NCCAM Protocol

FULL PROTOCOL TITLE

A pilot study of integrated treatment for Veterans with chronic pain and opiate misuse

Study Chairman or Principal Investigator:

Kevin E. Vowles, Ph.D., Associate Professor,
Department of Psychology, University of New Mexico

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STUDY TEAM ROSTER

PI - Kevin E. Vowles, PhD
Department of Psychology, University of New Mexico, MSC03 2220 – Logan Hall, Albuquerque, NM 87131; 505-277-5676 (tel); 505-277-1394 (fax); k.e.vowles@gmail.com (e-mail).

Co-I – Katie Witkiewitz, PhD
Department of Psychology, University of New Mexico MSC03 2220 – Logan Hall, Albuquerque, NM 87131; 505-277-4121 (tel); 505-277-1394 (fax); katiew@unm.edu (e-mail).

Co-I – Wesley Gilliam, PhD
Department of Primary Care, New Mexico Veteran Affairs Healthcare System; 1501 San Pedro Dr SE; Albuquerque, NM 87108; 505-265-1711 (ext. 5153) (tel); Wesley.gilliam2@va.gov (e-mail).

Co-I – Karen Cardon, MD
Department of Internal Medicine, New Mexico Veteran Affairs Healthcare System; 1501 San Pedro Dr SE; Albuquerque, NM 87108; 505-265-1711 (tel); Karen.Cardon@va.gov (e-mail).

Consultant – Sarah Bowen, PhD
Department of Psychology, , University of Washington, 1100 NE 45th, Suite 300, Seattle, WA 98105; 206-685-2995 (tel); swbowen@uw.edu (e-mail)

PARTICIPATING STUDY SITES

University of New Mexico, Department of Psychology, University of New Mexico MSC03 2220 – Logan Hall, Albuquerque, NM 87131

Raymond G. Murphy VA Medical Center, New Mexico Veteran Affairs Healthcare System 1501 San Pedro SE; Albuquerque, NM 87108

PRÉCIS

Objectives: Determine the feasibility and acceptability of a combined treatment for veterans with comorbid chronic pain and opioid misuse or dependence, as well as assess mechanisms of change during the combined intervention. A secondary objective is to examine weekly progress on specific therapy targets (e.g., pain acceptance, self-compassion, opioid craving) in the interventions in order to identify potential mechanisms of change and to identify the choice of intermediate endpoints for a larger randomized clinical trial. Approach—To test the feasibility of recruitment and retention, as well as study weekly progress on treatment targets, within a randomized clinical trial (RCT) of Acceptance and Commitment Therapy (ACT) + Mindfulness-Based Relapse Prevention (MBRP) or treatment as usual for chronic pain and opiate misuse.

Design and Outcomes: Veterans with chronic pain and opiate misuse, abuse, or dependence who are receiving long-term opioid therapy (i.e., 90+ days) will be recruited from the Raymond G Murphy Veterans Affairs (VA) Medical Center in Albuquerque, NM. Treatment will begin in Year 1 and conclude in Year 2 with follow-up assessment lasting through the first quarter of Year 3. At the time of enrolling in the trial, individuals will participate in a baseline assessment including self-report and behavioral measures. Participants (n = 120) will then be randomized to one of two treatment conditions: (1) treatment services-as-usual (i.e., standard care) or (2) standard care with eight weeks of group ACT plus four weeks of group MBRP. Participants will complete assessments at baseline (entry into the study), weekly during the first three months of the study (during treatment), three months after entry in the study (end of treatment), and nine months after entry in the study (six months after treatment conclusion).

Self-Report and Behavioral Assessment Batteries—Self-report and behavioral assessments will be used to evaluate study hypotheses. For the follow-up assessments we will use contact information collected at baseline to contact participants by phone one week prior to their scheduled follow-up date. Participants will be reminded about procedures and scheduled to complete all assessments at the VA.

Demographic Information (*Pre-treatment, Post-treatment, and 6 month follow-up assessment):* Patient demographics (e.g., gender, age, educational achievement) and pain-related information (e.g., duration, location, history of treatment) will be collected during the pre-treatment assessment. We will re-assess pain-related information and treatment history at post-treatment and the 6-month follow-up assessment.

Clinical Outcome Measures (*Pre-treatment, Post-treatment, and 6 month follow-up assessment)*: Given the relevance of interference from pain on key aspects of functioning in those with chronic pain, we will utilize the NIH PROMIS toolkit measures for pain behavior[1] and pain interference[2]. Both PROMIS measures have evidence of excellent psychometric properties in chronic pain. We will also collect information on current opioid misuse using the Current Opioid Misuse Measure, a measure of aberrant opioid-related behaviors over the past month[3]. The recommended cut-score of 12 has adequate sensitivity (77%) and specificity (77%) for a current diagnosis of prescription drug abuse[3]. Finally, current pain intensity, as well as least, most, and average over the past seven days, will be assessed via 0-10 numerical ratings scales and disability will be assessed via the Sickness Impact Profile[4].

Weekly Self-Report Progress Measures (20 minutes per week): In order to examine our secondary objective concerning mechanisms of change during treatment, we will collect weekly data during the 12 weeks of treatment to assess for change in specific therapy targets that are hypothesized to change during treatment. These weekly progress measures will include three self-report questionnaires, each of which has evidence for mediating treatment outcomes in either ACT for chronic pain[5] or MBRP for substance use disorder[6,7]. These measures include:

1. Chronic Pain Acceptance Questionnaire (CPAQ[8]). The CPAQ is a 20-item measure of acceptance and willingness to have chronic pain. It is perhaps the most widely used measure of pain acceptance in

the literature and its psychometric properties, factor structure, and sensitivity to treatment are well established[9,10].

2. Self-Compassion Scale (SCS[11]). The SCS is a 26-item questionnaire which evaluates numerous aspects of mindfulness and self-compassion. Initial psychometric evaluations of the measure have provided support for its reliability and validity[11].

3. Penn Alcohol/Drug Craving Scale (PACS[12]). A modified version of the PACS will be used to assess both alcohol and drug craving. The PACS is a 5-item measure including questions about frequency, intensity, and duration of craving, and an overall rating of craving for the previous week. The PACS has demonstrated good psychometric properties in our prior studies, including internal consistency reliability (α=.87) and criterion validity[6,7].

In addition to these three questionnaires, the weekly progress measure will also include items to assess mindfulness practice (days/times per day) and homework assignment completion, as well as items relating to pain intensity, distress intensity, willingness to experience pain, and engagement in valued activity[13].

Interventions and Duration: Intervention Conditions—All participants will continue to receive standard care for chronic pain within the VA. In addition, one-half of participants will be randomized to also receive ACT plus MBRP. Standard Care: Participants in all conditions will receive standard treatment as usual at the VA, as indicated by the individual's treatment plan which will not be manipulated by the research team. Consistent with national and VA standards[14,15], care at the recruitment sites typically consists of noninvasive interventions, such as analgesic pain medications (e.g., opioids, NSAIDs, anti-epileptics), topical solutions (e.g., lidocaine), physical therapy, and massage, as well as limited invasive interventions (e.g., injections, radiofrequency denervation). Acceptance and Commitment Therapy (Weeks 2–9): The ACT intervention is based on the standardized and manualized protocol of Vowles and Sorrell[16], which consists of weekly 90-minute group meetings over eight weeks. The protocol has been successfully used in previous clinical trials (e.g., [17,18]) and is currently available on the VA's Evidence-Based Practice SharePoint website. Over the course of the group meetings, participants will identify areas of meaningful functioning that have been adversely impacted by pain, learn methods to enhance pain willingness in the service of these meaningful areas, and practice present-focused awareness skills. Group sessions will include discussions of the impact of pain and distress avoidance, identifying alternatives to this avoidance and establish plans for behavior change, demonstration and role-playing exercises, and homework assignments. Participants will be provided with a treatment manual to help guide and inform practice outside of group sessions. Table 1 provides an outline of session content for the eight week ACT intervention. We anticipate enrolling approximately eight patients per group. Mindfulness Based Relapse Prevention (Weeks 10–13): The MBRP program is a standardized group psycho-educational intervention that consists of weekly 90-minute group meetings spanning four[19] to eight weeks[20]. For the current study, we will use the four-week program, which will eliminate redundancy with the ACT protocol (the eight-week MBRP group has some redundancy with ACT) and will also expand upon the 8 weeks of ACT by focusing on reactivity to substance cues, opioid misuse, and nonjudgmental awareness. Briefly, participants will be instructed in mindfulness techniques aimed at increasing concentration, improving awareness, and cultivating a nonjudgmental and accepting attitude toward craving and automatic thought patterns. Group sessions include discussions of mindfulness as a means of coping with craving and painful cognitions, role-playing exercises, meditation practice, and homework assignments. Each participant will be given audio CDs developed specifically for MBRP for independent practice outside of the group sessions.

