Title: Development of an Internet-based Behavioral Pain Management Intervention

Protocol Approval by VA Connecticut Healthcare System: 7/25/2016

NCT number: NCT01918189

RESEARCH PROTOCOL PROJECT DESCRIPTION

1. **Principal Investigator:** Alicia Heapy, Ph.D.*
   Co-Principal Investigator: Diana Higgins, Ph.D.*

Co-Investigators:
Joseph Goulet, Ph.D.* - VA Connecticut Healthcare System
Marc Rosen, M.D. – VA Connecticut Healthcare System
Cynthia Brandt, M.D.*– VA Connecticut Healthcare System
William Becker, M.D. – VA Connecticut Healthcare System
Woody Levin* – VA Connecticut Healthcare System

Co-Investigators not at VACHS
David Williams, Ph.D. – University of Michigan
Matthew Bair, M.D. – Richard L. Roudebush VA Medical Center, Indianapolis, Indiana
Sarah Krein, Ph.D. – VA Ann Arbor Healthcare System
Kenneth Weingardt, Ph.D. – Web Services, Office of Mental Health Services, Washington DC
Haseena Rajeevan, Ph.D. – Yale University
Robert Kerns, PhD – Yale University

Study Staff:
TBD* – VA Connecticut Healthcare System
TBD* – VA Connecticut Healthcare System
*Access to PHI

Title: Development of an Internet-based Behavioral Pain Management Intervention

2. Purpose:
The proposed study includes development, evaluation of preliminary efficacy, and usability testing of a behavioral self-management program (the VPMRC) involving cognitive-behavioral and progressive physical activity components for CLBP delivered via the Internet. The intervention will be developed and tested during 2 phases: (1) Development (Phase 1) and (2) Pilot Feasibility Trial of the VPMRC (Phase 2).

Phase 1: Development
The primary aim of this phase of the project is to develop an integrated, Internet-based behavioral pain self-management intervention called the Veteran Pain Management Resource Center (VPMRC). The first phase of the project will involve development of the VPMRC based on materials previously developed by our group in the context of several prior projects. During this phase, an Expert Panel (EP) of clinician investigators, including several with specific expertise and experience in developing and testing e-health interventions, will assist the PIs in preparing the initial content for the VPMRC. The EP will provide regular feedback that will be used to modify the VPMRC over a 14-month development period. This phase of the project also involves obtaining feedback from 15 Veterans with chronic low back pain (CLBP) to assess usability of the VPMRC, ease of navigation of the website, functionality of the website, and overall participant satisfaction with the VPMRC program.

Phase II: Pilot Feasibility Trial of the VPMRC
The primary aim of this phase of the project is to execute a pilot feasibility trial to evaluate the preliminary efficacy of, usability of, and satisfaction with the VPMRC.
The primary hypothesis is that a clinically meaningful reduction in pain interference with functioning post-exposure to the VPMRC will be observed compared to baseline ratings.
The secondary hypothesis is that Veterans who participate in the VPMRC will report a clinically meaningful reduction in pain intensity and statistically significant improvements on other important

problems commonly associated with CLBP including fatigue, sleep problems, depressive symptoms and negative mood, relative to baseline.
The tertiary hypothesis is that participants will report high levels of interest (credibility), use, and satisfaction with the VPMRC.

3. Background:
Limitations of current interventions for CLBP

For years, the practice of pain medicine has over-emphasized expensive and modestly effective treatments for CLBP, while under-utilizing inexpensive evidence-based behaviorally-oriented approaches that have demonstrated comparable or superior effect.[1,2,3,4,5] Non-pharmacological treatments such as education, exercise, and behaviorally-based therapies have been demonstrated to be efficacious and effective, but are rarely used in routine clinical practice. Optimal care should combine both pharmacological and non-pharmacological behavioral interventions – but again, this is rarely done. Patients have historically considered behavioral interventions to be "mental health" resulting in reluctance to accept the need for a "psychological" treatment for their pain. It is imperative that a viable delivery platform be developed to facilitate Veteran access to efficacious non-pharmacological interventions. Such integrated delivery has become the "gold standard" of care for other chronic medical conditions such as diabetes, congestive heart failure, and asthma. The development of the Veterans Pain Management Resource Center (VPMRC) represents a necessary "first step" in providing comparable evidence-based disease management for CLBP – a long anticipated transformation in how clinical pain medicine is practiced.

Behavioral interventions for pain self-management

Cognitive-behavioral therapy

Psychological interventions such as cognitive behavioral therapy (CBT) have demonstrated efficacy for reducing pain and improving function in persons with a broad spectrum of pain-related conditions and have become the most commonly cited alternatives to traditional medical and rehabilitation approaches to chronic pain management.[6,7,8] CBT is informed by a theory of chronic pain that suggests that patients' beliefs, attitudes, and coping resources play a central role in determining their experiences of pain.[8] The overarching goal of CBT for chronic pain is to assist patients in the development of an adaptive self-management approach to pain management based upon a conceptualization of pain as controllable and a personal attitude of self-efficacy and self-control. An important aspect of CBT is its foundation in a biopsychosocial and multidimensional perspective of chronic pain and the fact that it is specifically designed to simultaneously target reductions in pain and associated disability, emotional distress, and improve overall quality of life. CBT is a structured, time-limited, and goal-oriented therapeutic approach that can be delivered in either small groups or individual outpatient sessions. Therapy usually involves six to twelve outpatient treatment sessions during which a range of cognitive (e.g., attention diversion, development of coping self-statements) and behavioral (e.g., activity pacing, mental relaxation and other stress reduction) pain coping skills are taught. Progress toward individually-tailored goals for treatment and pain coping skill practice are encouraged through the collaborative development of intersession homework assignments. Kerns and colleagues published a meta-analysis of psychological interventions for chronic back pain and documented moderate to large effects of psychological interventions, including CBT, in reducing pain and pain-related interference relative to waiting list control conditions.[6] A similar Cochrane type review led to nearly identical conclusions.[7]

