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Whole Health Options and Pain Education (wHOPE): A Pragmatic Trial Comparing Whole Health Team vs Primary Care Group Education to Promote Nonpharmacological Strategies to Improve Pain, Functioning, and Quality of Life in Veterans—Rationale, Methods, and Implementation

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Abstract

Background. The Whole Health model of the U.S. Department of Veterans Affairs (VA) emphasizes holistic self-care and multimodal approaches to improve pain, functioning, and quality of life. *w*HOPE (Whole Health Options and Pain Education) seeks to be the first multisite pragmatic trial to establish evidence for the VA Whole Health model for chronic pain care. **Design.** *w*HOPE is a pragmatic randomized controlled trial comparing a Whole Health Team (WHT) approach to Primary Care Group Education (PC-GE); both will be compared to Usual VA Primary Care (UPC). The WHT consists of a medical provider, a complementary and integrative health (CIH) provider, and a Whole Health coach, who collaborate with VA patients to create a Personalized Health Plan emphasizing CIH approaches to chronic pain management. The active comparator, PC-GE, is adapted group cognitive behavioral therapy for chronic pain. The first aim is to test whether the WHT approach is superior to PC-GE and whether both are superior to UPC in

decreasing pain interference in functioning in 750 veterans with moderate to severe chronic pain (primary outcome). Secondary outcomes include changes in pain severity, quality of life, mental health symptoms, and use of nonpharmacological and pharmacological therapies for pain. Outcomes will be collected from the VA electronic health record and patient-reported data over 12 months of follow-up. Aim 2 consists of an implementation-focused process evaluation and budget impact analysis. **Summary.** This trial is part of the Pain Management Collaboratory, which seeks to create national-level infrastructure to support evidence-based nonpharmacological pain management approaches for veterans and military service personnel.

Key Words: Chronic PainVeterans; Complementary and Integrative Health; Cognitive Behavior Therapy; Primary Care; Pragmatic Trial

Background and Rationale

The opioid crisis has led to a breakdown in the management of chronic pain that has negatively impacted both patients and providers [1]. National policies intended to reduce harms from opioids have put pressure on health care systems to change their approach to pain management, especially in primary care. Nevertheless, health care systems lack guidance for implementing more effective systems of nonpharmacological chronic pain care. Recent research suggests that pain care that incorporates multiple nonpharmacological biopsychosocial modalities, such as exercise, behavioral health, and complementary and integrative health (CIH), can be as effective as medication or more effective than medication for treating chronic pain, with more durable impact and fewer harms [2].

The VA's Whole Health model [3] can be applied to multimodal pain care for veterans. At the center of the model are activated patients practicing pain self-management supported by Whole Health–informed clinical providers and coaches who both deliver and facilitate access to traditional and evidence-based CIH approaches. Specifically, in this trial, a Whole Health Team (WHT) approach will be tested that consists of a Whole Health–informed team of providers who collaborate with veteran participants with chronic pain to create a Personalized Health Plan. The WHT approach expands on the evidence-based VA Integrated Pain Team [4] in its structured, patient-centered approach to supporting the health and wellness of the whole person and its emphasis on self-management, skill-building, and the use of nonpharmacological and CIH modalities. The VA is currently implementing the Whole Health model to prevent and manage chronic disease in veterans, yet there has been no trial to support its effectiveness for chronic pain management. This trial will compare a WHT approach with another intervention—Primary Care-Group Education (PC-GE), an adapted form of evidence-based cognitive behavioral therapy for chronic pain (CBT-CP) [5], which will be delivered in a group format in primary care. The two active interventions will each be compared with usual primary care (UPC), which in the VA represents Step 1 of the VA's established Stepped Care Model of chronic pain treatment, in which primary care providers are trained in biopsychosocial pain management [6].

