



Co-Operative Pain Education and Self-management (COPES) Expanding Treatment for Real-World Access (ExTRA): Pragmatic Trial Protocol

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Funding sources: This work is supported by the National Institutes of Health (NIH) through cooperative agreement U24AT009769 from the National Center for Complementary and Integrative Health and cooperative agreement UG3/UH3-AT009767 from the National Center for Complementary and Integrative Health, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Nursing Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Disclaimer: Sarah L. Krein, Todd Wagner, and John D. Piette are Department of Veterans Affairs career research scientists. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the US government. This article is a product of the National Institutes of Health–Department of Defense–Department of Veterans Affairs Pain Management Collaboratory. For more information about the Collaboratory, visit <https://painmanagementcollaboratory.org/>.

Conflicts of interest: The authors report no conflicts of interest.

Supplement sponsorship: This article appears as part of the supplement entitled “NIH-DOD-VA Pain Management Collaboratory (PMC)”. This supplement was made possible by Grant Number U24 AT009769 from the National Center for Complementary and Integrative Health (NCCIH), and the Office of Behavioral and Social Sciences Research (OBSSR). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCIH, OBSSR, and the National Institutes of Health.

Abstract

Background. Given access barriers to cognitive behavioral therapy for chronic pain (CBT-CP), this pragmatic superiority trial will determine whether a remotely delivered CBT-CP intervention that addresses these barriers outperforms in-person and other synchronous forms of CBT-CP for veterans with musculoskeletal pain. **Design.** This pragmatic trial compares an asynchronous form of CBT-CP that uses interactive voice response (IVR) to allow patients to participate from their home (IVR CBT-CP) with synchronous CBT-CP delivered by a Department of Veterans Affairs (VA) clinician. Veterans (n=764; 50% male) with chronic musculoskeletal pain throughout nine VA medical centers will participate. The primary outcome is pain interference after treatment (4 months). Secondary outcomes, including pain intensity, depression symptom severity, sleep, self-efficacy, and global impression of change, are also measured after treatment. Where possible, outcomes are collected via electronic health record extraction, with remaining measures collected via IVR calls to maintain blinding. Quantitative and qualitative process evaluation metrics will be collected to evaluate factors related to implementation. A budget impact analysis will be performed. **Summary.** This pragmatic trial compares the outcomes, cost, and implementation of two forms of CBT-CP as delivered in the real-

world setting. Findings from the trial can be used to guide future policy and implementation efforts related to these interventions and their use in the health system. If one of the interventions emerges as superior, resources can be directed to this modality. If both treatments are effective, patient preferences and health care system factors will take precedence when making referrals. Implications of COVID-19 on treatment provision and trial outcomes are discussed.

Key Words: Chronic Pain; Nonpharmacologic Treatment; Pragmatic Trial; Cognitive Behavioral Therapy; Interactive Voice Response; Technology

Background and Rationale

Cognitive behavioral therapy for chronic pain (CBT-CP) is one of the most widely used evidence-based nonpharmacologic interventions for pain [1, 2]. CBT-CP is a manualized, skills-based psychological treatment that typically entails 8–12 weekly 50-minute in-person sessions delivered in an individual or group format. Barriers to the uptake of evidence-based psychological interventions including CBT-CP are common [1]. A shortage of trained therapists and expertise in psychological treatments for pain [3], especially in rural areas and outside academic medical settings, often limits access to psychological treatments for pain [4, 5]. In response to this shortage, the Department of Veterans Affairs (VA) Evidence-Based Psychotherapy (EBP) program trained over 400 VA mental health clinicians to deliver CBT-CP to VA patients [5]. Despite this larger workforce, CBT-CP providers may face high caseloads (including non-CBT-CP cases) and competing demands within a health system that delivers care for multiple mental health conditions. Even when CBT-CP is available, patient-level barriers to engagement in CBT-CP such as stigma and scheduling and transportation difficulties exist [6]. Attending multiple in-person visits increases patient burden and is associated with patient attrition and lower-than-optimal treatment dose [7].

