Supplement 1

Protocol

Original Protocol

Amendments

Amendment 1 - Approved 01/01/2010

- Create peer experience testimonials from Veterans who previously completed CBT for Chronic Pain plus addition of voice consent
- Addition of study recruitment flyer

Amendment 2- Approved 05/19/11

- Approval to post recruitment flyers in the following venues: 1) patient care waiting areas, 2) craigslist under the "volunteer" section, 3) flat screen informational TVs around the hospital and 4) VA Good Morning VA Connecticut
- Recruit at Pain Education table
- Change defined score for absence of dementia for SLUMS (13 to 20)
- In addition to current DSM-IV axis 1 diagnosis, we also will access past major depressive disorder
- Substitute new satisfaction treatment questionnaire from the modified VHA Customer Service Standards to Satisfaction with Therapy and Therapeutic Scale
- Addition of monitoring pain medication
- Addition of the following scales: PSC, PSCOQ, SF36-V, SPQI, SOPA
- Add daily IVR questions – sleep, pain coping, mood
- Change sample size in protocol from 128 to 230 since incorrectly written
- Update 'Safety' section to accurately describe AE monitoring with current IRB rules and regulations
- Based on feedback from pilot, altered treatment manual – changed Module 9 from 'Pacing – Pleasant Activities' to 'Sleep – Sleep Hygiene Tips'
- ICBT prerecorded explanation of skills on the second day was changed so patients could listen to the explanation whenever they wanted
- Updated 'Risks & Protection' section about data storage outside the VA (Michigan Academic Computing Center – MACC)
- Deleted eligibility criteria of urine toxicology test at baseline
- Changed treatment cut off from 12 weeks to 14 weeks to allow for cancelations and rescheduling
- Stated we would track the reason for drop-out
- Changed how the IVR calls would occur – originally stated the patient would call the IVR system, but changed to say the IVR system will call the patient
- Modified the method for assessment completion – mail or via TrialDB
- Deleted the section about needing a RA to collect data via telephone if the patient missed an IVR call
- Changed randomization procedures – instead of using numbered envelopes, we will use a database that has a stratified factor that will auto assign the patients completed by the study biostatistician

Amendment 3- Approved 07/07/2011

- Modified protocol to state that we will provide the patient's first name to U. of Mich for the IVR system to personalize the call
- Minor changes to the medical clearance form

Amendment 4- Approved 11/03/2011

- Modified method of getting medical clearance by putting note into CPRS since providers didn't use email encryption
- Addition of short interview at the end of the IVR condition to provide feedback
- Addition of prescreening people during recruitment – created screener, WIC and WOA

Amendment 5- Approved 01/05/2012

- Remove medical clearance
- Provide patients feedback about to progress in graph forms
- 1 week baseline assessment of pain intensity, sleep duration and activity level
- Change language from tape recording to digital audio recording

- Remove the names of the MACC employees as they are not having access to PHI and only maintaining equipment
- Change language for how patients will be paid – by voucher and check

Amendment 6- Approved 03/15/2012
- Replace the SCID with the MINI
- Transfer data to and from VINCI

Amendment 7-Approved 03/16/2013
- Provide flyers to providers for direct referral
- Advertise via VACHS Facebook
- Place flyers at Veteran Centers and with Veteran Coordinators at local Universities and throughout the local New Haven area
- Conduct the educational pain table at all VACHS location

Amendment 8- Approved 11/21/2013
- Expand recruitment by adding study brochure

Amendment 9- Approved 02/06/2014
- Add additional language regarding information security and data flow of trial – clarify what information is at Yale, how often data is to be returned to the VA, the manner it will be returned and the transfer of data from Yale via secure server transfer

Amendment 10- Approved 05/21/2015
- Send de-identified data to University of Michigan to train artificial intelligence (AI) engine for newly funded grant

Amendment 11-Approved 06/30/2016
- Review of medical records in order to compare patients who enrolled vs. those expressed interest, met eligibility but didn't enroll. Extract demographics: age, race, sex, pain medication use, distance from VA, and number/location of pain sites

DESCRIPTION OF RESEARCH PROJECT
Human Studies Subcommittee
VA Connecticut Healthcare System

1. **Principal Investigators**: Alicia Heapy, Ph.D – VA Connecticut Healthcare System
2. **Co-investigators**:

Access to PHI:

Robert Kerns, Ph.D – VA Connecticut Healthcare System, VA Central Office, Yale University
Cynthia Brandt, M.D.- VA Connecticut Healthcare System , Yale Center for Medical Informatics
Mary Dallas, PhD., RPT – VA Connecticut Healthcare System
Gerald Grass, M.D. - VA Connecticut Healthcare System
John Sellinger, Ph.D. – VA Connecticut Healthcare System
Rebecca Czlapinski, M.A. – VA Connecticut Healthcare System

No access to PHI:

Carman Hall, Ph.D., RN. - Polytrauma/Blast-related Injury QuERI, Minneapolis VAMC
John Piette, Ph.D. – Ann Arbor VA, University of Michigan
Sarah Krein, Ph.D., RN. - Ann Arbor VA, University of Michigan
Caroline Richardson, M.D. – Ann Arbor VA, University of Michigan
Joseph Goulet, Ph.D. - VA Connecticut Healthcare System

3. **Title:** IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain

4. **Purpose:** The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention. The primary Clinical equivalence hypothesis states that Veterans with Chronic Low Back Pain (CLBP) receiving IVR-based CBT (ICBT) will demonstrate, relative to standard face-to-face CBT (CBT), equivalent declines in reports of pain intensity as measured by the numeric rating scale at post-treatment and follow-up. The secondary hypothesis states that Veterans with CLBP receiving ICBT, relative to CBT, will demonstrate equivalent declines in reports of pain-related interference and emotional distress at post-treatment and follow-up. Lastly, it is hypothesized that a) Veterans with CLBP receiving ICBT, relative to those receiving CBT, will demonstrate equivalent treatment dropout rates, behavioral goal accomplishment, IVR call adherence, treatment satisfaction ratings and treatment credibility ratings at post-treatment and follow-up and b) moderators of significant improvements in treatment outcomes will include age, sex, race/ethnicity, and psychiatric comorbidities.

5. **Background:**

Chronic Pain and Cognitive Behavioral Therapy: CBT is the most commonly cited psychological alternative to more traditional medical and rehabilitation approaches to chronic pain management and has demonstrated efficacy for reducing pain and improving function in persons with a broad spectrum of pain-related conditions.[13,14] CBT is informed by a theory of chronic pain that hypothesizes that patients' idiosyncratic beliefs, attitudes and coping resources play a central role in determining their experiences of pain.[15] The overarching goal of CBT is to assist the patient in the development of an adaptive problem-solving, self-management approach to pain management based on 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 it is specifically designed to simultaneously target reductions in pain and associated disability, emotional distress, and overall quality of life. CBT is a structured, time-limited, and goal-oriented therapeutic approach that can be delivered in either small group or individual outpatient sessions. During therapy 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 overall treatment goals and pain coping skill practice are encouraged through the development of intersession homework assignments. Kerns and his colleagues recently published a meta-analysis of psychological interventions for CLBP and documented moderate to large effects of psychological interventions, including CBT, in reducing pain and pain-related interference relative to waiting list control conditions. [14] A similar Cochrane type review led to nearly identical conclusions.[13]

CBT has several limitations that have hindered its use in clinical care settings. First, CBT requires that patients attend treatment sessions regularly. A typical CBT treatment schedule might require weekly, 60-minute sessions for 6 to 12 weeks. This schedule may put treatment out of reach for patients with limited funds or transportation options, health and mobility limitations, busy schedules, and those who work during the day. Further, patients who are geographically removed from centers where CBT for chronic pain is offered may not be aware of this treatment option or may not be able to participate if they are aware. Second, therapists who use this time intensive treatment schedule can deliver service to a limited number of patients, likely a smaller number than could benefit from the services. Finally, assessment of pain intensity, pain-related interference, affective functioning, and adherence to behavioral goals set in prior sessions occurs during the patient's therapy sessions, making the reports retrospective in nature. Retrospective patient report, often using pencil and paper methods, is the most common technique for collecting information regarding a person's pain experience in both clinical research and treatment. Despite the popularity and ease of use of retrospective self-reports, this method is vulnerable to recall and cognitive biases that attenuate their validity and reliability.[16]These biases include disproportionate weight given to recent and extreme (positive or negative) events, influence of emotional state at the time of recall, omission of distal information, and reliance on ease of retrieval to estimate the frequency of a behavior.[17]

For these reasons, CBT is often not the most accessible, convenient, and efficient means of providing treatment. An alternative is to improve treatment access and efficiency of treatment provision, and to enhance the validity and reliability of assessment techniques through the use of electronic methods such as interactive voice response technology.

Interactive Voice Response (IVR): IVR is a computerized interface that allows patients to report and receive information via their telephone. Patients contact the IVR system using a toll free telephone number. Data are collected when patients answer pre-recorded voice prompts using their telephone key pad. In the context of a CBT intervention for chronic pain, the IVR system can be used to collect data regarding a patient's pain intensity, pain-related disability, emotional functioning, medication adherence, and adherence to coping skills practice goals set during prior sessions. All of the information reported during a call is automatically captured in a database and time and date stamped. Patients can also receive information via IVR. The IVR system can be programmed to provide patients with pre-recorded standard didactic information regarding pain coping skills or personalized therapist feedback based on the patient's self-reported pain-related symptoms, adherence to skill practice and behavioral goals, or their mood. In addition to the convenience, accuracy and efficiency benefits of IVR, the system also maintains the therapist's ability to be responsive to each patient's progress, symptoms and

circumstances. The therapist is able to monitor a patient's daily IVR report and to tailor subsequent feedback based on pain-related symptoms or adherence to skill practice goals.

Use of IVR to deliver treatment: There is emerging evidence that IVR-based interventions are effective for providing education, peer support, providing tailored messages to enhance adherence, and maintaining and enhancing treatment gains for patients with a range of chronic conditions.[18-20] One of the most well developed areas of investigation is the use of IVR-based therapy for the treatment of Obsessive Compulsive Disorder (OCD). A recent review found that an IVR-based CBT treatment for OCD was as good as therapist delivered CBT treatment and superior to relaxation only treatment.[21] Within the realm of pain-related research, use of IVR after traditional CBT to reinforce pain coping skills and prevent relapse has been successful in maintaining and even enhancing gains made in treatment.[19,22] The authors also note high levels of adherence to daily IVR telephone calls both during the study when they received $.70 per call, but also after the study concluded when payment was no longer offered and 9 out of 10 participants continued to call.[19] Despite these promising results, to our knowledge there have been no trials of IVR-based treatment for chronic pain.

Use of IVR to collect data: Although still a relatively new data collection method, several studies have used IVR technology to collect daily participant data [20,23] and administer validated assessment measures.[24-26] In our lab we have used IVR to monitor daily ratings of pain, pain-related symptoms, medication side effects and adherence pain coping skill practice in two studies.[20,27] We have found that participants are readily able to learn and navigate the IVR system and that they demonstrate a high rate of adherence to the daily calling schedule (see Work Accomplished section for more details).

Equivalence trial of IVR-based CBT for chronic pain: Given the empirical evidence to support the use of CBT for persons with CLBP, the proposed research can be conceptualized as an equivalence trial of IVR-based CBT relative to standard CBT treatment. An equivalence trial is designed to determine if a new treatment is therapeutically equal to an established treatment.[28] A new treatment can be recommended as therapeutically similar to the established treatment when it falls within a pre-defined range of efficacy in a primary patient outcome.[28] For example, in an equivalence trial of pain management treatments such as the one proposed, we must define the minimum difference in pain intensity that would represent a meaningful decrease in pain. Because equivalence trials present methodological challenges not present in trials designed to evaluate treatment superiority and because these trials are being used more frequently, the CONSORT statement on the conduct of clinical trials has been extended recently to include the reporting of non-inferiority and equivalence trials.[17] We have designed the proposed study to be consistent with CONSORT recommendations for equivalence trials and will note when methodological and design choices have been made in the service of CONSORT guidelines. If IVR-based CBT is found to have clinically equivalent outcomes relative to standard CBT, an additional treatment option and enhanced access to treatment will be open to Veterans with CLBP. It is unlikely, as well as inadvisable, that traditional CBT be eliminated as a potential treatment for CLBP. Rather, it is recommended that both IVR-based and traditional CBT remain available to enhance treatment options for Veterans.

6. **Significance:** CLBP is one of the most prevalent and costly healthcare problems in industrialized nations.[29-31] Low back pain is the fifth most common reason for all physician office visits in the U.S. and the second most common symptomatic reason. Total incremental direct health care costs attributable to CLBP in the U.S. were estimated at $26.3 billion in 1998. In addition, indirect costs related to days lost from work are substantial, with approximately 2% of the U.S. work force compensated for back injuries each year.[32-34] Several studies demonstrate a particularly high prevalence and costs of musculoskeletal disorders, particularly

CLBP, among Veterans receiving care in VHA facilities.[8-10] Data suggest that as many as 50% of Veterans receiving primary care services in VHA facilities report significant pain.[35] Among OEF/OIF Veterans, painful musculoskeletal conditions represent the most prevalent of all diagnosed medical and psychiatric conditions.[11] Costs to Veterans and their families associated with pain, suffering, diminished functioning and employability, and quality of life as well as economic costs associated with the delivery of healthcare services and disability compensation are documented to be particularly high.[36]

The VHA National Pain Management Strategy was initiated November 12, 1998, and established Pain Management as a national priority. The overall objective of the strategy is to develop a comprehensive, multicultural, integrated, system-wide approach to pain management that reduces pain and suffering for Veterans experiencing acute and chronic pain associated with a wide range of conditions, including terminal illness. Central to this objective is the goal to assure access to an interdisciplinary approach to pain care across VHA facilities. It is in this context that the current study is proposed. Given the large number of Veterans who could potentially benefit from empirically validated treatment such as CBT for chronic pain, it is essential that factors that limit access to this treatment are addressed. An IVR-based CBT approach can be used to enhance care for patients in geographic areas where face to face access is not available. Establishment of the equivalence of an IVR-based CBT is viewed as an important step in meeting the objective of the VHA Pain Management Strategy.[37] IVR will allow Veterans to access CBT from their home via a touch-tone telephone 24 hours/day, thereby promoting convenient access to treatment without travel to the VA. In our prior studies of CBT for chronic pain and in providing care through the Comprehensive Pain Management Center (CPMC) at VA Connecticut Healthcare System (VACHS) we have found that many Veterans experience significant barriers that negate their ability to access potentially helpful treatments. Many lack reliable transportation, cannot afford gasoline, are geographically removed from our facility, or have health and mobility issues that make travel difficult. Veterans who work, particularly younger Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) Veterans may not have the workplace flexibility to attend weekly outpatient sessions. We believe that IVR-based CBT may address these barriers. If IVR-based CBT proves to have equivalent efficacy to traditional CBT, it could provide an additional avenue to treatment for those who are otherwise unable to participate in face-to-face treatment.

7. **Subjects:** Subjects will be 128 patients receiving care at the VACHS who report chronic low back pain. Women and minorities will be recruited. The sample characteristics will most likely be similar to the characteristics of those persons who have participated in our other recent studies. The age range of the sample is expected to be between 18 and 80 with a mean age of approximately 55. It is expected that approximately 5 to 15 % of the subjects will be women, and between 10 and 15% are likely to represent racial/ethnic minorities. The majority of subjects are expected to have a high school diploma. Subjects are expected to have been diagnosed of a range of chronic medical conditions in addition to low back pain. Chronic psychiatric disorders are also expected be common, including a rate of current major depressive disorder of approximately 40-50%. All subjects will be Veterans. No specific subpopulations will be specifically included or excluded. No specifically identifiable vulnerable populations will be targeted for enrollment

Eligibility criteria: (1) Presence of at least a moderate level of low back pain for a period of 3 months immediately prior to enrollment (i.e., scores of 4 or greater on a 0 [no pain] to 10 [worst pain imaginable] numeric rating scale of average pain.). (2) Absence of any life threatening or acute medical condition that could impair the subject's ability to participate (e.g., severe COPD, limb amputation, end stage renal failure, terminal cancer). (3) No psychiatric condition (e.g., active substance abuse, psychosis or suicidality) that could impair a subjects' ability to

participate as defined by their response to a validated depression measure, a review of their medical chart, and/or their responses during the baseline assessment interview (e.g., BDI score >30 or presence of suicidal intent, in-patient psychiatric admission within the prior 30 days, non-compliance with antipsychotic medication and/or uncontrolled psychiatric symptoms). *Presence of suicidal ideation or intent will prompt immediate medical/psychiatric attention to assure safety and institution of appropriate treatment.* (4) Ability to participate safely in the daily walking portion of the intervention as evidenced by ability to walk at least one block at baseline and medical clearance from the participant's primary care provider that the patient is physically able to participate in daily walking (see Appendix). (5) Absence of dementia defined by a score of 13 (or 20 if high school education) or greater on the Saint Louis University Mental Status (SLUMS).[60] (6) Urine toxicology screen confirming the absence of illegal substances or non-prescribed opioids. (7) Provision of participant consent to consult their primary care physician and review their medical records to ensure that eligibility criteria are met. (8) Absence of surgical interventions for pain during their participation in this study. Participants undergoing surgery will be discharged from the study in order to maintain the integrity of the active treatments. (9) Availability of a touch-tone telephone in the participant's residence to facilitate the provision of IVR data.