Sample Size and Population: This study will recruit veterans with chronic pain (n = 120) who are currently misusing, abusing, or dependent on prescription opioids. Participants will be recruited from the Co-Occurring Disorders Clinic (a specialty clinic for patients with chronic pain and evidence of problematic opioid use), as well as the Ambulatory Care and Primary Care Clinics of Raymond G. Murphy VA Medical Center in Albuquerque, New Mexico.

1. STUDY OBJECTIVES

1.1 **Primary Study Aims**: **Determine the feasibility of an integrated psychosocial treatment (ACT + MBRP) in veterans with chronic pain with evidence of opioid-related problems.** Chronic pain patients (*n* = 120) who are receiving opioid therapy and who are identified as opioid misusing, abusing, or dependent will be recruited from the Albuquerque Veterans Administration (VA) Hospital. Participants will be randomized to receive standard care or standard care in addition to ACT+MBRP.
Hypothesis 1: Feasibility of recruitment: Given the high prevalence of both chronic pain and opioid-related problems in VA populations, we hypothesize it will be possible to recruit our target sample size (*n* = 120) within a 15-18 month timeframe.
Hypothesis 2: Feasibility of retention: Drop-out rates will be consistent with other trials of similar psychosocial interventions for chronic pain (i.e., < 20%[5,21–23]).

1.2 **Secondary Study Aims**: **To examine weekly progress on specific therapy targets (e.g., pain acceptance, self-compassion, opioid craving) in the interventions in order to identify potential mechanisms of change and to identify the choice of intermediate endpoints for a larger randomized clinical trial.**
Hypothesis 1: Evidence of treatment mechanisms: The combined ACT+MBRP treatments will be associated with changes in treatment mechanisms specified within the therapeutic models and in a manner consistent with that of previous work on ACT and MBRP, in comparison with standard care.
Hypothesis 2: Selection of intermediate endpoints: Weekly progress measures will provide data indicating measures of treatment-specific mechanisms that are most sensitive to change. We hypothesize that acceptance of pain discomfort will be most sensitive to change in ACT and that reductions in reactivity to substance craving will be most sensitive to change in MBRP.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Prescription drug abuse and opioid use disorders are a significant public health problem in the United States. According to the most recent data from the National Survey on Drug Use and Health[24], approximately 13% of the U.S. population (more than 34 million people) aged 12 or older reported lifetime nonmedical use of prescription pain relievers. Likewise, in 2011, nearly two million Americans reported abuse or dependence on prescription pain relievers within the past year. Since 1999, there has been a 300% increase in overdose deaths caused by prescription opioids, with 14,800 overdose deaths in 2008 alone.[25] Overdose deaths due to opioids are more common than overdose deaths due to cocaine and heroin combined[26]. The societal costs of prescription opioid misuse, abuse, and dependence was estimated at $55.7 billion in 2007, with workplace and healthcare costs accounting for 91% and criminal justice approximately 9% of those costs[27].

Substantial increases in morbidity and mortality associated with opioid misuse are particularly relevant in the case of chronic pain, a common healthcare concern in primary and specialist care settings[28,29] costing approximately $100 billion annually in the United States[30,31]. The available evidence suggests opioids are increasingly used in the treatment of chronic pain[32] with a recently published study indicating that 61% of 26,000 primary care patients surveyed were on long-term (i.e., 90+ consecutive days) chronic opioid therapy[33]. Unfortunately, aberrant opioid use behaviors, such as opioid dependence and overuse or use of other substances, are quite common, occurring in up to 25% of patients on long-term opioid therapy[34,35]. Furthermore, while comprehensive psychosocial treatments that address pain-related distress and disability have a strong evidence base[36], patients meeting criteria for opioid dependence are at risk for poorer outcomes and noncompletion[37]. Therefore, development of interventions that address the core issues of distress and disability as well as aberrant opioid use are a high priority.

In military veterans, the issues of chronic pain and opioid-related problems seem even more pronounced. Chronic pain is common, distressing, and debilitating, particularly in those that have served since the first Gulf War, with prevalence estimates reaching as high as 68%[38–42]. As in civilian healthcare settings, opioids are commonly - and increasingly - used in the treatment of chronic pain in veterans[38,43], with one recent large scale study indicating that two-thirds (978 of 1,478) of veterans with a chronic pain diagnosis were prescribed opioids as part of their treatment[44]. Furthermore, in that same study, half of those prescribed opioids (478 of 978) were receiving in excess of 180 mg total daily morphine milligram equivalents, a level that represents a substantial increase in overdose risk in comparison with lower dosages[45]. There is evidence of a vicious cycle of comorbidity amongst chronic pain, opioid abuse, and adverse events in veterans[46,47]. For example, in one study of over 6,000 veterans, the mere presence of a chronic pain diagnosis almost doubled the risk of prescription drug abuse (OR: 1.9; 95% CI: 1.4-2.5)[48], while another large scale survey of over 15,000 veterans indicated a prescription for opioids for chronic pain was related with an increased risk of adverse clinical outcome (e.g., accidents resulting in wounds, opioid-related accidents, overdose, violence-related injuries) in a manner that was independent of mental health diagnoses or other prescribed medications[43]. Clinicians in Veteran Affairs (VA) hospitals are well aware of these issues and have noted both frustration and uncertainty in treating chronic pain patients, as well as the lack of evidence-based approaches that simultaneously treat problems related to both chronic pain and opioid misuse[49,50].

2.2 Study Rationale

In combination, the above data highlight the need for focused treatment development, especially in veterans who served in the recent conflicts, including Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), and Operation New Dawn (OND). Two promising approaches are Acceptance and Commitment Therapy (ACT) for chronic pain and Mindfulness-Based Relapse Prevention (MBRP). ACT for chronic pain decreases problematic pain avoidance behaviors and enhances engagement in effective and meaningful activities which contribute to fewer pain-related restrictions in functioning over the longer term[51]. Mindfulness-Based Relapse Prevention (MBRP) for substance use disorders may be an ideal behavioral intervention for helping individuals cope with the desire, or "craving," to use opioids, as well as the automatic tendency to use opioids when experiencing pain. MBRP for substance use disorders was designed to target these behaviors, with the ultimate goal of reducing problematic substance use[52,53].

While there have been no direct examinations of ACT and MBRP in combination, research in ACT and MBRP separately presents a number of parallel, compatible findings which support their efficacy. We therefore hypothesize that their combination in veterans experiencing chronic pain and opioid-related difficulties will be both appropriate and feasible. Further, we hypothesize that the combination of these treatments will affect specific therapy targets (e.g., pain acceptance and opioid craving) in a manner consistent with existing trials.

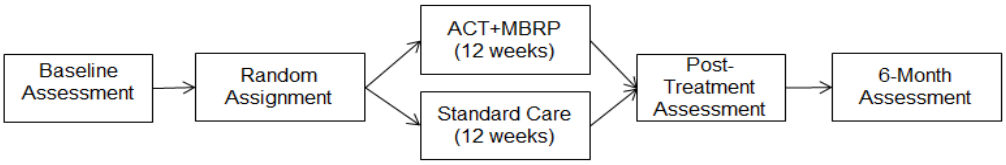
ACT and MBRP are each promising interventions with good efficacy data[7,54] and are likely to complement one another in treating this population. Thus, the proposed research is significant in that we are proposing to empirically test a combination of interventions that could greatly decrease pain interference, improve functioning, and decrease opioid misuse among the very large number of veterans treated for chronic pain.

3. STUDY DESIGN

As noted above, the primary objective of the study is to determine the feasibility and acceptability of a combined treatment for veterans with comorbid chronic pain and opioid misuse or dependence, as well as assess mechanisms of change during the combined intervention. Participants will include veterans with chronic pain and opiate misuse, abuse, or dependence who are receiving long-term opioid therapy (i.e., 90+ days) and who are receiving treatment from the Raymond G. Murphy Veterans Affairs (VA) Medical Center in Albuquerque, NM. Treatment will begin in Year 1 and conclude in Year 2 with follow-

up assessment lasting through the first quarter of Year 3. At the time of enrolling in the trial, individuals will participate in a baseline assessment including self-report and behavioral measures. Participants (*n* = 120) will then be randomized to one of two treatment conditions: (1) treatment services-as-usual (i.e., standard care) or (2) standard care with eight weeks of group ACT plus four weeks of group MBRP. Participants will complete assessments at baseline (entry into the study), weekly during the first three months of the study (during treatment), three months after entry in the study (end of treatment), and nine months after entry in the study (six months after treatment conclusion). The trial design is shown in Figure 1.