Technology can be used to address these barriers through both synchronous and asynchronous treatment delivery. Synchronous delivery (i.e., in real time), such as through videoconferencing, allows patients to attend treatment from home, thereby reducing travel burden and stigma while maintaining real-time interaction between the therapist and patient. Asynchronous treatment delivery (i.e., without real-time interaction) uses technology to acquire patient data and transmit it to a clinician for later review and feedback. Similar to synchronous delivery, asynchronous treatment delivery allows treatment from home and reduction of stigma and travel barriers, but because treatment does not involve a real-time interaction, it can occur at the patient's convenience (e.g., outside normal business hours). Finally, providers spend less time per patient, so more patients can receive CBT-CP at a given staffing level.

Interactive voice response (IVR) is a telephonic-based treatment approach that allows asynchronous monitoring of patient progress and delivery of personalized feedback. Prior studies have shown that the use of IVR calls and feedback following in-person CBT-CP resulted in maintenance and even improvement of treatment effects [8, 9]. The Co-Operative Pain Education and Self-management (COPEs) program is an IVR-delivered CBT-CP program. In a non-inferiority trial comparing in-person CBT-CP to COPEs IVR-delivered CBT-CP, statistically significant improvements in physical functioning, sleep quality, and physical quality of life relative to baseline occurred in both treatments, with no significant advantage for either treatment [10]. Patients participating in the COPEs program reported comparable treatment satisfaction and a significantly larger dose (i.e., greater number of CBT contacts) relative to patients who had to travel to a health center to receive treatment [10, 11]. However, given that COPEs addresses problems that are largely related to system and feasibility concerns, a tightly controlled trial may not reflect the true effectiveness of the intervention when accounting for real-world factors, such as how closely the trial participants correspond to the patients in the clinical setting where the treatment will eventually be delivered, patient access to treatment, and therapist availability [12]. Instead, a pragmatic trial, which tests interventions in real-world settings with fewer restrictions than standard clinical trials, may be a more accurate indication of the effectiveness of IVR-delivered CBT-CP.

This article describes the study protocol for one of the pragmatic trials within the National Institutes of Health (NIH)–Department of Defense (DOD)–VA Pain Management Collaboratory [13] called Co-Operative Pain Education and Self-management: Expanding Treatment for Real-World Access (COPEs ExTRA). COPEs ExTRA builds on the findings from the original COPEs trial by assessing the relative effectiveness in real-world clinical practice settings, comparing COPEs IVR CBT-CP with standard CBT-CP with clinicians delivering the treatment as part of their normal clinical duties. The large sample size and broader inclusion criteria will make it possible to identify the relative effectiveness of the interventions within patient populations that are

commonly excluded from explanatory trials, such as patients with pain and comorbid substance abuse. To inform future implementation efforts, the trial includes a budget impact analysis and qualitative interviews to identify barriers to implementation related to treatment referral, uptake, and adherence.

Methods

Study Objectives

The aims of the study are as follows:

Aim 1a: Determine whether asynchronous COPES (IVR CBT-CP) plus usual care (UC) are superior to synchronous CBT-CP plus UC at 1, 4 (primary end point), 6, and 12 months after enrollment, with respect to 1) pain interference (Brief Pain Inventory [BPI] Interference subscale—primary outcome) [14]; 2) secondary outcomes, including total BPI score, pain intensity, overall pain impact, insomnia, pain catastrophizing, pain self-efficacy, depressive symptoms, alcohol misuse, and patient-rated change in condition; and 3) health care use.

Aim 1b: Evaluate uptake, engagement, and variation in outcomes across groups where treatment disparities are possible (e.g., gender, race or ethnicity) and among patients with comorbid substance use disorders who have traditionally been excluded from similar trials.

Aim 2: Evaluate the intervention costs and conduct a budget impact analysis.

Aim 3: Conduct a process evaluation using the Consolidated Framework for Implementation Research (CFIR) framework to guide our evaluation [15].