Exercise

Exercise or progressive physical activity programs also have a demonstrated role in helping to control pain. Of particular importance, physical activity helps to maintain function among persons with chronic pain conditions.[9-11] While pain severity shares an imperfect relationship with function, the presence of chronic pain can result in decreased activity levels and self-protective behaviors such as guarding and avoidance of physical activity due to fear of pain exacerbation or potential re-injury.[9,10] Over time, such behaviors can lead to reduced muscle tone, increased pain, and functional disability – a vicious cycle that perpetuates the persistence of pain and low levels of functioning.[9] It has been hypothesized that interventions that specifically target increasing physical activity and functioning may serve to disrupt this downward spiral. Research shows that physical activity can help prevent recurrence

or reduce pain, improve functional status, and decrease sick leave and disability for patients with chronic pain.[5, 11-14] It has been suggested that the most effective strategy for improving pain includes a supervised, yet individually designed home-based exercise program, consisting of high-dose intensity exercise (defined by the amount of time spent exercising). However, studies also suggest that a variety of exercise programs or interventions including yoga as well as aerobic (e.g., walking) and strengthening exercises result in both clinically and statistically significant improvements in outcomes for patients with CLBP.[5,11,13] Despite the importance of exercise in managing chronic pain, efficient and effective strategies for promoting exercise therapy among patients with CLBP are not widely available, and the use of exercise as a management strategy among patients with CLBP remains relatively low.[15-17]

Internet as a delivery platform for behavioral interventions

Internet-based Interventions in Veterans

While new technology, such as telemedicine, has been introduced with success for chronically ill Veterans,[18] few Internet-based interventions have focused on US Veteran populations. McMahon and colleagues examined a web-based intervention compared to usual care for management of blood pressure and glucose among Veterans with diabetes.[19] Participants in the web-based condition demonstrated lower and clinically meaningful hemoglobin A1c (HbA1c) values and systolic blood pressure over 12 months post-intervention compared with control participants. Using the same sample of participants cited by McMahon,[19] Fonda and colleagues compared "diabetes distress" in Veterans receiving usual care for diabetes to those receiving an Internet-based care management program for diabetes.[20] Results indicated that participants (mean age 61 years) in both conditions demonstrated a decrease in diabetes distress; however, those with sustained usage of the Internet-based program showed significantly greater decreases in diabetes distress compared to non-users. In addition, glycemic control was positively correlated with a measure of diabetes-related distress, such that reductions in HbA1c were associated with reductions in distress. These results suggest the promise of an Internet-based program, even among older Veterans.

Internet-based interventions for chronic pain

To date, few published studies have evaluated Internet-based interventions for chronic pain. A recently published meta-analysis included 11 studies of Internet-based interventions that included pain intensity as an outcome.[21] Studies involved persons with back pain, osteoarthritis, headache, fibromyalgia, and rheumatoid arthritis. The nature of the interventions varied considerably across the studies and included delivery of email, discussion groups, live chat groups, information promoting exercise or relaxation therapy, and more comprehensive psychoeducational approaches based on principles of CBT and pain self-management. Across all studies, an overall small effect of the Internet-based interventions on reports of pain intensity relative to control conditions was noted. In the sole study of persons with CLBP with an intervention similar to that proposed in this study, participants were randomized to waiting list or to receive access for six weeks to an Internet-based intervention comprised of education, cognitive skills acquisition, behavioral rehearsal, and generalization and maintenance.[22] Statistically significant improvements on measures of pain catastrophizing, control over pain, and "ability to reduce pain" were reported. None of the reported studies were noted to include Veterans. The authors concluded that, although only small improvements in pain were noted across the studies, greater improvement in pain-related disability was noted in studies that examined this variable, and that the efficacy of cognitive behavioral interventions was particularly supported.

4. Significance:

VHA has recognized numerous challenges in achieving its Pain Management Strategy objectives. Of particular relevance to the current proposal, VHA has specifically recognized the need to develop systems of care that promote equitable access to specialty healthcare services for Veterans regardless of geography and socioeconomic barriers. Pain management has been identified by the PACT leadership as the top priority area for this initiative.

The short term objective of this project is to conduct a pilot feasibility trial of an Internet-based self-management program, the VPMRC, for Veterans with CLBP that is compatible with VA IT architecture and MHV. The evaluation will examine preliminary efficacy of the VMPRC for reducing pain-related interference, pain severity, and related problems commonly associated with CLBP, and will also test the usability of and satisfaction related to the VPMRC. If successful, the long term objective is to migrate the

VPMRC to the MHV platform to provide widespread and easy access for Veterans across VHA regardless of geography or other access barriers.

5. Research Plan:

The proposed study includes development, evaluation of preliminary efficacy, and usability testing of a behavioral self-management program (the VPMRC) involving cognitive-behavioral and progressive physical activity components for CLBP delivered via the Internet. The intervention will be developed and tested during 2 phases: Development (Phase 1) and Pilot Feasibility Trial of the VPMRC (Phase 2). Because the proposed study includes 2 phases, each phase will be described separately.

Phase 1: Development

The primary aim of this phase of the project is to develop an integrated, Internet-based behavioral pain self-management intervention called the Veteran Pain Management Resource Center (VPMRC). The first phase of the project will involve development of the VPMRC based on materials previously developed by our group in the context of several prior projects. Five specific studies from our investigative team provide additional background for the development of the VPMRC and for informing this phase of the project. : A Clinical Science R&D Service Merit Award to Dr. Kerns titled "Efficacy of tailored cognitive behavior therapy for chronic back pain", HSR&D funded Short Term Project, "Piloting Interactive Voice Response Modules for Chronic Pain Treatment", an efficacious web-based behavioral self-management program (WEB-SM) known as "Living Well with Fibromyalgia.", an Internet-mediated exercise intervention for Veterans with CLBP that was tested at the Ann Arbor VA Medical Center, and a RR&D study examining a motivational interviewing intervention for Veterans with mental health conditions applying for VA disability benefits that has recently been translated for delivery via the Internet at VACHS.

During this phase, an Expert Panel (EP) of clinician investigators, including several with specific expertise and experience in developing and testing *e*-health interventions, will assist the PIs in preparing the initial content for the VPMRC. The EP will provide regular feedback that will be used to modify the VPMRC over a 14-month development period.