8. **Privacy:**
(1) To protect the privacy of participants during recruitment, several measures will be taken. A HIPAA waiver and Waiver of informed consent will be sought from the Human Studies Subcommittee to use administrative data to identify potential subjects. After obtaining agreement from each patient's primary care provider, a letter will be sent to the identified Veterans (see Appendix) from their primary care provider informing them about the study and inviting them to participate. Veterans will be informed of the option of "opting out" of the study or further contact by calling the study research assistant or returning a stamped and addressed response card. In order to avoid any perception of coercion, the letter will explicitly state that Veterans may contact the opt out phone number after usual business hours and leave a voice mail if they wish to avoid interaction with study personnel and that declining to be in the study will not affect their care at VACHS in any way. The research associate will have access to the voicemail. We will ask Veterans to leave the following information when leaving a voice message: (1) full name, (2) phone number, and (3) that they do not want to be contacted again. In the absence of such notification, 10 days after mailing the letter, Veterans will be called to solicit their involvement in the study. If the Veteran is not available during the phone call, the research associate will keep the conversation minimal and only ask for a call back from the Veteran to a phone number regarding a letter he or she should have received in the mail. Phone call guidelines would include stating the research associate's name, that he/she is associated with VA Connecticut Healthcare System and was calling about a letter the Veteran should have received. Conversation would include asking if the Veteran was interested in the study and if agreeable, Veterans will be screened regarding several of the key eligibility criteria for the study (e.g., confirmation of presence of chronic pain, and absence of medical and psychiatric comorbidities that preclude eligibility). If not agreeable, the research associate will thank the Veteran for his/her time. (2) Potential subjects will meet privately with study staff that will consent the subjects and receive written signatures from subjects on informed consent, voice consent and HIPAA documents. (3) Subjects will be informed during consent procedures that study personnel will review their medical records pertinent to their chronic low back pain in CPRS. Information will be included in a final assessment of eligibility for the study which will be determined thorough review of medical records by the study physician and psychologists and consultation with participants' primary care provider to ensure medical clearance for participation in the daily walking regimen required by the active interventions. This information will be accessed only after informed consent has been provided.

9. **Selection:** Potential subjects will be selected by seeking a HIPAA waiver from the Human Studies Subcommittee to use administrative data to identify all patients with a diagnosis of back pain (CPT codes 721, 722, and 724) reporting a pain score of ≥ 4 during their most recent clinic visit. After obtaining agreement from each patient's primary care provider, a letter will be sent to the identified Veterans from their primary care provider informing them about the study and inviting them to participate. Veterans will be informed of the option of "opting out" of the study or further contact by calling the study research assistant or returning a stamped and addressed response card. In order to avoid any perception of coercion, the letter will explicitly state that Veterans may contact the opt out phone number after usual business hours and leave a voice mail if they wish to avoid interaction with study personnel and that declining to be in the study will not affect their care at VACHS in any way. In the absence of such notification, 10 days after mailing the letter, Veterans will be called to solicit their involvement in the study. If agreeable, Veterans will be screened by phone regarding several of the key eligibility criteria for the study (e.g., confirmation of presence of chronic back pain, and absence of medical and psychiatric comorbidities that preclude eligibility). If screening suggests potential eligibility, and if the Veteran is interested and willing, a face-to-face appointment for obtaining written informed consent and to begin the pre-treatment assessment process will be scheduled. Solicitation letters will be mailed in waves in order to prevent overwhelming our capacity to provide timely treatment for interested Veterans.

We have elected to use the more proactive opt-out form of recruitment as opposed to an opt-in or general advertisement method of recruitment in order to obtain a pool of participants who are representative of all VACHS patients with chronic low back pain. Our usual recruitment method of placing advertisements in patient care areas and screening of referrals to the Comprehensive Pain Management Center (a multidisciplinary pain management program directed by RK) results in a pool of participants that primarily obtain their care at the West Haven campus of VACHS and may not adequately represent patients who obtain care at the Newington campus, the six Community-Based Outpatient Centers in Connecticut, or those who limit their appointments due to financial, transportation, mobility or scheduling restrictions. Additionally, use of opt-in techniques has been shown to result in a less representative sample and lower response rates than opt-out techniques.[51] Use of the opt-out method has been approved by the VACHS HSS in the past.

10. **Recruitment**: Approximately 128 patients receiving care at the VACHS who report chronic low back pain will be enrolled into the study. Potential subjects will be recruited via opt out letter that will be sent from their primary care physician informing them about the study and inviting them to participate (see Selection section for details).

11. **Research Plan:** After consent, the final assessment of eligibility for the study will be determined by thorough review of medical records by the study physician and psychologists, consultation with participants' primary care provider, and completion of a semi-structured interview described below. First, medical clearance for participation in the daily walking regimen required by the active interventions will be sought from each participant's primary care provider. We are using a medical clearance form developed and previously used in a walking intervention by our consultants Drs. Krein and Richardson (see Appendix). A urine toxicology screen will be completed in order to identify the presence of non-prescription drugs of abuse and to confirm that participants are taking prescribed opioid medications. A doctoral level psychologist associated with the study will review each participant's chart to identify if any disqualifying psychiatric issues are present. Following eligibility determination, baseline assessment will be initiated. The study coordinator (trained research associate or doctoral psychologists) or therapist (doctoral level clinical psychologist), will administer the SCID to identify the presence of any DSM-IV psychiatric disorders. The SLUMS will be administered to screen for cognitive

deficits likely to interfere with treatment participation, and a semi-structured interview regarding the nature and course of the pain complaint will be conducted.

The research assistant will then administer a battery of self-report outcome measures described below. Participants will be trained in the use of a pedometer to facilitate its use in the walking portion of the CBT and ICBT interventions. The research assistant will remain blind to participants' treatment assignments throughout the study. Subsequent assessments employing these self-report measures will occur via the internet using a secure, encrypted interface called TrialDB. TrialDB allows participants to use a login and password to access a data collection interface via the internet. Participants may then provide their answers to the self-report questionnaires via their home computer without the need to travel to VACHS. All self-report questionnaires will be de-identified. This system has been successfully used to collect data in the HSR&D Merit-funded Women Veterans Cohort Study (WVCS; PI: C. Brandt). Because not all Veterans have home internet access, we will provide Veterans with the option of completing the assessment at the VACHS location closest to their home or work or to have study staff bring a laptop to their home to allow then to complete the questionnaires. This strategy is being successfully used in the WVCS. These evaluations will occur at each evaluation interval.

Daily pain scores for all participants and adherence to coping skill practice will be assessed using IVR. The study research assistant will have responsibility for training subjects in the use of this method and for monitoring the data collection. The IVR system will generate a phone call to participants in the event of missing data with a prompt to call and supply the data. If a participant misses two consecutive daily calls the research assistant will call him/her in order to attempt to elicit the adherence ratings. Any data collected by the research assistant in this manner or collected via IVR call on a subsequent day will be marked to identify it as retrospectively collected. Participants will also use the IVR system for one week to report their pain intensity scores just prior to the collection of the 3- and 6-month follow-up data.

Once eligibility has been confirmed and all of the baseline assessments have been completed, participants will be randomized to one of the two treatment conditions according to the randomization procedure described below. Participants will be randomized within two weeks of the completed baseline assessments.

Randomization. Persons who meet eligibility criteria, provide informed consent, and complete the baseline assessment will be randomized to either CBT or ICBT. Randomization will be implemented by computerized random number generator (SAS version 8.2). The randomization codes will be created by the study biostatistician. The treatment allocation ratio for the two treatment arms will be 1:1 using a random permuted block design of varying block size. Treatment assignments will be placed in sequentially numbered, opaque sealed envelopes. These envelopes will be kept by the study coordinator. After a participant has provided informed consent and is deemed eligible to participate, the study coordinator will open the next sequentially numbered envelope and inform the therapist of the condition assignment. Individual outpatient treatment will be initiated immediately following random assignment.

Treatments:

Treatment structure: Both CBT conditions involve 10 treatment modules delivered over 10 consecutive weeks. The 10-week course of therapy will consist of an introductory module, followed by four consecutive two-session pain coping skills modules, and conclude with a tenth module emphasizing skill consolidation and relapse prevention. Both conditions will present the same 4 pain coping skills: relaxation, exercise, activity pacing and adaptive response to stress. A therapist manual for each CBT conditions has been developed. The CBT manual was used in our "Tailored CBT" study, and the ICBT manual was recently developed through funding from an HSR&D Short Term Project award. The study psychologist(s) will meet weekly with RK (the PI) for clinical supervision and audiotapes of treatment sessions will be rated for adherence to the treatment manuals (see Treatment Fidelity). ICBT involves four key components: (1) reading

handbook materials; (2) retrieval of pre-recorded information about the coping skills and IVR assessment of comprehension; (3) daily reporting using IVR on (a) pain intensity, (b) progress related to a behavioral treatment goal, and (d) pain coping skill practice; and (4) retrieval of pre-recorded therapist feedback and encouragement related to comprehension of module-specific information, daily reporting of pain and activities, goal accomplishment, pain coping skill practice, and potential associations among pain, goal accomplishment, and pain coping skill practice. CBT involves ten, weekly, 60-minute, individual face-to-face sessions with a doctoral level psychologist. The following table describes the key components of CBT.

Week	Module	Coping skill	Description	Goals
1	Introduction	None	Present rationale for treatment, explain pain cycle, and introduce goal setting.	Use pedometer to track steps for baseline measure
2	Exercise	Walking	Instructions for walking and benefits of increased activity,	-Increase daily steps based on +10% of baseline steps -Select a goal in service of attaining overall treatment goals
3	Exercise	Stretching/Body mechanics	Instructions for stretching and body mechanics and benefits	-Increase daily steps +10% of prior weeks steps -Select a goal in service of attaining overall treatment goals -Continue to practice prior week's skills
4	Relaxation	Diaphramatic breathing	Instructions for diaphragmatic breathing and benefits	-Practice diaphragmatic breathing 20 minutes/day - Select a goal in service of attaining overall treatment goals -Continue to practice prior week's skills
5	Relaxation	Progressive muscle relaxation	Instructions for progressive muscle relaxation and benefits.	-Practice progressive muscle relaxation 20 minutes/day - Select a goal in service of attaining overall treatment goals - Continue to practice prior week's skills
6	Adaptive stress response	Identifying negative thoughts	Influence of negative thoughts on pain, activities, and mood	-Monitor negative statements - Select a goal in service of attaining overall treatment goals - Continue to practice prior week's skills
7	Adaptive stress response	Positive coping statements	Countering negative thoughts with coping statements	-Use provided coping statements daily - Select a goal in service of attaining overall treatment goals -Continue to practice prior week's skills
8	Pacing	Activity pacing	Pace activities based on time rather than pain.	-Engage in one activity/day using pacing - Select a goal in service of attaining overall treatment goals -Continue to practice prior week's skills
9	Pacing	Pleasant activity scheduling	Scheduling pleasant activity scheduling to increase activity and enhance mood.	-Engage in one pleasant activity per day - Select a goal in service of attaining overall treatment goals -Continue to practice prior week's skills
10	Treatment wrap-up	Skill consolidation and relapse prevention	Planning for relapse and pain flares.	-Continue practicing all skills

Goals: Goal setting and skill practice is a common component of CBT and is designed to promote home practice of adaptive pain coping skills and other relevant goals. Goal setting communicates the importance of skill practice and prompts the actual practice and mastery of pain coping skills that allow patients to successfully use the skills on their own to manage chronic pain. Thus, goal setting is an important part of both CBT treatments. Near the end of each treatment session, beginning with the first treatment session, the participant will be assigned one overall treatment goal and from one to four (depending on the session) specific, quantifiable goals for coping skill practice for the participant. Weekly goals will include one goal that will support the accomplishment of the overall treatment goal, and one goal which will include specific expectations for home practice of a newly presented pain coping skill (e.g., practice relaxation exercise for 20 minutes daily) and continued practice of prior session treatment goals. Our clinical experience is that patients often have difficulty setting measurable, achievable, and timely goals without the assistance of a therapist, particularly at the outset of treatment. In order to avoid the frustration and failure that often accompany poorly defined, unachievable, or too easily attained goals, we have elected to include pre-selected goals in both CBT and ICBT. Participants in both treatments will receive the same goals.

After completing treatment, patients will continue practicing all of the skills they have learned during treatment and continue to set small goals in the service of their overall treatment goal. At

the 3- and 6-month post-treatment follow up intervals they will report on their adherence to this skill practice and goal attainment by calling the IVR system daily for one week.

CBT: Session 1 will begin with an overview of the goals of treatment and an introduction to the self-management approach to chronic pain that emphasizes acquisition and practice of adaptive pain coping skills. Treatment will emphasize the weekly identification of intersession goals and homework assignments, the importance of home practice of pain coping skills, and the use of the IVR system for the daily ratings of adherence.

- Sessions 2 through 9 will be comprised of four, two session coping skills training modules. The specific pain coping skills presented in these sessions will be relaxation, activity pacing, exercise, exercise and adaptive response to stress. Each module will include: (1) the presentation of an explicit rationale for development and use of the specific coping skill being taught, (2) a description of each coping skill and in session modeling and practice of the skill, as is appropriate, (3) problem-solving about the practice and use of the specific skill, and (4) discussion of specific goals for skill practice and use. Goal setting related to the practice and use of the specific skill for coping with pain and for achieving the overall treatment goal will be incorporated.
- Session 10 will emphasize skill consolidation and relapse prevention. An explicit review of skills learned during the treatment will be followed by a discussion targeting continued practice and application of the skills. Areas of poor adherence to recommendations for skill practice and application will be explicitly addressed. The session will conclude with elicitation of specific concerns about relapse (e.g., in the context of “pain flares” or anticipated stressful life events) and problem-solving discussion designed to reinforce perceptions of self-efficacy and a commitment to continued skill application.
- Throughout treatment, patients will call the IVR system daily to report on their pain, pain-related symptoms, and adherence to skill practice.

ICBT: ICBT is an adapted form of CBT specifically designed for the IVR environment. Following enrollment into the study, participants will receive a patient handbook and instructions for using the IVR system. Because the intervention will occur exclusively by phone, we were particularly aware of the need for the materials to be understandable, engaging, and informative because no face to face interaction will be available to determine participant understanding of the material or to provide clarification. To that end, we have taken care to create patient materials that are written at the 6^{th} to 7^{th} grade reading level. Each module includes a set of true/false comprehension questions designed to determine if the module information was successfully conveyed to the participant. If it was not, corrective information will be given during a weekly pre-recorded therapist feedback session. Treatment will occur over 10 weeks and will consist of the same 4 coping skills modules presented in SCBT. As in SCBT, treatment consists of an introductory module, followed by four consecutive two-session pain coping skills modules, and concludes with a tenth module emphasizing skill consolidation and relapse prevention.

- On the first day of each week, the patient will read the patient handbook section that corresponds to that week’s module. The handbook will contain instructions for setting weekly goals that promote practice of the current and former session coping skills. Participants will also receive information and support in attaining one overall treatment goal that they select from a menu of options.
- The next day they will then listen to a 10- to 15-minute pre-recorded treatment session that includes an elaboration of the treatment module information. They will answer a series of 5 questions to determine if they understand the content.
- Patients may record a question for their therapist at any time during the treatment. This will allow participants to obtain clarification or feedback on specific topics and avoid frustration that may impair progress or prompt dropout.

- On the last day of the week, they will listen to pre-recorded feedback from their therapist regarding their goal adherence during the week that includes a review of progress and adherence, praise for effort, corrective information regarding any incorrect answers that the participant provided to the true/false comprehension questions, answers to specific questions posed by the patient, and identification of areas for improvement. The therapist will also discuss any changes in the patient's self-reported pain and highlight any apparent relationships between symptoms and adherence.
- Throughout treatment, patients will call the IVR system daily to report on their pain and adherence to skill practice. The patient handbook, scripts for the treatment sessions, and therapist guidelines for delivering personalized feedback and scripts for common feedback themes can be found in Appendix A.

Participants assigned to both conditions will continue to receive routine care of their CLBP by their current healthcare providers as clinically indicated (not research staff). Study staff will not attempt to influence care in any way.

Outcome Measures:

The Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT) among other groups has called for the routine assessment of multiple domains of the pain experience in all pain treatment trials and have made recommendations for choice of measures for each core domain.[48] We have followed these IMMPACT recommendations in the development of our plan for assessing outcomes. A variety of standardized and reliable interview and questionnaire measures, supplemented by IVR methods, 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 therefore consistent with CONSORT guidelines on equivalence trials that outcome measures be similar to those used in studies to establish efficacy of the reference treatment. In addition to these outcomes we also propose to examine treatment satisfaction, treatment credibility, drop-out rate, goal accomplishment, IVR call adherence and skill practice adherence. See the table below for an explanation of the timing of assessment procedures.