Overall Design

This is a randomized hybrid type 1 pragmatic superiority trial comparing a technology-based form of CBT-CP allowing patients to participate from their homes and including IVR monitoring and psychoeducation (IVR CBT-CP) vs CBT-CP delivered by a VA clinician at an outpatient center (see [Supplementary Data](#) for Consolidated Standards of Reporting Trials [CONSORT] flowchart). As illustrated by the PRagmatic-Explanatory Continuum Indicator Summary (PRECIS) figure (see [Supplementary Data](#)), where possible, pragmatic rather than explanatory trial methods are used [16]. Explanatory trials are conducted in ideal conditions and emphasize internal validity, whereas pragmatic trials attempt to mimic real clinical practice and emphasize generalizability. Consistent with a pragmatic approach, screening, consenting, randomization, and outcome collection are conducted by telephone from the study coordinating center so that research staff are not needed at the recruitment sites and the study does not disrupt clinic flow. The eligibility criteria are inclusive and designed to accrue participants that are representative of patients with chronic musculoskeletal pain receiving care from the VA, including patients with comorbid pain and substance abuse. The data analysis plan includes nonadherent participants to capture real-world attendance patterns. Nonpragmatic

aspects of the trial include addition of central clinical staff and an IVR system to support IVR CBT-CP because it is not part of standard VA clinical care. In addition, few relevant treatment outcomes are collected by the health system, requiring the addition of research assessments that limit truly pragmatic outcome collection. Finally, the frequency of outcome assessment is greater than typical in clinical care to allow for examination of initial treatment response and durability of treatment effects.

Study Population: Inclusion and Exclusion Criteria

Participants are veterans with chronic musculoskeletal pain (N=764) from nine VA health care systems. This study was approved by the VA Central Institutional Review Board and the Yale School of Medicine Human Investigation Committee (NCT03469505). Inclusion criteria are as follows:

An electronic health record (EHR)-identified Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) musculoskeletal and connective tissue (M code) condition. Eligible codes include the most commonly diagnosed musculoskeletal and connective tissue conditions in VA settings, including spine conditions, osteoarthritis, joint pain, fibromyalgia, rheumatoid arthritis, and two commonly used non-M-code diagnoses: chronic pain syndrome and pain disorder with related psychological factors.

Presence of chronic pain of at least moderate severity (two or more pain intensity numeric rating scale [NRS] ratings of ≥ 4 in for a period of 12 months, with at least 30 days between occurrences, collected via EHR).

Ability to participate safely in the walking portion of the intervention (patient-reported ability to walk at least one block and absence of foot ulcers and recurring falls at enrollment).

Availability of a touch-tone landline or cellular telephone.

Exclusion criteria are as follows:

Current inpatient psychiatric hospitalization for detoxification of alcohol or drugs or acute psychotic episode.

Receipt of hospice or end-of-life palliative care.

Dementia-related diagnosis.

Patient-reported or verified vision or hearing deficits that would impede participation.

Current participation in CBT-CP.

Any medical intervention that would cause a meaningful increase in pain such as surgery, chemotherapy, or radiation therapy.

Screening, Recruitment, and Randomization Procedures

An EHR referral alert developed for the trial will be triggered during a patient's clinical visit when EHR data indicate inclusion criteria 1 and 2 and do not indicate exclusion criterion 3 (see [Supplementary Data](#) for details). The EHR alert 1) states that the patient could benefit from CBT-CP; 2) describes CBT-CP and how to present it to the patient; and 3) facilitates an interfacility consult to coordinating center staff. When a site has agreed, patients may self-refer to the study team using a

toll-free number included in recruitment materials placed in outpatient clinics.

After receiving a provider- or patient-initiated referral, study staff at the study coordinating center contact patients by telephone; assess patient interest; and confirm eligibility, including pain chronicity, walking safety, touch-tone phone availability, absence of sensory deficits, and no current involvement in CBT-CP or medical interventions that may increase pain. Interested patients provide consent using a web-based or mailed consent document—assessed for high-impact chronic pain [17], over-the-counter pain reliever use, and complementary and integrative health use—and are scheduled for an automated IVR baseline assessment. After completing the baseline assessment, participants are randomly assigned in a 1:1 ratio to either IVR CBT-CP or synchronous CBT-CP. Participants who are randomly assigned to synchronous CBT-CP are assigned using local site procedures to a VA CBT-CP therapist who delivers treatment as part of their usual clinical duties. Participants randomly assigned to IVR CBT-CP will be enrolled in the IVR system by study staff. The randomization sequence was generated by the study statistician using statistical software and is concealed in the study database until the time of randomization. Randomization is stratified by site and gender and uses a permuted block design with a variable block size (four and six) to maintain balanced treatment assignment.