Whole Health Options and Pain Education (*w*HOPE) seeks to be the first large, multisite pragmatic trial to establish evidence for the VA Whole Health model for chronic pain care and, as part of the National Institutes of Health (NIH)–Department of Defense (DOD)–VA Pain Management Collaboratory (PMC), will contribute to the overall mission to build national-level infrastructure to support evidence-based nonpharmacological pain management approaches for veterans and military personnel. As a pragmatic trial, *w*HOPE recently completed a 2-year developmental formative evaluation to determine how best to tailor implementation of the trial interventions to the needs, preferences, and resources of each participating enrollment site [7]. Now, with the COVID-19 global pandemic, the trial has needed to incorporate pragmatic adaptations to intervention delivery and data collection.

Methods

Study Objective

The overarching goal of this four-year, three-arm, multisite pragmatic randomized controlled trial is to compare two health care delivery approaches to chronic pain management. For Aim 1, a pragmatic randomized controlled trial design will be conducted in 750 veterans with moderate to severe chronic pain across five geographically diverse VA facilities to test the hypothesis that WHT will be superior to PC-GE and both will be superior to UPC with respect to the primary outcome, pain interference, as well as the following secondary outcomes: pain intensity, functioning and quality of life, use of higher-risk pain medications (e.g., opioids), engagement in nonpharmacological pain management activities, and improvement in mental health symptoms. Aim 2 is to facilitate future implementation and dissemination by a process evaluation and budget impact analysis.

Overall Design

Study participants will be screened for trial eligibility during recruitment (telephone screen) and enrollment (baseline assessment); approximately 750 eligible and

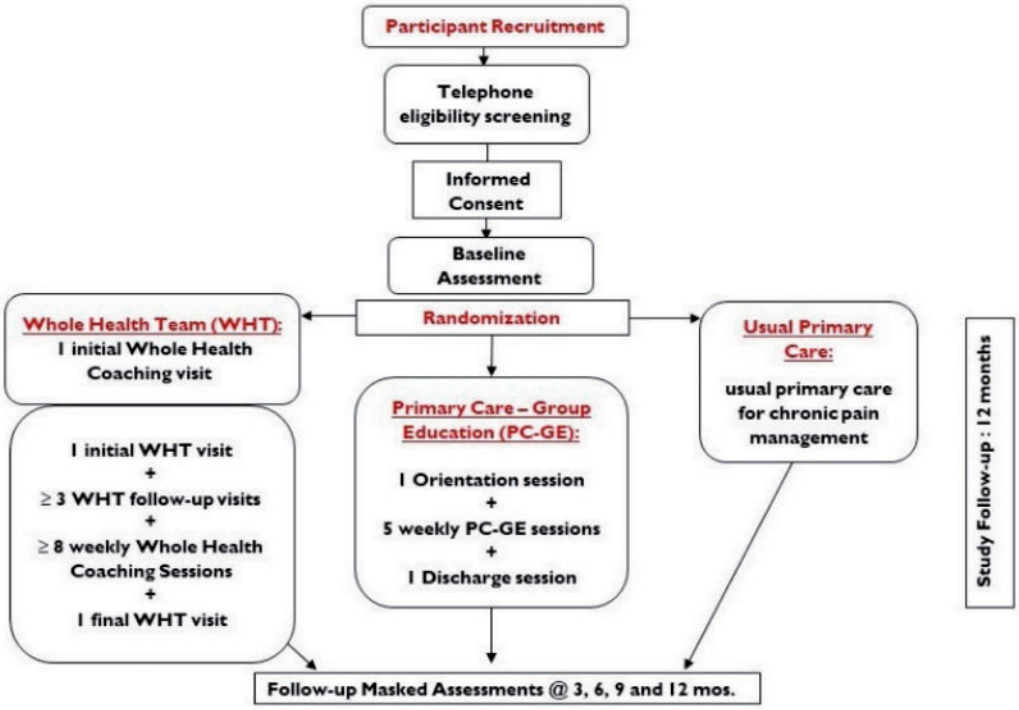

Figure 1. *w*HOPE trial flowchart.

consenting veterans with moderate to severe chronic pain will be randomized over a 24-month enrollment period (Figure 1 and Supplementary Data). The follow-up period for the three arms is 12 months, with data obtained from the VA electronic health record (EHR) and through patient self-report at baseline and 3, 6, 9, and 12 months. Concurrently, a process evaluation consisting of qualitative semi-structured interviews will be conducted with veteran participants and study stakeholders to better understand barriers to and facilitators of implementation of the study interventions across diverse enrollment sites. In addition, the costs of implementation and intervention activities will be collected for a budget impact analysis.