Figure 1. Proposed Trial Design



Based on the preliminary data described above and our experience in working with chronic pain patients who misuse/abuse their prescription opioids, we hypothesize that the combination of ACT with MBRP may be particularly suited for treating this population. Other interventions (e.g., cognitive-behavioral therapy, exercise therapy) were also considered; however, our recent work has suggested that both ACT and MBRP may be superior or more suitable in comparison to these other interventions. Also, ACT and MBRP are theoretically aligned, which makes their combination more seamless than other interventions that are not theoretically aligned. Several research designs incorporating ACT and MBRP were also considered (e.g., including an MBRP-only condition, a wait-list control group, or a no-treatment control group); however, these designs were ruled out because *1)* MBRP was designed and has been empirically supported as an after-care intervention and has not been empirically studied as a stand-alone intervention for chronic pain, and *2)* wait-list and no-treatment control groups were considered unethical for a treatment seeking population already enrolled in treatment. We hypothesize that training in ACT will help reduce pain interference and improve functioning and that the addition of the MBRP mindfulness skills to ACT will help individuals with chronic pain who currently meet criteria or are at high risk for opioid misuse to reduce patterns of opioid misuse until they are no longer of clinical concern.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

Recruitment Sites and Participants— This study will recruit veterans with chronic pain (*n* = 120) who are misusing, abusing, or dependent on prescription opioids. Participants will be recruited from the Co-Occurring Disorders Clinic (a specialty clinic for patients with chronic pain and evidence of problematic opioid use), as well as the Ambulatory Care and Primary Care Clinics of the Raymond G. Murphy VA Medical Center in Albuquerque, New Mexico.

The Albuquerque VA is an ideal recruitment site for the present study for several reasons. First, it has approximately 321,140 veterans enrolled in Primary and Ambulatory Care and facility records indicate that nearly a quarter of these are currently prescribed chronic opioid therapy as defined by a prescription of 90 or more days. Second, the issue of comorbid chronic pain and problematic opioid use has been identified as a priority within this VA, such that a specialty medication management clinic has been established. This clinic receives approximately 25 referrals per month, with only approximately 30% of these appropriate for the primary treatment option of Buprenorphine (an opioid agonist)[50]. These data suggest that there is a large proportion of patients who are seeking help for chronic pain with potential opioid misuse who are in need of intervention beyond the currently available treatment options. These individuals, as well as veterans in Primary and Ambulatory Care, may be appropriate for recruitment into the present study. Finally, the close proximity and history of collaboration between the University of New

Mexico (UNM) and the Albuquerque VA should aid in decreasing institutional barriers and facilitating progress. Historically, Veterans treated at the Albuquerque VA are primarily male, average 62 years of age, and are of considerable racial/ethnic diversity, including over 40% Hispanic and about 10% Native Americans.

Recruitment methods: The study PI and the research team will work closely with staff in Co-Occuring Disorders, Primary and Ambulatory Care clincs at the VA Medical Center. In-service seminars will be held to explain the purpose of the study and eligibility criteria to hospital staff at the beginning of the study and periodically throughout the recruiting period. An IRB approved recruitment flyer will also be distributed to these clinics (see Microsoft Publisher attachments to protocol materials for IRB approved flyer and informational brochure).

Before a patient is contacted by the study team, the patient's primary clinician will be asked to: a) confirm patient is between the ages of 21-65; b) confirm a chronic pain diagnosis of six months or longer; c) review medications to confirm that patient has been prescribed opioids for ninety days or longer; d) confirm that patients pain severity level has been four or greater over the past seven days on a 0 to 10 scale, where 0 is no pain and 10 is worst pain possible and e) provide the patient with the study flier describing the study and invite the patient to meet with the research team to learn about the study and be screened for eligibility. If the patient expresses interest in the study and requests that the study team contact him/her for screening, the primary clinician will then alert the study PI via the electronic medical record or with PKI encrypted email containing name and last four indicating that the patient is interested in being contacted for screening. No assessments will be administered for research purposes, including screening, until the patient has signed the informed consent.

Once potential participants have made voluntary contact with the investigators (e.g. after seeing a study flier at the VA facility) or once a member of the research team makes contact with potential participants after they express interest to their treatment providers, a full screening will take place via telephone to confirm eligibility for the study (using the Telephone Screening Form, which contains all exclusion and inclusion criteria listed in section 5). In order to inquire about PHI relevant to all inclusion and exclusion (i.e., designated special population membership) criteria, the investigators have obtained a HIPPA waiver from the governing IRB. Further, details of the study will also be discussed to better inform potential participants about the study requirements. Potential participants will be free to ask any questions about the study. At no time during the telephone screen is identifiable information collected that can link answers to the potential participant. If participants meet the above eligibility criteria and remain interested in taking part in the study, an appointment will be set up to meet with the participant at the data collection site, which take place in a private office. At this appointment, the participant will complete all baseline assessment information. In the event that a potential participant is ineligible or declines to take part in the study, any protected health information will be destroyed pursuant to VA information security policy. The electronic medical record will be utilized to alert the primary care provider that a patient on his/her panel has been enrolled in the study and which study arm the patient was assigned to. The payment schedule as according to the section of the Protocol on Participant Compensation will be clearly explained to potential participants during the consent process and following assignment into study condition.

4.1 Inclusion Criteria

All participants must meet the following inclusion criteria: *1)* be between 21 and 65 years old; *2)* have had chronic pain for >6 months in duration; *3)* averaged 4 or greater on usual pain intensity over the past week on a scale of 0–10 with medication; *4)* daily use of prescribed opioids for chronic pain for at least 90 consecutive days preceding assessment; *5)* identified as having current opioid misuse [Current Opioid Misuse Measure (COMM) score of > 12][3] or meeting diagnostic criteria for opiate abuse or dependence based on the Structured Clinical Interview for the DSM (SCID)[56]; *6)* consent to randomization of

treatment to usual care with or without ACT+MBRP; *7)* be willing to consent to assessment procedures and to be contacted for follow-ups; and *8)* the ability to read written English.

4.2 Exclusion Criteria

With regard to exclusionary criteria, participants will not be eligible for study participation if they: (1) meet diagnostic criteria for current substance abuse/dependence on a drug other than opioids, (2) meet diagnostic criteria for a current or past DSM diagnosis of schizophrenia, delusional disorder, psychotic or dissociative disorders, (3) are currently prescribed medications for opioid addiction (e.g., Buprenorphine/Naloxone/Suboxone)., or (4) history of suicide attempts or inpatient hospitalization for risk of suicide in the past six month. In addition, we will screen for significant suicidal ideation (e.g., marked intent or established plan) using a self-report measure at the baseline, post-treatment, and follow-up assessments. If significant ideation exists, the study RA will contact the VA's Acute Psychiatric Clinic, which provides on-call and immediate consultation and liason services for the VA. The service is often consulted when significant ideation is identified.

During the study period, participants may become ineligible and may be involuntarily removed. The conditions for removal are detailed in the Consent Form. These conditions are summarized as follows: (1) Individuals may be removed if the study team discerns a significant worsening of stress or mood symptoms as a result of study participation, (2) if an participant is incarcerated, they cannot attend treatment sessions and will be remvoved, (3) if an individual becomes pregnant, their primary care provider will wean them off of opioids (due to documented birth defect risk associated with opioid use) which will render the participant ineligible for the study as they will no longer be taking opioids, and (4) if the participant displays behaviors that are deemed overly disruptive to other participants in the treatment group.

4.3 Study Enrollment Procedures

A brief screening questionnaire that inquires about eligibility criteria will be administered via telephone to patients receiving opioid therapy as part of their treatment for chronic pain at the VA who are interested in participating in the research study. Interested individuals who meet initial screening criteria will be seen at the VA for an in-person screening where the procedures and voluntary nature of the study will be fully explained. Participants will meet with a trained Research Assistant (RA) in a private assessment office at the VA for the opioid use and psychiatric screening and to obtain Human Research Protections Office (HRPO) approved informed consent. The in-person screening will consist of self-reported opioid misuse behaviors on the COMM, as well as a structured clinical interview using the Substance Use Disorders model of the SCID, which will enquire about opioid use patterns.

Anticipated wait time from screening to baseline assessment and randomization. After the initial screening, eligible participants will be scheduled for an in person assessment to complete informed consent and baseline assessments. This assessment will occur within 14 days (and ideally within 7 days) of screening. Immediately following completion of informed consent and assessment, participants will be randomized to treatment condition.

Anticipated wait time from randomization to intervention beginning. We plan to begin at least one new group per month, therefore, wait time for most participants is anticipated to be less than one month from the time of study enrollment. As noted, we have planned for recruitment of eight individuals per month, which corresponds to our target group size. Should recruitment be faster than expected, we can accommodate up to ten individuals in each group to keep waiting times to a minimum. Furthermore, by the third month of providing intervention, we will be running three treatment groups at any one point in time (as each group will receive treatment for three months total). If the participant backlog surpasses six individuals (which is sufficient to compose a group for treatment), we will be able to add a fourth treatment group.

5. STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

Intervention Conditions—All participants will continue to receive standard care for chronic pain within the VA. In addition, one-half of participants will be randomized to also receive ACT plus MBRP.

Standard Care: All conditions will also receive standard treatment as usual, as indicated by treatment plan and not manipulated by the research team. Consistent with national and VA standards[14,15], care at the recruitment sites typically consists of noninvasive interventions, such as analgesic pain medications (e.g., opioids, NSAIDs, anti-epileptics), topical solutions (e.g., lidocaine), physical therapy, and massage, as well as limited invasive interventions (e.g., injections, radiofrequency denervation).

Acceptance and Commitment Therapy (Weeks 2–9): The ACT intervention is based on the standardized and manualized protocol of Vowles and Sorrell[16], which consists of weekly 90-minute group meetings over eight weeks. The protocol has been successfully used in previous clinical trials (e.g., [17,18]) and is currently available on the VA's Evidence-Based Practice Sharepoint website. Over the course of the group meetings, participants will identify areas of meaningful functioning that have been adversely impacted by pain, learn methods to enhance pain willingess in the service of these meaningful areas, and practice present-focused awareness skills. Group sessions will include discussions of the impact of pain and distress avoidance, identify alternative to this avoidance and establish plans for behavior change, demonstration and role-playing exercises, and homework assignments. Participants will be provided with a treatment manual to help guide and inform practice outside of group sessions. Table 1 provides an outline of session content for the eight week ACT intervention. We anticipate enrolling approximatley eight patients per group.

Table 1: Overview of ACT Treatment Sessions

Session	Objectives and Content
1	a. Treatment orientation and overview. b. Review treatment history and evaluate it in terms of how it has worked relative to patient's goals and expectations.
2	a. Review interactions among thoughts, feelings, and action, which often serve to make one another worse (e.g., become a "vicious cycle"). b. Exercises to attempt to control thoughts and/or emotions. Review patient experiences about the difficulty inherent in control attempts. c. Introduce the idea that changes in action may mean changes that directly contribute towards meaningful and successful living (i.e., values), rather than changes in stubborn, avoidant, or "just do it" ways. d. Introductory awareness training practice consisting of 2 short exercises (sitting and breathing) and 1 longer exercise (breathing). All exercises followed by discussion to review experience.
3	a. Values clarification exercises. Emphasis on identification and awareness. May include analysis of ways in which patients' lives have not been as values-oriented as they would like since pain, and the effort to control it, has begun. b. Awareness training (breathing). Emphasis on awareness and "just noticing", including noticing distractions.
4	a. Continued values clarification, emphasis on personal values versus those that are dictated by others.

	b.	Discussion of barriers and exercises exploring possibilities for values-based action with continuing aversive experiences. Exercises relating to willingness and unwillingness to have discomfort.
	c.	Introduction to effective goal setting, as related to values.
	d.	Awareness of body sensations exercise, followed by discussion.
5	a.	Discussion of activity pacing and activity cycling.
	b.	Exercises to raise awareness of language-based influences on action, including those that are arbitrary or fail to work over the longer term. Purpose is to increase awareness of these processes and highlight opportunities for choosing to behave in ways consistent or inconsistent with identified values.
	c.	Awareness exercise (body awareness, including awareness of pain). Fewer cues and guidance by therapist during exercise. Followed by discussion of experience.

(Table continues)

Table 1 (con't)

6	a.	Continued discussion of willingness to have discomfort in the service of meaningful living, including exercises to explore the longer term impacts of willingness and unwillingness.
	b.	"Thought watching" exercise. Discussion in middle or at end of exercise to explore experience of honest, non-avoidant observation.
	c.	Discussion of effective communication.
7	a.	Awareness exercise, pertaining to the ways in which humans add additional, often unnecessary, distress onto already distressing situations.
	b.	Continued discussion of willingness, especially related to meaningful living.
	c.	Walking mindfulness exercise, preferably outside of treatment room.
8	a.	Values clarification exercise, emphasizing commitment and future planning.
	b.	Preparation for relapses and set-backs.

Mindfulness Based Relapse Prevention (Weeks 10–13): The MBRP program is a standardized group psycho-educational intervention that consists of weekly 90-minute group meetings lasting from four[19] to eight weeks[20]. For the current study, we will use the four-week program, which will eliminate redundancy with the ACT protocol (the eight-week MBRP group has some redundancy with ACT) and will also expand upon the eight weeks of ACT by focusing on reactivity to substance cues, opioid misuse, and nonjudgmental awareness. Briefly, participants will be instructed in mindfulness techniques aimed at increasing concentration, improving awareness, and cultivating a nonjudgmental and accepting attitude toward craving and automatic thought patterns. Group sessions include discussions of mindfulness as a means of coping with craving and painful cognitions, role-playing exercises, meditation practice, and homework assignments. Each participant will be given audio CDs developed specifically for MBRP for independent practice outside of the group sessions.

Table 2: Overview of MBRP Treatment Sessions

Session		Objectives and Content
9	a.	Treatment orientation and overview.
	b.	Introduce the concept of "automatic pilot" in relation to opioid use and the tendency to act upon cravings, pain, or other negative-affective states without awareness.
	c.	Discussion of triggers for opiate use that include situations, thoughts, emotions, and sensations (including pain),
	d.	Mindfulness exercise to increase awareness in daily life.
10	a.	Review home practices of mindfulness to increase awareness.
	b.	Continue discussion of triggers and high-risk situations for opiate misuse.
	c.	Introduce "urge surfing" as a method for dealing with urges and other challenging situations.
11	a.	Review home practice of urge surfing and challenges over the past week.
	b.	Discuss the relapse cycle and the process of discomfort, difficult sensations or emotions, and negative thoughts leading to opiate misuse and craving.
	c.	Introduce the "SOBER" breathing space as an exercise that can be used to deal with craving and other discomfort in the moment.
12	a.	Review home practice of the SOBER breathing space and triggers/challenges over past week.
	b.	Discuss lifestyle balance and increasing daily activities that are nurturing, while reducing depleting activities or those activities that can trigger opiate misuse.
	c.	Create reminder cards with people to call and alternative activities to prevent opiate misuse.
	d.	Preparation for incorporating mindfulness into daily life and building a support network.
	e.	Concluding meditation and closing discussion of skills learned throughout the past 12 weeks.

5.2 Handling of Study Interventions

Interventions will be delivered in a group format. The target number of participants for each group will be up to eight individuals, although it is possible to conduct the group with as few as four participants or as many as ten. Both interventions will be manualized as described in section 5.1 above. Due to the nature of the intervention, blinding to condition will not be possible.

Number of therapists: There will be a minimum of two study therapists for each group (one the RA paid on the grant and the other a volunteer RA). Study therapists will be appointed through the University of New Mexico's (UNM) graduate program in clinical psychology. The volunteer RA will receive practicum credit through UNM in lieu of payment. All therapists will be advanced post-Masters degree doctoral students (i.e. with necessary approval of the UNM's Clinical Committee to engage in clinical work) who will have received four and one half days of training (32.5 hours total) in ACT (provided by Dr. Vowles; training completed January 2015) and MBRP (provided by Dr. Bowen; training completed December 2014). Prior to leading any treatment sessions, therapists will be required to demonstrate a minimum level of competency, as outline by ACT and MBRP training guidelines. Instructors will also receive weekly supervision from an outside supervisor with specific expertise in ACT and MBRP.

5.3 Concomitant Interventions

Standard care, which will be received by all participants, will proceed as indicated by the patient's pre-existing treatment plan (as determined by their primary care of speciality pain treatment provider). As noted above, standard care will be consistent with national and VA standards[14,15], and will therefore typically include noninvasive interventions, such as analgesic pain medications (e.g., opioids, NSAIDs, anti-epileptics), topical solutions (e.g., lidocaine), physical therapy, and massage, as well as limited invasive interventions (e.g., injections, radiofrequency denervation).

Prohibited interventions, as noted in section 4.2 above will include: (1) active treatment for substance abuse/dependence for a drug other than opiates opioids (as this active treatment would indicate current criteria for substance abuse/dependence for that other drug); (2) current prescription of medication for opioid addiction (e.g., Buprenorphine/Naloxone/ Suboxone, Methadone).

Commented [KV1]: Comment 5 – How are we going to track concomitant interventions?

5.3.1 Allowed Interventions

All interventions noted in section 5.3 as "standard care" will be allowed. Aside from the medications noted in section 5.3 (e.g., Buprenorphine/Naloxone/Suboxone, Methadone), there will be no drug restrictions (e.g., opioids, NSAIDs, anti-epileptics, anti-depressants are all allowed).