Process: Development of the VPMRC will follow an iterative process between the informatics experts and the Expert Panel (EP; described below). The initial content will be developed based upon the Veteran-centered materials for self-management of CLBP described above. A prototype web site with a single module (i.e., Introduction Module) will be developed in conjunction with the informatics expert and programmer (Dr. Haseena Rajeevan) and a graphic designer incorporating User-Centered Design processes. Once a draft of the first module is completed, the EP will be convened by teleconference (with LiveMeeting capability) to review the content and prototype navigation for the site. Draft materials for each of the remaining modules will be developed iteratively by the writing team and Dr. Rajeevan and added to the VPMRC prototype. On a monthly basis, the EP will be asked to review and comment on new content. Once all modules are completed and reviewed, an initial version of the entire VPMRC will be evaluated by the EP and by 15 Veterans (see below for further detail) to assess usability, ease of navigation, and functionality. Based upon feedback from this round of review, modifications will be made to the beta version of the VPMRC program followed by a second review by the EP. Final modifications to the VPMRC program will be made prior to releasing it into the production environment for the Phase II pilot feasibility trial.

Compatibility with VA WebOps Standards: Compatibility with VA WebOps Standards and VA IT architecture requirements is ensured by the close involvement of three additional co-investigators. Dr. Kenneth Weingardt is National Director of Web Services for the Office of Mental Health Services. Dr. Cynthia Brandt is Director of the Informatics Core of the PRIME Center and is a member of the *e*Health QUERI project. Dr. Rajeevan will work with the EP and with Drs. Weingardt and Brandt to develop the VPMRC using guidelines provided by VHA (i.e., WebOps standards) to ensure that the VPMRC is compatible with the VHA's web environment and can ultimately be integrated into the MHV platform. Initially, the VPMRC will be hosted on a Yale University server and will not be tied to the VHA's Intranet. TheWebOps standards specify software and server compatibility (i.e., Dr. Rajeevan will build the VPMRC using Microsoft tools to ensure compatibility), security and privacy (i.e., no PHI will be collected in the VPMRC), accessibility (e.g., section 508 guidelines), compatibility with web browsers, space quotas, and file type restrictions. Attention will also be given to representation of VHA using correct decals, symbols, and disclaimers about content while in development phases, although the interface design may be

somewhat flexible because MHV has a templated interface. Dr. Rajeevan will also build the VPMRC with knowledge of the "Clinic in Hand" chronic pain mobile application for smartphones to ensure compatibility.

Composition of the VPMRC

As currently envisioned, the VPMRC program will contain two components, a participant home page and several behavioral and cognitive pain coping skill modules containing evidence-supported methods of managing CLBP.

Home Page: The home page will contain a number of features including (a) the ability to log in and be recognized by the program (which will be required to access features of the program), (b) a self-assessment survey to guide users to the modules of most relevance based upon problem areas (e.g., low scores on measures of adaptive coping such as exercise, pacing, mental relaxation), readiness to make behavioral changes, and preferences, (c) a site map indicating utilization and progress within skill modules, (d) a link to summary information associated with self-monitoring or activities tied to each module, and (e) optional customization applications such as daily tips, pain news, links to resources, and similar functionality.

Pain Coping Skill Modules: Table 1 provides an overview of the preliminary modules to be adapted for the VPMRC program. Each module will adhere to a common structure composed of the following: (1) a video lecture on the specific skill topic by a subject matter expert, (2) an opportunity for self-assessment regarding the content covered in the video lecture followed by automated feedback comparing the participant's current behavior with known or recommended standards, (3) a demonstration video or animation modeling how skills can be used to modify the behaviors associated with the content of each module, and (4) a tool for setting goals and for developing an action plan for achieving desired behavioral changes. This behavioral action plan can also be shared with family or clinicians. In addition, each module will include tools for identifying and overcoming barriers to change, and supporting resource materials specific to each module (e.g., self-monitoring forms, information about the skill that can be shared with a physician).

Table 1. Introduction to Intervention and Pain Coping Skill Modules

Module	Coping Skill	Description
Introduction to VPMRC		Present rationale for treatment, explain pain cycle, introduce goal setting
1. Progressive Physical Activity	Walking	Instructions for walking and benefits of increased activity; goal setting (increase distance walked by 10%/week)
2. Physical Activity	Stretching/Body Mechanics	Instructions for stretching and body mechanics benefits; goal setting (perform stretching exercises once/ day)
3. Relaxation	Diaphragmatic Breathing	Instructions for diaphragmatic breathing and benefits; goal setting (practice 20 minutes/day)
4. Relaxation	Progressive Muscle Relaxation	Instructions for progressive muscle relaxation and benefits; goal setting (practice 20 minutes/day)
5. Adaptive stress response	Identifying negative thoughts	Influence of negative thoughts on pain, activity, and mood; self-monitoring negative thoughts (maintain daily diary)
6. Adaptive stress response	Using positive coping statements	Countering negative thoughts with coping statements; self-monitoring (maintain daily diary)
7. Pacing	Activity pacing	Pace activities based on time rather than pain level; goal setting (set daily goals and maintain daily diary)
8. Pacing	Pleasant activity scheduling	Using pleasant activity scheduling to increase activity and enhance mood; goal setting (select daily goals and maintain daily diary)
9. Addressing pain flares	Skill consolidation and relapse prevention	Planning for relapse and pain flares; goal setting for sustaining improvements

Expert Panel

The EP will be comprised of several co-investigators and led by Drs. Higgins, Kerns, and Williams. Members of the EP have expertise in pain management and clinical, rehabilitation, and health services pain research, conduct of clinical trials using behavioral interventions, and adaptation of therapy materials for Internet delivery. Table 2 includes a list of the EP members, their disciplines, and a brief description of their areas of particularly relevant expertise.

