan for notifying all local facility directors and LSIs when a multi-site study reaches the point that it no longer requires engagement of the local facility (e.g., all subsequent follow-up of subjects will be performed by the PI from another facility):

- The PI will notify the LSIs when the study reaches the point at which it no longer requires engagement of the local facility.
- The LSIs will submit Form 117b Local Site Project Participation Closure Report to the PI, who will submit the signed form to the VA Central IRB.
- The LSI will notify their respective local site Facility Director and R&D Committee that their facility will no longer be engaged in the research.

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