Brief Cognitive Behavioral Therapy for Chronic Pain to Improve Functional Outcomes among Primary Care Veterans

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Background and Significance

Chronic pain is highly prevalent among primary care Veterans and impacts health and safety.

Pain has a significant impact on the VA healthcare system with 50% or more of Veterans in primary care reporting pain (1-2). Chronic musculoskeletal conditions are among the most common sources of pain and are, therefore, the focus of this application. Chronic musculoskeletal pain has been associated with a range of disabling health outcomes, including diminished functional status and quality of life as well as increased health care costs associated with high rates of medical care utilization (3-5). Attention to chronic pain among Veterans has also increased given its relation to high priority safety issues identified by VA: suicide and opioid use. Chronic pain is associated with suicide risk, particularly among those with moderate or severe pain intensity (6). The safety of opioids has also been called into question because of well-documented adverse outcomes including substance misuse, accidental poisoning, and death (7).

Cognitive Behavioral Therapy for Chronic Pain (CBT-CP) is effective but designed for specialty care.

The CBT-CP treatment approach is consistent with the biopsychosocial model of pain and targets the biological (e.g., relaxation training), psychological (e.g., cognitive coping), and social (e.g., decreasing isolation) aspects of pain to improve health outcomes. CBT-CP encourages clients to adopt an active, problem-solving approach to cope with the many challenges associated with chronic pain (8). Behavioral targets of CBT-CP emphasize activity pacing that helps with re-engaging in pleasurable events (or new activities) in a safer manner. Relaxation training is used to directly address the stress associated with chronic pain. CBT-CP also targets the maladaptive thoughts that occur in relation to pain. Learning and applying thought monitoring, evaluation, and disputation can result in more balanced and useful ways of responding to pain and its consequences. Abundant evidence suggests that CBT-CP produces small to moderate improvements in important clinical outcomes, including measures of disability (e.g., pain-related activity interference), pain intensity, mood (e.g., depression symptoms), and quality of life (9).

Within the VA system, a protocolized full-length CBT-CP treatment is currently available as part of the Evidence-Based Psychotherapy Program which has been shown to be effective at improving pain intensity, catastrophic thinking, pain-related activity interference, and overall psychological distress. This protocol is typically delivered by behavioral health providers with pain management expertise who work in specialty care settings due to its time-intensive nature (i.e., 11-12 sessions of 50-mintues each). Many patients who could benefit from CBT-CP never receive it due to limited access to specialty CBT-CP providers (10). Adding more specialty providers is likely beneficial to a point, but the sheer volume of patients who could benefit from CBT-CP prohibit specialty care from being the chief source of CBT-CP. Thus, there has been a suggestion for improved integration of behavioral treatment into medical settings, such as primary care, to reach more patients in need.

Figure 1: Overview of Brief CBT-CP Sessions

Session	Content summary
1	**Education and Goal Identification**: Acute versus chronic pain; factors that impact pain/biopsychosocial model; chronic pain cycle; SMART goals
2	**Activities and Pacing**: Address fear of movement; activities pacing; avoiding withdrawal or disengagement
3	**Relaxation Training**: Relaxation benefits and techniques (Deep breathing and abbreviated progressive muscle relaxation)
4	**Cognitive Coping 1**: Recognize unhelpful thoughts that negatively impact the pain experience
5	**Cognitive Coping 2**: Modify thoughts that are unhelpful when managing pain
6	**The Pain Action Plan**: Reviewing progress made and skills acquired; Plan for future success

Brief CBT-CP provides essential components of treatment in less time.

Our team adapted the full-length protocol into *Brief Cognitive Behavioral Therapy for Chronic Pain (Brief CBT-CP;* 11) which is designed for use by Primary Care Mental Health Integration (PCMHI) providers to reduce functional limitations related to pain while conforming to the brief treatment format (≤6, 15-30-minute appointments). Brief CBT-CP is significantly shorter in duration (~3 hours total) than the original protocol (up to 12 hours). The resulting manualized protocol for Brief CBT-CP is summarized in Figure 1.

Preliminary studies: Brief CBT-CP is associated with improvement in patient outcomes.

We conducted a clinical demonstration project to gather preliminary data regarding Brief CBT-CP effectiveness and acceptability among patients and providers (12). Nationally, 22 PCMHI providers across 22 primary care clinics responded to an invitation to participate in a 12-month demonstration project that included training in Brief CBT-CP. At the end of the project period, data from 118 unique patients treated with Brief CBT-CP by a participating PCMHI provider were analyzed to assess changes in outcomes. Although not a randomized controlled trial (RCT), patient reported outcome data collected by the PCMHI providers at each visit showed statistically significant improvement in the PEG (13) of moderate effect size by session three (d = 0.65). This one-point decrease in PEG scores indicated that clinically significant improvement in outcomes can potentially be made in as few as three, 30-minute appointments of Brief CBT-CP. Pain self-efficacy showed smaller but also statistically significant improvements (d = 0.22).