Pain intensity: We will assess participants' global pain intensity using the Numeric Rating Scale of pain intensity (NRS-I)[52] an 11-point numeric rating scale (0 = no pain, 10 = worst pain imaginable). Participants will be asked to rate their usual, worst and least pain over the past week. The average of these numbers will serve as the primary outcome measure. Additionally, participants will rate their pain intensity using a single question (average pain that day on an 11-point numeric rating scale as above) when making daily calls to the IVR system.

Pain-related disability: The Interference subscale of the WHYMPI and by the Roland and Morris Disability Questionnaire will be used to assess pain-related disability.[53,54]

Emotional functioning: Overall functioning will be assessed using the Profile of Mood States (POMS),[55] a multidimensional measure of emotional functioning designed to be used in non-psychiatric or physically ill populations. Depression will be assessed using the Beck Depression Inventory[56] a widely used self-report measure with excellent reliability that is designed to detect depressive symptom severity.

Study Variable	Instrument	Baseline	Daily IVR	Post-treatment and 3- and 6-month follow-up	Purpose
Demographic (age, sex, race) and pain-relevant variables (duration, location, treatment)	Semi-structured interview	X			Covariate
Psychiatric comorbidities	Structured Clinical Interview for DSM-IV (SCID)[xx]	X			Covariate
Pain intensity	Numeric Rating Scale[xx-xx] Daily IVR diary	X	X	X	Primary Outcome Measure Clinical Outcome
Pain-related interference	Interference subscale WHYMPI[xx] Roland-Morris Disability Questionnaire[xx]	X		X	Clinical Outcome
Emotional functioning	Beck Depression Inventory[xx]	X		X	Clinical Outcome
Emotional functioning	Profile of Mood States[xx]	X		X	Clinical Outcome
Skill practice adherence	Daily IVR diary*		X		Treatment Feasibility Outcome
Goal accomplishment	Daily IVR diary*		X		Treatment Feasibility Outcome
IVR daily call adherence	Daily IVR diary*		X		Treatment Feasibility Outcome
Patient satisfaction	VHA patient satisfaction survey[xx]			X	Treatment Feasibility Outcome
Drop-out rate	N/A			X	Treatment Feasibility Outcome
Treatment credibility	Treatment Credibility Scale[xx]			X	Treatment Feasibility Outcome

* The Daily IVR diary consists of questions regarding pain intensity, skill practice adherence and goal accomplishment adapted from our prior work.

Treatment feasibility outcomes:

Adherence to coping skill practice will be assessed via IVR. The system that employs the use of a toll-free telephone number, computerized voice prompts for elicitation of adherence ratings, and automated recording of these ratings in a computerized database. Specifically, subjects will be instructed to call a toll-free number daily, typically in the evening, to provide ratings of their adherence to each of the specified intersession goals. They will then be instructed in the use of their touchtone telephone keypad to provide ratings on a 0 (not at all accomplished) to 10 (completely accomplished) scales for each of the specified goals. The IVR system is programmed to monitor the collection of these data on a daily basis. When a daily phone call is missed, the system will initiate a reminder call to the patient. If this is not successful a research assistant will call the subject at home in an effort to retrieve the missing data. If this method is still unsuccessful, adherence ratings for the days of missing data will be entered as 0. It is important to note that a high prevalence of missing data has the potential to undermine the integrity of this key dependent measure, so extensive efforts will be undertaken to assure the timely collection of these data. Ultimately, these adherence ratings will be aggregated across all goals and all days during the treatment and for the seven day periods associated with each follow-up assessment.

Goal accomplishment: In collaboration with the psychologist, participants will develop one specific, quantifiable behavioral treatment goals (e.g., increase amount of household chores completed to 30 minutes each day, increase outside social activities to two times per week) at baseline. At post-treatment, patients will rate their achievement of the goal on a 5-point scale ranging from -2 (100% decline) to 0 (no change) to +2 (100% improvement).

IVR call adherence will be at each evaluation interval. Call adherence will be total number of IVR calls made as expected divided by the total number of expected calls. Total number of

expected calls during treatment is 70 (7 daily calls X 10 weeks of treatment). Total number of follow-up calls is 7 per follow-up period (7 daily calls X one week follow-up reporting period.

Treatment credibility: Participants' judgments of treatment credibility will be assessed at post-treatment and follow-up using a questionnaire adapted from Borkovec and Nau.[57]

Patient satisfaction: Patient satisfaction will be assessed by a modified version of the VHA ambulatory care patient satisfaction survey designed to assess several specific VHA Customer Service Standards.[58] The measure will assess global perceptions of health care at the VACHS, as well as specific perceptions of care delivered in the context of this study.

Treatment attendance and drop out: Session attendance will be tracked, and the number of participants who do not complete follow-up assessments will be calculated.

Treatment fidelity measures:

CBT and ICBT Treatment Receipt/Comprehension: The measures of treatment receipt (i.e., the five item "content" questionnaire) have been described above. We will analyze and report these data regarding average level of correct treatment receipt and if any treatment modules were more difficult for participants to understand. These data will also allow us to comment on the absolute and relative fidelity of the treatments and to provide context regarding the efficacy results in this study. This will allow us to draw conclusions about the benefit of ICBT and to guide future research examining the use of this treatment for CLBP.

Treatment integrity will be assessed by students who will rate audiotapes of 30% of the CBT sessions and the ICBT personalized feedback sessions to assure that key components of the manuals are covered. Checklists for the use of these strategies will be available for the raters. Percentages of treatment integrity/violations will be calculated. The PI will provide corrective feedback to the psychologist whenever drift occurs.

Covariates:

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 of pain sites, and treatment regimen shown to be associated with outcomes will also be assessed at baseline.
Psychiatric comorbidities: Structured Clinical Interview for DSM-IV (SCID)[59] is a semi-structured interview designed to generate reliable Axis I DSM-IV psychiatric diagnoses. The SCID-I assesses for the presence of Mood Disorders, Anxiety Disorders, Substance Use Disorders, Psychotic symptoms, Somatoform Disorders, and Eating Disorders according DSM-IV.

Sample Size Calculation. This study will determine whether interactive voice response-based cognitive-behavior therapy (ICBT) is equivalent to standard cognitive-behavior therapy (CBT) on the primary outcome measure of pain intensity, as measured by the Numeric Rating Scale (NRS-I). Because the efficacy of CBT has been well established (REFS), a placebo comparison group was deemed unnecessary and potentially unethical.

The sample size was calculated based on a test of non-inferiority comparing ICBT to CBT, with 90% power and Type I error (1-sided) of 0.025. Based on available data from Veterans in a study of the efficacy of CBT for chronic back pain (Kerns, R.D. (PI), "Efficacy of tailored cognitive-behavior therapy for chronic back pain"), the estimated baseline NRS pain intensity score will be 7 ± 1.6 units. A 20% reduction in the NRS pain score, from 7 to 5.6 or 1.4 units, at 12 weeks post baseline is considered to be clinically relevant. The equivalence margin was set one NRS pain scale unit (e.g. if the mean score for ICBT is more than one unit lower than the CBT score, it will be deemed inferior). Based on these assumptions and 15% inflation for losses, the total required sample size is 128 participants (64 per group) [Hintze, J. (2005). Number Cruncher Statistical Systems (Version 2005) [Computer software].

Analytic Plan.

Baseline Analysis. The adequacy of the randomization will be assessed by comparing baseline demographic and clinical characteristics between the two treatment groups. Variables will be summarized (means, proportions, etc.) and continuous compared using two-sample t-tests, while differences in categorical variables will be examined using chi-square tests. Characteristics found to be significantly different between conditions will be included as covariates in analyses to determine if they alter the conclusions of the study.

Non-inferiority Analysis. We will compare ICBT to CBT on the NRS pain intensity scores at 12 weeks follow up using a one-sided, two-sample t-test. Non-inferiority will be demonstrated by the mean score for ICBT participants being less than one point less than those in the CBT. Non-inferiority analyses will be conducted on a *per protocol* basis. All other analyses will be conducted according to intent-to-treat basis, that is, by considering patient group status as randomized.

Analyses of outcome measures. Further analysis of primary and secondary outcome measures will employ mixed-effects models, which will account for the clustering induced by repeated measures on individual patients (SAS Institute Inc., Cary, NC). Mixed effects models include both between-groups and within-subject effects and allow for missing data, and measurements at different time intervals. Data from different subjects are assumed to be independent, while the correlation structure of the repeated measurements within subjects is modeled via parameterization of the covariance structure.

Between group comparisons of the effectiveness of treatments at 12 weeks (post-treatment), 3 months post-treatment, and 6 months post-treatment will demonstrate the post-treatment effects and whether benefits are maintained over time. Each of these hypotheses can be tested separately within the same mixed-effect model using a treatment dummy variable, time dummy variable, and treatment by time interaction terms and appropriate contrasts. The outcome variable in each model will be changes at the three follow-up visits relative to baseline, with the baseline value included as a covariate in the model. Separate models will be analyzed for the three clinical outcomes of interest: pain severity; pain-related disability; and affective distress.

Missing Data. If more than 15% of an outcome variable or a major covariate is missing, we will use multiple imputation method based on sequential regression imputation methods using SAS MI Procedure (SAS Institute).

12. **Risks and Benefits:**

Potential Risks and Protection from Risks:

1. Cognitive behavioral treatment - Participation in the psychological treatment is not expected to be associated with any significant risk or discomfort. The standard CBT treatment used in this study has been used safely by this research team in many prior studies and in the course of providing clinical care to Veterans. Subjects in the face-to-face CBT condition will be monitored in weekly sessions for worsening of psychiatric symptoms and suicidal ideation and plan, as is standard clinical practice. Study therapists are doctoral-level clinical psychologists with extensive training in therapeutic interventions, patient safety, and assessment of suicidality. Although we have never delivered CBT treatment via IVR, we have no reason to believe that this form of CBT would confer any additional risks to subjects. Because we will not have face-to-face contact with patients that would allow us to monitor any psychiatric or suicidal symptoms we will provide them with an information sheet in their patient handbook that explains where they may access treatment if they notice these symptoms or their current symptoms worsen. Patients who exhibit suicidal symptoms will be immediately referred for evaluation. For example, in the event that a patient endorses suicidal ideation when completing the BDI through TrialDB

(i.e. a response of 2 or higher on item 9: “suicidal thoughts or wishes”), the patient will be contacted via phone by the study coordinator (a trained, doctoral level psychologist), who will provide the necessary referral to ensure patient safety. A research assistant will be monitoring data collected via TrialDB each day during the week, including reviewing the BDI for endorsement of the suicide item.

2. Questionnaires, interviews and rating scales - Minor inconvenience may occur during the completion of the interviews and questionnaires, which may be viewed as frustrating and time-consuming. Some subjects may experience distress as a result of the psychiatric diagnostic interview (SCID). Interviewers are trained research associates or doctoral level psychologist with explicit training in the interview and management of subjects who experience emotional upset. Trained research associates will also be supervised by a doctoral level psychologist. Participants may take a break from the interview process as necessary. No risk is associated with participation in completing these measures.

3. Audiotaping of therapy sessions – Audiotaping is necessary to ensure the fidelity of the face-to-face CBT sessions and the personalized therapist feedback in the IVR-based CBT condition. Only participants in the CBT sessions will be asked to sign a separate consent to audiotape form. Participants who are in the IVR- based CBT will not have their actual voice audiotaped so voice consent is not necessary. Participants who decline will be referred for CBT treatment outside the study. Therapists will conduct the audiotaping and will label each tape with the subjects study ID# and the session number. Only approved research personnel will have access to the audiotapes and they will be stored in locked file cabinets in secure offices. Tapes will be destroyed according to recommended VA ISO procedures following fidelity ratings.

4. Walking intervention - Participants may experience a brief increase in pain or discomfort associated with participation in the walking portion of the intervention. The extent and duration of increased pain during or after walking is not expected to differ from that encountered in the pursuit of any mildly intensive physical activity regimen. Nonetheless, we have created several procedures designed to reduce any risks associated with regular walking. All subjects will have to obtain medical clearance from the physician prior to engaging in the treatment. We will actively solicit information on adverse events from subjects. Subjects who experience adverse events will be evaluated by their primary care provider or the study physician prior to re-entry into the study. These processes are described more fully in the “Adequacy of Protection against Risks” section.

Ultimately, any risks are best characterized as psychological or physical, and no known social or legal risk is identified. These risks, to the extent that they are present, are specifically associated with participation in the research. Potential study participants are informed that they may choose not to participate in the research study, and that cognitive behavior therapy for chronic pain management, similar to the intervention being evaluated in this study, is available in our facility without participation in the research.

<u>Potential Benefits:</u>

Since psychological and other interventions for pain management are generally available at the VA Connecticut Healthcare System, there is no direct benefit to Veterans agreeing to participate in this study. There is considerable potential benefit of this research to others given the specific promise of developing methods for promoting pain management that are available to a greater number of Veterans who suffer from chronic pain. Given the low potential for risk to the individual participant and the potential benefit to others with chronic pain, the risk-benefit ratio is judged to be favorable.

Importance of Knowledge to Be Gained

Chronic non-cancer pain remains a devastating problem for many people in our society in terms of the experience of pain, associated high rates of disability and emotional distress. Although psychological interventions, particularly cognitive-behavior therapy, have demonstrated efficacy for chronic pain, lack of access to treatment undermine their potential benefit for large numbers of persons who are otherwise judged to be appropriate for these treatments. The primary aim of the proposed study is to compare a more accessible version of IVR-based cognitive-behavioral therapy for chronic pain to standard cognitive behavior therapy to improve access for Veterans who are not able to regularly attend face-to face treatment sessions. Results of the study may lead to improvements in cognitive-behavioral approaches to pain management that may improve their utility for an increasing proportion of patients who could potentially benefit from this treatment. Given the low level of risk to individual participants, and the potential clinical and scientific benefits likely to be accrued from this research, risks to participants are reasonable.

13. **Safety:**

Assessment of level of risk: minimal

Oversight for this investigation will be provided by: Alicia Heapy, PHD and Robert Kerns, PhD. All research conducted at VACHS is provided with oversight by the VACHS Human Subjects Subcommittee (HSS) along with Yale University Human Investigation Committee.

Definition of adverse events: The following definitions of adverse events are included in the Standard Operating Procedures of the VACHS HSS and we have adopted these same definitions for use in monitoring the safety of participants in the proposed project.

Adverse event (AE) An AE is defined as any untoward physical or psychological occurrence in a human participant taking part in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research, or any risk associated with the research or the research intervention, or the assessment.

Serious Adverse Event (SAE) A SAE is defined as death; a life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the participant and may require medical or surgical treatment to prevent one of the preceding outcomes.

Unexpected Adverse Event (UAE) An UAE is any adverse event and/or reaction, the specificity or severity of which is not consistent with the informed consent, current investigator brochure or product labeling. Further, it is not consistent with the risk information described in the general investigational plan or proposal.

Monitoring of AEs Subjects in both treatment arms will be monitored regularly for adverse events by the study therapists and research assistant. Staff is trained to report any AEs promptly to the PIs. In both treatment conditions subjects are prompted during their daily IVR call to report any adverse events they have experienced. We anticipate that using this active identification method will allow us to identify all AEs in a timely manner. The study RA will be responsible for reviewing the AE reporting of all subjects each day and reporting the information to the PIs.

Reporting of Unanticipated Problems or Adverse Events. As per local HSS/HIC rules, we will notify the HSS promptly using the VACHS Adverse Event/Unanticipated Problem Report form and the Yale University HIC using the Adverse Event Form 6b, when any AE occurs. If the incident is serious, unanticipated and /or requires revision of the Project Description and/or Consent Form, we will notify the Research Office by telephone as soon as possible and always within 24 hours. A formal report will be provided within 2 business days. As per our local HSS and HIC policy, *all* AEs must be reported to the HSS/HIC *as they occur* for review regardless of

seriousness and/or relationship to the research. Because of this policy, the local HSS will be providing parallel review of AEs along with the PIs. We believe this will insure stringent oversight and early identification of any unexpected risks to human subjects.
Study progress including subject recruitment, completion of protocol, and adverse events will be reviewed by Joseph Goulet, PHD, study biostatistician, on a monthly basis. These results will be presented to the study PIs monthly.

14. **Informed Consent:** If an individual passes the screening process and is interested in enrolling in the study, study staff approved for obtaining consent will initiate the process of obtaining written informed consent. Written informed consent will be obtained in the context of a face-to-face discussion in a private office setting. Staff obtaining consent will have completed a web-based course with post-test on Human Research Protections, and all will have had specific training by the PI in obtaining informed consent for this study. All staff obtaining consent will be authorized to do so by the VA Connecticut Healthcare System Human Studies Subcommittee. Written informed consent will be obtained using a document for this purpose that has previously been approved by the VA Connecticut Healthcare System Human Studies Subcommittee. The original copy of the signed written consent form will be available in the Veterans' medical record and a copy will be given to the Veteran.