5.3.2 Required Interventions

N/A

5.3.3 Prohibited Interventions

No interventions for pain treatment will be prohibited.

5.4 Adherence Assessment

In relation to the primary aims of this study, concerning recruitment and retention, no pre-determined adherence requirement will be established. We will track treatment attendance for all participants and examine it as part of our evaluation. We have no plans to exclude patients for non-adherence, nor do we have plans to restrict re-entry into treatment following a period of absence.

5.4.1 Therapist Adherence: Treatment fidelity in ACT will be assessed using the ACT Core Competency Rating Form (ACT-CCR)[57] and in MBRP will be assessed using the MBRP Adherence and Competence Scale (MBRP-AS)[58]. Inter-rater reliability of adherence ratings will be ascertained by double coding randomly selected practitioner audiotapes throughout the course of the 12-week treatment. Therapists who consistently fail to meet the criteria rating on adherence checklists will be decertified and will be required to undergo remedial training before they are allowed to resume seeing participants.

6. STUDY PROCEDURES

6.1 Schedule of Evaluations

Assessment	Telephone Screening: (Day-30 to Day -1)	Baseline, Enrollment, Randomization Visit 1 (Day 0)	Treatment Visit Visit 2-12 (W2-12)	Final Treatment Visit 13 (W13)	6 mo. follow-up Visit 14 (W37)
Screening	X				
Informed Consent Form	X	X			
Demographics		X			
Pain-Related Information		X			X
Clinical Outcomes		X		X	X
Weekly Assessments		X	X	X	X

6.2 Description of Evaluations

6.2.1 Screening Evaluation

Screening

Once potential participants make contact with the study team to voice interest in taking part in the study, a brief screening questionnaire that inquires about eligibility criteria will be administered via telephone. The screening questionnaire will determine if the participant is:

(a) Between 21 and 65 years of age.
(b) Has experienced pain daily for at least the past 6 months
(c) Has been taking prescribed opioids for the treatment of chronic pain daily for at least the past 3 months
(d) Experiencing average weekly pain of a four or greater on a 0-10 scale of pain intensity

Each of these criteria will be evaluated by “yes/no” responses from potential participants and responses recorded on our IRB-approved telephone script assessing these details (see Appendix I).

Consenting Procedure for Screening

There will be two consenting procedures. The first will be part of the telephone screening evaluation. Our IRB has approved the telephone script and determined that verbal consent to complete the screening is allowed.

The consent for screening and screening procedure will take place within a single telephone conversation. Study RAs will complete the procedure. All study RAs have completed the appropriate Human Subject’s Protection Training (completion certificates on file with our local IRB).

For most participants, screening will be completed < 30 days prior to entry into the treatment study (as a new course of treatment will begin each month). In some cases, participant preference may delay entry into treatment.

6.2.2 Enrollment, Baseline, and/or Randomization

Study consenting, enrollment, baseline assessment, and randomization will all take place during a clinic visit. All procedures will be completed by study RAs.

Consenting Procedure for Enrollment

This study will follow the *Informed Consent Process for Research* (UNM HRP-090). Each participant's consenting process will be recorded by the study RA. The consent document will be stored in a locked cabinet in Co-I Gilliam's office in the VA. No minors will be involved in this study, thus parental/guardian permission and minor assent is not relevant. None of the identified groups of vulnerable populations are included in this study.

The informed consent process will take place in a private office, and participants will have the opportunity to choose their seating, read the consent form, and ask any questions they may have at the beginning of the data collection session. Signed consent forms will be transported in a locked file separate from other paper measures. Participants will be reminded that their involvement in this study is completely voluntary, and that they can withdraw it any time without any negative repercussions whatsoever (e.g., with regard to clinical care or healthcare access). They will also be explicitly told that they may leave any question blank for questionnaires or unanswered for the clinical interview if they do not feel comfortable answering. See Appendix II for the consent form.

Non-English Speaking Participants – Individuals who do not speak or understand English will not be recruited to the study. While we recognize the limitations of this approach, practical considerations necessitate the inclusion of only those who are able to speak or understand English.

Enrollment date will be recorded on a case report form, which will also include documentation of inclusion/exclusion criteria. See Appendix III for case report form and site screening & enrollment log.

Baseline Assessments (Appendix IV)

Demographic Information:

- Patient demographics (e.g., gender, age, educational achievement)
- Pain-related information (e.g., duration, location, history of treatment)

Opioid Use:

- Current Opioid Misuse Measure (COMM) - We will also collect information on current opioid misuse using the COMM, a measure of aberrant opioid-related behaviors over the past month[3]. The recommended cut-score of 12 has adequate sensitivity (77%) and specificity (77%) for a current diagnosis of prescription drug abuse[3].

- Structured Clinical Interview for DSM-IV (SCID) – The Substance Abuse and Dependence module of the SCID will be conducted with all participants.

Clinical Outcomes:

- Pain Behavior - *PROMIS Bank v1.0 Pain Behavior*

- Pain Interference - *PROMIS Bank v1.0 Pain Interference*

- Disability – *Sickness Impact Profile* (SIP) – The SIP is a measure of health-related disability[4]. It has demonstrated utility in chronic pain settings and provides a detailed assessment of

functioning across multiple domains. The SIP has been widely used in chronic pain settings and has demonstrated sensitivity to intervention[5,59,60].

- Pain intensity, including current and least/most/usual over the past week, will be assessed via a 0 (no pain) -10 (maximum possible pain) numerical rating scale (NRS). Assessing pain intensity via NRS is a widely-used and well-established method in studies of pain[61,62].

Randomization

Randomization will occur following baseline assessment. We will use a random order variable-sized block randomization procedure with block sizes of 2, 4, and 6. The investigators will be blind to the size of each block and randomization allocation.

6.2.3 Blinding

PI Vowles and Co-I's Witkiewitz (study statistician), Gilliam, and Cardon will be blinded. Unblinded staff will include the Research Coordinator from the Biomedical Institute of New Mexico (BRINM) and Graduate Research Assistant as these individuals will handle randomization and delivery of treatment, respectively. These individuals will have no access to data and no involvement in data monitoring or analyses.

6.2.4 Follow-up Visits

Weekly Assessments (Appendix IV)

As noted, participants will complete assessments measures at each week's visit. Measures will include:

- *Chronic Pain Acceptance Questionnaire* (CPAQ[8]). The CPAQ is a 20-item measure of acceptance and willingness to have chronic pain. It is perhaps the most widely used measure of pain acceptance in the literature and its psychometric properties, factor structure, and sensitivity to treatment are well established[9,10].

- *Self-Compassion Scale* (SCS[11]). The SCS is a 26-item questionnaire, which evaluates numerous aspects of mindfulness and self-compassion. Initial psychometric evaluations of the measure have provided support for its reliability and validity[11].

- *Penn Alcohol/Drug Craving Scale (PACS[12]).* A modified version of the PACS will be used to assess both alcohol and drug craving. The PACS is a 5-item measure including questions about frequency, intensity, and duration of craving, and an overall rating of craving for the previous week. The PACS has demonstrated good psychometric properties in our prior studies, including internal consistency reliability (α=.87) and criterion validity[7,63].

6.2.5 Completion/Final Evaluation

Six months following the last treatment session, all participants will again complete:

- Pain-related information (e.g., duration, location, history of treatment)
- Opioid Use - COMM
- Pain Behavior - *PROMIS Bank v1.0 Pain Behavior*
- Pain Interference - *PROMIS Bank v1.0 Pain Interference*
- Disability – SIP

- Pain Intensity – NRS for current and least/most/average over past week.
- Pain Acceptance - CAPQ
- Self-Compassion – SCS
- Alcohol/Drug Craving – PACS

Commented [KV2]: Added Depression? BCMDI with suicide items

The Study Completion Record is in Appendix V.

6.2.5.1 **Participant Compensation**

Remuneration for each of the assessments is as follows: Participants will receive $60 for completion of the baseline session, $5 per week for completing weekly assessments during active treatment ($60 total), $50 for completing the end of treatment assessment (week 13), and $50 for completing the six-month follow-up (week 37), totaling $220. Individuals who complete all assessments will be given a $50 bonus at the 6-month follow-up, for a maximum compensation of $270.

Participant costs per year are as follows:

Year 1: $9,680	(*64 baseline, 64 X $60=$3840; 64 weekly treatment, 64 X $60=$3840; 40 post-treatment; 40 X $50=$2000*).
Year 2: $19,520	(*56 baseline, 56 X $60=$3360; 56 weekly treatment, 56 x $60= $3360; 80 post-treatment, 80 X $50=$4000; 88 six month follow-up, 88 X $50=$4400; 88 bonus six month maximum completion, 88 X $50=$4400*).
Year 3: $3,200	(*32 six month follow-up, 32 X $50=$1600; 32 bonus six month maximum completion, 32 X $50=$1600*).