Significance and Relevance for Veterans and VA Healthcare

The long-term goal of this research is to promote recovery among Veterans with chronic musculoskeletal pain. The focus of the intervention (i.e., a CBT intervention to improve functional outcomes commonly impacted by chronic pain) directly addresses the current RR&D special emphasis area related to non-pharmacological activity-based interventions for chronic pain. Taken together, these related high priority topics reflect ORD-wide clinical priorities and the VA's current Strategic Plan (FY19-24).

Research Design and Methods

Participants.

We will recruit and randomize 184 Veterans (not including screening failures) who utilize one of the primary care clinics located at the regional VAMC and CBOCs in Western and Central New York. Eligible participants will be randomized in a 1:1 ratio into either (1) Brief CBT-CP plus primary care TAU or (2) primary care TAU only.

Eligibility and recruitment.

Screening procedures. Our primary method of recruiting Veterans with chronic musculoskeletal pain who self-report functional impairment will replicate our successful case-finding method. This method has proven especially effective in identifying primary care patients with chronic pain of at least moderate intensity that could benefit from intervention but who have not otherwise received behavioral treatment for pain. Note that we will additionally accept referrals for potential participants directly from the primary care team, should they arise or directly from the Veteran by contacting the PI or study staff after hearing of the study by word of mouth or other sources, including ClinicalTrials.gov. For case-finding, VA electronic medical record data will be initiated to identify potential participants. Based on prior work, we estimate that about 7,000 individuals will initially be accessed through VINCI/CPRS from which to do additional screening for *initial eligibility criteria*: Veterans who are age ≥18 and ≤79 years, conversant in English, have an established history of VA primary care utilization at the regional VAMC/CBOCs (i.e., at least one primary care visit in the past year), and a diagnosis of a musculoskeletal condition based on ICD-10 code linked to their primary care encounter(s). We will also remove patients with a diagnosed major or minor neurocognitive disorder (e.g., dementia) based on ICD-10 code. Those Veterans meeting initial eligibility criteria will be sent a study invitation letter signed by the primary care lead. Following the letter, Veterans will be contacted by phone (after a period of one week to allow patients to decline participation, if desired) for additional screening. They are first asked to verify the presence of current musculoskeletal pain for ≥ 3 months (consistent with the consensus definition of chronic pain from the International Association for the Study of Pain). The PEG (13), a well-validated 3-item composite measure of pain intensity and functional impairment, will also be administered. Veterans must score ≥4 on the PEG pain intensity item and ≥4 on the PEG pain interference items to verify impact of at least moderate intensity. *Initial exclusion criteria:* Veterans will be excluded if they score positive on the Drug Abuse Screening Test (DAST-10). We will exclude those with a positive score on the Alcohol Use Disorders Identification Test (AUDIT) which would exclude those with a more significant alcohol use disorder. Veterans will be additionally excluded at this stage if they self-report current or prior engagement (in the past 12 months) in behavioral health services specifically for chronic pain, such as pain psychology services or behavioral medicine interventions, given the potential for overlap in content with Brief CBT-CP. Veterans who are already receiving a stable course of on-going mental health services that are not focused on pain (e.g., PCMHI, specialty mental health clinic, PTSD clinic, etc.) or psychopharmacological intervention from a mental health prescriber will not be excluded. We will ask patients to clarify if they have had any recent changes (last 2 months) in pain medication or medications for mental health conditions. Use of over-the-counter (OTC) analgesic medications/topicals will not be considered an exclusion criterion, even if these agents are recorded in the

patient's medical record by a VA provider. Similarly, routine or PRN use of prescribed anti-inflammatory medications (i.e., acetaminophen, aspirin, ibuprofen, naproxen, diclofenac) or topical agents will not be considered an exclusion criterion. Veterans who are engaging in interventional procedures for chronic pain management (e.g., epidural), have recently had (i.e., in the past three months) or plan to have surgery or other hospitalizations, or have a pending pain-related disability claim will be excluded.