15. **Confidentiality:** Confidentiality will be protected by assigning numeric codes to subjects and using these codes any time forms and assessment measures are administered to subjects. A code list with names and numeric codes and written evaluations will be stored in locked file drawers in locked offices on VA property when not in use. All study related electronic data will be stored behind the VA firewall.

The only investigators who will have access to identifiable data are Drs. Heapy, Kerns, Brandt, Dallas, Grass, Schulman, Sellinger and Ms. Czlapinski.

16. **Location of Study**: All research will be conducted at the West Haven VACHS. Conduct of the proposed study will be supported by two existing Centers at the VACHS. Particularly relevant is the recently funded VA HSR&D Research Enhancement Award Program PRIME Center (PI: R. Kerns). The Comprehensive Pain Management Center (CPMC), also directed by the PI, is an established clinical, research, and training center that has the full and continuing support of referring physicians throughout VACHS and will serve to support recruitment and will provide a clinical context for the conduct of the study.

17. **Payment:** Participants will receive payment for participation in the four pain assessments. Participants will be paid $20 for participating in the first evaluation; $30 for participating in the questionnaire assessment after the tenth treatment session; $40 for participating in the 3-month follow-up questionnaire $50 for participating in the 6-month follow up questionnaire assessment. If subjects participate in each of these evaluations, they will receive a total of $140.

18. **Funding:** This study is currently under review for a VA HSD&D Merit Review, but funding is pending.

19. **Duration:** The duration of the study is expected to be four years. The duration of individual subject's involvement is expected to be 10 consecutive weeks of treatment, a three month follow-up and a six month follow-up. Subjects have the option in the consent form, to be contacted in the future for further studies.

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Department of Veterans Affairs

Memorandum

Date: July 20, 2010

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain" (#0004) was reviewed and approved by the Human Studies Subcommittee on 7/1/10. Neither you nor any of the identified co-investigators participated in the review and decision-making.

This amendment requires approval by the Yale HIC before implementation. For a timely review, where appropriate, submit a copy of this amendment request with the VACHS HSS approval letter to the Yale HIC without delay.

The approval for this project expires 3/17/11, when it will be subject for continued approval by the subcommittee on Human Studies. This will require that you submit a progress report. Request for this information will be forwarded to you one month before the end of the current approval period.

The Subcommittee reminds you of several important requirements:

1. All procedures and interventions employed must be those as approved by the HSS subcommittee.
2. Any changes to the protocol must be proposed to the subcommittee in writing (identifying the title, project number and sign by the PI) as a modification to an approval project and must be approved before they are initiated.

If any questions, please contact me at ext. 3350.

for Cora Milewski

Department of Veterans Affairs

REPORT OF SUBCOMMITTEE ON HUMAN STUDIES

Amendment

Project/Program Title: IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain

Principal Investigator: Heapy, A., Ph.D. (#0004)

VAMC: VA Connecticut Healthcare System/689 Review Date: 7/1/10

no change in findings

COMMITTEE FINDINGS

1. The information given in the Informed Consent under the Description of Research by Investigator is complete, accurate, and understandable to a research subject or surrogate who possesses standard reading and comprehension skills. ☐ YES ☐ NO

2. The informed consent is obtained by the principal investigator or a trained and supervised designate under suitable circumstances. ☐ YES ☐ NO

3. Every effort has been made to decrease risk to subject(s)? ☐ YES ☐ NO

4. The potential research benefits justify the risk to subject(s)? ☐ YES ☐ NO

5. If subject is incompetent and surrogate consent is obtained, have all of the following conditions been met; a) the research can't be done on competent subjects; b) there is no risk to the subject, or if risk exists the direct benefit to subject is substantially greater; c) If an incompetent subject resist, he/she will not have to participate; d) If there exists any question about the subject's competency, the basis for decision on competency has been fully described. ☐ YES ☐ NO

6. If the subject is paid, the payment is reasonable and commensurate with the subject's contribution. ☐ YES ☐ NO ☐ NA

7. Members of minority groups and women have been included in the study population whenever possible and scientifically desirable. ☐ YES ☐ NO

8. Comments: (Indicate if Expedited Review) Addition of Advertisement, Interview Questions and Form 10-3202 Consent for Use of Picture and/or voice approved.

RECOMMENDATION: ☑ APPROVED ☐ DISAPPROVE/REVISE

SIGNATURE OF CHAIRMAN: [signature] DATE: 7/20/2010

VA FORM 10-1223 EXISTING STOCK OF VAF 10-1223,

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: June 24, 2010 Amendment Initiated by: Local Investigator

Name of Principal Investigator: Alicia Heapy Ph.D.

Title: **IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain (AH0004)**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☐Recruitment Material
☐Consent	☐Administrative Letter	☐Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We are requesting an amendment in order to recruit and interview veterans who have participated in cognitive behavioral therapy (CBT) for chronic pain at VA Connecticut Healthcare System. We also are requesting an addition of a study flyer to assist in recruitment efforts.

1. We request a change to the project to include the recruitment and interviewing of veterans who have participated in CBT for chronic pain in order to improve our treatment materials. We wish to create "peer experiences testimonials" for inclusion in the patient handbooks and other study materials. We believe it will enhance engagement in the study if participants are able to listen to recordings of veterans describe in their own words how CBT has helped them manage their chronic pain conditions and what parts of treatment have been most helpful. We would also like to include the veterans' pictures in the patient handbooks along with their name and a brief description of their pain complaint. The recordings will be provided to participants in our study in the form of a CD for participants in the face-to-face treatment condition and as an optional part of the IVR phone call for person in the IVR condition (i.e, press 1 if you would like to hear from a VA Connecticut veteran who has used relaxation to manage his pain). Veterans will be recruited by approaching psychologists who deliver CBT for chronic pain and asking them to contact candidates that they have treated. The provider will introduce the opportunity to their patient. If patients are interested in participating, providers will then ask patients if it is okay for the PI to contact them and will get a verbal agreement for the plan. Patients will also have the option of contacting the PI directly. We will use only those patients who were seen clinically for the treatment of chronic pain, not those seen in the context of prior research studies as we did not request permission to recontact study participants. In order to avoid any perception of coersion, only patients who have completed treatment will be contacted. We will ask these patients several general open-ended questions about their treatment experiences (see attached list of interview questions). It is important to note that some of their responses will prompt follow up questions that cannot be

anticipated, so while we will ask all of the questions on the script that we create, and we may also ask additional questions for clarification. We will record these interviews and incorporate portions into the study treatment materials. Veterans will be asked to sign a voice and picture consent prior to the interview. Pg. 10, Research Plan

2. We request the addition of a study recruitment flyer which will be placed in patient care areas in order to help us meet the targeted enrollment criteria. Although the protocol states that we will be using the "opt-out" letter as our preferred method of recruitment, we do not want to limit our recruitment methods.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

These changes will not increase the risk to subjects. The recording will not include any patient identifyers and the picture will be used to personalize the recording. The flyer will not increase patient risks since is used to open up our recruitment strategies. The protocol for patient contact for those recruited from flyers, will be the same as when receiving "opt-out" letters and/or calls.

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects*	☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No (2) Does the change increase risk to research personnel or others? ☐Yes ☒No
If the answer to (1) is yes, submit a revised Research Protocol Safety Survey *If the answer to (2) is yes, describe the increased risk below*

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

–

Signature of Principal Investigator

7/20/10
Date

Department of Veterans Affairs

Memorandum

Date: May 19, 2011

From: HSS Coordinator /Research/151

Subj: Approval of Amendment and Consent Form(s)

To: Alicia Heapy, Ph.D.

Your Amendment and Consent Form(s) to the project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) were reviewed and approved by the Chairperson of the Human Studies Subcommittee on 5/19/11 and approved by the Subcommittee on Research Safety on 1/11/11. Neither you nor any of the identified co-investigators participated in the review and decision making.

If you have a dual appointment (VA Connecticut Healthcare System and Yale University) this amendment requires approval by the Yale HIC before implementation. For timely review, submit a copy of this amendment request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 2/29/12 for this project. The Request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. Only the stamped Consent Form(s) (with no revisions) and HIPAA Authorization may be used. The Consent Form(s) and HIPAA Authorization used must be the most recently approved by the Subcommittee. Be sure that both are filled in completely.
2. All procedures and interventions employed must be those as approved by the R&D Committee.
3. Any changes to the protocol or the Consent Form(s) must be proposed to the Subcommittee in writing (identifying the title, project number and signed by the PI) as a modification to an approved project and must be approved before they are initiated.
4. Any adverse event an AE report form with accompanying supporting documentation (this applies to both on and off site reports).
5. The VACHS Pharmacy must dispense any drugs used in this project.

If any questions, please contact me at ext. 3350 or Brendan Sullivan at ext. 3351.

Cora Milewski

Department of Veterans Affairs

REPORT OF SUBCOMMITTEE ON HUMAN STUDIES

Amendment

Project/Program Title: IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain

Principal Investigator: Heapy, A., Ph.D. (#0004)

VAMC: VA Connecticut Healthcare System/689 Review Date: 5/5/11

COMMITTEE FINDINGS

1. The information given in the Informed Consent under the Description of Research by Investigator is complete, accurate, and understandable to a research subject or surrogate who possesses standard reading and comprehension skills. [X] YES [ ] NO

2. The informed consent is obtained by the principal investigator or a trained and supervised designate under suitable circumstances. [X] YES [ ] NO

3. Every effort has been made to decrease risk to subject(s)? [X] YES [ ] NO

4. The potential research benefits justify the risk to subject(s)? [X] YES [ ] NO

5. If subject is incompetent and surrogate consent is obtained, have all of the following conditions been met; a) the research can't be done on competent subjects; b) there is no risk to the subject, or if risk exists the direct benefit to subject is substantially greater; c) If an incompetent subject resist, he/she will not have to participate; d) If there exists any question about the subject's competency, the basis for decision on competency has been fully described. [ ] YES [ ] NO [ ] N/A

6. If the subject is paid, the payment is reasonable and commensurate with the subject's contribution. [X] YES [ ] NO [ ] NA

7. Members of minority groups and women have been included in the study population whenever possible and scientifically desirable. [X] YES [ ] NO

8. Comments: (Indicate if Expedited Review) The PI requested to amend the recruitment, measures procedures, Consent Form, data storage and Project Description

RECOMMENDATION: [✓] APPROVED [ ] DISAPPROVE/REVISE

SIGNATURE OF CHAIRMAN: [signature] DATE: 5/17/2011

VA FORM 10-1223 EXISTING STOCK OF VAF 10-1223.

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program
Information Security Officer Approval
Human Subjects Research

Incorporates all Information Security elements located in the Department of Veterans Affairs Checklist for Reviewing Privacy, Confidentiality and Information Security in Research (2010).

This form to be completed by VACHS Information Security Officer		
Date: 5/5/11	VA Project #:	
VACHS (PI): Alicia Heapy, PhD	Email Address: alicia.heapy@va.gov	
Project Title:	IVR-based CBT for Chronic Low Back Pain	
Information Security Officer	Mathew Cotton	
Information Security Officer email/phone	Mathew.Cotton@va.gov (203) 932-5711 x4431	

	N/A	Met	Not Met	Comments
Initial Application (*Information Security Plan – Confidentiality and Security of Data*, page 1a) In accordance with VHA Handbook 1200.05, VA Handbook 6500 – Appendix D, VHA Handbook [illegible] 10-1, and VA Directive 6609.				
PI attests that all study staff are up-to-date with *VHA Information Security Awareness Training and Rules of Behavior*, and proof of training (i.e. certificates of completion) can be provided if requested.	☐	☒	☐	
Any specially obtained Software is identified and explained.	☐	☒	☐	
Individually identifiable information is to be collected or used.	☐	☒	☐	
Data flow is identified and explained.	☐	☒	☐	
Data storage and corresponding security measures are identified and explained.	☐	☒	☐	
Research data intended to be removed from the VA protected environment is identified and explained.	☐	☒	☐	
Those whom have access to data are identified and explained.	☐	☒	☐	
The use of mobile/portable devices is identified and explained.	☒	☐	☐	
Data return is identified and explained.	☐	☒	☐	
Reporting plan for a suspected or confirmed loss of VA information is appropriate.	☐	☒	☐	
Consistency				
The Initial Application contains similar language as the protocol and project description with regard to the Confidentiality and Security of Research Data.	☐	☒	☐	

Based on all submitted documents for this protocol:

1. ☒	All applicable local, VA and other Federal requirements for Information Security policy have been met.
Or	
2. ☐	Specific deficiencies identified: Suggestions of available options for correcting these deficiencies:

Signature of Information Security Officer

3/16/11
Date

ISO Approval

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program
Information Security Checklist
Human Subjects Research

Date: May 16, 2011	VA Project #: 0004
VACHS (PI): Alicia Heapy, Ph.D.	Email Address: alicia.heapy@va.gov
Project Title:	IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain
Privacy Officer	Nancy Katz-Johnson
Privacy Officer email/phone	Nancy.Katz-Johnson@va.gov (203) 932-5711 x4109
Information Security Officer	Michael Raffanello
Information Security Officer email/phone	Michael.Raffanello@va.gov (203) 932-5711 x3444

Instructions: If you answer 'NO' to any one of the statements, you may not remove or transmit the VA sensitive research information outside VA unless you have approval in writing from your supervisor, ACOS/R, Information Security Officer, and Privacy Officer. If the research will not obtain any VA sensitive information the statements below should be marked as not applicable (N/A).

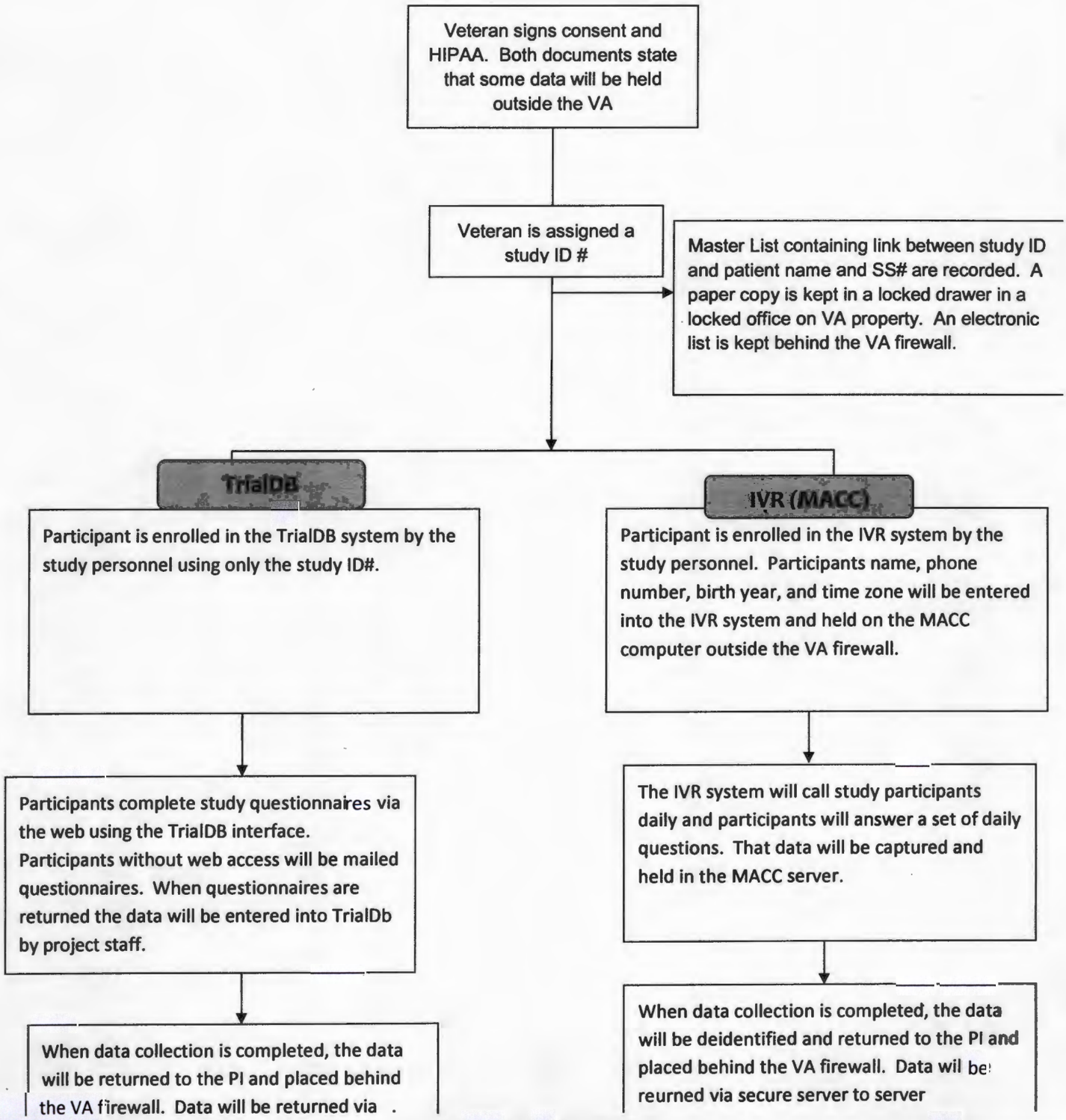
Yes	No	N/A	Specific Requirements
☐	☒	☐	All VA sensitive research information is used and stored within the VA
☐	☒	☐	All copies of VA sensitive research information are used and remain within the VA

If you have answered **Yes or N/A** to both statements above, **stop here.**
If the original or copies of VA sensitive research information (data) are removed from the VA answer the following statements:

Yes	No	N/A	Specific Requirements
☒	☐	☐	Permission to remove VA sensitive research information has been obtained from your (1) immediate supervisor, (2) ACOS/R, (3) VA Information Security Officer (ISO), (4) VA Privacy Officer, and (5) Facility Director
☐	☐	☒	A property pass for VA issued laptop computers has been obtained.
☐	☐	☒	The laptop or other portable media is encrypted and password protected.
☐	☐	☒	VA sensitive research information transmitted as an attachment to e-mail messages is protected.
☐	☒	☐	Names, addresses, and Social Security Numbers (real and scrambled) and other HIPAA Privacy Rule identifiers have been replaced with a code.
☒	☐	☐	VA sensitive research information sent via mail or delivery service on CD will be encrypted. Note: a delivery service is preferable because there is a "chain of custody".
☐	☒	☐	For VA sensitive research information that will reside on a non-VA server: The server has been certified and accredited as required by Federal Information and Security Management Act of 2002 (FISMA). This certification and accreditation meets Federal Information Protection Standards (FIPS 140-2) established by the National Institute of Standards and Technology.
☒	☐	☐	Access to VA sensitive research information is only by those who are authorized to access it and the access is related to VA-approved research.
☒	☐	☐	Procedures for reporting theft or loss of VA sensitive research information or the media (laptop) containing sensitive information are in place and familiar to the researcher and all others who have access to, use, store, or transport the data.