The Pragmatic Explanatory Continuum Indicator Summary (PRECIS)-2 (see Supplementary Data), a tool to help investigators design their studies on the pragmatic–explanatory continuum, was applied during the design of the *w*HOPE trial to maximize pragmatism with regard to 1) eligibility (includes most patients with chronic pain), 2) setting (geographically diverse VA facilities, including medical centers and community clinics); and 3) flexibility of intervention delivery (intervention tailored to site) [8]. The primary outcome, pain interference, is highly pragmatic because it captures patients' lived experiences and the impacts of chronic pain. The primary analytic strategy, intention to treat, is highly pragmatic in using data from all originally randomized participants. Less pragmatic trial design elements are recruitment and follow-up intensity. The use of centralized VA EHR databases for recruitment is aimed at addressing known barriers to recruiting patients with chronic pain, especially those receiving opioids [9]. Given the importance of patient-reported outcomes in pain research, the study design includes frequent telephone assessments by blinded study staff members. Finally, the VA's policy of converting as many clinic visits as possible to telehealth consultations during the COVID-19 pandemic pushed the trial design toward greater pragmatism, with UPC, WHT, and PC-GE visits designed to be flexibly delivered, either in person or by telehealth, depending on varying shelter-in-place and recovery plans at each of the enrollment sites.

Study Population

Because this is a pragmatic trial, the study inclusion criteria are selected to be as representative as possible while ensuring the safety of study participants. For study enrollment, participants must meet the following inclusion criteria: 1) have had at least one clinic visit to a primary care provider at a VA facility in the past year; 2) report pain present every day or nearly every day for $\geq$6 months; and 3) report overall pain severity on the Pain, Enjoyment of Life, and General Activity (PEG) scale of $\geq$5 [10]. Exclusion criteria are as follows: 1) moderate or severe cognitive impairment, as determined by a failed six-item, validated cognitive screener [11]; 2) active suicidal ideation, as determined by chart review or by the Patient Health Questionnaire (PHQ)–9 at baseline assessment; 3) unstable psychiatric or medical condition or receiving hospice care; or 4) other factors precluding study participation, such as lack of telephone service, being a non-English speaker, plans to relocate within

12 months, or concurrent participation in another pain trial. Phone eligibility screening will be used to ascertain eligibility criteria not available in the VA EHR (see section on Recruitment, Screening, and Enrollment Procedures).

Recruitment, Screening, and Enrollment Procedures

With a Health Insurance Portability and Accountability Act waiver for recruitment, the study will use VA EHR data as the primary source for recruitment. Patients eligible for recruitment will meet the following criteria: 1) had at least one clinic visit to a primary care provider at a VA enrollment site within the past year and reside within 100 miles of the site; 2) reported having at least two instances of the same pain diagnosis at two separate clinical visits at least 90 days apart within the past 2 years; and 3) reported a Numerical Rating Scale pain score of $\geq$4 on at least two clinical visits within a single year. Secondary recruitment streams for *w*HOPE include primary care referral and veteran self-referral.

The enrollment period will be 24 months. Contact information for eligible participants will be entered and securely stored in the San Francisco VA Health Care System's Data Coordinating Center's database. Each enrollment site's study coordinator will access the database to mail potentially eligible veterans recruitment materials, including study information sheets and opt-out letters. If opt-out letters are not returned in 10 days, potentially eligible veterans will be contacted by phone (up to five attempts) for eligibility screening with a phone eligibility screener. Preliminarily eligible and interested participants will be scheduled with the local site coordinator to complete a baseline assessment. At the appointed date and time, at the beginning of the baseline assessment, the study coordinator will e-mail a link to the electronic informed consent form. If a participant does not have e-mail, the coordinator will mail out the informed consent document before baseline assessment. The coordinator will read through the consent document, describing the purpose of the study, study procedures, and risks and benefits of participating, to ensure comprehension. If interested, eligible participants will be asked to electronically sign the online informed consent document or physically sign and return a mailed copy. After obtaining the e-signed or mailed consent, the study coordinator can begin the telephone baseline assessment. The baseline assessment will determine final eligibility for the trial, ensuring the absence of severe untreated mental health disorders, active suicidal ideation, obvious intoxication, delirium, or other severe cognitive impairment.