Consenting and baseline assessment. We will aim to conduct all study procedures by phone/VVC as the safest option during the pandemic. We have therefore requested a waiver of documentation of informed consent and a full HIPAA waiver. Veterans who meet initial telephone screening criteria will be scheduled for consenting procedures and a baseline interview to confirm eligibility. We will send potential participants study related materials (e.g., baseline appointment reminder letter, informed consent information, etc.) in advance of their baseline appointment using secure Azure RMS email, a VA-approved encrypted email, or through standard mail. We will also send study measures in advance of the baseline and subsequent assessments based on request of the participant or judgment of the study team. Verbal consent will be and a check of participant understanding of key consent items will be administered prior to collecting baseline assessment data. Our primary outcome, pain-related activity interference, will be assessed with the Brief Pain Inventory (BPI) interference subscale. Only those potential participants with a score ≥4 (indicating at least moderate pain-related disability) will be included. Potential participants who endorse active suicidal ideation at time of assessment will be further evaluated by study staff following a standard suicide risk prevention protocol and consultation with study PI (or designee). Individuals who are deemed at elevated risk (e.g., suicidal ideation with intent and plan) will be connected to the appropriate emergency service (see Suicide Protocol, including warm handoff procedures to Vet's Crisis Line). Electronic medical record review will be used to confirm screening self-report of prescribed pain or psychiatric medications are on a stable dose for the past two months. Use of over-the-counter (OTC) analgesic medications/topicals will not be considered an exclusion criterion, even if these agents are recorded in the patient's medical record by a VA provider. Similarly, routine or PRN use of prescribed anti-inflammatory medications (i.e., acetaminophen, aspirin, ibuprofen, naproxen, diclofenac) or topical agents will not be considered an exclusion criterion. Patients will be asked to confirm medical record information regarding psychotropic medication, such as whether or not medications are currently being taken as prescribed. Similarly, chart review will be used to confirm select telephone screening items noted above, i.e., that the patient has not 1) used behavioral services for chronic pain management in the past 12 months, 2) has no recent (i.e., in the past three months) or upcoming interventional procedures for chronic pain management (e.g., epidural), 3) have recently had (i.e., in the past three months) or plan to have surgery or other hospitalizations, or 4) have a pending pain-related disability claim. Additionally, patients will be excluded if chart review indicates either of the following: 1) unstable psychiatric status (e.g., active psychosis, current mania), 2) major or minor neurocognitive disorder (e.g., dementia), or any other illness or condition (e.g., active cancer treatment for new diagnosis, end-of-life care, etc.) that would preclude or predictably influence ability to appropriately engage in study visits, as determined by the study team. Participants will also be excluded if they are unwilling to have their treatment sessions audio recorded. Patients who are excluded at this stage due to recent changes in medications, use of mental health services for chronic pain management within the past year, or recent/upcoming interventional procedures who otherwise meet all inclusion criteria and are interested in participating will be asked if they would like to be re-contacted in the future by study staff when appropriate timeframes have passed for re-evaluation of eligibility.

Procedures.

Upon completing baseline measures and meeting all eligibility criteria, participants will be randomly assigned to (1) Brief CBT-CP plus TAU or (2) TAU only. Assignment to Brief CBT-CP will be stratified based on degree of pain interference as measured by the Brief Pain Inventory (14). Participants will be classified as moderate interference (mean BPI interference subscale score ≥4 and <7) or severe interference (mean BPI interference subscale score ≥7). All participants will complete a follow-up (face-to-face, telephone, or VVC) with the study coordinator, who will be blinded to participants' condition at 12 weeks (post-treatment) randomization for re-administration of study measures. On an as-needed basis, we will contact participants through telephone, secure Azure RMS email, or through standard mail to provide appointment reminders and follow-up in case of missed appointments. Participants will be compensated $50 for the initial assessment and $50 for each of three follow ups (total $200).

Measures of Patient Outcomes.

Administration of all study measures below will take about one hour at each time point:

Brief Pain Inventory (BPI). The BPI is an extensively validated 9-item scale that includes a subscale to assess pain-related interference in daily activities and social functioning (14). It is the primary patient outcome for this trial. The BPI also includes an assessment of pain intensity which will be used as a secondary outcome. Both subscales are considered core outcome measures for pain management effectiveness trials.

*Patient Health Questionnaire-9 (PHQ-9).*This is a 9-item measure of depressive symptoms validated for use in primary care (15). Respondents are asked to rate symptoms experienced over the past two weeks on a four-point scale ranging from not at all (0) to nearly every day (3). The PHQ-9 is included because depression, as an indicator of emotional functioning, is a core outcome domain for all pain clinical trials.

World Health Organization Quality of Life - BREF (WHOQOL-BREF). This 26-item abbreviated version of the well-validated, full-length WHOQOL measure evaluates quality of life in several domains such as social relationships and satisfaction with person-environment interactions (16). WHOQOL-BREF is included to determine if Brief CBT-CP can improve overall quality of life across multiple domains of function.

Ability to Participate in Social Roles and Activities – Short Form (APSRA-SF). This 8-item measure was developed to evaluate one's perceived ability to perform usual social roles and activities. Negatively worded items about social role engagement are rated on a scale from 1 (always) to 5 (never) such that higher scores represent fewer limitations. This measure has been shown to have excellent psychometric properties and clinical utility (17).

Demographics. We will gather participant background information by asking them to self-report standard demographic variables (e.g., age, gender, race/ethnicity, income, education, service era, etc.) for purposes of describing our sample and for potential effect modifiers (i.e., age and gender).