Table 2. Expert Panel Membership

Expert Panel Clinician	Study Role	Expertise
Diana Higgins, Ph.D. (Clinical Psychologist)	*EP lead; Project Coordinator; oversee production of VPMRC (content and patient interface)*	• Adapting behavioral interventions for delivery via the Internet for Veterans • Psychologist therapist in clinical trials of cognitive behavioral interventions for chronic pain
Robert Kerns, Ph.D. (Clinical Psychologist)	*EP lead; oversee content of VPMRC; dissemination lead*	• National Program Director for Pain Management • Director, PRIME Center • Pioneered development and evaluation of CBT for chronic pain, psychosocial pain assessment instruments, and a model of readiness to adopt behavioral changes for pain management
David Williams, Ph.D. (Clinical Psychologist)	*EP lead; development of VPMRC; translation of face-to-face treatment for Internet delivery*	• Leading contributor to development of pain coping construct and its measurement • Lead author of cognitive behavioral intervention in prior Gulf War Veteran Illness VA Cooperative Studies Project • Developed Internet-based interventions for pain including “Living-well with FM”
Alicia Heapy, Ph.D. (Clinical Psychologist)	*Development of VPMRC; translation of face-to-face treatment for Internet delivery for Veterans*	• Associate Director, PRIME Center • Developing/implementing clinical trials using IVR to disseminate CBT for Veterans with chronic pain who have limited access to specialized care
Marc Rosen, M.D. (Psychiatrist)	*Development of VPMRC; translation of face-to-face treatment for Internet delivery for Veterans*	• Adapting a behavioral intervention for Veterans with mental health conditions who are applying for VA benefits for Internet delivery
Matthew Bair, M.D.,M.S. (Primary Care Physician)	*Development and content expert; implementing VPMRC into primary care setting*	• Investigator at the Center of Excellence on Implementing Evidence-Based Practice • HSR&D Career Development Awardee, focus on pain management in VA primary care settings
William Becker, MD (Primary Care Physician)	*Development and content expert; implementing VPMRC into primary care setting*	• Investigator at the PRIME Center • HSR&D Career Development Awardee, focus on pain management in VA primary care settings
Sarah Krein, Ph.D., RN (Doctoral-level Nurse)	*Development of VPMRC; translation of face-to-face treatment for Internet delivery for Veterans; content expert for progressive physical activity modules*	• Investigator at the VA Center for Clinical Management Research • Utilizing the Internet as a delivery platform for exercise interventions

Pre-pilot testing

Once a complete initial version of the VPMRC is developed, the intervention will be piloted with a small sample of Veterans (N=15) to determine usability, ease of navigation, and functionality. Based on suggested sample sizes for qualitative research, which recommend using at least 6 participants[23,24]for a phenomenologic approach (i.e., designed to capture the essence of the experience[25] to obtain thematic saturation), we opted to enroll 15 participants to achieve thematic saturation and to reduce the likelihood

that we will obtain bimodal opinions of the program. This phase is designed to solicit feedback from participants to further develop and modify the VPMRC program.

Procedure: Eligible participants (N=15) will be asked to participate in two, 2.5 hour visits during which they will complete informed consent, complete the tailoring self-assessment, and review the modules using a computer at VACHS while the Research Assistant (RA) prompts the participant for feedback and records his/her feedback. During the first visit, participants will be asked to complete the informed consent, review the program's homepage, complete the tailoring self-assessment, and review the first 3 treatment modules while providing verbal, audio-recorded feedback (e.g., using the "Think Aloud" method). Participants will be given a homework assignment to login to their account on 2 separate occasions to revisit the modules they have reviewed and choose one skill to practice during the week following the first study visit. This will provide information about the ease of logging in, sufficient speed of Internet connection, and so forth, in addition to ensuring that they are able to provide a thorough evaluation of their experience with the VPMRC. During the second visit, participants will be asked to provide brief feedback regarding their experience with the homework assignment and will review the final 6 treatment modules, again while providing verbal feedback. At the end of the second visit, participants will be asked to complete the Post-intervention Measure to obtain quantitative feedback. Table 3 describes study visits, assessment measures, and qualitative and quantitative data collection for Phase I.

Table 3: Phase I Visits and Assessments

Visit	Visit description	Assessments
Consent, Self-Assessment & First 3 Modules	• Consent • Issue userID and temporary password • Review first 3 treatment modules	• Informed Consent • Participant will provide verbal feedback about his/her experience with the homepage, self-assessment, and first 3 modules which will be recorded by the RA (Think Aloud Method)
Final 6 Modules & Data Collection	• Report experience accessing modules at home • Review final 6 treatment modules • Post-intervention assessment	• Participant will provide verbal feedback about his/her experience with the final 6 modules which will be recorded by the RA (Think Aloud Method) • Post-intervention questionnaire assessing participants' experience with the intervention

Feedback from Veterans will be reviewed with the EP which will subsequently make recommendations to the VPMRC developers for further modifications to the program. As the refinements are made, the EP will continue to interact with the developers to ensure that the feedback from the Veterans is adequately addressed and incorporated in the final version of the VPMRC.

Assessments: The primary focus of assessment during Phase I is to gather qualitative and quantitative feedback during and after completion of the intervention regarding the layout of the website, ease of navigation and use, relevance of the materials presented, appeal of the program, understanding of key concepts, appropriateness of the graphics and multimedia interface, problems encountered, amount of material presented, and general likes, dislikes, overall functionality of the program, and recommendations for change.

Intra-intervention Assessment: Qualitative information will be collected through a "Think Aloud" process in which the participants provide unstructured verbal feedback while engaging in the computer task. This feedback is recorded by a member of the study staff who will be present in the room with the participant. Think Aloud is a popular method for testing usability and for revision of novel applications that involves a participant providing verbal feedback about an application to a "listener" (i.e., a research assistant [RA]) that is recorded and then transcribed for coding and analysis.[26]

Post-intervention Measure: Participants will be administered an investigator-created measure designed to assess the layout of the website, ease of navigation, relevance of the materials presented, appeal of the program, understanding of key concepts, appropriateness of the graphics and multimedia interface, ease of use, problems encountered, amount of material presented, and general likes, dislikes. These data will be used to guide modification of the VPMRC.

Phase II: Pilot Feasibility Trial of the VPMRC

Design

The primary aim of this phase of the project is to execute a pilot feasibility trial to evaluate the preliminary efficacy of, usability of, and satisfaction with the VPMRC. A single treatment condition (Usual Care [UC] plus VPMRC) X two evaluation periods (baseline and 10 weeks post-baseline) design with multiple dependent measures will be employed. Participants in the study will be 55 Veterans with CLBP. Participants will continue to receive care as usual from their primary care providers (PCPs) and other healthcare providers.