IVR-Based CBT for Chronic Low Back Pain (Heapy)

Data Flow Diagram



VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: April 28, 2011 Amendment Initiated by: Local Investigator Study #: 0004

Name of Principal Investigator: Alicia Heapy, Ph.D.

Title: **IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☒Consent	☐Administrative Letter	☒Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

Please excuse the length of this amendment request. This study was originally approved after the project was first submitted for funding. Since that time, the project has evolved based on reviewer suggestions and feedback from a pilot study. In an effort to be efficient, we elected to make all of the changes to the protocol just prior to the start of study enrollment.
We request to make changes to the following areas: recruitment, measures, and procedures.

I. We request approval to expand our recruitment methods to ensure that we are able to meet our recruitment goals.

a.) We would like to post approved advertisements and or flyers in the following venues: 1) patient care waiting areas, 2) Craigslist under the "Volunteers" section of the site, 3) flat screen informational televisions around the hospital, and 4) Good Morning VA Connecticut. Public relations will coordinate posting advertisements on the informational screens in the hospital and Good Morning VA Connecticut. (Selection, pg. 6; Recruitment pg. 7) See attached appendix for advertisement language.

b.) We would like to recruit patients at a Pain Education table positioned outside the Patient Education room in Building 2, 1st floor. This table will be staffed by study research staff including research assistants and/or co-investigators. We plan to include approved recruitment flyers at the table and information about chronic pain and chronic pain management, pertinent VACHS resources, and other currently approved research studies conducted by our group (separate amendments will be submitted for each study). Research staff will not approach patients but will wait for patients to approach and indicate interest in the materials. Participants who indicate interest in the study will be given information and will complete a study screening instrument. The screening instrument will allow staff the

ability to make an preliminary eligibility ruling. No patient identifiable information will be collected, unless the patient is eligible for the study. If they are eligible and interested, contact information will be collected so an appointment for consenting and baseline procedures can be arranged. Participants will be offered a semi-private area for completing the screening measure. (See attached screener). (Selection, pg. 6)

II. We are requesting changes or additions to the assessment instruments as detailed below. We do not believe these changes will add significantly to the response burden of the participants but will provide us with finer grained information about their pain and their response to treatment.

a.) We would like to change the defined score for absence of dementia for the approved Saint Louis University Mental Status (SLUMS) measure. By error, the original protocol stated that we would define an absence of dementia by a score of 13; however, the literature states that the defined score is actually 20. (Eligibility Criteria, pg. 5)

b.) In addition to assessing for current DSM-IV Axis 1 disorders via the SCID, we would like to assess for past Major Depressive Disorder. Prior research has indicated that persons with any history of Major Depressive Disorder (MDD) demonstrate differences from persons without a history of MDD in how they cope with pain flares, their appraisal of the efficacy of their coping efforts, and their mood-related reactivity in response to pain flares. Because of these prior findings we plan to include history of MDD as a covariate in some analyses. (Research Plan, pg. 7)

c.) We would like to substitute a new treatment satisfaction questionnaire. Initially, we had proposed to use the modified VHA Customer Service Standards questionnaire to assess treatment satisfaction, which measures global perceptions of pain care. The new published and validated measure, the Satisfaction with Therapy and Therapist Scale will specifically assess the participants' perceptions of treatment and their therapist. This is important since we are interested in the efficacy of IVR-based treatment when compared to standard face-to-face CBT, and satisfaction with treatment, not more global pain care, is a specific outcome of interest. (Treatment Feasibility Outcomes, pg. 15) See attached modified treatment satisfaction questionnaire.

d.) We are going to examine pain medication use at baseline and throughout treatment for both treatment conditions. At baseline, medication use will be assessed by the study coordinator or trained research associates, using VACHS computer pharmacy records and confirmation with the participant. Once a week during the IVR calls, patients will be asked if their medication use changed in any way from what they reported at the beginning of the study. A change could be taking more of a medication, taking less of a medication, taking a new medication or stopping a medication. Pain medication use will serve as a covariate in the analysis. (Covariates, pg. 16; consent)

e.) We are adding the following published and validated measures: Pain Catastrophizing Scale (PCS), Pain Stages of Change Questionnaire (PSOCQ), SF-36V, Pittsburgh Sleep Quality Index (PSQI), and Survey of Pain Attitudes (SOPA). (Outcome Measures, pg. 12). These outcome measures are similar to those we have used in prior CBT efficacy studies and are consistent with CONSORT guidelines on equivalence trials that outcome measures be similar to those used in studies to establish efficacy of the reference treatment. Attitudes about pain (PCS, SOPA) and readiness to change (PSOCQ) have been found to be associated with outcomes in prior pain treatment studies. Sleep (PSQI) is frequently compromised by chronic pain and will be added as a secondary outcomes measure.

f.) We are going to add daily questions regarding sleep, pain coping and mood to the set of questions that patients will answer daily via IVR. This will allow us to track the status of our participants more closely, especially in the ICBT condition where there is no face to face patient contact. This additional information will allow us to provide better weekly feedback to these patients even though they are not seen in person. (Research Plan, pg. 7; Treatments, pg. 8 & 10; consent) See attached daily questions worksheet.

III. We request approval to make the following changes the procedures of the project.

a. Project Description

i. We request a change in sample size from 128 to 230. We mistakenly included a sample size of 128 in the original project description. The study was originally designed to have 230 participants. (Subjects, pg 4; Recruitment, pg. 7; Sample Size Calculations, pg. 16; Consent)

ii. We updated the Safety section of the project description to accurately describe the monitoring of Adverse Event in accordance with current Human Studies Subcommittee policy and procedures. (Safety, pg. 19-20)

iii. Based on feedback from pilot participants we altered the topics in the treatment manual slightly. Module 9 has been changed from Pacing-Pleasant Activities to Sleep – Sleep Hygiene Tips. (Treatment; Table, pg. 9)

iv. We have changed the ICBT treatment slightly to allow greater flexibility for participants. Instead of having the participant listen to a pre-recorded explanation of each treatment module skill on the second day of each week. We will give them the option of listening to an elaboration of the treatment skill information on any day of the week they choose. For those participants who have an adequate understanding of the material from reading their patient handbook do not require or want any further explanation, they can elect to skip the explanation. (Treatment: ICBT, pg.10)

v. We updated the Potential Risks and Protections section regarding suicidal ideation. The IVR system will allow participants to connect directly to the Suicide Hotline during their daily call. (Risks and Benefits, pg. 17)

vi. We have updated the Potential Risks and Protections section to notify participants that some of their data will be stored outside the VA firewall. The study uses a large computer server (Michigan Academic Computing Center or MACC at the University of Michigan in Ann Arbor, Michigan) for collecting the IVR data, which has extensive data security protections. The study team will use a secure, password-protected web page to enter participants' name, birth year, and phone number so that the automated telephone system can make calls to participants. No other information about participants, such as social security numbers or medical record information will be used for the automated calling system. The data obtained from the weekly calls will be stored on a computer at the MACC. When the study is complete, all the research study data will be removed from the MACC. Participants will be made aware of the IVR data being stored off VA firewall in the consent form. (Risks and Benefits, pg. 18; Consent)

vii. We deleted the eligibility requirement of a urine toxicology at baseline to rule out illegal drug use or non-prescribed opioids. Review of the medical records for the most recent clinical urine toxicology reports and review of most recent substance abuse clinic and mental hygiene notes will be examined during the routine eligibility review. This will reduce the burden to participants while still allowing us to identify persons who may be ineligible due to active substance abuse. (Eligibility Criteria, pg. 5; Research Plan, pg. 7; consent)

viii. We changed the treatment cut-off date from 12 weeks to 14 weeks, to give leeway for reschedules and schedule conflicts, before treatment is cut-off. The treatment cut-off time will allow for treatment delivery to be standardized across all patients. (Treatment, pg. 8; Analytic Plan, pg. 16-17)

ix. We will track reasons for treatment dropout which will allow us to have a better understanding of reasons for treatment drop-out and if dropout is related to use of IVR. (Recruitment, pg. 7)

x. We are changing how the daily IVR calls will occur. The IVR system will now call patients instead of participants calling the IVR system. Co-investigators with experience using IVR systems (Piette and Tennen) advise that adherence to the call schedule is improved and patients report that the treatment is more convenient when the system initiates the daily call instead of the patient. (Treatments, pg. 9- 10; Treatment feasibility outcomes, pg. 15; Consent)

xi. We will allow participants to complete questionnaire assessments either via TrialDB, a web-based interface, as originally proposed or by mail. We will allow completion by mail as not all participants will have internet access. (Research Plan pg. 7; Consent)

xii. We will no longer ask RAs to contact participants and collect data via the phone when participants miss a scheduled daily IVR phone call. In prior studies we have had high rates of compliance with the daily IVR call (between 85-90%). Thus, we do not believe that it is necessary to have RA collect data by phone. (Research Plan, pg. 7-8; Treatment feasibility outcomes, pg 15)

xiii. The randomization procedure has been changed in order to enhance its integrity. Instead of placing treatment assignments in sealed and sequentially numbered envelopes, we have constructed a database that will collect data regarding the stratification factors (type of pain and distance from the VA) and automatically assign participants according to the randomization schedule created by the study biostatistician. We believe this is an improvement that will allow for enhanced security of the randomization schedule and reduce the ability of study staff to anticipate the treatment assignment. (Research Plan: Randomization, pt.8)

b. Consent form:

i. We request to have the witness signature deleted from the consent form. This does not increase the risk for participants.

ii. Since the IVR data will be stored outside the VA firewall on the Michigan Academic Computing Center or MACC at the University of Michigan in Ann Arbor, Michigan, the consent form will state this additional risk to confidentiality. Please see attached consent forms for these changes.

iii. Other changes to conform with changes made to the protocol as outlined above.

c. Research Authorization:

i. We changed the research authorization form to reflect the current format.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

These changes will not increase the risk to subjects. The project has evolved based on reviewer suggestions and feedback from a pilot study.

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects*	☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No

(2) Does the change increase risk to research personnel or others? ☐Yes ☒No

If the answer to (1) is yes, submit a revised Research Protocol Safety Survey

If the answer to (2) is yes, describe the increased risk below

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Alicia Hofstetter — 4/28/11

Signature of Principal Investigator — Date

Department of Veterans Affairs

Memorandum

Date: July 7, 2011

From: HSS Coordinator /Research/151

Subj: Approval of Amendment and Consent Form(s)

To: Alicia Heapy, Ph.D.

Your Amendment and Consent Form(s) to the project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) were reviewed and approved by the Chairperson of the Human Studies Subcommittee on 7/7/11 and approved by the Subcommittee on Research Safety on 1/11/11. Neither you nor any of the identified co-investigators participated in the review and decision making.

If you have a dual appointment (VA Connecticut Healthcare System and Yale University) this amendment requires approval by the Yale HIC before implementation. For timely review, submit a copy of this amendment request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 2/29/12 for this project. The Request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. Only the stamped Consent Form(s) (with no revisions) and HIPAA Authorization may be used. The Consent Form(s) and HIPAA Authorization used must be the most recently approved by the Subcommittee. Be sure that both are filled in completely.
2. All procedures and interventions employed must be those as approved by the R&D Committee.
3. Any changes to the protocol or the Consent Form(s) must be proposed to the Subcommittee in writing (identifying the title, project number and signed by the PI) as a modification to an approved project and must be approved before they are initiated.
4. Any adverse event an AE report form with accompanying supporting documentation (this applies to both on and off site reports).
5. The VACHS Pharmacy must dispense any drugs used in this project.

If any questions, please contact me at ext. 3350 or Brendan Sullivan at ext. 3351.

Cora Milewski

Department of Veterans Affairs

REPORT OF SUBCOMMITTEE ON HUMAN STUDIES

Amendment

Project/Program Title: IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain

Principal Investigator: Heapy, A., Ph.D. (#0004)

VAMC: VA Connecticut Healthcare System/689 Review Date: 7/7/11

COMMITTEE FINDINGS

1. The information given in the Informed Consent under the Description of Research by Investigator is complete, accurate, and understandable to a research subject or surrogate who possesses standard reading and comprehension skills. [X] YES [ ] NO

2. The informed consent is obtained by the principal investigator or a trained and supervised designate under suitable circumstances. [X] YES [ ] NO

3. Every effort has been made to decrease risk to subject(s)? [X] YES [ ] NO

4. The potential research benefits justify the risk to subject(s)? [X] YES [ ] NO

5. If subject is incompetent and surrogate consent is obtained, have all of the following conditions been met; a) the research can't be done on competent subjects; b) there is no risk to the subject, or if risk exists the direct benefit to subject is substantially greater; c) If an incompetent subject resist, he/she will not have to participate; d) If there exists any question about the subject's competency, the basis for decision on competency has been fully described. [ ] YES [ ] NO [ ] N/A

6. If the subject is paid, the payment is reasonable and commensurate with the subject's contribution. [X] YES [ ] NO [ ] NA

7. Members of minority groups and women have been included in the study population whenever possible and scientifically desirable. [X] YES [ ] NO

8. Comments: (Indicate if Expedited Review) Revision of the Consent Form, HIPAA Form, Voice Consent Form and Recruitment material approved.

RECOMMENDATION: [✓] APPROVED [ ] DISAPPROVE/REVISE

SIGNATURE OF CHAIRMAN: [illegible] Bell, PhD DATE: 7/12/2011

VA FORM 10-1223 EXISTING STOCK OF VAF 10-1223.

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB #:	Promise #: 0004
Project Title:	IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 5/7/09			
Current Approval Period: 2/29/12		Expiration: 2/19/12	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☐	☐	☑

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☐ No

Has the investigator complied with all regulations and HSS decisions? ☐ Yes ☐ No

The research should be:
- ☐ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

M Bell, PhD
Signature of Reviewer

7/7/2011
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: June 30, 2011 Amendment Initiated by: Local Investigator Study #: 0004

Name of Principal Investigator: Alicia Heapy, Ph.D.

Title: **IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☐Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☒Consent	☐Administrative Letter	☐Data Collection Tools
☒Other *Describe:* Research HIPAA Authorization		
☒Other *Describe:* Voice Consent Form		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

1) We would like to add participant's first name to the list of already approved information that will be sent to and held at the University of Michigan on our study's IVR system. Having the participant's first name will allow the IVR system to address the caller by name when contacting them. The transmittal of this information to the University of Michigan will be disclosed to participants in the consent and HIPAA form. This is already stated in the approved, stamped consent form.

2) We would like to make a minor amendment to the study's medical clearance form. We currently ask each participant's primary care provider to give medical clearance for their patient to participate in the daily walking program that is part of the study treatment. We would like to add clearance to engage in stretching exercises also. The stretching exercises have always been part of the approved protocol, we just wish to explicitly inform providers that their patients will be asked to engage in specific stretching exercises selected by a physical therapist for patients with chronic low back pain. See attached medical clearance form for changes.

3) We would like to update the recruitment letter by changing the contact information due to new approved RAs on the study. The contact information will be for Kathryn LaChappelle and Joseph Kirlin, instead of Rebecca Czlapinski. See attached recruitment letter for changes.