Randomization Procedures

After baseline assessment and study enrollment, each site will randomize enrolled patients to WHT, PC-GE, or UPC in randomly permuted blocks of three, six, and nine, stratified by site, gender, and current prescription opioid therapy status, yielding 20 strata. Randomization will be performed within strata, ensuring that the main covariates are balanced across treatment arms. Randomization code will be concealed and completed only once per study subject, preventing staff from influencing treatment allocation.

Participating Sites

The study consists of five geographically diverse enrollment sites: the San Francisco VA Health Care System (Data Coordinating Center), San Francisco, California; the VA Connecticut Healthcare System, West Haven, CT; VA Portland Health Care System, Portland, Oregon; James A. Haley Veterans Hospital, Tampa, Florida; and the VA St. Louis Health Care System, St. Louis, Missouri. In addition, the Central Arkansas Veterans Healthcare System, Little Rock, Arkansas, will serve as a back-up site should study enrollment fall below target. Co-investigators at the Minneapolis VA Health Care System, Minneapolis, Minnesota, will provide methodological support.

Interventions

WHT Intervention

WHT Core and Optional Intervention Elements. Given the pragmatic research framework, the WHT intervention is described in terms of *core* and *optional* components. The first core element of the WHT model is the interdisciplinary team of providers: a medical provider (e.g., physician, nurse practitioner) and an integrative health provider (e.g., mindfulness instructor, acupuncturist). At a minimum, WHT providers will have participated in one of VA's Whole Health trainings or an equivalent that emphasizes a nonpharmacological approach to chronic pain management based on the eight dimensions of Whole Health (e.g., emotional health, physical health, sleep, nutrition) [3]. The second core element of the WHT intervention is personalized health planning, in which the WHT guides the participant in developing pain management goals. Whole Health coaching is the third core element. Whole Health coaches will have completed the VA Whole Health coaching course and have prior experience in coaching veterans via the Whole Health model as well as in motivational interviewing and shared decision-making [12]. Coaches will support veterans in implementing and refining pain management goals. The WHT will meet weekly to coordinate pain care for participants. Optional elements of the WHT include 1) the addition of a mental health provider, 2) co-located (preferred) or sequential visits with team members, and 3) embedding the WHT in primary care (preferred) or an alternative location.

WHT Fidelity Monitoring. Fidelity to the core elements of the WHT model will be monitored by 1) auditing at least 5% of templated WHT clinic notes,

2) requiring that the site principal investigator observe at least one WHT visit monthly, and 3) hosting monthly all-site WHT conference calls to standardize the WHT intervention across sites. Fidelity to Whole Health coaching will be monitored by a co-investigator/psychologist with expertise in supervising Whole Health coaching [13], who will audit a random 10% of all audio-recorded coaching sessions per quarter. In addition, Whole Health coaches will participate in a monthly all-site virtual coaching supervision call.

WHT Protocol. Within 30 days after randomization, before the first WHT visit, a Whole Health coach will conduct a personalized health inventory by telephone or video telehealth (approximately 1 hour) to inventory participants' current vs desired status on eight dimensions of Whole Health, as well as their overall values and goals (see Figure 1). Personalized health inventory results will be communicated to the WHT through a templated EHR note and during weekly WHT meetings. After the personalized health inventory, the first collocated interdisciplinary WHT visit will be 1 hour, will be guided by templated notes in the EHR, will be conducted in person or by video telehealth or telephone (depending on local site COVID-19 guidance), and will consist of an initial pain-focused assessment, culminating in a personalized health plan. Also, after the initial visit, Whole Health coaches will conduct eight weekly 30-minute telehealth/telephone coaching sessions to encourage participants to implement their pain management goals in the personalized health plan, with optional monthly "booster" coaching sessions. Coaching visits will be guided by an EHR note template. Over the 12-month follow-up period, there will be a total of at least three 30-minute WHT visits (two visits in the first 6 months and one visit in the latter 6 months) to assess interval progress on pain management goals and to update the personalized health plan as needed. The final WHT visit will address post-study plans for ongoing pain management.