Recruitment

VistA Search: We will identify potential Veterans for inclusion from available electronic medical record (EMR) data in VistA. All Veterans 18 years or older from VACHS (Station 689) with low back pain defined using the *International Classification of Diseases, Ninth Revision* diagnostic codes related to low back pain (724, 7240x, 7241x, 7242x, 7243x, 7244x, 7245x, 7246x, 7247x, 8460x, and 8472x) will be considered eligible. We will attempt to oversample OEF/OIF/OND, female, and minority Veterans, as these Veterans have high prevalence rates of chronic musculoskeletal pain conditions and are of particular interest in the context of the proposed study. We will then identify Veterans in this group to exclude psychiatric hospital admissions in the previous 30 days, suicide flag in the Electronic Medical Record (EMR), or behavioral alert flag in the EMR.

A letter will be sent to the identified Veterans from their PCPs informing them about the study and inviting them to participate. Veterans will be provided with information about the voluntary nature of the study and the option to "opt out" from further contact with study staff by notifying us of their lack of interest by phone, email or letter. Veterans who do not contact us will be called by the study RA to be further informed about the study and, if interested, to be screened for participation. Screening will include several of the key eligibility criteria for the study (e.g., confirmation of presence of CLBP, readiness to engage in self-management for pain, interest in Internet-based pain care, and absence of medical and psychiatric comorbidities). If screening suggests potential eligibility, and if the Veteran is interested, an in-person appointment for obtaining written informed consent and baseline assessment data will be scheduled. Solicitation letters will be mailed in waves in order to prevent overwhelming our capacity to offer participation in a timely manner.

We also will post the already approved flyer in the following venues: 1) patient care waiting areas, 2) flat screen informational televisions around the hospital, 3) Good Morning VA Connecticut 4) VA Connecticut's Facebook page, 5) vet centers (after securing their permission) and 6) at the Pain Education table. We also will provide advertisement language in "The Prime Times", a PRIME Center community newsletter.

Procedures

Veterans meeting eligibility criteria based on screening (e.g., by phone) will be scheduled to meet in person with the RA to obtain written informed consent and to complete all baseline study measures. Immediately upon completing the measures, the participant will meet separately with the study coordinator to receive instructions for accessing the VPMRC, and additional logistical details related to their participation in the study. Participants will be provided with a userID and temporary password for accessing the VPMRC program.

Questionnaires and inventories that comprise the principle outcome measures will be reassessed at 10 weeks post-baseline, online using a secure, encrypted Internet-based interface called TrialDB. TrialDB allows participants to complete the self-report questionnaires via their home computer without the need to travel to VACHS. This system has been successfully used to collect data in the HSR&D funded "Women Veterans Cohort Study" (WVCS; PI: C. Brandt). The RA and TrialDB data manager will check the TrialDB reports for accurate and timely completion. The RA will contact participants by phone or email at 10 weeks post-baseline to prompt them to complete post-baseline measures online. If participants are unable to complete the assessments online using TrialDB, alternative arrangements for data collection will be made, such as administering the measures to the participant in person or mailing the measures to the participant with a postage-paid return envelope. The 10 weeks post-baseline timeframe was chosen to allow sufficient time to complete the tailored skills modules and will serve as the post-intervention assessment. Table 4 outlines specific assessment measures to be collected at each assessment point. Participants will be paid $75 for their participation in each of the two assessments.

Table 4. Phase II Assessment Schedule

	Baseline in-person	Weekly Telephone	10 weeks Post-baseline TrialDB
Regular computer/Internet access	X		
Readiness to Change Checklist	X		
Interest in Internet-based pain self-management	X		
Can walk one block?	X		
Consent Form	X		
Chart/Medication Review	X		X
WHYMPI-Interference Scale	X		X
Numeric Rating Scale of Pain Intensity (0-10)	X		X
Profile of Mood States	X		X
Beck Depression Inventory	X		X
Multidimensional Fatigue Scale	X		X
MOS Sleep Scale	X		X
Behavioral Goal Adherence		X	X
Patient Treatment Satisfaction Scale			X
Treatment Credibility Scale			X
Module(s) completed		X	
Usability of Module		X	
Time and content accessed		X	
Post-intervention Measure			X

In addition to completing assessments at baseline and 10-weeks post-baseline, participants will be contacted by the study staff via telephone on a weekly basis beginning 1 week post-baseline and ending at 10 weeks post-baseline. The brief phone contacts will serve to confirm continued Internet access to the VPMRC and to remind participants to continue to complete the VPMRC modules. Qualitative and quantitative feedback will be obtained. Questions will be asked on the following dimensions: goal adherence for previous week's goals (using a 0-10 Likert scale, where 0 indicates no adherence to completing the goal and 10 indicates complete adherence), feedback regarding usability of the previous week's module(s), and specific indication of modules most recently completed. The study staff member will also solicit questions about the content of the VPMRC and provide clarifying answers to these questions. Strict limits will be placed on the nature of the responses and length of time of the calls (i.e., no greater than 10 minutes).

Intervention Description (UC+VPMRC)

Usual Care (UC): All participants will continue to receive whatever pain care they have been receiving. There will be no attempt by study personnel to influence ongoing pain care. Although it is beyond the scope of this project to influence pain care at VACHS, it may be important to know that VACHS continues to work to implement the VHA's stepped care model and to ensure that accepted standards for pain assessment and treatment are met for all Veterans. Within the primary care setting, a Primary Care Pain Workgroup works to promote system improvements related to pain care. Facility performance improvement data document a high rate of adherence to performance criteria related to documentation of pain assessments, treatment plans, and reassessment of the effectiveness of the interventions. Participants in this study will be encouraged to discuss pain concerns with their PCP. Results from the Stepped Care for Affective Disorders and Musculoskeletal Pain (SCAMP) trial conducted in both VHA and non-VHA settings and involving a collaborative care intervention for improving pain outcomes indicated that spill-over for pain outcomes are likewise minimal.[27] Whatever minor spillover does occur, results in a conservative estimate of the intervention's efficacy.

Veteran Pain Management Resource Center (VPMRC): Participants will continue to receive UC as described above, in addition to receiving access and being encouraged to complete the VPMRC program. The VPMRC will be accessed via the Internet at the participant's home or other regular access point. The VPMRC will guide participants in initially completing a self-assessment screening tool for module selection and in setting personally-relevant goals, in addition to assisting them with tracking progress made toward goal accomplishment. The skill modules identified by the self-assessment will be listed and available to the patient to access, learn, and practice through written text, guided narration, video demonstration, and interactive printable action plans to assist patients in learning and practicing

pain self-management skills. Participants will be encouraged to complete the skill modules at their own pace. Participants will also be able to access other modules not identified by the self-assessment if they are interested in completing them. Participants will be provided with a pedometer at the baseline assessment to facilitate completion of the exercise/walking module, which requires patients to track the number of steps walked each day.