4) We would like to include information in the consent and HIPAA forms that notifies participants that some study information will be shared with Yale University. As you may recall, study assessment data will be collected electronically using theTrial DB web-based interface and the data will be captured on a secure server housed at Yale University. We believe the data will be de-identified as we are using a study ID only to identify participants in the Trial DB system, however dates may be collected and it is not entirely clear if this can be considered an identifier. Since we cannot be

certain that identifiers will not be included, we have decided to notify participants that these data will be shared with Yale and stored on a secure server.

Consent form:
On page 5, under Expected Risks of Study
-after 1st paragraph: added "The study also uses a large computer server (TrialDB at Yale University in New Haven Connecticut) that has extensive data security protections. TrialDB is outside the VA computer network and will not be protected with the same high standards of security established inside the VA. The VA cannot guarantee security of research data after it is transmitted outside the VA. The data obtained from your questionnaires throughout treatment will be stored on a computer at Yale University. When the study is complete, all the research study data will be removed from TrialDB and sent back to the VA."
- On page 5, under Confidentiality of Information
- paragraph 1, 2nd sentence: add paper in second sentence and "at the VA Connecticut Healthcare System (VACHS) in West Haven".
- add "electronic format will be stored in secure servers at Yale University and University of Michigan (MACC)."
- paragraph 2, 3rd sentence: correct GAO to "Government Accountability Office"
- paragraph 2, 5th sentence: added "and other authorized individuals at Yale University and University of Michigan (MACC)"
- paragraph 2, 8th sentence: add "participating in clinical trials"

This amendment correctly describes where information is stored. The change in procedure follows directions provided in the recent Information Technology Office of Compliance (ITOC) site visit.

HIPAA Authorization
Page 2 - Under Use & Disclosures: Who
- added under Others: "and other authorized individuals at Yale University."
-deleted under Others: "nurse case manager, post docs and interns" - these are considered "authorized study staff"
-changed under Others: "approved" to "authorized"

This amendment correctly describes who will describe, receive, and/or use information covered by this authorization.

Voice Consent:
Updated voice consent for - 1/7/2011 version.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects* ☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No

(2) Does the change increase risk to research personnel or others? ☐Yes ☒No

If the answer to (1) is yes, submit a revised Research Protocol Safety Survey

If the answer to (2) is yes, describe the increased risk below

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

6/30/11
Date

Department of Veterans Affairs

Memorandum

Date: January 5, 2012

From: HSS Coordinator/ Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain" (#0004) was reviewed and approved by the Human Studies Subcommittee (HSS) on 11/3/11. Neither you nor any of the identified co-investigators participated in the review and decision-making.

If you have a dual appointment (VA Connecticut Healthcare System and Yale University) this may require approval by the Yale HIC before implementation. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 2/29/12 for this project. The Request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. All procedures and interventions employed must be those as approved by the HSS subcommittee.
2. Any changes to the protocol must be proposed to the subcommittee in writing (identifying the title, project number and sign by the PI) as a modification to an approval project and must be approved before they are initiated.

If you have any questions, please contact me at ext. 3351.

Brendan Sullivan

Department of Veterans Affairs

REPORT OF SUBCOMMITTEE ON HUMAN STUDIES

Amendment

Project/Program Title: IVR-based Cognitive Behavioral Therapy for Chronic Low Back Pain

Principal Investigator: Heapy, A., Ph.D. (#0004)

VAMC: VA Connecticut Healthcare System/689 Review Date: 11/3/11

COMMITTEE FINDINGS

1. The information given in the Informed Consent under the Description of Research by Investigator is complete, accurate, and understandable to a research subject or surrogate who possesses standard reading and comprehension skills. — [X] YES [ ] NO

2. The informed consent is obtained by the principal investigator or a trained and supervised designate under suitable circumstances. — [X] YES [ ] NO

3. Every effort has been made to decrease risk to subject(s)? — [X] YES [ ] NO

4. The potential research benefits justify the risk to subject(s)? — [X] YES [ ] NO

5. If subject is incompetent and surrogate consent is obtained, have all of the following conditions been met; a) the research can't be done on competent subjects; b) there is no risk to the subject, or if risk exists the direct benefit to subject is substantially greater; c) If an incompetent subject resist, he/she will not have to participate; d) If there exists any question about the subject's competency, the basis for decision on competency has been fully described. — [ ] YES [ ] NO [ ] N/A

6. If the subject is paid, the payment is reasonable and commensurate with the subject's contribution. — [X] YES [ ] NO [ ] NA

7. Members of minority groups and women have been included in the study population whenever possible and scientifically desirable. — [X] YES [ ] NO

8. Comments: (Indicate if Expedited Review) Revision of Project Description, Ad and HIPAA Waiver. Addition of Screening tool, script and WWIC.

RECOMMENDATION: [X] APPROVED [ ] DISAPPROVE/REVISE

SIGNATURE OF CHAIRMAN: [signature] DATE: 12/30/11

VA FORM 10-1223 EXISTING STOCK OF VAF 10-1223,

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist
Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB #: 01281	Promise #: 0004
Project Title:	IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 5/7/09			
Current Approval Period: 3/1/11 - 2/29/12		Expiration: 2/29/12	

Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***		Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☐	☐	☑

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☑ No

Has the investigator complied with all regulations and HSS decisions? ☑ Yes ☐ No

The research should be:
- ☑ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

Signature of Reviewer

12/30/11
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request for Waiver of Written Informed Consent (WWIC)
Human Subject Research

Date: **December 28, 2011**

Name of Principal Investigator: Alicia Heapy, Ph.D.

Title of Study: **IVR-based Cognitive Behavioral Therapy for Chronic Low Back Pain**

I am requesting a waiver of the requirement to obtain written informed consent.

1. Subjects (choose a or b)

a. ☐ This request to waive written consent is intended to cover all subjects

OR

b. ☒ This request to waive written consent is intended to cover only a specific segment of the potential subjects

If you chose B, identify in the area below the subjects covered by this waiver for written consent.

For eligibility screening (screening questions and review of medical records). We will obtain verbal consent from patients to conduct an initial telephone and medical record screening (see attached script).

2. Basis (choose a or b)

☐ a. 38 CFR 16.117(c)(1)

The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research , and the subject's wishes will govern,

☐ The research is not FDA regulated

If you have chosen option a, a consent form must be submitted for approval.

☒ b. 38 CFR 16.117(c)(2)

The research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context

Provide in the space below protocol specific reasons why your study is no more than minimal risk

The only risk to patients is the loss of privacy and confidentiality. Patients will be asked to provide verbal consent and we will not proceed with screening unless verbal consent is obtained. Patients will ultimately choose whether they wish to undergo screening and a medical record review, prior to consent.However, only members of the research team will have access to this information. All electronic documents will be stored behind VA firewalls and paper documents will be kept in locked VA off.

Signature Principal Investigator

Date 1/4/12

Area Below for HSS Use Only

The Requirement for obtaining written informed consent is: ☑ Waived ☐ Not Waived

Signature of HSS Chairperson
(or designated reviewed)

Date 12/30/11

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program
Request for Waiver of HIPAA Authorization (WOA)
Human Subject Research

Date: October 27, 2011	VA Project #: 0004
VACHS (PI): Alicia Heapy, Ph.D.	Email Address: alicia.heapy@va.gov
Project Title:	IVR-based Cognitive Behavior Therapy for Chronic Low Back

I am requesting to use and/or disclose protected health information (PHI) in the conduct of this research under a waiver of HIPAA Authorization. This request is based on 45 CFR 164.512(i) and VHA Handbook 1200.05 37.b.(3),(4).

1. Purpose (choose a, b, or c – more than 1 may apply)

This waiver request:
a. ☐ Covers the full study(no HIPAA Authorizations will be obtained)
b. ☒ Is for screening or recruitment purposes only
c. ☐ Only applies to a specific component of the study or to a specific group of subjects

If item c was checked, describe below the component of the study and the specific group of subjects

If your request for a HIPAA waiver is for screening purposes only, you should only use information related to the screening in completing the sections below.

2. Description of the Protected Health Information (PHI) that will be used/disclosed

Briefly describe in the area below the protected health information (PHI) and the identifiers (name, SSN, etc.) that will be used or disclosed in your protocol. Specify if the research involves drug or alcohol abuse, HIV infection, or sickle cell anemia.

A research assistant will conduct an in person or telephone screening and review the charts of patients who contact study staff in response to a flyer or recruitment letter, to identify those who are potentially eligible for our study before written consent. Study staff will obtain a verbal approval from patients to review their medical records before proceeding with the review. An approved screening tool will be used to collect the following information: name, last 4, pain score, veteran status, low back pain, if one block can be walked, access to touch-tone telephone on a daily basis, name of primary care physician, and any active SI/HI.

3. Disclosures

☒ The PHI will only be used by members of the research team and will be disclosed only to the following individuals or entities.

(Describe below any individual who may be given access to the PHI. Justify the need to make the information available to anyone outside of VHA).

No PHI will be reused or disclosed outside of VHA. Only members of the research team as identified in the project description will have access to PHI for recruitment and pre-screening eligibility assessments.

4. Justification

a. ☒ The proposed use and/or disclosure involves no more than minimal risk to the privacy of individuals because:
Items (1), (2), and (3) must be checked to check box a

☒ (1). Identifiers will be protected from improper use and disclosure and will be destroyed at the earliest opportunity consistent with the research and the disposition instructions approved by the National Archives and Records Administration and published in VHA Records Control Schedule (RCS 10-1).

☒ (2). Identifiable information will not be reused or disclosed to any other person or entity outside VHA, other than those identified in the protocol, except as required by law, for authorized oversight of this research study, or for other research approved by the IRB and for which the use or disclosure would be permitted by the Privacy Rule.

4. Justification	
	☒ (3). The identifiable information will be protected from improper use or disclosure. *Describe below your plan to protect the identifiable information from improper use or disclosure.*
	We will collect the above information and only store such information along with our other research materials in locked file cabinets and behind secure VA firewalls.
b. ☒ The proposed study could not practicably be conducted without the waiver (*describe why, below).*	
We are targeting Veterans who do not receive pain care at the West Haven campus, so driving to West Haven for a handful of screening questions, will be burdensome and intractable for patients. Additionally, we must have a mechanism that allows study staff to be certain that potential participants meet eligibility criteria that does not unduly impose upon the veteran.	
c. ☒ The proposed study could not practicably be conducted without the access to and use of the proposed information (describe why, below).	
In order to increase our referral volume, phone or in-person screening and a CPRS chart review is necessary to provide a preliminary screen of potential participants for inclusion in the study. It is burdensome to ask the veteran to travel for a screening appointment when a simple pre-screen can prevent unnecessary trips to the West Haven campus.	

5. Information protected by 38 USC 7332	
☐	If the research involves drug or alcohol abuse, HIV infection, or sickle cell anemia, check this box to provide the following assurance that patient identities will not be disclosed: *No personnel involved may identify, directly or indirectly, any individual patient or subject in any report of such research or otherwise disclose patient or subject identities in any manner*

Signature Principal Investigator

10/27/11
Date

Area Below for HSS Use Only

IRB of record: Human Studies Subcommittee, VA Connecticut Healthcare System, West Haven, CT

The waiver was reviewed under: ☑ Full review procedures

☐ Expedited review procedures

☑ A waiver of authorization has been granted for use with this protocol.

The approval is based on the determinations that:

I. The risk to the privacy of individuals is minimal based on:
- The investigator's plan to protect the identifiers from improper use or disclosure
- The investigator's intent to destroy the identifiers at the earliest opportunity consistent with the research and the current record's control schedule and
- The investigator's written assurance that the PHI identified will not be reused or disclosed outside of VHA, except as detailed in this waiver request

II. The research could not be practicably conducted without this waiver of authorization

III. The research could not be practicably conducted without the PHI identified

☐ A waiver of authorization for use with this protocol has been denied. (*Explain reasons for denial below)*

Signature of HSS Chairperson
(or designated voting member)

12/30/11
Date

DEPARTMENT OF VETERANS AFFAIRS

12/28

Memorandum

Date: December 28, 2011

From: Alicia Heapy, Ph.D.

Subj: Response to HSS Minutes, November 3, 2011

To: Chair, Human Studies Subcommittee

RE: IVR-based CBT for Chronic Low Back Pain

In response to the minutes of November 3, 2011, I have ...

1. In response to the contingent approval of our request to conduct telephone screening interviews and to review potential participants' electronic medical records to confirm eligibility status, we are requesting a WWIC (attached) and have included consent language in our phone screening script as requested by the committee (see attached script).

Note, we are no longer obtaining medical clearance (amendment dated 12/28/11) so the WWIC will only be to screen patients over the telephone and review medical records for eligibility purposes, before written consent.

Thank you for your consideration.

Alicia Heapy, Ph.D.

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: October 27, 2011 Amendment Initiated by: Local Investigator Study #: 0004

Name of Principal Investigator: Alicia Heapy, Ph.D.

RECEIVED
OCT 27 2011
RESEARCH SERVICE/151

Title: **VR-based Cognitive Behavior Therapy for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☐Consent	☐Administrative Letter	☐Data Collection Tools
☒Other *Describe:* interview		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We are requesting changes to the procedures for securing medical clearance to participate, adding a post-treatment interview for the IVR condition only, adding a screener, and updating the flyer.

1. Medical clearance - We had originally proposed to obtain medical clearance for participants to engage in the study's walking and stretching program by sending the clearance form to participants' providers via email. It has come to our attention that many primary care physicians do not have PKI, so we are unable to securely send an email with patient information. We are requesting permission to place the HSS approved medical clearance form into the prospective subjects' medical record and add the primary care physician as a co-signer. We will ask primary care providers to check the appropriate box in the form to indicate if the subject is approved, disapproved or pending. This will only be undertaken when a subject has passed a prescreening, given verbal consent and has an appointment for a consent and baseline interview. We are requesting a WIC and WoA to allow us to obtain medical clearance prior to a subject consenting to be in the study (see attached). This is necessary because we wish to avoid asking potential participants to travel to West Haven for a 2-3 hour consent and baseline appointment if they will not be cleared to participate.

2. Interview- We are requesting permission to add a short interview to the end of the IVR treatment condition. Because we have never provided CBT treatment via IVR we are interested in feedback from participants regarding the IVR treatment. Research assistants will ask patients if they want to come into the VA to complete the interview or if they prefer, the interview can be completed over the telephone. (Research Plan, pg 10). See attached interview questions.

3. Screener – We are requesting permission to add a screener tool so that research assistants can prescreen participants into the study. We are requesting a WIC and WoA to allow us to obtain verbal consent from patients to conduct an initial

telephone or in person screening (see attached screening tool). Those who pass the initial phone screening and wish to schedule a consent and baseline appointment will be asked if they will allow us to review their medical records to ensure eligibility. We require a mechanism to screen patients over the telephone so they do not have to drive to the West Haven campus to be asked a small number of screening questions. We are specifically targeting Veterans who may live far away from West Haven campus and who receive care at Newington and/or the CBOCs, for whom driving to the West Haven campus for screening would be impractical and burdensome.

3. Flyer - We are requesting a change to the name of the research assistant on the flyer due to personnel changes.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects* ☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No

(2) Does the change increase risk to research personnel or others? ☐Yes ☒No

If the answer to (1) is yes, submit a revised Research Protocol Safety Survey

If the answer to (2) is yes, describe the increased risk below

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

10/27/11
Date

Department of Veterans Affairs

Memorandum

Date: January 20, 2012

From: HSS Coordinator /Research/151

Subj: Approval of Amendment and Consent Form(s)

To: Alicia Heapy, Ph.D.

Your Amendment and Consent Form(s) to the project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) were reviewed and approved by the Human Studies Subcommittee on 1/5/12 and approved by the Subcommittee on Research Safety on 12/13/11. Neither you nor any of the identified co-investigators participated in the review and decision making.

If you have a dual appointment (VA Connecticut Healthcare System and Yale University) this may require approval by the Yale HIC before implementation. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 1/16/13 for this project. The Request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. Only the stamped Consent Form(s) (with no revisions) and HIPAA Authorization may be used. The Consent Form(s) and HIPAA Authorization used must be the most recently approved by the Subcommittee. Be sure that both are filled in completely.
2. All procedures and interventions employed must be those as approved by the R&D Committee.
3. Any changes to the protocol or the Consent Form(s) must be proposed to the Subcommittee in writing (identifying the title, project number and signed by the PI) as a modification to an approved project and must be approved before they are initiated.
4. Any adverse event an AE report form with accompanying supporting documentation (this applies to both on and off site reports).
5. The VACHS Pharmacy must dispense any drugs used in this project.

If any questions, please contact me at ext. 3351.