Participating Sites

Nine VA medical centers that are part of the VA Women's Health Practice-Based Research Network (WH-PBRN) have agreed to participate as recruitment sites and to provide the synchronous CBT-CP locally. Because women are underrepresented in the VA, the WH-PBRN was engaged to facilitate obtaining a sample of 50% women in order to test for gender differences in outcomes. The VA Connecticut site serves as the coordinating center and provides screening, randomization, and IVR CBT-CP.

Interventions: Interactive Voice Response Cognitive Behavioral Therapy for Chronic Pain and Synchronous Cognitive Behavioral Therapy for Chronic Pain

COPEs IVR CBT is a 10-week asynchronous IVR-facilitated program of CBT-CP that includes daily IVR assessment of pain and treatment-relevant data, a graduated walking program, goal-based skill practice, and weekly therapist feedback messages [11]. Prior to treatment, all participants are mailed a pedometer and provided access to the COPEs patient manual. The treatment includes an introductory module that presents the rationale for CBT-CP, eight pain coping skill modules, and a relapse prevention module. A single self-management skill (e.g., paced physical activity,

stretching, or relaxation) is the focus of each week. Therapists use a manual developed in prior trials to guide the creation of participant feedback messages. After therapists complete initial training, the senior IVR CBT-CP therapist monitors treatment fidelity and provides feedback to therapists for 30% of treatment sessions. Participants have three weekly goals: 1) practice the current week's pain coping skill as assigned in the patient manual (e.g., practice deep breathing for 5 minutes each day this week); 2) meet a daily step target calculated by their therapist, based on their prior week's average daily step count plus an additional 10%; and 3) accomplish a self-generated weekly meaningful activity using the specific, measurable, achievable, relevant, and timely (SMART) framework.

One week prior to starting treatment and continuing through an immediate 1-week post-treatment period (12 weeks total), participants receive daily IVR assessments of pain interference, pain intensity, sleep duration, sleep quality, pedometer-measured step count, catastrophizing, task persistence, skill practice rating, and pain self-efficacy and weekly meaningful goal attainment rating. Participants select a time between 6:00 PM and 10:30 PM to receive their daily IVR assessment call. Participants have three opportunities per day to complete an IVR system-initiated call or they may call into the system before it is considered missed for the day. Participants can connect automatically to the VA Suicide Prevention Hotline during any IVR call. Therapists use daily IVR assessment data to construct a weekly 2- to 4-minute personalized feedback message. The message is recorded and made available to participants at the end of the usual IVR assessment call on the final day of each treatment week.

Synchronous Cognitive Behavioral Therapy for Chronic Pain Intervention

Synchronous (in-person, telephone, or videoconference) CBT-CP is delivered by a VA clinician as part of their usual duties. CBT-CP is part of VA's EBP initiative, and therapist training includes didactic attendance, recording and evaluation of treatment sessions, and ongoing expert consultation. The treatment is a 10- to 11-week structured intervention that teaches patients to manage chronic pain and has been shown to support patient improvements in areas such as pain interference and quality of life [18,19]. Each CBT-CP session includes agenda-setting, pain-related content review, and patient materials for learning and home practice. A detailed CBT-CP therapist manual [20] includes pain education, case examples, treatment guidance, and materials.

Participants will receive CBT-CP as delivered at their medical center, which will include individual or group treatment sessions with a CBT-CP therapist, defined by completion of the VA's CBT-CP EBP program and/or prior training and experience in a doctoral or

postdoctoral setting or employment as a VA pain psychologist. Given the COVID-19 pandemic, treatment will be delivered using various methods, including individual and group in-person sessions, telephone sessions, and videoconferencing. In the spirit of a pragmatic trial, we will not attempt to influence how synchronous CBT-CP is provided, but we will track treatment method, fidelity, and treatment engagement (see the *Treatment Provision Characteristics* section).

Baseline and Follow-Up Procedures

Demographic variables, covariates, and outcome measures are extracted from the EHR when possible and supplemented with automated IVR patient-reported data collection. Outcomes and covariates are assessed at baseline and at 1, 4, 6, and 12 months after baseline. The fourth-month outcome is the primary outcome. To refine and evaluate the implementation and use of the study interventions, we will conduct a two-phase evaluation using qualitative interviews occurring during and following site start-up. This evaluation supplements an initial evaluation of sites that occurred in the planning phase of the study and contributed to final site selection.