PC-GE Intervention

PC-GE Description. The PC-GE model is an adapted, abbreviated version of VA's CBT-CP [5], delivered as open group sessions as opposed to individual sessions or closed groups, such that participants can start any of five CBT-CP modules after completing an initial 90-minute PC-GE session, offered at least once monthly, to orient them to CBT-CP. Afterward, they will begin the next of five rotating CBT-CP modules that will be delivered during 90-minute weekly group treatment sessions: 1) Activation and Pacing, 2) Relaxation Training, 3) Pleasant Activities, 4) Reframing Thinking, and 5) Sleep. Groups will range from two to ten participants, and with rolling admission, the groups will be "open," likely consisting of a different combination of study participants each time. In addition, depending on COVID-19 guidance, participants may attend the groups in person or by video-telehealth or telephone, such that groups may also be mixed with respect to mode of delivery. After completion of five different PC-GE modular sessions, participants will be required to attend a 90-minute discharge session held each month to develop plans for the future and anticipate barriers to implementing their new skills. Participants will also be invited to attend 90-minute PC-GE booster sessions offered monthly during follow-up. The PC-GE arm was adapted from an evidence-based manualized therapy to be an active pragmatic comparator to the WHT intervention, but one that is less intensive, less individualized, and more reliant on the participant's primary care provider to prescribe or de-prescribe medications and to refer for other nonpharmacological pain management services. In contrast, the WHT includes a medical provider who can prescribe and order pain management services directly for study participants.

PC-GE Training and Fidelity Monitoring. Psychologists will lead the group PC-GE sessions at each site and will be experienced with manualized CBT-CP and the adapted version used in this intervention. Fidelity will be monitored by psychologists using a treatment fidelity checklist embedded in the PC-GE note to document the treatment elements delivered. Psychologists will participate in a weekly PC-GE case review at each of the sites with the study coordinator, as well as a monthly all-site case conference call, during which PC-GE providers will review cases with expert CBT-CP consultants in an effort to standardize PC-GE intervention delivery across sites.

UPC (Control Condition)

UPC Description. In the VA, interdisciplinary teams in primary care represent Step 1 of the VA's Stepped Care Model for the treatment of chronic pain. VA primary care providers and allied health team members (e.g., registered nurse care managers, social workers, pharmacists, dieticians) are trained in the biopsychosocial management of chronic pain, including the coordination of multimodal care that incorporates patient preferences and values. Participants randomized to this arm will continue to have their primary care providers and allied health teams serve in this role.

Elements Common Across Study Arms

First, all participants (regardless of study treatment arm) will continue to see their primary care providers throughout the study. Primary care providers will be added as co-signers on the clinic note templates to either inform or request changes to participants' pain regimens, as needed. Second, after randomization, all participants will be oriented to the study arm and be informed about the web/mobile Whole Health Resource Directory, which primary care providers, study clinicians, and participants can search to identify CIH pain management services mapped