Attrition

The RA and study coordinator will monitor the study for attrition and follow-up with participants when they appear at risk for withdrawal or report the intent to withdraw. If a participant contacts the study coordinator to withdraw, s/he will first ask if there is a problem that s/he can address that would allow them to stay in the study. If not, s/he will ask subjects who wish to withdraw from treatment if they will consider continuing to complete the follow-up assessments. To keep losses-to-follow-up at a minimum, every effort, including reminder e-mails and follow-up phone calls, will be made to collect post-baseline data. We will also prospectively collect the reasons for missing data such as "patient refusal due to difficulty completing skill modules" or "patient moved away". Reasons for missing data will be evaluated during data analysis.

Outcome Measures

Standardized and reliable interview and questionnaire measures will be used to assess outcome and process variables. These outcome measures are similar to those we have used in prior CBT efficacy studies and are consistent with CONSORT and IMMPACT guidelines. In addition to these outcomes we also propose to examine treatment satisfaction, treatment credibility, and goal accomplishment.

Primary Outcome:

Pain Interference: The 9-item Interference subscale of the West Haven-Yale Multidimensional Pain Inventory (WHYMPI) assesses pain-related interference in social, work and household functioning and has demonstrated good internal consistency (0.86) and stability (0.85 over 2 weeks).[28] The WHYMPI-Interference Scale was recommended by IMMPACT as a core outcome measure for this domain.[29] A reduction in WHYMPI-Interference Scale scores of 0.6 or greater has been identified as an indicator of meaningful improvement in physical functioning and will be employed in this study.[30]

Secondary Outcomes:

Pain intensity: Self-report of pain is recognized as the gold standard for pain assessment given the inherently subjective nature of pain. Although the numeric rating scale (NRS), verbal rating scale (VRS), and the visual analogue scale (VAS) are all reliable and valid measures of pain, there are differences that led to the IMMPACT recommendation and our selection of the NRS as the primary measure of pain. Of particular note is the fact that the NRS is the accepted measure for screening for the presence and intensity of pain for the VHA, and it is quite familiar to Veterans. Data from several studies suggest that use of this measure, relative to the VRS and VAS, yields fewer missing observations and is preferred by more participants, especially among older persons and among those prescribed opioids.[31] The NRS can be easily administered by either a research assistant, via the telephone, or online as is proposed for this study. In this trial, participants will be asked, "Please rate your pain by indicating the number that best describes your average pain in the last 24 hours on a 0 (no pain) to 10 (pain as bad as you can imagine) scale".[32] A clinically-meaningful reduction in pain intensity will be defined as a reduction in pain of 30% on the NRS relative to baseline NRS. This threshold is also consistent with IMMPACT recommendations based on an analysis of ten studies that examine changes in absolute ratings of pain intensity and independent ratings of treatment satisfaction.[33]

Emotional functioning: Overall functioning will be assessed using the 65-item Profile of Mood States (POMS), a multidimensional measure of emotional functioning designed to assess six dimensions of mood and can be used in non-psychiatric or physically ill populations.[34] Internal consistency (0.84 to 0.95, depending on subscale) and test-retest reliability (0.65 to 0.74, depending on subscale) is good. Depressive symptom severity will be assessed using the 21-item Beck Depression Inventory (BDI) a widely used self-report measure with excellent internal consistency (.92) and stability (.80-.90).[35] Both measures were recommended by IMMPACT.[26]

Fatigue: Clinical fatigue will be assessed using the Multidimensional Fatigue Inventory (MFI).[36] The MFI can be scored to produce 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity.

Sleep Problems: Sleep problems will be assessed using the MOS Sleep Scale. The MOS is segregated into subscales addressing seven sleep domains (i.e. sleep disturbance, snoring, awaken short of breath or with headache, adequacy of sleep, somnolence, a problems index 1 and a problems index 2). An additional single item assesses quantity of sleep.[37]

Behavioral Goal Adherence: Goal adherence for previous week's goals will be assessed via telephone on a weekly basis for 10 weeks post-baseline using a 0-10 Likert scale, where 0 indicates no adherence to completing the goal and 10 indicates complete adherence.

Tertiary outcomes:

Module completion: Participants will be asked during weekly (for 10 weeks) phone calls placed by the study staff about completion of modules (i.e., how many modules completed, which modules) during the previous week. In addition, the web developer will build a database to track time spent on each module, which modules were accessed, and number of times each participant accessed the program. This database will be linked only to userID and will not be linked with PHI.

Module usability: Participants will be asked during weekly phone calls about usability of modules. Specifically, they will be asked to rate each completed module on a 0-10 scale where 0= very difficult and 10=very easy, in terms of accessing information presented, understanding information presented, setting a module goal, navigating the module.

Treatment credibility: Participants' judgments of treatment credibility will be assessed at the post-baseline assessment interval using a questionnaire adapted from Borkovec and Nau.[38] This measure has been shown to have an internal consistency of .85 and test-retest reliability of .83.

Patient satisfaction: Patient satisfaction will be assessed by the Pain Treatment Satisfaction Scale which is a 5-item satisfaction survey designed to assess patient satisfaction with 5 domains of pain care.[39] This measure shows good internal consistency (.83-.90 across two samples) and significant associations to follow-up treatment satisfaction and staff and patient ratings of patient improvement.

VPMRC program-specific feedback: Participants will be administered an investigator-created measure designed to assess the layout of the website, ease of navigation, relevance of the materials presented, appeal of the program, understanding of key concepts, appropriateness of the graphics and multimedia interface, ease of use, problems encountered, amount of material presented, and general likes and dislikes

Sociodemographic status and pain-relevant variables: Participants' age, sex, education level, racial/ethnic background, and marital status will be assessed at the time of the baseline examination. Pain-specific factors such as pain duration, number and location of pain sites, past and current pain treatments, cause of pain, and presence of radicular symptoms, will also be assessed at baseline.