Primary and Secondary Outcomes

Automated IVR assessment calls allow blinded assessment of patient-reported outcomes. Outcome assessment calls take approximately 7–9 minutes to complete. The primary outcome is the Interference subscale of the BPI score [14], which is not collected routinely as part of standard CBT-CP in the VA and assesses patient-reported pain-related interference. Total pain impact will be assessed with the total BPI score and the Pain, Enjoyment of life, and General activity (PEG-3) scale, which is a common measure collected across Pain Management Collaboratory Coordinating Center trials [14, 21]. Depression symptom severity will be assessed using the eight-item Patient Health Questionnaire (PHQ-8) [22]. Sleep quality will be measured using the Insomnia Severity Index [23]. Catastrophizing will be measured using the Short Form of the Pain Catastrophizing Scale (PCS-SF), a two-item self-report scale that examines thoughts and feelings people may experience when they are in pain, including rumination, magnification, and helplessness [24]. Self-efficacy will be assessed using the two-item Short Form of the Pain Self-Efficacy Questionnaire (PSEQ-2) [25]. The Patient Global Perception of Change scale, will measure a participant's overall perception of improvement since beginning treatment [26]. The Alcohol Use Disorders Identification Test—Concise (AUDIT-C) identifies problematic drinking [27]. Each participant's self-reported COVID-19 status and its effect on their ability to access health care, obtain social support, and meet basic needs and its effect on their mental health will be assessed using

the Pain Management Collaboratory Coronavirus Pandemic Measure.

Covariates and Outcomes Extracted from Electronic Health Record

Other covariates and outcomes will be extracted from the EHR, including sociodemographic characteristics, musculoskeletal (prior 12 months) and psychiatric (prior 18 months) diagnoses, distance to the nearest VA facility, NRS pain intensity ratings, opioid medications dispensed in morphine equivalent daily dose, and service use (e.g., specialty care, urgent care, emergency department visits). See [Supplementary Data](#) for details.

Treatment Provision Characteristics

A trained research assistant will review each participant's EHR or IVR data at the completion of treatment to collect treatment characteristics (mode), treatment initiation (yes or no, completed the first CBT-CP session or IVR CBT-CP call week), time to treatment initiation, number of sessions completed, time to completion, completion of all 10 sessions (yes or no), and treatment quality using a standardized data extraction tool.

Qualitative Interviews

Interview guides will be developed using constructs and questions derived from the CFIR [15] and tailored to the informant group being interviewed (mental health provider, primary care provider, or administrator). Interviews will be audio-recorded and professionally transcribed. Individual telephone interviews will be conducted with staff who provide clinical care, are directly involved in patient referral to CBT-CP, or supervise primary care or mental health clinics.

Sample Size Determination

Assuming a standard deviation of BPI interference of 2.4 (as observed in a previous study [Stepped Care to Optimize Pain Care Effectiveness, SCOPE]) [28], a total sample size of 610 participants (305 per group) would provide 80% power to detect a mean difference in BPI interference of 0.55 between groups at 4 months using a two-sided t test at a significance level of $\alpha=0.05$ and 90% power to detect a difference of 0.63. To account for an expected attrition rate of 20%, we will enroll a total of 764 participants (382 per group). Half of the participants will be female.

Analytic Methods

The analysis will be done at $\alpha=0.05$ according to the intent-to-treat (ITT) principle. We will compare IVR CBT-CP and CBT-CP in terms of BPI interference by using a linear mixed-effects model that simultaneously models all BPI interference measurements, including baseline. The model will contain fixed effects for treatment (categorical: IVR CBT-CP vs CBT-CP); time

(categorical: baseline and 1, 4 [primary end point], 6, and 12 months); the treatment \times time interaction; and the stratification variables: site (categorical) and gender (categorical). An unstructured matrix will be used for modeling within-subject correlations, and a therapist random effect will be used for modeling the correlation of outcomes in participants with the same therapist. In the aforementioned model, we will impose the constraint that the means for the two groups must be equal at baseline (i.e., we will perform a constrained longitudinal data analysis). Results will be summarized as least-squares means (and their 95% confidence interval).