Table 1. Schedule of patient-reported outcome measures

Measures	Domain Measured	Baseline Full Assessment	Follow-up Full Assessment (6 and 12 months)	Follow-up Brief Assessment (3 and 9 months)
Demographics		X		
Brief Pain Inventory	Pain severity and interference	X	X	X
Veterans Rand 12-Item Health Survey	Quality of life	X	X	X
Nonpharmacological and Self-Care Approaches	Inventory of CIH measures	X	X	X
Pain Catastrophizing Scale (4-item)	Pain catastrophizing	X	X	
Pain Self-Efficacy Questionnaire (4-item)	Pain self-efficacy	X	X	
Patient Global Impression of Change Scale	Change in pain		X	X
Pain Medications Used	Inventory of pain medications	X	X	X
Godin Leisure-Time Exercise Questionnaire	Exercise	X	X	X
PROMIS: Sleep Disturbance	Sleep	X	X	X
Perceived Stress Scale (4-item)	Stress	X	X	
COVID-19 Impacts Questionnaire	Psychosocial impacts	X	X	X
Patient Health Questionnaire (PHQ-9)	Depression	X	X	X
Generalized Anxiety Disorder 7-item Scale	Anxiety	X	X	X
Primary Care PTSD Screen (PC-PTSD-5)	PTSD	X	X	
AUDIT-C (Brief Alcohol Screen)	Alcohol	X	X	X
Tobacco, Alcohol, Prescription Medications, and other Substance Part 2 (TAPS-2)	Illicit use of substances	X	X	
EPOCH—Pain Treatment Satisfaction	Treatment satisfaction	X	X	X
CDC High Impact Chronic Pain Measure	Pain	X	X	

PTSD = posttraumatic stress disorder.

to the eight dimensions of Whole Health at their VA facility and in their local communities (see Supplementary Data).

Baseline and Follow-up Procedures

Study outcomes will be derived from three sources: 1) point-of-care data, 2) VA EHR data, and 3) patient-reported assessments (Schedule of Assessments, Table 1).

Point-of-Care Data

Data from the validated three-item PEG [10], assessing pain severity and interference, and the four-item PHQ-4 [14], assessing depression and anxiety, will be collected at each PC-GE and WHT study visit via VA Clinical Reminder software embedded in the EHR note templates, which can be searched through VA EHR databases. Because most study visits will be virtual in the context of COVID-19, local study coordinators will instead call participants within 24 hours of WHT and PC-GE sessions to collect PEG and PHQ-4 data and then will send study clinicians results via encrypted email so they can record them in the clinic note templates during study visits. When in-person visits resume, the original protocol for handling of point-of-care will be reinstated.

VA EHR Data

VA EHR data will be used to 1) ascertain pain-related study visits and other clinical visits within and outside VA and 2) capture changes in pain medication use. VA EHR data are contained within a number of different VA databases, available to researchers with human subjects research approval. Using these databases, we will capture utilization data for VA health services and VA-reimbursed non-VA health services, along with associated *International Classification of Diseases* (9th and 10th revisions) pain diagnostic codes and pharmacy data by date. In addition, other clinic codes denoting CIH wellness and clinical care (i.e., 139 and 159, respectively), CHAR4 codes, and Current Procedural Terminology codes will be used to identify VA and community CIH services (reimbursed by VA) for chronic pain. Study visits for each of the two active interventions (WHT and PC-GE) can be tracked with special codes for research; UPC visits associated with pain-related diagnoses will also be tracked.

Patient-Reported Outcomes Data

Patient-reported outcomes data will be collected at baseline and at 3, 6, 9, and 12 months during telephone assessments conducted by blinded research staff and entered directly into VA-approved REDCap data collection and management software. Full-length outcome assessments (60–75 minutes) will be conducted at baseline and at 6 and 12 months. Abbreviated assessments (30–45 minutes) will be conducted at 3 and 9 months. Participants will receive stipends for each telephone assessment ($50 for full-length and $25 for brief assessments). A complete list of the outcome assessment measures and the domains measured are shown in Table 1.

Statistical Methods

Sample Size Determination

Sample size determination was based on the primary outcome: the total Brief Pain Inventory (BPI) interference subscale [15]. On the basis of repeated-measures ANOVA, using the F test, we focused on two types of pairwise comparisons. For the first pairwise comparison of the active interventions (WHT vs PC-GE), an alpha of 0.03 and effect size of 0.15 were used. On the basis of a prior published study [9], for the second pairwise comparison of each active intervention compared with UPC (WHT vs UPC and PC-GE vs UPC), an alpha of 0.01 and effect size of 0.30 were used, with the assumption that the difference in pain interference would be greater when comparing the active interventions with UPC (control) than when comparing each active intervention with the other (family-wise error rate=0.05). For the first pairwise comparison, a power of 0.90 and two repeated measures with an equal allocation (ratio 1:1) were assumed. For the second pairwise comparison, an unequal allocation ratio was assumed for computing sample size for the UPC arm. On the basis of data from a prior pilot study, the correlation between repeated measures was 0.66 and the variance 5.90, in this case yielding a sample size of 273 per arm for the first pairwise comparison and 50 for the UPC arm in the second pairwise comparison. Allowing for a 20% attrition rate, the final sample size was 745 (341 each for WHT and PC-GE and 63 for UPC). On the basis of prior studies, 70% of those screened will be eligible, and of those, roughly 20% will enroll. Therefore, over 24 months' enrollment, roughly 5,360 will need to be screened to yield 3,750 eligible patients, for a final sample size of 745.