Brendan Sullivan

Department of Veterans Affairs

REPORT OF SUBCOMMITTEE ON HUMAN STUDIES

Amendment

Project/Program Title: IVR-Based Cognitive behavioral Therapy for Chronic Low Back Pain

Principal Investigator: Heapy, A., Ph.D. (#0004)

VAMC: VA Connecticut Healthcare System/689 Review Date: 1/5/12

COMMITTEE FINDINGS

1. The information given in the Informed Consent under the Description of Research by Investigator is complete, accurate, and understandable to a research subject or surrogate who possesses standard reading and comprehension skills. [X] YES [ ] NO

2. The informed consent is obtained by the principal investigator or a trained and supervised designate under suitable circumstances. [X] YES [ ] NO

3. Every effort has been made to decrease risk to subject(s)? [X] YES [ ] NO

4. The potential research benefits justify the risk to subject(s)? [X] YES [ ] NO

5. If subject is incompetent and surrogate consent is obtained, have all of the following conditions been met; a) the research can't be done on competent subjects; b) there is no risk to the subject, or if risk exists the direct benefit to subject is substantially greater; c) If an incompetent subject resist, he/she will not have to participate; d) If there exists any question about the subject's competency, the basis for decision on competency has been fully described. [ ] YES [ ] NO [ ] N/A

6. If the subject is paid, the payment is reasonable and commensurate with the subject's contribution. [X] YES [ ] NO [ ] NA

7. Members of minority groups and women have been included in the study population whenever possible and scientifically desirable. [X] YES [ ] NO

8. Comments: (Indicate if Expedited Review) Revision of Project Description, Consent Form and HIPAA.

RECOMMENDATION: [X] APPROVED [ ] DISAPPROVE/REVISE

SIGNATURE OF CHAIRMAN: M Mahell, PhD DATE: 1/19/2012

VA FORM 10-1223 EXISTING STOCK OF VAF 10-1223,

12/28

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: December 28, 2011

Amendment Initiated by: Local Investigator

Name of Principal Investigator: Alicia Heapy

Title: **IVR-based CBT for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention. The primary clinical equivalence hypothesis states that veterans with chronic low back pain (CLBP) receiving IVR-based CBT (ICBT) will demonstrate, relative to standard face-to-face CBT (CBT), equivalent declines in reports of pain intensity as measured by the numeric rating scale at post-treatment and follow-up. The secondary hypothesis states that veterans with CLBP receiving ICBT, relative to CBT, will demonstrate equivalent declines in reports of pain-related interference and emotional distress at post-treatment and follow-up.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☒Consent	☐Administrative Letter	☐Data Collection Tools
☒Other *Describe:* HIPAA		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

The following amendment request contains both an amendment to the protocol from an earlier contingently approved amendment request along with several new requests.

Contingently Approved Amendment:

1. We have requested a WWIC and have included consent language in our phone screening script as requested by the committee. This amendment involves the request to add screening language on page 7 (Selection) of the protocol.

We are also requesting approval for the following amendments to the protocol.

2. We had initially proposed to require that all participants receive clearance from their primary care provider in order to engage in the walking portion of the intervention. We would like to remove this clearance. As you may recall, participants in this study will be asked to record their daily steps using a study-provided pedometer and be given a goal of increasing their average steps by 10% over the previous week's steps. Recent discussions with several primary care providers revealed that they felt that completing the clearance form would be burdensome and is not necessary to safely conduct the study given the low risk nature of the walking intervention. Providers did specify that prior to consent we ask patients if they experience chest pain as a result of walking and disqualify patients who endorse this symptom. Patients are

already asked if they are able to walk one block before beginning the study. Pg. 5 (Eligibility criteria), Pg. 6 (Privacy), (Research Plan), Pg 17 (Risks and benefits) WIC

3. We request approval to give participants feedback about their treatment progress in the form of graphs detailing their self-reported pain, sleep and activity levels as well as their goal accomplishment and use of pain coping skills over the course of the study. Participants who are randomized to the IVR condition (ICBT), will be mailed the materials and those in CBT condition will be given these materials during treatment session. Pg 9 (Treatments)

4. We request approval to add a post treatment telephone interview for patients who complete the IVR (ICBT) condition to assess their satisfaction with the treatment. To our knowledge this is the first trial of CBT for pain conducted solely via IVR, consequently, we are very interested in participant's reactions to the treatment. Pg 14 (Treatment feasibility outcomes)

5. We have added a one week baseline assessment of pain intensity, sleep duration and activity level at baseline. These variables will be assessed via automated telephone call.Pg 8 (Treatments) Consent Form - pg 1

6. We have altered the protocol description language regarding "tape recording" of treatment sessions. We will not be using a tape; we will be using an ISO approved digital audio recorder. Therapists will conduct the digital audio recording and will label each digital file with the subjects study ID# and the session number. Only approved research personnel will have access to the audiotapes audio files and they will be stored behind the VA firewall. Pg 16 (Risks and benefits)

7. We have removed the names of personnel at the Michigan Computing Center who had been listed as having access to PHI. We have learned that these personnel will be responsible for maintaining the computing equipment but they will not have access to PHI. Pg 19 (Confidentiality)

8. We have added language to the protocol to indicate that we will pay participants by voucher in addition to check. Participants can choose whichever method is most convenient for them. Pg 20 (Payment).Consent Form - pg 6

9. We have updated the consent form and HIPAA form to be consistent with the most current format.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

The modification to remove physician consent for participation in the walking portion of the intervention was suggested by physicians and we will exclude persons who report experiencing chest pain when walking. We will also be actively soliciting reports of walking related AEs from participants on a weekly basis.

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects*	☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No (2) Does the change increase risk to research personnel or others? ☐Yes ☒No
If the answer to (1) is yes, submit a revised Research Protocol Safety Survey *If the answer to (2) is yes, describe the increased risk below*

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

–

_____ _____

Signature of Principal Investigator Date

Department of Veterans Affairs

Memorandum

Date: March 19, 2012

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was reviewed and approved by the Human Studies Subcommittee (HSS) on 3/15/12. Neither you nor any of the identified co-investigators participated in the review and decision making.

If you have a dual appointment (VA Connecticut Healthcare System and Yale University) this amendment may require approval by the Yale HIC before implementation. For timely review, submit a copy of this amendment request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 1/16/13 for this project. The forms for requesting Continued Approval can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. All procedures and interventions employed must be those as approved by the Human Subjects Subcommittee.
2. Any changes to the protocol must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated.

If any questions, please contact me at ext. 3350 or 3351.

Brendan Sullivan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist Amendment(s)

Principal Investigator: Heapy, Alicia, Ph.D	MIRB #: 01281	Promise #: 0004
Project Title:	IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain	
Initial Approval Date (mm/dd/yy): 03/19/09		
Current Approval Period: 01/17/12	Expiration: 01/16/13	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☑	☐	☐

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☑ No

Has the investigator complied with all regulations and HSS decisions? ☑ Yes ☐ No

The research should be:
- ☑ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

Signature of Reviewer

3/15/2012
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: February 27, 2012 2/28/12 Amendment Initiated by: Local Investigator

Name of Principal Investigator: Alicia Heapy

Title: **IVR-based CBT for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention. The primary clinical equivalence hypothesis states that veterans with chronic low back pain (CLBP) receiving IVR-based CBT (ICBT) will demonstrate, relative to standard face-to-face CBT (CBT), equivalent declines in reports of pain intensity as measured by the numeric rating scale at post-treatment and follow-up. The secondary hypothesis states that veterans with CLBP receiving ICBT, relative to CBT, will demonstrate equivalent declines in reports of pain-related interference and emotional distress at post-treatment and follow-up.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☐Consent	☐Administrative Letter	☐Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We request the following changes to the protocol and recruitment letter:

We would like to replace the Structured Clincal Interview for DSM Disorders (SCID) with the Mini International Neuropsychiatric Interview (MINI) as a measure of current psychiatric comorbidities. The MINI has been found to be reliable and valid and is much less burdensome to patients than the SCID. The SCID takes on average one hour or more to administer and the MINI takes approximately 15 minutes.

We would like to transfer data to/from the VINCI system, which is a VA internal secure computing environment, for the purpose of performing data analysis. VINCI is located behind the VA firewall.

Lastly, we request to change the opt out recruitment letter to be consistent with the current approved protocol.

IIIb. **Does the modification increase the risk to subjects?** ☐Yes ☒No *Describe below, if applicable*

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No (2) Does the change increase risk to research personnel or others? ☐Yes ☒No
If the answer to (1) is yes, submit a revised Research Protocol Safety Survey *If the answer to (2) is yes, describe the increased risk below*

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

2/27/12
Date

Department of Veterans Affairs

Memorandum

Date: May 17, 2013

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was granted approval by the Human Studies Subcommittee (HSS) on 03/16/13. Neither you nor any of the identified co-investigators participated in the review and decision-making.

If you have a faculty appointment at Yale University, this may require approval by the Yale HIC before implementation. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 12/19/13. The request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Human Studies Subcommittee reminds you of several important requirements:

1. All procedures and interventions must be those as approved by the Human Subjects Subcommittee.
2. Any changes to the protocol must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated.

If any questions regarding HSS issues, please contact me at ext. 3350.

Brendan Sullivan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist
Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB #:	Promise #: 0004
Project Title:	IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 05/07/09			
Current Approval Period: 12/20/12		Expiration: 12/19/13	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☑	☐	☐

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☑ No

Has the investigator complied with all regulations and HSS decisions? ☑ Yes ☐ No

The research should be:
- ☐ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

M. Bell, PhD
Signature of Reviewer

5/16/2013
Date

Amendment

Risk Level: Not greater than minimal

2. **DeVito, Elise, Ph.D.** Education Requirement Met? ☐

Influence of Sex Hormones and Substance Use on Cognition

ID: **01555** Prom#: **0001** Protocol#: **N/A** Protocol Dt:

STATUS: Active

HSS Init Approval Dt: 12/15/2011 [Risk Level: Not greater than minimal]
HSS CR Approval Dt: 11/15/2012 [Risk Level: Not greater than minimal]
Research Staff [(*) = on committee]: Babuscio, T.; Barnes, L.; Herman, A.; Minnix, S.; Mitchell, E.

Reviewer: Fichtenholtz, H.

ITEMS REVIEWED (* = stipulations):

- Amendment Memo (05/08/2013)
- Project Description (05/08/2013)

The PI submitted an amendment requesting to expand the incluson criteria to allow participants with a BMI of 17.0-34.99 to enter the study. The Subcommittee reviewed the requested change, determined it does not reduce the scientific merit of the study and that the risk level remains not greater than minimal.

A motion to Approve was seconded and passed.

Approved [For: 11 Against: 0 Abstained: 0 Recused: 1 (Sofuoglu, M.) Excused: 2 (Peixoto, A.; Ranganathan, M.) Total: 14]

3. **Heapy, Alicia, Ph.D** Education Requirement Met? ☐

IVR-Based Cognitive Behavorial Therapy for Chronic Low Back Pain

ID: **01281** Prom#: **0004** Protocol#: **N/A** Protocol Dt:

STATUS: Active

HSS Init Approval Dt: 05/07/2009 [Risk Level: Not greater than minimal]
HSS CR Approval Dt: 12/20/2012 [Risk Level: Not greater than minimal]
Research Staff [(*) = on committee]: Buta, E.; Cervone, D.; Clark, E.; Fenton, L.; Gaetano, V. S.; Goodin, B.; Ibsen, L.; Kirlin, J.; LaChappelle, K.; Spreyer, K.

Sponsor: VA - Health Services R&D (9024) • Admin: VA (02)

Reviewer: Fiszdon, J.

ITEMS REVIEWED (* = stipulations):

- Advertisement - Facebook Add (05/07/2013)
- Advertisement - Fliers (05/07/2013)
- Amendment Memo (05/07/2013)
- Project Description (05/07/2013)

The PI submitted an amendment requesting to expand recruitment in the following ways:

a. provide study flyers to VACHS providers for direct referral;
b. advertise on VACHS FaceBook page;
c. place study flyers at Vet centers;
d. provide approved flyers to veteran coordinators at local universities;

Amendment

e. place flyers in grocery stores and libraries within the greater New Haven area;
f. conduct pain education tables at all VACHS locations.

The Subcommittee reviewed the requested changes, determined they do not reduce the scientific merit of the study and that the risk level remains not greater than minimal.

A motion to Approve was seconded and passed. One member abstained from the vote due to concerns over the photo included in one advertisement.

Approved [For: 10 Against: 0 Abstained: 1 Recused: 0 Excused: 3 (Heapy, A.; Peixoto, A.; Ranganathan, M.) Total: 14]

Notification

1. **Petrakis, Ismene L., M.D.** Education Requirement Met? ☐
Cosgrove, Kelly, Ph.D
George, Tony P., M.D.
Gonzalez-Haddad, Gerardo, M.D.
Jane, Serrita, Ph.D
Kim, Nancy, MD
O'Malley, Stephanie, Ph.D
Ralevski, Elizabeth, Ph.D
Rounsaville, Bruce J., M.D.
Staley, Julie K., Ph.D.
Terlecki, Meredith, BS
Wilkinson, Patrick, Med., RN,C
Treatment with Mecamylamine in Smoking and Non-Smoking Alcohol Dependent Patients
ID: **00573** Prom#: **0023** Protocol#: **N/A** Protocol Dt:
STATUS: Active
HSS Init Approval Dt: 11/06/2003 [Risk Level: Moderate]
HSS CR Approval Dt: 03/07/2013 [Risk Level: Moderate]
Sub-Investigators [(*) = on committee]: Drew, S.; Edens, E.
Research Staff [(*) = on committee]: Dean, E.; Dwan, R.; Earley, C.; Frolich, E.; Genovese, A.; Hayden, R.; Keegan, K.; Limonecelli, D.; McHugh-Strong, C.; Newcomb, J.; Russo, A.; Terlecki, M.
Sponsor: VA MIRECC (9299) • Admin: VA (02)

Dr. Petrakis notified the committee that she received the Yale School of Medicine Center for Translational Neuroscience of Alcoholism (CTNA) Data Safety Monitoring Board (DSMB) Report dated December 12, 2012. The CTNA DSMB found no concerns regarding this project. The study will continue to move forward as planned.

Acknowledged

Department of Veterans Affairs

Memorandum

Date: November 25, 2013

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was granted approval by the Human Studies Subcommittee (HSS) on 11/21/13. Neither you nor any of the identified co-investigators participated in the review and decision-making.

If this project uses any Yale resources, it may require review by the Yale HIC. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 12/19/13. The request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Human Studies Subcommittee reminds you of several important requirements:

1. All procedures and interventions must be those as approved by the Human Subjects Subcommittee.

2. Any changes to the protocol must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated.

If any questions regarding HSS issues, please contact me at ext. 3350.

Brendan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB #: 01281	Promise #: 0004
Project Title:	IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 05/07/09			
Current Approval Period: 12/20/12		Expiration: 12/19/13	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☐	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☐	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☐	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☐	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☐	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☐	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☐	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☐	☐	☐

Reviewer Recommendations
Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☐ No Has the investigator complied with all regulations and HSS decisions? ☐ Yes ☐ No The research should be: ☐ Continued ☐ Continued with modifications ☐ Suspended ☐ Terminated
Reviewer Comments:

☑ Convened HSS
☐ Determination by Expedited Reviewer, as minor changes in previously approved research

M. Bell. PhD
Signature of Reviewer

4/21/2013
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: 11/05/13 Amendment Initiated by: Local Investigator Study #: 0004

Name of Principal Investigator: Alicia Heapy

Title: **IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention. The primary clinical equivalence hypothesis states that veterans with chronic low back pain (CLBP) receiving IVR-based CBT (ICBT) will demonstrate, relative to standard face-to-face CBT (CBT), equivalent declines in reports of pain intensity as measured by the numeric rating scale at post-treatment and follow-up. The secondary hypothesis states that veterans with CLBP receiving ICBT, relative to CBT, will demonstrate equivalent declines in reports of pain-related interference and emotional distress at post-treatment and follow-up.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☐Protocol	☐Investigator Drug Brochure	☒Recruitment Material
☐Consent	☐Administrative Letter	☐Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We would like to expand our recruitment by adding a study brochure which will allow us to provide more detailed study information to patients. We will make the brochure available via our previously approved recruiting mechanisms such as the informational pain table and by giving them to providers who will be asked to offer them to potentially eligible patients.

We also request to update our approved advertisement to include the word "Are you a Veteran" and update the contact information. Adding the Veteran language decreases the burden of screening individuals who would not meet study criteria as we are not recruiting non-Veterans.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects*	☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No (2) Does the change increase risk to research personnel or others? ☐Yes ☒No
If the answer to (1) is yes, submit a revised Research Protocol Safety Survey *If the answer to (2) is yes, describe the increased risk below*

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

11/5/13
Date

Department of Veterans Affairs

Memorandum

Date: February 10, 2014

From: HSS Coordinator/Research/151

Subj: Approval of Amendment and Consent Forms(s)

To: Alicia Heapy, Ph.D.

Your amendment with Consent Forms to your approved project entitled "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was reviewed and approved by the Human Studies Subcommittee (HSS) on 02/06/14. Neither you nor any of the identified co-investigators participated in the review and decision making.