The participant compensation record is displayed in Appendix VI.

7. SAFETY ASSESSMENTS

No vulnerable classes of human participants will be targeted for recruitment, although it is possible that participants may, for example, become pregnant during the trial or be incarcerated. ***We do not foresee that the intervention conditions will cause harm to the fetus or distress the pregnant participant. In the case that a participant is incarcerated during the course of the study, the research team will make every attempt to provide the opportunity for completing assessments only if continued assessment presents no more than minimal risk and if adequate assurances can be made that parole boards will not take into account prisoners' participation in the research in making decisions regarding parole or probation. Further, each prisoner must be clearly informed in advance that participation in the research will have no effect on his or her parole.***

Sources of Material: Research material will consist of data collected from participants using structured clinical interview and self-report questionnaires. The structured clinical interview will be conducted during the baseline assessment to evaluate for mood, anxiety, or psychotic disorders, as well as the presence of substance use disorders (prescribed opioid and otherwise). The self-report questionnaires will assess a range of relevant constructs, including demographic information (e.g., age, gender, educational history), pain-related details (e.g., location, duration, current and past treatments), hypothesized treatment mechanisms (i.e., pain acceptance, self-compassion, alcohol and drug craving), and aspects of current and past functioning and substance use behaviors (i.e., pain behavior, pain interference, aspects involved in current opioid use).

A linkage between personal identification numbers (PINs) and individually identifiable private information (participants' names and contact information) is necessary to facilitate follow-up communication. Great care will be taken to maintain the confidentiality of data provided by participants. All data collected on participants will be identified with a randomly generated, unique personal identification number (PIN).

Master lists of PINs and individually identifiable private information will be stored in locked file cabinets and computers with restricted access, and will be available only to research staff on this project. The linkage and the individually identifiable private information will be destroyed at the earliest opportunity consistent with conduct of the research. All data will be collected specifically for the proposed research study.

Potential Risks: Risks to participants are primarily psychological in nature and may include discomfort associated with answering sensitive questions (e.g., about mental health and substance abuse). The information requested may be viewed as private, and therefore the questions may be perceived as intrusive. The act of completing assessment materials may cause participants to become cognizant of certain behaviors and personal problems which may cause distress. In the event that a participant becomes overly anxious, he or she will be evaluated for risk by a licensed mental health clinician. Participants are also asked to report on potentially illegal behaviors such as use of illicit and controlled substances. Answers to these questions could pose social and legal difficulties if this information were linked to their identity and became known to someone outside of the research team.

The therapies employed in the current study, ACT and MBRP, do not involve any known risks. Both interventions have been empirically validated. However, participants could become anxious or distressed during a session, or they could arrive in crisis to a session. Should this occur, the therapist will abort the scheduled materials for that day and implement crisis reduction therapy. In the event of an emergency, therapists will be able to reach the PI or study Co-I's (all of whom are licensed clinical psychologists, with the exception of Dr. Cardon, who is a licensed physician) or another designated licensed psychologist who is on call for this purpose. Therapists will always have a list of licensed VA psychologists to call in the event of an emergency. This practice is standard in the VA and is used, for example, when trainee psychologists are in need of consultation or assistance.

Finally, there is the risk that some participants may not benefit from the interventions.

Adverse events will be identified and reported initially to Dr. Gilliam, as part of his role as VA Co-I. Dr. Gilliam will be responsible for the assessment, intervention and treatment (if necessary) of these adverse events and for the reporting of adverse events to the required oversight entities (i.e., Institutional IRB). The known potential risks will be described in the informed consent document and protocol. Study team members will no longer have access to paper or electronic records when they are no longer part of the research team.

We believe this research does *not* cross the threshold of Minimal Risk for participants for the following reasons:

1. There are no known substantial risks associated with questionnaire completion or with engagement in psychotherapy. While these activities may result in transient increases in distress, the evidence base reliably indicates that any distress associated with questionnaire completion is not sustained and engagement in psychotherapy is associated with decreases in distress for the majority of participants.
2. Participant identifying information will not be stored beyond record of consent, which will not include a record of whether an individual provided full data/achieved completion of study procedure.
3. Participants will not be informed of the results of any assessment procedure.
4. Participant treatment providers, family members, friends, etc. will not be informed of the results of any assessment procedure.

The approving IRB body has agreed with our risk assessment and granted us permission to conduct the study.

7.1 Specification of Safety Parameters

Recruitment and Informed Consent: The investigators have taken several steps to protect participants against potential risks inherent to the proposed research. First, every effort will be made to protect the confidentiality of participant records. We will obtain a Certificate of Confidentiality from the Federal government, because we are asking participants about the use of illegal drugs. However, complete confidentiality can never be absolutely guaranteed because records may be examined by personnel from the UNM Human Research Protections Office and because accidents or other unforeseen circumstances sometimes occur despite the best protections put in place. Participants will be informed of this possibility prior to signing any consent forms for this study. All records will be kept strictly confidential and will not be inspected by any other agency except if required by law. Only research staff and staff of the UNM Human Research Protections Office will have access to PHI. Signed consent forms will be kept separately from any documents containing Personal Health Information (PHI) or participants' unique ID numbers. The database linking ID numbers to participants' identity will be kept separately from all PHI and ID numbers and only the PI and research staff on this study will have access to this link. Any hard copies of data (e.g., consent forms, audiotapes of sessions) will be kept in double locked rooms designated for the storage of PHI. Data will be destroyed 7 years after the last publication. The results of this research may be presented at meetings or in publications, however participants' identities will not be disclosed. All computers with ID-coded data will be encrypted and password protected.

Distress. Potential psychological risks, including discomfort associated with disclosure of information, feelings of compromised privacy and distress that may be caused by increased awareness of one's opiate misuse, will be addressed in the consent form. Participants will be encouraged to contact investigators and/or study staff if they have any concerns about their participation or if they experience any psychological distress. All study investigators are clinical psychologists with extensive experience in the treatment of chronic pain and substance abuse and/or substance misuse, abuse, or dependence. They will train and supervise research staff and the study therapists to utilize data provided at each assessment point as well as clinical judgment to monitor and evaluate the condition of participants. Therapists will always have a list of licensed psychologists to call in the event of an emergency. If a participant discloses suicidal or homicidal intentions or ongoing child or elder abuse, the therapist will notify the licensed psychologist on call who will evaluate the participant for risk and follow the NM state law regarding mandated reporting. Therapists will disclose these limits of confidentiality to participants at their first therapy session. If a participant arrives for treatment or assessment in an intoxicated state, the therapist or research assistant will reschedule their session and be advised not to drive and seek appropriate transportation back to their homes. All participants will be informed of the right to withdraw from the study at any time and still receive full compensation for their time.

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

N/A

7.3 Adverse Events and Serious Adverse Events

As noted above, we deem the risk of adverse events to be negligible within this study. Adverse events can include a breach of study procedures (e.g., use of an expired consent form), distress requiring the services of a healthcare provider, or inadvertent breach of confidentiality.

There is no evidence that participation in this treatment trial will increase risk of a serious adverse event.

All adverse events will be recorded and reported within 5 days of occurrence, as required by our IRB of record (https://spa.unm.edu/common/documents/irb-guidelines.pdf).

7.4 Reporting Procedures

The PI of the study (Dr. Vowles) will be responsible for reporting all adverse events to the IRB of record. The IRB uses the "Click" system (http://hsc.unm.edu/som/research/hrrc/click.shtml), which includes a reporting mechanism that is sent directly to the IRB. For any adverse events, a course of remediation will be proposed (e.g., in the event of a protocol violation, safeguards will be put in place to decrease the probability of repeated violation) to the IRB, although the IRB itself will approve/disapprove the remediation.

7.5 Follow-up for Adverse Events

All AE's will be reported to the IRB of record within five days. Follow-up remediation will occur within five days of the IRB's response or decision.

7.6 Safety Monitoring

We have established a Data Safety Monitoring Board (DSMB), consisting of three individuals. The first member is Professor Barbara McCrady, who is a Distinguished Professor within the Department of Psychology at UNM and also director of the Center on Alcoholism, Substance Abuse, and Addictions (CASAA). She brings with her 40 years of experience conducting funded clinical trials with substance abusing populations. The second member is Professor Ronald Yeo, a Regents' Professor within the Department of Psychology at UNM. Dr Yeo also has extensive experience working with complex clinical populations, chiefly schizophrenia and brain injury. He is also a member of the UNM Institutional Review Board (IRB) and has expertise in research ethics. The third and final member is Dr J Scott Tonigan, a Research Professor within the Department of Psychology and CASAA, as well as Chair of the UNM IRB. Dr Tonigan brings with him significant expertise in trial design and research ethics. He also is a highly accomplished statistician. Please see biosketches for all three members of the DSMB in Appendix VII.