Analytic Methods

The primary hypothesis is that the WHT approach will be superior to PC-GE and both will be superior to UPC in improving pain interference as measured with the BPI, which includes seven numeric ratings of pain interference (general activity, mood, walking, work, relationships, sleep, and enjoyment of life) and is scored as the average of individual item scores [15]. An intention-to-treat analysis will be conducted with a mixed-effects linear regression, with the BPI interference score (averaged by number of items with non-missing values) used as the primary outcome for each of the three pairwise comparisons. Intervention time (6 and 12 months) and its interaction term will be included. Primary analyses will be adjusted for the baseline BPI interference score and stratification variables, including site, gender, and prescription opioid use. Analyses will not be adjusted for clustering because although the PC-GE intervention is conducted in group format, the groups will be open with rolling admission, creating no consistent clustering effect. Post hoc–identified covariates that are imbalanced between groups will be relegated to sensitivity analysis.

During the COVID-19 pandemic, there may be fluctuating adherence to some of the study interventions and outcome assessments. Consequently, additional time-dependent variables, including sites' access to clinical care (i.e., fully closed vs partially open vs fully open [categorical]), mode of study treatment delivery (i.e., in person, video telehealth, phone [categorical]), and degree of availability of nonpharmacological pain services within VA and the local community will be captured by study staff at each site or via the EHR and will be included in analyses. Exploratory analysis will be stratified by time periods, sites, and site characteristics but may be limited by inadequate power from partitioning the sample. Information on individual-level variables, including COVID-19 infection status, other psychosocial and health impacts, and number of missed intervention visits and outcome assessment time points (numerical), will be collected. Depending on the COVID-19 impacts on study completion rates, in addition to the planned intention-to-treat analysis, we will consider a per-protocol analysis that includes only patients completing the protocol to pre-determined thresholds for the originally allocated treatments [16]. All analyses will be performed in SAS (from SAS Institute, Cary, NC) and VA SQL Service Management Server (SSMS).

Procedures for Handling Missing Data

Strategies will be used to minimize missing data. Most importantly, participants wishing to withdraw from the allocated study interventions will be encouraged to participate in outcome assessments and contribute EHR data. Nevertheless, the amount and patterns of missing data and impact on statistical power will be ascertained. The main analysis will reflect the "missing-at-random" assumption, in which there is no systematic difference between subjects who are and are not lost to follow-up, and the probability of missingness depends only on observed data that will be collected that could explain the missingness. Under the missing-at-random assumption, planned analytical strategies are unbiased, including mixed-effects linear regression, inverse probability weighting, and multiple imputation. Sensitivity analyses will test whether results from the main analysis are robust when there is a departure from the missing-at-random assumption. Here, a "missing-not-at-random" mechanism is assumed, in which the probability of missingness depends on unobserved data, and there are systematically worse outcomes in those lost to follow-up than in those adherent to their assigned treatment.

Implementation and Dissemination

The trial will include a process evaluation of the implementation of the two active interventions (WHT and PC-GE) and will consist of semi-structured patient "exit" interviews and evidence-based quality improvement meetings with study stakeholders (e.g., VA facility

leadership in primary care, pain care, and Whole Health; study clinicians and veteran opinion leaders) [17]. Goals of the process evaluation are fourfold: 1) to increase the relevance of the primary research findings to patients, clinicians, and health care decision makers; 2) to increase the likelihood of timely translation of research findings into diverse practice settings; 3) to generate information to guide interpretation of primary trial findings; and 4) to create an implementation toolkit to support future implementation and dissemination of study interventions in diverse practice settings. The RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) Framework [18] will guide the process evaluation. Rapid analysis of process evaluation findings will inform iterative improvements to the implementation strategy as the trial progresses. In addition, costs, broadly classified as implementation costs, intervention costs, and other health care costs, will be collected for each of the three study arms. Results from this budget impact analysis will be included in the implementation toolkit to help inform future implementation and dissemination efforts. In addition to the implementation toolkit, findings from this trial will be disseminated through reports, manuscripts, abstracts, cyberseminars, and other PMC products.