Therapist training and assessment of fidelity.

The interventionists will be trained by the PI in how to apply the protocol. Training will include at least 20 hours of didactic explanations of the principles of each intervention, role play and feedback exercises, discussion of case examples, and skill rehearsal. Following the above training requirements, audio recorded sessions will be reviewed from the first three patients assigned to each interventionist during weekly supervision to provide additional feedback/instruction based on rating scale scores. As shown in the Brief CBT-CP Adherence Ratings Scale, critical components are protocol-specific aspects of the intervention related directly to psychoeducation or skill development (e.g., describing the biopsychosocial model of pain or providing instruction in relaxation training). Non-critical components (e.g., agenda setting, reinforcing at-home practice, session length) are important aspects of most CBT-based treatment for the PCMHI setting but are not intervention specific and, therefore, do not necessarily adversely impact dose of CBT. If adherence measure scores are below cut off, the interventionist will receive feedback and be assigned additional role play/training cases until deficiencies are corrected.

Study conditions.

Brief CBT-CP plus TAU: In summary, Brief CBT-CP is a manualized protocol that includes six, 30-minute sessions over the course of 12 weeks. Session one focuses on foundational pain education and the development of treatment goals. Session two emphasizes balanced engagement in physical activity and pleasurable events. Session three emphasizes skills training for easily implemented relaxation techniques. Sessions four and five focus on recognizing and modifying unhelpful thoughts that negatively impact pain. Session six focuses on relapse prevention and independent implementation of CBT-CP skills following treatment. Progress across sessions is measured by routine use of the PEG and two items inquiring about completing homework and skills practice. These brief items are administered by the study interventionists as part of the treatment protocol. Brief CBT-CP will be delivered face-to-face (primary care clinics or reserved clinical research space), telephone, or VVC depending on patient preference and safety issues related to COVID-19. Patients will be provided with the Brief CBT-CP Patient Guidebook as part of their treatment. Sessions will be audio recorded for review by PI or designee for fidelity assessment.

TAU only: Participants assigned to TAU only will receive standard medical care from their primary care provider including pain medications, brief advice (e.g., use of relative rest and self-care strategies), or referral to adjunctive interventions (e.g., physical therapy, chiropractic, standard PCMHI, etc.), as indicated.

Power Analyses.

Our primary aim of this longitudinal, two-arm, parallel RCT is to adequately test our primary null hypothesis of no differences in pain-related activity inference measured by the BPI Interference (BPI-I) subscale between Brief CBT-CP plus TAU and TAU-only across a 12-week treatment period. Multilevel

modeling (MLM) using a random coefficients model will be used to test this hypothesis by assessing the group by time fixed effect coefficient. A sample size of 184 (92 per group) offers at least 80% power to detect a small to medium effect of .35 in the group by time coefficient with an experiment-wise alpha of .05 (2-tailed). To estimate sample size, we employed the method proposed by Hedeker, et al. for multilevel longitudinal designs (18) using results from our Brief CBT-CP clinical demonstration project. Our sample size is adjusted for an overall 25% attrition rate split across treatment (12%) and follow-up (13%) study periods.

Statistical Analysis

Statistical analyses will be conducted using SAS v9.4. The primary analysis will be conducted using the intention-to-treat approach; participants who are randomized will be analyzed according to their assigned group regardless of amount of treatment received. The data will be screened for missing cases, outlier scores, and non-normal response distributions. Assumptions underlying statistical models will be assessed by examining standardized residuals, influence diagnostics, and homogeneity of variance (e.g., among groups).

A multilevel model (MLM) will be used to test the primary null hypothesis of no difference in pain-related activity interference measured by the BPI Interference subscale between Brief CBT-CP plus TAU and TAU-only against the two-sided alternative. Our MLM will consist of fixed and random effects. Fixed effects will consist of group, time of assessment, and a cross-level interaction between condition and time. The condition effect compares the baseline BPI-I score between Brief CBT-CP plus TAU and TAU-only. Time will be entered in our model as a nominal variable representing effects relative to baseline at weeks. In other words, baseline (t0) will be defined as the reference level allowing dummy indicators to estimate differences in BPI-I from baseline. The β of the 12-week primary treatment effect will be tested against a two-sided alternative.

Similar to our primary outcome measure of pain-related activity interference, we intend to utilize MLM to assess secondary subjective outcomes (i.e., pain intensity, depression symptoms, suicidal ideation, quality of life, and social role engagement). Comparing multiple correlated outcomes on the same set of patients tends to inflate the number of incorrect rejections of the null hypothesis. Thus, the Benjamini-Hochberg False Discovery Rate (FDR) procedure (19), described in further detail below, will be utilized to preserve the proportion of incorrect rejections (among rejected hypotheses) at 5% .

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