Pain medication: At baseline, medication use will be assessed by the study coordinator through participant interview and VACHS computer pharmacy records. Medications will be coded into several categories, namely non-steroidal anti-inflammatory, non-opioid analgesics, opioid analgesics, and benzodiazepines and other sedative/hypnotics using a recording sheet used in our prior studies. The specific medication used, its dose, and schedule of administration will be recorded. At 10 weeks post-baseline, this information will again be collected via patient self-report using Trial DB, and participants' medical records will be independently reviewed for changes in medication regimen from baseline by the RA for corroboration.

Analytic Plan

Because the overall goal of the project is to develop a pain self-management resource for Veterans, the VPMRC, we will employ an iterative process of formative evaluation through two distinct Phases in order to optimally revise and modify the VPMRC. All analyses will be conducted in the service of further refining and optimizing the usability and effectiveness of the program. Ultimately, these data and the subsequent modifications to the VPMRC will produce a resource that can be submitted to examination of efficacy through a randomized controlled trial.

Phase I: Development of the VPMRC

Using the Think Aloud protocol, qualitative data will be collected regarding participants' verbal, audio-recorded feedback of their experiences with navigating the VPMRC homepage, self-assessment, resources, and reviewing the treatment modules. Consistent with a phenomenologic approach (i.e., capturing the essence of the participant's experience), the qualitative feedback collected from each of the two study visits for each participant will be transcribed, coded, and systematically analyzed for emerging themes. These analyses will be shared with members of the EP and will be used to inform modification of

the VPMRC with respect to the layout of the website, ease of navigation, relevance of the materials presented, appeal of the program, understanding of key concepts, appropriateness of the graphics and multimedia interface, ease of use, problems encountered, amount of material presented, as well as general likes, dislikes, overall functionality of the program, and recommendations for change.

Quantitative data collected from the Post-intervention Measure will provide information regarding the usability, ease of navigation, and functionality of the program and specific modules. Descriptive statistics (e.g., means, standard deviations, frequencies) will be calculated for these data.

All quantitative and qualitative data collected, with input from members of the EP, will be used to guide modification of the VPMRC to reduce identified issues with navigation of the site, graphics and audio effects, relevance of materials for the population, ease of use with respect to the self-assessment, homepage functions, and other related issues. These changes will be made prior to initiating the pilot feasibility trial described in Phase II.

Phase II: Pilot Feasibility Trial of VPMRC

We will analyze the primary and secondary hypotheses according to the Intent-to-Treat principle. If missing data are minimal (e.g., <5%), we will conduct a complete case analysis; otherwise, imputation methods will be used to fill in the missing values. Several imputation approaches will be considered after inspection of the missing data rates and before any analyses of treatment effects are conducted. These approaches would include imputing the worst and best value (i.e., bounds on the treatment effects) and using multiple imputation assuming missing at random. These approaches would be supplemented by sensitivity analyses assuming nonignorable missingness. Only pre-specified baseline variables that may affect the outcome will be considered as adjustment variables in a sensitivity analysis. These variables include age, race/ethnicity, gender, educational attainment, and depressive symptom severity.

The primary endpoint is the mean difference in baseline to post-baseline follow-up scores on the primary measure of pain interference (i.e., WHYMPI-Interference Scale) at 10 weeks post-baseline. T-tests will be utilized to evaluate the effect of treatment on the primary outcome, and an ordinary least squares regression model will be used to control for potential confounders. The treatment will be represented by an indicator variable. The model fit will be assessed using graphical techniques and regression diagnostics. In a sensitivity analysis, we will examine the effect of treatment adjusted for the pre-specified set of baseline covariates. Analyses of covariance (ANCOVAs) will be employed to control for differences among participants in baseline scores and to determine whether participant characteristics are associated with changes in scores on outcome variables across time.

Because the primary and secondary hypotheses test differences in outcome measure scores across time, we will use paired t-tests, or their non-parametric analogs (e.g., Mann-Whitney test) to compare mean (or median) scores on the outcomes across time. Given the multiplicity of tests for secondary outcomes (i.e., six outcomes) and the power of the study, in addition to maximizing sample size, we will use the Bonferroni procedure p-value, which we conservatively estimate to be $p = 0.008$, based on an overall significance of $p=0.05/6$, to account for the number of comparisons. Our six secondary outcomes will be examined with the purpose of informing future modifications to the VPMRC and additional hypothesis generation. We have not grouped within subsets in order to ensure a more conservative approach. Tertiary hypotheses will examine data related to usability (use of and functionality) and satisfaction (satisfaction, credibility) with the VPMRC and will be collected only at 10 weeks post-baseline. Descriptive statistics will be employed to examine these data in order to describe participants' experiences with the VPMRC.

As in Phase I, quantitative data from the Post-intervention Measure with added data from the weekly phone calls for Phase II regarding usability of and satisfaction with the VPMRC will be used to modify the program. In addition, we will use specific primary and secondary outcomes data to inform modification of the VPMRC. For instance, if the data suggest a significant reduction in pain interference, but more modest changes in fatigue or depression, specific modules, such as Pacing (the pleasant activity scheduling coping skill) or Adaptive Stress Response (the using positive coping statements coping skill) will be targeted for further content and presentation enhancement to increase benefit to patients on these important related outcomes. We will also use data from tertiary outcomes to further modify presentation of the various treatment modules. For example, if certain modules are clearly preferred, as indicated by participant report of modules completed and satisfaction with the modules, other, less-preferred modules may be further enhanced (e.g., changes to audio-visual aspects, presentation of content within modules) to increase use, interest, and satisfaction.