Discussion

*w*HOPE was designed to be the first large, multisite, pragmatic trial to establish evidence for the VA Whole Health model for chronic pain care. *w*HOPE is one of several studies that are a part of the NIH-DOD-VA PMC, which affords several benefits. First, cross-study comparisons of pain management interventions can be made relatively easily because of the standardization of independent and dependent variable phenotypes (e.g., definition of chronic pain and pain interference as a common primary outcome). Second, several PMC studies are using the same secondary outcome measures, which also facilitates cross-study comparisons. Third, the PMC has organized work groups in areas such as biostatistics, ethics and regulatory issues, and implementation that provide real-time consultation when questions arise with regard to study design or methodology. In turn, each study can contribute meaningfully to the overall mission of the NIH, DOD, and VA to build national-level infrastructure to support evidence-based nonpharmacological pain management approaches for veterans and military personnel.

As a pragmatic trial, *w*HOPE recently completed a 2-year developmental formative evaluation to determine how best to tailor implementation of the trial interventions to the needs, preferences, and resources of each participating enrollment site. The following changes to the study design reflect feedback from qualitative interviews and evidence-based quality improvement meetings with study stakeholders. First, stakeholders recommended making the composition and workflow of the WHT more flexible. Enrollment sites agreed that it was more feasible to include a medical and CIH provider on the WHT while making inclusion of a mental health provider optional, because of shortages of VA mental health personnel and to better differentiate the WHT from the PC-GE intervention, which requires a mental health provider. In addition, because of scheduling conflicts, some sites may need to conduct sequential rather than fully collocated interdisciplinary WHT visits. Second, study stakeholders, including veteran patients, suggested changes to the language in the informed consent, eligibility screener, and study orientation scripts to highlight that the goal of the study is not to taper or "take away" opioids but instead to learn more about nonpharmacological approaches to chronic pain management. Finally, stakeholders emphasized the importance of garnering leadership buy-in for the trial and apprising middle management of leadership support when negotiating "study asks" such as clinical space, release time for study clinicians to participate in the trial, and the use of the local EHR for study note templates. Stakeholders also emphasized the importance of ensuring workload credit for study clinicians by using particular research stop codes. Finally, making volunteer study clinicians "study collaborators" may facilitate more sustained engagement in the trial because, as collaborators, study clinicians will be invited to collaborate with co-investigators on study products.

In response to the COVID-19 global pandemic, after shelter-in-place orders were issued across the United States, the trial was modified such that all study interventions could be delivered virtually via telehealth (video and telephone platforms). To capture the psychosocial, financial, and health impacts of COVID-19, as well as experiences with virtual care from the perspective of study participants and study clinicians, surveys and qualitative interview questions were developed that included a set of questions common across PMC studies. In addition, the PMC biostatistics groups advised supplementing the intention-to-treat analysis with a per-protocol analysis in the event participants could not complete the treatment intervention or outcomes assessments. In addition, the protocol was amended to conduct quarterly environmental scans of the fluctuating availability of VA and community pain management services in response to local COVID-19 guidance and to include these variables in time-varying sensitivity analyses. A silver lining to the COVID-19 pandemic is that not only will this study produce the first trial evidence for the Whole Health model applied to pain care in comparison with an evidence-based pain care approach (PC-GE/CBT-CP), but it will also yield evidence for the virtual delivery of two nonpharmacological pain management approaches in veterans, which is likely to be highly relevant for the foreseeable future.

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Supplementary Data

Supplementary Data may be found online at http://painmedicine.oxfordjournals.org.

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