We will perform a sensitivity analysis of the primary outcome (BPI interference at 4 months) that accounts for the synchronous CBT-CP delivery mode. The treatment group will be a three-level variable: video or telephone CBT-CP, in-person CBT-CP, and IVR CBT-CP. This will allow us to compare the two types of synchronous CBT-CP with each other and separately with IVR. Because participants in the synchronous arm will not be randomly assigned to mode of delivery, we will use propensity score methods to balance the three groups in terms of baseline covariates. We will use Holm's correction to adjust for multiple secondary analyses. We will also conduct a per-protocol analysis as an adjunct to the ITT primary analysis, defining a "dose" of treatment as having attended or answered calls for three treatment sessions. Analysis of the continuous secondary outcomes collected by IVR will be similar to the primary analysis. We will use a generalized mixed model for ordinal data to analyze the Patient Global Impression of Change. Analysis of pain intensity NRS scores will use a mixed model with fixed effects for treatment; site; gender; time of clinic visit (days since randomization); the treatment \times time interaction; and random effects for intercept, slope, and therapist. We will use a polynomial function of time (e.g., quadratic) if appropriate. We will consider within-subject correlation structures for unequally spaced data and will select the best structure based on the Akaike information criterion.

"Treatment initiation" will be defined as a patient attending at least one session of CBT-CP or completing at least one treatment week of IVR CBT-CP. Time from randomization to treatment, number of sessions attended, time from randomization to completion, completion (yes or no completed at all 10 sessions; binary variable), and treatment satisfaction at 4 months (continuous variable) will be examined. We will compare initiation, number of treatment sessions, completion, and treatment satisfaction at 4 months between groups by using a negative binomial logistic generalized linear mixed model and a linear mixed model as appropriate. Time to treatment and completion will be analyzed using Cox proportional hazards models. All models will include treatment, site, and gender as fixed effects and a random effect for therapist. To test whether between-group differences in outcomes vary by gender, race or ethnicity,

comorbid substance use disorder, and alcohol use, subgroup analyses will be performed via interaction tests.

For the budget impact analysis, we will measure the cost of the intervention using direct measurement. Data from CBT-CP therapists' time records will be combined with VA wage data to produce estimates of intervention-specific personnel costs. We will also estimate intervention costs related to other personnel, supplies, CBT-CP therapist training, and IVR costs. The budget impact analysis will compare the intervention costs relative to patient downstream costs. Costs for medical care, such as medications, will be obtained from the VA Managerial Cost Accounting System. The budget impact analysis will be based on the VA's perspective with a short-term, 1-year time horizon. Cost analysis will be conducted in accordance with the study conducted by Sullivan et al. [29]. Cost comparisons will be adjusted for observed differences in baseline characteristics. Because costs of resource utilization are usually skewed, alternative modeling techniques (e.g., log-transformed costs, negative binomial regression) will be used in sensitivity analyses.

When considering missing data, the inferences from the mixed model for the primary analysis are valid under the missing at random (MAR) assumption. Because it is not possible to distinguish between MAR and missing not at random (MNAR) based on observed data, we will conduct our primary analysis under the MAR assumption (mixed model) and conduct sensitivity analyses to see how results change under different missing data assumptions.

Qualitative Analysis

We will develop a template summary of data at each facility according to a small set of predetermined domains that align with the interview guides developed for each group of respondents. Once we have developed that summary for each facility, we will create a matrix across all facilities to understand the major issues with regard to implementation. Matrices streamline the process of noting the similarities, differences, and trends in responses across a group of informants [30]. Analysis of qualitative data will be conducted using ATLAS.ti software.