6. References:

1. Chou R, Huffman LH. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med.* 2007;147:492-504.
2. Martel B, O'Connor P, Kerns RD, Becker W, Morales KH, et al. Opioid treatment for chronic back pain: a systematic review and meta-analysis of their prevalence, efficacy, and association with addiction. *Ann Intern Med,* 2007;146:116-127.
3. Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain.*Clin J Pain.*2002;18:355-365.
4. Hoffman BM, Papas RK, Chatkoff DK, Kerns RD. Meta-analysis of psychological interventions for chronic low back pain. *Health Psychol.* 2007;26:1-9.
5. Van Tulder MW, Ostelo R, Vlaeyen JWS, Linton SJ, Morley SJ, et al. Behavioural treatment for chronic low back pain (Cochrane Review). 2004; Issue 3. In *The Cochrane Library*, Chichester, UK.
6. Lamb SE, Hansen Z, Lall R, Castelnuovo E, Withers EJ, Nichols V, Potter R, and Underwood MR. Group cognitive behavioral treatment for low-back pain in primary care: a randomized controlled trial and cost-effectiveness analysis. *Lancet.* 2010;375:916-923.
7. Dobscha SK, Corson K, et al. Collaborative care for chronic pain in primary care: a cluster randomized trial. *JAMA- J Am Med Assoc.* 2009;301:1242-1252.
8. Kerns RD, Jacob M. Psychological aspects of back pain. In S. Newman & M. Jacob (Eds.), Psychological aspects of rheumatic disease. London: Bailliere Tindall. 1993.
9. Krein SL, Heisler M, et al. Overcoming the influence of chronic pain on older patients' difficulty with recommended self-management activities. *Gerontologist.* 2007;47(1): 61-68.
10. Krein SL, Heisler M, Piette JD, Makki F, Kerr EA. The effect of chronic pain on diabetes patient's self-management. *Diabetes Care.* 2005;28(1):65-70.
11. Clark JD. Chronic pain prevalence and analgesic prescribing in a general medical population. *J Pain Symptom Manag.* 2002;*23*(2):131-137.
12. Wodcock J. A difficult balance – pain management, drug safety and the FDA. *New Engl J Med*, 2009;361:2105-2107.
13. Crosby FE, et al. Survey of pain among veterans in Western New York. *Pain Management Nursing.* 2006;7(1):12-22.
14. Kerns RD, et al. Veterans' reports of pain and associations with ratings of health, health-risk behaviors, affective distress, and use of the healthcare system. *J Rehabil Res Dev.* 2003;40(5):371-379.
15. Mitchinson AR, Kerr EA, Krein SL. Management of chronic noncancer pain by VA primary care providers: when is pain control a priority?. *Am J Manag C.* 2008;14(2):77-84.
16. Kerns RD, Sellinger J, Goodin BR. in press. Psychological treatment of chronic pain. *Ann Rev Clin Psychol*.
17. Smeets RJEM, Vlaeyen JWS, Hidding A, Kester ADM, Van der Heijden GJMG, Van Geel ACM, Knottnerus JA. Active rehabilitation for chronic low back pain: Cognitive-behavioral, physical, or both? First direct post-treatment results from a randomized controlled trial. *BMC Musculoskeletal Disorders*. 2006;7:5.
18. Christensen H, Griffiths KM, Farrer L. Adherence in internet interventions for anxiety and depression. *J Med Internet Res.* 2009;*11*(2):1438-8871.
19. Hollon SD, Muñoz RF, et al. Psychosocial intervention development for the prevention and treatment of depression: promoting innovation and increasing access. *Biol Psychi.* 2002;52(6):610-630.
20. Wagner B, Knaevelsrud C, Maercker A. Internet-based cognitive-behavioral therapy for complicated grief: a randomized controlled trial. *Death Stud*. 2006;30:429-453.
21. Ybarra ML, Eaton WW. Internet-Based Mental Health Interventions. *Ment Health Serv Res.* 2005;7(2):75-87.
22. McInnes DK, Gifford AL, Kazis LE, Wagner TH. Disparities in health-related internet use by US veterans: results from a national survey. *J Informat Prim Care.* 2010;18(1): 59-68.
23. Fonda S, McMahon G, Gomes H, Hickson S, Conlin P. Changes in Diabetes Distress Related to Participation in an Internet-Based Diabetes Care Management Program and Glycemic Control. *Journal of Diabetes Science and Technology.* 2009;3(1):117-124.

24. Macea DD, Gajos K, Calil YAD, Fregni F. The Efficacy of Web-Based Cognitive Behavioral Interventions for Chronic Pain: A Systematic Review and Meta-Analysis. *Pain.* 2010;11(10):917-929.
25. Keogh E, Rosser BA, Eccleston C. e-Health and chronic pain management: Current status and developments. *Pain.* 2010;151:18-21.
26. Boris-Karpel S. Policy and practice issues in pain management. In M.E. Ebert & R.D. Kerns (Eds.). *Behavioral and psychopharmacologic pain management:* London, England*:* Cambridge University; 2011.
27. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates: estimates from U.S. national surveys. *Spine.* 2002;31(23):2724-2727.
28. Kerns RD, Rosenberg R, Jamison RN, Caudill MA, Haythornthwaite J. Readiness to adopt a self-management approach to chronic pain: The Pain Stages of Change Questionnaire (PSOCQ). *Pain.* 1997;72: 227-234.
29. Kerns RD, Habib S. A critical review of the pain readiness to change model. *Pain.* 2004;5:357-367.
30. Jensen MP, Nielson WR, Kerns RD. Toward the development of a motivational model of pain self-management. *Pain.* 2003;4:477-492.
31. Jensen MP, Turner JA, Romano JM, Strom SE. The chronic pain coping inventory: development and preliminary validation*. Pain*. 1995;60(2):203-216.
32. Nielson WR, Armstrong JM, Jensen MP, Kerns RD. Two brief versions of the multidimensional pain readiness to change questionnaire, version 2 (MPRCQ2). *Clin J Pain.* 2009*;*25*:* 48-57.
33. Farrar JT, Young JP, LaMoreauxb L, Werthb JL, Pooleb RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain.* 2001;94(2):149-158.
34. McNair D, Lorr M, Doppleman L. *Profile of Mood States*. San Diego, CA: Educational and Industrial Testing Service;1971.
35. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clin Psychol Rev.* 1988;8:77-100.
36. Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res.* 1995;39(3):315-325.
37. Stewart AL, Sherbourne C, Hays RD, et al. Summary and discussion of MOS measures. In Stewart AL, Ware JE (eds.), *Measuring functioning and well-being: The Medical Outcomes Study approach.* Durham, NC: Duke University Press;1992:pp. 345-371.
38. Borkovec TD, Nau CD. Credibility of analog therapy rationales. *J Exp Psychol Gen.*1972; 3: 257-269.
39. Kerns RD, Otis JD, Rosenberg R. Veterans' reports of pain and associations with ratings of health, health risk behaviors, affective distress, and use of the healthcare system. *J Rehabil Res Dev.* 2003;40:371-380.