8. INTERVENTION DISCONTINUATION

- Participant choosing to discontinue.
-
- Because this is a feasibility trial, we will not discontinue intervention based on non-attendance.

No other discontinuation criteria are identified.

Commented [KV3]: Need to add discontinuation criteria from the consent

9. STATISTICAL CONSIDERATIONS

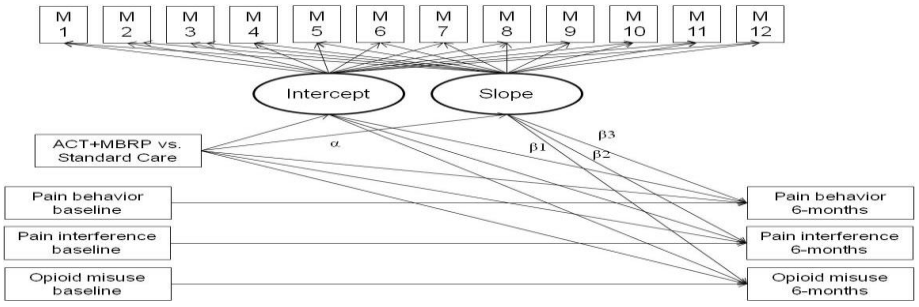
9.1 General Design Issues

Preliminary Analyses: Data will be analyzed for missing cases to detect any bias across research groups that might result from differential attrition and/or response omission. For example, participant characteristics to include gender, minority status, age, drinking history, pain duration and intensity, educational achievement, and previous treatment experiences will be compared for those participants retained in the study versus those lost to attrition. Furthermore, the data will be examined for both missing cases and outlier scores on measures. Variable distributions will be checked for normality and if necessary, transformations will be performed to normalize the distributions. We will compare demographics and primary study measures at baseline between randomized treatment groups, using Analyses of Variance (ANOVA) for continuous variables (or Kruskal-Wallis if parametric assumptions are violated) and using chi-square tests for categorical variables. Subsequent analyses will adjust for significant baseline differences among the randomized groups at $\alpha = 0.05$.

Analyses to Test Primary Aim Hypotheses: The primary analyses for Aim 1 will be descriptive, including calculating the percent of individuals enrolled in the study versus those eligible and the percent of individuals who remain in the study. We will pay particular attention to issues of retention, as the treatment program will occur over 12 weeks and this length may impact treatment completion (previous programs of ACT alone, which have lasted eight weeks, have had drop-outs of < 20%[17,21]). Therefore, we will define multiple levels of treatment retention, including partial treatment completion (% of individuals who do not complete all sessions), treatment dropout (% of individuals who dropout of treatment but continue to do assessments), research dropouts (% of individ
uals who remain in treatment, but do not complete research assessments), and treatment + research dropouts (% of individuals who do not complete treatment for research assessments). We will further break down the enrollment and retention calculations by examining enrollment/retention differences by treatm
.ent group, gender, age race/ethnicity, and initial severity using cross-classification tables.

Analyses to Test Secondary Aim Hypotheses. The primary goal of Aim 2 is to identify potential mechanisms of change and intermediate endpoints for future randomized clinical trials comparing ACT+MBRP to standard care. We will accomplish this goal by examining initial level and changes in targeted mechanisms over time during the course of treatment, as well as the association between changes in targeted mechanisms during treatment and 6-month follow-up measures of clinical outcomes. Targeted mechanisms will include (1) pain acceptance (2) psychological flexibility, (3) experiential avoidance, (4) opioid craving, and (5) reactivity to pain and craving, and will be examined using latent growth curve models with fixed effects of treatment and random effects of time. These analyses will provide an estimate of the initial level of each targeted mechanism (i.e., intercept) and the change in the targeted mechanisms over time (slope). Clinical outcome measures will include pain interference, pain behavior, and opioid misuse and will be examined using mediation analyses within the context of latent growth curve modeling[64], as we have done in prior studies[63,65]. Specifically, as shown in simplified form in Figure 2, we will examine whether initial level (intercept) or changes (slope) in the targeted mechanisms ("M" in figure 2) during treatment mediate the effect of treatment on 6-month clinical outcomes, controlling for baseline levels of the outcomes. These analyses will also provide a test of Aim 2 Hypothesis 2, which is to identify those measures that are most sensitive to change (measures with the largest slope). Identifying measures that are more sensitive to change will help us in identifying intermediate endpoints for a larger RCT. Validation of intermediate endpoints is challenging and it is often recommended that meta-analytic methods be used[66], but alternative methods have been developed that allow for the evaluation of endpoints in mental-health clinical trials[67].

Figure 2. Simplified mediation model (excludes residual terms and covariances)



Mediation models will be estimated using the product of coefficients method[68], which provides an estimate of the mediated effect by multiplying regression coefficients for the regression of the mediators (e.g., slope of targeted mechanism) on treatment condition (i.e., a-path or α) and for the regression of the clinical

outcome on the mediators (i.e., b-path or β). We will use bootstrapping to obtain 95% confidence intervals of the mediated effect[69]. We will use maximum likelihood estimation for all analyses, which provides the variance-covariance matrix for all available data and is the preferred method for estimation when some data are missing[70]. Attrition analyses will determine whether there are any differences in study variables between those with missing and complete data. Study variables associated with missing data will be covaried in all analyses.

9.2 Sample Size and Randomization

Commented [KV4]: Blocking

Statistical Power for Secondary Aims: We estimated statistical power for the mediation analyses using parameter estimates from prior studies of mediation following ACT for chronic pain[5] and following MBRP for substance use disorders[7,63] to estimate the effect sizes for the behavioral measures in the current study. Following ACT, numerous behavioral measures significantly mediated changes in disability, depression, pain-related anxiety, medical visits, and number of classes of prescribed analgesics, with large mediation effect sizes. The prior studies of MBRP have found that experiential avoidance, awareness, and nonjudgment significantly mediated the association between treatment and changes in craving (α = 0.56; β = -0.43) and that craving significantly mediated the association between treatment and changes in substance use (α = -0.20; β =0.71). Based on these effect sizes and power estimates for testing mediation derived from a simulation study[71], we will have power greater than 0.80 to detect significant mediating effects with the proposed sample size of 120.

Examining mechanisms of change assumes that treatment influences change in the clinical outcome measures at follow-up, thus we also estimated the power to detect a main effect of treatment on the clinical outcome measures. Effect size estimates were drawn from prior studies of ACT for patients with chronic pain[5,23,60,72] and MBRP for substance use disorders[52,63,73]. The effect sizes for ACT in comparison to treatment as usual or active treatment for chronic pain have ranged from 0.29 to 1.09. The effect sizes for MBRP in comparison to treatment as usual for substance use and craving have ranged from 0.21 to 0.52. Based on these studies, we estimate a minimum average effect size of d=0.25. Using a mixed-effects linear model with α=0.05 (two-tailed test), three repeated assessments (baseline, end of treatment, 6-month follow-up), and a correlation among repeated measures of 0.43 (based on prior studies) we will need 60 subjects per condition (total *n* = 120) for 80% power to detect a main effect of ACT+MBRP in comparison to standard care.

Treatment Assignment Procedures

We will use a random order variable-sized block randomization procedure with block sizes of 2, 4, and 6. The investigators will be blind to the size of each block and randomization allocation.

9.3 Definition of Populations

Because of the primary aim of feasibility, and corresponding dependent variables of recruitment and retention, we do not plan to differentiate ITT and per protocol populations for the analyses.

9.4 Interim Analyses and Stopping Rules

We have no plans for interim analyses.

9.5 Outcomes

Please see response to Section 9.1 above. We have no plans for outcomes to be reviewed and adjudicated by a committee.

9.5.1 Primary Outcome

The outcome for Aim 1 will be descriptive, including calculating the percent of individuals enrolled in the study versus those eligible and the percent of individuals who remain in the study. We will pay particular attention to issues of retention, as the treatment program will occur over 12 weeks and this length may impact treatment completion (previous programs of ACT alone, which have lasted eight weeks, have had drop-outs of < 20%[17,21]. The assessment of this latter primary outcome will occur at each treatment meeting (as this is the only way to assess retention) and follow-up.

9.6 Data Entry and Analyses

Data will be entered into the Statistical Package for Social Sciences Software (SPSS; IBM Corp). We will update the software license yearly so that the most recent version is used (currently version 22 is used). We will use an audit trail for entry, which will include a "sign-in" mechanism, where each session of data entry will be recorded. Recorded information within this mechanism will include the RA doing data entry, as well as case numbers entered and descriptive information with regard to the data entered (e.g., "cases 14-19; post-treatment data entered". A new database will be saved and individually labeled after each session of data entry (e.g., NCCIH R34 – Jan.22.2015).