Implementation and Dissemination Procedures

The findings of this trial, including information on treatment effect, engagement, cost, and barriers and facilitators to implementation, will be shared with VA operations leadership, clinicians, and patients. The clinical impact of the treatments will be evaluated in terms of their effectiveness, reach, and cost, both in absolute terms and relative to other available treatments, thus providing information beyond that obtained from our prior efficacy and implementation trials. We will focus on disseminating information related to the implementation and potential program maintenance of COPES as a sustainable, compatible program within the VA health system. We

will share results about the outcomes and implementation of both CBT-CP interventions with VA operational leaders in the National Pain Management Program Office and the EBP program. Dissemination efforts will take advantage of existing resources, including the VA Pain/Opioid Consortium of Research and the Pain Research, Informatics, Multi-Morbidities, and Education Center. We will prepare patient- and provider-facing information describing the relative strengths and weaknesses of the two forms of CBT-CP and the variation in outcomes across groups if present (e.g., gender, race or ethnicity) to inform provider referral and patient engagement in treatment. Our use of an EHR-based referral to enhance recruitment and automated IVR calls to collect outcomes with reduced participant burden may prove to be useful methods for future investigators. Although these methods are not entirely novel, their use on a large scale and in support of pragmatic methods may bolster future use in similar large-scale pragmatic trials.

Discussion

CBT-CP is an evidence-based intervention that is available through the VA, and significant resources have been committed to its widespread dissemination throughout the EBP program. Although it is not currently widely implemented, IVR CBT-CP offers a highly scalable approach that could provide an enterprise-wide treatment option. The treatments have different strengths and weaknesses, which may emerge more clearly in a pragmatic trial that evaluates how treatments perform when examined as provided in real-world settings. If synchronous CBT-CP or IVR CBT-CP demonstrates superior effectiveness in this trial, there will be evidence to recommend one over the other as the first-line treatment option for patients with chronic musculoskeletal pain. Increased efforts can then be directed toward enhancing capacity for this treatment option. Alternatively, we may find that the treatments are not significantly different. In this case, patient preference and feasibility concerns within the health care system, such as costs and the need to train therapists, will be more salient factors in the recommendation of treatment. The pragmatic nature of the study also provides the opportunity to examine whether common comorbidities of chronic musculoskeletal pain such as substance use disorders and individual difference variables (including gender and race or ethnicity) modify treatment engagement, participation, and outcomes.

The trial began recruiting participants in November 2019, shortly before the COVID-19 pandemic prompted the VA to discontinue most in-person clinical appointments and move to virtual treatment delivery in March 2020. In the original study design, the comparison group was in-person CBT-CP. Due to VA clinical guidelines limiting face-to-face outpatient interactions during the COVID-19 pandemic, the comparison group has been modified to allow additional modes of treatment

delivery, including via live telephone and video chats. The IVR intervention remains unchanged. We have consulted with the Pain Management Collaboratory Coordinating Center Biostatistics Work Group to adapt our analysis plan to the changes in the in-person condition. Access to treatment from home was one of the factors that justified the hypothesized superiority of IVR CBT-CP. However, we still expect IVR CBT to be superior. We assume that the dose will be greater in the IVR condition because patients can access treatment at any time, even outside business hours; session time is shorter, reducing therapist and participant burden; and time to treatment will be shorter because the centralized delivery of IVR CBT allows more efficient use of therapist resources. We developed a plan to monitor the treatments for evidence of a difference in treatment initiation, number of treatment sessions, and time to treatment (see the *Treatment Provision Characteristics* section); enact a futility analysis if the advantage is not present; and conduct sensitivity analyses to evaluate the impact of treatment modality on the primary outcome.

Despite COVID-related challenges, this trial is well positioned to contribute needed evidence in the realm of technology-based psychological treatment for chronic pain and to explore differences in the engagement, outcomes, cost, and implementation of an asynchronous technology-based intervention relative to in-person and synchronous technology-based care. When COVID conditions improve, in-person CBT-CP treatment can resume, allowing us to assess how many patients receive virtual vs in-person care and to examine patient and therapist factors associated with those choices. Many patients do not receive recommended evidence-based care due to barriers to its widespread implementation and uptake. Understanding factors that impede widespread use of CBT-CP is necessary to ensure that more patients have access to and receive this evidence-based, low-risk pain care. Planned sensitivity analyses to compare outcomes across treatment delivery modes will address a key knowledge gap regarding the relative effectiveness of IVR, in-person, and videoconferencing treatment provision.

Supplementary Data

[Supplementary Data](http://pain-medicine.oxfordjournals.org) may be found online at <http://pain-medicine.oxfordjournals.org>.

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