If this project uses any Yale resources, it may require review by the Yale HIC. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 12/04/14. The forms for requesting Continued Approval can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Subcommittee reminds you of several important requirements:

1. The Consent Form(s) and HIPAA Authorization used must be the most recently approved by the Subcommittee. Be sure that both are filled in completely.
2. The procedures and interventions must be those proposed in the protocol and that have been approved.
3. Any changes to the protocol or the Consent Form(s) must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated. HIPAA forms may be amended as necessary and, a copy forwarded to the Research Office.
4. Please Note: All Consent Form(s) must be reviewed, and signed by the Principal Investigator. (Co-investigators may sign, if PI is unavailable, however the PI must co-sign as soon as possible.)
5. Please Note: Signatures of the Witness and the Person Obtaining Consent cannot be the same person.
6. Any adverse event, unanticipated problem or protocol deviation must be promptly reported to the Subcommittee.
7. Any drugs used in this project must be dispensed by the VACHS Pharmacy.
8. For each signed HIPAA Authorization and Consent Form(s) there must be:
    - A copy in your file
    - A copy given to the subject (or representative)
    - A research alert must be created in the electronic medical record containing the date of enrollment, the title of study, the name of PI, the name of the person obtaining consent and any other pertinent information regarding this study.

If any questions, please contact me at ext. 3350.

Brendan Sullivan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist
Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D	MIRB #: 01735	Promise #: 0006
Project Title:	IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain	
Initial Approval Date (mm/dd/yy): 05/07/09		
Current Approval Period: 12/05/13	Expiration: 12/04/14	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☑	☐	☐

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☑ No

Has the investigator complied with all regulations and HSS decisions? ☑ Yes ☐ No

The research should be:
- ☑ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

M Bell, PhD
Signature of Reviewer

2/06/2014
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: 01/30/14 Amendment Initiated by: Local Investigator Study #: 0004

Name of Principal Investigator: Alicia Heapy, Ph.D.

Title: **IVR-based Cognitive Behavior Therapy for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of interactive voice response (IVR) for delivering an empirically validated psychological treatment (cognitive behavior therapy) for chronic pain in order to improve access and sustainability of this intervention.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☐Recruitment Material
☒Consent	☐Administrative Letter	☐Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We would like to add additional information to the study consent form and project description regarding the information security and data flow aspects of the trial. We currently have approval for identifiable information to be held outside the VA at Yale University and the University of Michigan and participants are informed of this in the consent and HIPAA forms. However, we would like to clarify what information will be held at Yale, how often data will be returned to the VA from both sites and the manner of return. We would like to make revisions to the consent form that will provide participants with more information and more clearly specify our data flow processes in the project description.

1) Yale and TrialDB- We inform participants that data will be held outside the VA and the VA cannot protect data once it leaves. We specify that data collected via questionnaires completed using the TrialDB database will be held at Yale. In an earlier amendment we stated that although we believed the data held at Yale would be de-identified, dates would be collected and because dates could be considered an identifier we wanted to notify participants that identifiable data would be collected and held at Yale. We were not specific in the consent form about the nature of the identifiable data that would be held. We have recently become aware that the TrialDB system requires a birth date be entered when enrolling a new participant. The PI was not aware of this requirement because this data field was not part of the data collection form. Although patients were not specifically informed that their birth date was being held at Yale, they were informed that data would be held outside the VA and this data is collected during the questionnaire completion process. We would like to specify in the protocol and consent the exact nature of the identifiable information being held outside VA. Additionally, we would like to update the project description to accurately reflect that idenifiable data will be held on TrialDB. In looking at our project description we had never updated to it to reflect our amendment approved on July 7, 2011 (attached).

2) Transfer of data to VA
University of Michigan - We have clarified that data will be returned periodically to VA, not just at the end of the study.

Yale University- We originally proposed to return the data from Yale via encrypted disk, we would like to add the option of returning the data via secure server to server transfer. We have added language to the project description that details the secure process by which the data will return periodically and at the conclusion of the data collection period.

IIIb. Does the modification increase the risk to subjects? ☐Yes ☒No *Describe below, if applicable*

IIIc. Is this amendment being requested because of new information or findings that may impact on the subject's willingness to continue participation? *If Yes, describe in the space below how the new information will be communicated to the currently enrolled subjects* ☐Yes ☒No

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No
(2) Does the change increase risk to research personnel or others? ☐Yes ☒No

If the answer to (1) is yes, submit a revised Research Protocol Safety Survey

If the answer to (2) is yes, describe the increased risk below

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

1/30/14
Date

Department of Veterans Affairs

Memorandum

Date: May 27, 2015

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was granted approval by the Human Studies Subcommittee (HSS) on 05/21/15. Neither you nor any of the identified co-investigators participated in the review and decision-making.

If this project uses any Yale resources, it may require review by the Yale HIC. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 11/19/15. The request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Human Studies Subcommittee reminds you of several important requirements:

1. All procedures and interventions must be those as approved by the Human Subjects Subcommittee.

2. Any changes to the protocol must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated.

If any questions regarding HSS issues, please contact me at ext. 3350.

for Brendan Sullivan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB 01281	Promise #:0004
Project Title:	IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 03/19/09			
Current Approval Period: 11/20/14		Expiration: 11/19/15	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☑	☐	☐

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☐ No

Has the investigator complied with all regulations and HSS decisions? ☐ Yes ☐ No

The research should be:
- ☐ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

M Bell, PhD
Signature of Reviewer

5/21/2015
Date

VA CONNECTICUT HEALTHCARE SYSTEM
Research and Development
Request to Modify an Approved Research Protocol
Human Subject Research

Version Date: May 8, 2015

Amendment Initiated by: Local Investigator

Name of Principal Investigator: Alicia Heapy

Title: **IVR-based CBT for Chronic Low Back Pain**

SECTION I: PROTOCOL BACKGROUND

In the area below, provide a brief statement about the purpose of the research and identify the interventions and procedures that are being performed for research purposes

The primary purpose of this study is to test the efficacy of an innovative method, interactive voice response (IVR), for delivering an empirically validated psychological (cognitive behavior therapy [CBT]) treatment for chronic pain in order to improve access and sustainability of this intervention. The primary clinical equivalence hypothesis states that veterans with chronic low back pain (CLBP) receiving IVR-based CBT (ICBT) will demonstrate, relative to standard face-to-face CBT (CBT), equivalent declines in reports of pain intensity as measured by the numeric rating scale at post-treatment and follow-up. The secondary hypothesis states that veterans with CLBP receiving ICBT, relative to CBT, will demonstrate equivalent declines in reports of pain-related interference and emotional distress at post-treatment and follow-up.

SECTION II. COMPONENTS OR PROTOCOL ELEMENTS(S) TO BE MODIFIED

Mark all items below that apply. The new/revised document(s) must be submitted with the Request for Modification. When applicable, attach the currently approved document with track changes, and a final version with changes incorporated.

☒Protocol	☐Investigator Drug Brochure	☐Recruitment Material
☐Consent	☐Administrative Letter	☐Data Collection Tools
☐Other *Describe:*		
☐Other *Describe:*		

SECTION III. AMENDMENT DESCRIPTION, RATIONALE, AND IMPACT

IIIa. In lay language, describe the proposed modification and rationale in the space below.

We would like to transfer de-identified data to University of Michigan investigators who are being submitted for approval on the study. The investigators (Satinder Singh (Baveja) and Sean Newman) will receive and analyze de-identified study data. This data will be used to "train" an artificial intelligence (AI) engine that we will be using to deliver cognitive behavioral treatment in a newly funded study. Briefly, the AI engine will use patients' daily reports about their progress in treatment to automatically personalize the intensity and type of patient support (50 minute telephone session, 15 minute telephone session or 5 minute pre-recorded, personalized feedback); thereby ensuring that scarce therapist resources are used as efficiently as possible and potentially allowing programs with fixed budgets to serve many more Veterans. In order to "learn" which patients benefit most from which sessions and how many days of data are required to make the best assignment, the engine requires data from patients. Often an engine will learn on the initial group of 50 trial participants, but this means that the participants who are used for learning may not achieve as positive outcomes as those who were entered into the trial after the engine has had some initial learning. In order to avoid this potentially negative outcome for the initial participants, we would like to use deidentified data from the above mentioned trial to teach the AI engine that will be used in the soon to be started trial. The ongoing trial collects much of the same information, uses the same population (Veterans with chronic low back pain), and delivers a similar treatment (cognitive behavioral therapy for chronic pain delivered in real time versus brief pre-recorded feedback).

IIId. (1) Does the change involve biological, chemical, physical and/or radiation hazards? ☐Yes ☒No (2) Does the change increase risk to research personnel or others? ☐Yes ☒No
If the answer to (1) is yes, submit a revised Research Protocol Safety Survey *If the answer to (2) is yes, describe the increased risk below*

Investigator's Assurance

I assure the IRB that the proposed changes will not be initiated without required committee approval(s), except when necessary to eliminate apparent, immediate hazards to the subjects.

If the amendment is initiated by the Yale HIC, attach a copy of the Yale minutes requesting this change.

Signature of Principal Investigator

5/11/15
Date

Department of Veterans Affairs

Memorandum

Date: July 1, 2016

From: HSS Coordinator/Research/151

Subj: Approval of Amendment

To: Alicia Heapy, Ph.D.

Your amendment to your approved project entitled, "IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain" (#0004) was granted approval by the Human Studies Subcommittee (HSS) on 6/30/16. Neither you nor any of the identified co-investigators participated in the review and decision-making.

If this project uses any Yale resources, it may require review by the Yale HIC. For timely review, submit a copy of this request with the VACHS HSS approval letter to the Yale HIC without delay.

Review and approval of your Request for Continued Approval by the HSS is required prior to the expiration date of 11/4/16. The request for Continued Approval forms can be found on the SharePoint site and a reminder to complete the required paperwork will be forwarded to you approximately eight (8) weeks prior to the end of your current approval period.

The Human Studies Subcommittee reminds you of several important requirements:

1. All procedures and interventions must be those as approved by the Human Subjects Subcommittee.
2. Any changes to the protocol must be proposed to the Subcommittee in writing as a modification to an approved project and must be approved before they are initiated.

If any questions regarding HSS issues, please contact me at ext. 3350.

Brendan Sullivan

VA CONNECTICUT HEALTHCARE SYSTEM
Human Research Protection Program

Human Studies Subcommittee (HSS) Review Checklist
Amendment(s)

Principal Investigator: Alicia Heapy, Ph.D.		MIRB #: 01281	Promise #: 0004
Project Title:	IVR-based CBT for Chronic Low Back Pain		
Initial Approval Date (mm/dd/yy): 5/7/09			
Current Approval Period: 11/5/15		Expiration: 11/4/16	

	Criteria for IRB Approval of Research: The following information is designed to assist the reviewer in determining that the Federally required criteria for HSS approval codified in the Common Rule at 38 CFR Part 16.111, and in FDA regulations, are met. ***The following criteria must be met for all reviews of amendments.***	Yes	No	N/A
a.	**Risks to subjects are minimized: (i)** By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and (ii)** whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.	☑	☐	
b.	**Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.** In evaluating risks and benefits, the HSS should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The HSS should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.	☑	☐	
c.	**Selection of subjects is equitable**. In making this assessment the HSS should take into account the purposes of the research and the setting in which the research will be conducted.	☑	☐	
d.	**Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116.** (or has previously been waived by the HSS)	☑	☐	☐
e.	**Informed consent will be appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117.** (or has previously been waived by the HSS)	☑	☐	☐
f.	**When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.**	☑	☐	
g.	**When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.**	☑	☐	☐
h.	**When some or all of the subjects are likely to be vulnerable to coercion or undue influence,** such as children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects.**	☑	☐	☐

Reviewer Recommendations

Has any new information emerged either from the research itself or from other sources that could alter the HSS's previous determinations, particularly with respect to risk to subjects? ☐ Yes ☐ No

Has the investigator complied with all regulations and HSS decisions? ☐ Yes ☐ No

The research should be:
- ☐ Continued
- ☐ Continued with modifications
- ☐ Suspended
- ☐ Terminated

Reviewer Comments:

- ☑ Convened HSS
- ☐ Determination by Expedited Reviewer, as minor changes in previously approved research

Mona Bell, PhD
Signature of Reviewer

6/30/2016
Date

Amendment

ADVERTISEMENT

1. The advertisement was missing from the hardcopy of the amendment provided by the PI, however, the reviewer stated she did see an electronic version of the flyer posted on the Research SharePoint site. Provide a hardcopy of the missing flyer, which will then be reviewed by the HSS chairman for final approval.

The PI submitted a revised Waiver of Informed Consent (WIC) and a Waiver of HIPAA authorization to reflect the review of the problems list in CPRS. The revised WIC is based on 38 CFR 16.116(d). All four required elements are adequately addressed. The Request for Waiver of Authorization describes the PHI that the PI proposes to use, and contains information that satisfies the three criteria stated at 45 CFR 164.512(i)(2)(ii).

A motion to grant Contingent Approval was seconded and passed. A written response to the minutes signed by the PI is required along with a clean copy of the flyer. The template for the written response memo can be found on the Research SharePoint site and is entitled "Response to Minutes Memo template."

Contingent Approval [For: 14 Against: 0 Abstained: 0 Recused: 1 (Fiszdon, J.) Excused: 0 Total: 15]

3. **Heapy, Alicia, Ph.D** Education Requirement Met? ☐

IVR-Based Cognitive Behavioral Therapy for Chronic Low Back Pain

ID: **01281** Prom#: **0004** Protocol#: **N/A** Protocol Dt:

STATUS: Active

HSS Init Approval Dt: 05/07/2009 [Risk Level: Not greater than minimal]
HSS CR Approval Dt: 11/05/2015 [Risk Level: Not greater than minimal]
Research Staff [(*) = on committee]: Bertschinger, E.; Buta, E.; Cervone, D.; Fenton, L.; Gaetano, V. S.; Ibsen, L.; Kirlin, J.; LaChappelle, K.; Rinadli, A.; Simone, L.; Spreyer, K.

Sponsor: VA - Health Services R&D (9024) • Admin: VA (02)

Reviewer: Sevarino, K. A.

ITEMS REVIEWED (* = stipulations):

- Amendment Memo (06/10/2016)
- HIPAA Waiver (WOA) - revised (06/10/2016)
- Project Description - clean (06/10/2016)
- Project Description - tracked (06/10/2016)
- Request for Waiver of Informed Consent (WIC) - Revised (06/10/2016)

The PI submitted an amendment to her protocol requesting to conduct a medical record review in order to compare patients who enrolled in the intervention versus those that expressed interest and met eligibility criteria, but did not enroll. The PI will extract demographic information from the medical record, to include: age, race, sex, pain medication use, distance from the VA and the number and location of pain sites.

The Subcommittee reviewed the requested change, determined it does not reduce the scientific merit of the study and that the risk level remains not greater than minimal. The PI submitted an updated Waiver of Informed Consent for the medical record review. The waiver request is based on 38 CFR 16.116(d).

Amendment

All four required elements are adequately addressed.

A motion to Approve was seconded and passed.

Approved [For: 14 Against: 0 Abstained: 0 Recused: 1 (Heapy, A.) Excused: 0 Total: 15]

4. **Heapy, Alicia, Ph.D** Education Requirement Met? ☐

Cooperative Pain Education and Self-Management (COPES)

ID: **01997** Prom#: **0012** Protocol#: **VA** Protocol Dt:

STATUS: Active

HSS Init Approval Dt: 10/15/2015 [Risk Level: Not greater than minimal]

Sponsor: None Specified

Reviewer: Sevarino, K. A.

ITEMS REVIEWED (* = stipulations):

- Amendment Memo (06/23/2016)
- Project Description - clean (06/23/2016)
- Project Description - tracked (06/23/2016)
- Request for Waiver of Written Informed Consent - Add focus groups (06/08/2016)

The PI submitted an amendment requesting the following changes to her protocol:

a. Pilot a previously-approved qualitative interview guide with staff and patients at VACHS and pilot surveys with staff at VACHS prior to their use at the implementation sites;
b. Conduct focus groups with patients to get their feedback on the recruitment material and a patient handbook to be used in the intervention;
c. Clarify that surveys being administered to providers will be conducted using VA REDCap;

The Subcommittee reviewed the requested changes, determined they do not reduce the scientific merit of the study and that the risk level remains not greater than minimal. The proposed changes included a revised Waiver of Written Informed Consent (WWIC) and two new information sheets. The WWIC was revised so that it now covers the focus groups, and remains approved under 38 CFR 16.117 (c) (2). The Subcommittee agreed that the research presents no more than minimal risk of harm to the subjects and involves no procedures for which consent is normally required outside of the research context.

A motion to Approve was seconded and passed.

Approved [For: 14 Against: 0 Abstained: 0 Recused: 1 (Heapy, A.) Excused: 0 Total: 15]

5. **Justice, Amy, M.D.** Education Requirement Met? ☐

Braithwaite, Ronald Scott, M.D.
Erdos, Joseph J., M.D., Ph.D.
Fiellin, David A., M.D.
Kim, Nancy, M.D.
Latkany, Paul, M.D.
Mattocks, Kristin, Ph.D

Consortium to improve Outcomes in HIV/AIDS, Alcohol, Aging, and Multi-Substance Use