In addition to responses to section 9.1 and 9.2, where details regarding the data analyses can be found, the following information addresses the queries listed in the instructional set for completing this protocol. We do not anticipate any confounding variables, although we will assess for the role of gender, age, ethnicity, educational achievement, pain duration, and pain location in influencing dependent variables.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

All data will be collected by study RAs in a pen-and-paper format. Each participant's data will be coded with their Personal ID number (PID).

10.2 Data Management

All initial data storage will be performed by study RAs. It will be double entered and checked for accuracy. All data will be stored initially at the Albuquerque VA on a password-protected computer in a locked office within a patrolled area (Co-I Dr. Gilliam's office). Once all data are collected and ready for analysis, data will be transported to the Department of Psychology onto a password-protected computer in a locked office suite (PI Dr. Vowles' laboratory space) for data analysis. At the time of transport, data will be de-identified and a back-up copy will be kept on the VA premises. All data collection forms are displayed in Appendix IV and detailed in Section 6.2.

Commented [KV5]: Comment 8 – Type of database used to capture study information; whether it will have an audit trail

10.3 Quality Assurance

10.3.1 Training

All staff will complete the human participants protection training required by the University of New Mexico (UNM). The University uses the "CITI" training program (Collaborative Institutional Training Initiative; https://www.citiprogram.org/). All study members have completed the "Social and Behavioral Research" Training program, which includes 13 modules, including:

- History and Ethical Principles

- Defining Research with Human Subjects
- The Federal Regulations
- Assessing Risk
- Informed Consent
- Privacy and Confidentiality
- Research with Prisoners
- Research with Children
- Research in Public Elementary and Secondary Schools
- International Research
- Internet-Based Research
- Conflicts of Interest in Research Involving Human Subjects
- Unanticipated Problems and Reporting Requirements in Social and Behavioral Research

All staff must provide at least 80% correct responses to pass a required test on each module. A refresher course must be passed every 24 months.

10.3.2 Quality Control Committee

There is not a quality control committee. Therapist adherence to the study protocol will be assessed as detailed in section 5.4.1.

10.3.3 Metrics

All self-report outcome measures have demonstrated psychometric soundness, including reliability and validity. Please see sections 6.6.2 and 6.6.4 for details and supporting citations.

10.3.4 Protocol Deviations

Protocol deviations will be recorded on the Protocol Deviation Tracking Log and, if appropriate, on the Adverse Events Form and, if necessary the Serious Adverse Events Form (although as noted, we do not foresee any reasonable risk of Serious Adverse Events). See Appendix VIII for all forms.

10.3.5 Monitoring

We will monitor data and safety issues throughout the study. See Data and Safety Monitoring Log in Appendix IX. The study RA will be responsible for completion of the log, which will be reviewed by the Steering Committee at their monthly meeting.

As noted in section 7.6, we have also established a DSMB. The DSMB will meet at least yearly to review Data and Safety Monitoring Logs. In addition, all adverse events will be reported to the DSMB on a monthly basis to allow for ad hoc DSMB meetings should the Board determine they are necessary. Any Serious Adverse Event will be reported to the DSMB within 5 days and will occasion a meeting of the full Board to review the event within 30 days.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

This protocol and the informed consent document (Appendix II) and any subsequent modifications will be reviewed and approved by the IRB responsible for oversight of the study.

11.2 Informed Consent Forms

A signed consent form will be obtained from each participant. Participants who cannot consent for themselves in English will not be included in the study. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. Each participant will receive a copy, which will be documented in the participant's record.

11.3 Participant Confidentiality

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality. All records will be kept in a locked file cabinet in a locked office within a patrolled security environment. All computer entry and networking programs will be done using PIDs only. Information will not be released without written permission of the participant, except as necessary for monitoring by IRB, the FDA, the NCCAM, and the OHRP.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NCCAM, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected.

12. COMMITTEES

12.1 Steering Committee – Study PI (Dr. Vowles) and Co-I's (Drs. Cardon, Gilliam, and Witkiewitz) and RAs (TBD) will meet monthly to discuss study progress relative to milestones, coordinate efforts, and review any protocol violations or other issues requiring adjustment.

13. PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by the Steering Committee. Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NCCAM prior to submission.

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15. SUPPLEMENTS/APPENDICES

List of Appendices

I. Telephone Script
II. Consent Form
III. Case Report Form & Site Screening and Enrollment Log
IV. Questionnaires
V. Study Completion Record
VI. Participant Compensation Record
VII. Biosketches - Data Safety Monitoring Board
VIII. Protocol Deviation Tracking Log/Adverse Event Form/Serious Adverse Event Form
IX. Data and Safety Monitoring Log

Appendix I

A pilot study of integrated treatment for Veterans with chronic pain and opiate misuse
Telephone Screening Form
07/29/2014

"The purpose of this screening interview is to see if you meet the criteria for taking part in our treatment study for people with chronic pain. This interview will take approximately 10 minutes. I am going to go through a list of questions. You may choose not to answer these questions. You also may choose to stop participating in this interview at any time; if you want to stop, please tell me. Information about you that you give me during this interview will be kept as confidential as possible as required by law.

You can choose if you want or do not want to take part in this research screening procedure – it is up to you. If you refuse to answer the questions or stop answering them at any time, there will be no penalty, and you will not lose any benefits to which you otherwise would be entitled.

The risk to taking part in this interview is small. The screening interview is not designed to ask you for sensitive personal information, but it is possible that some people may feel uncomfortable answering these questions with a person they do not know. If you qualify to take part in the study and are *interested* in taking part, then I will record your name and information; this will be kept confidential, but there is a small risk that people outside of the research team could learn this information. If you are *not interested* in the study, then I will destroy the personal information you give me.

There are no benefits to you to taking part in this screening interview. However, it is possible that the information from the study that we will be doing may help researchers to learn more and may benefit others in the future.

If you do not want to answer these questions, you have other choices. You can talk to your doctor about chronic pain and treatment options. Your choice to participate or not participate in this screening interview will not affect your treatment in any way.

You will not be paid for answering questions in this interview since it is only to see whether you qualify to take part in the study.

If you have any questions, concerns or complaints at any time about the research study, Dr. Wes Gilliam, or his/her associates will be glad to answer them at (505) 265-1711. If you would like to speak with someone other than the research team, you may call the UNMHSC HRPO at (505) 272-1129."

I will now ask you three questions to determine your eligibility to participate in this study.

1. "Are you between 21 and 65 years of age?" *<u>Answer for eligibility must be</u>: Yes*
2. "Have you been diagnosed with a chronic pain condition for past 6 months or longer?" *2a. If clarification needed: "Have you experienced pain each day for the past 6 months or longer?"* *<u>Answer for eligibility must be</u>: Yes*
3. "On a 0 to 10 scale, where 0 is no pain and 10 is worst pain possible, what has your average pain intensity been over the past seven days?" *<u>Answer for eligibility must be</u>: four or greater*
4. *"Have you been using prescribed opioids for chronic pain daily for the last three months or longer?"* *<u>Answer for eligibility must be</u>: Yes* *<u>If clarification needed: Types of opioids</u>:* ○ Opium ○ Darvon, Darvocet ○ Percodan ○ Dilaudid, Hydromorpone ○ Oxycodone (Oxycontin, Percodan/-cet, , Roxicet) ○ Morphine, ○ Methadone (Dolophine) ○ Codeine ○ Demerol ○ Hydrocodone (Vicodin, Lorcet) ○ Fentanyl (Duragesic, "percopop")

ELIGIBLE - SCRIPT 1

Based on the information you gave me, it looks like you are eligible for this study. At this point, you have three choices: (1) I can take down your contact information and can set up an appointment with you; (2) I can give you the number to call when you are ready to set up an appointment; (3) if you are not interested in this study, the information just collected will be destroyed. I am also happy to answer any questions you have about the study.

_____ OK TO CONTACT *(collect contact info)*
_____ SUBJECT TO CONTACT STUDY TEAM *(give contact info)*
_____ NOT INTERESTED → **(*destroy <u>all</u> information collected*)**
_____ CALL BACK → (Phone #: _____)
_____ MAIL ADDRESS → _____)

INELIGIBLE - SCRIPT 2
Based on the information you gave me, you are not eligible for this study. Thank you for your time. I am happy to answer any questions you have about the study.

Appendix II

Department of Veterans Affairs	VA RESEARCH CONSENT FORM		
Subject Name :		**Date:**	
Title of Study :	A pilot study of integrated treatment for Veterans with chronic pain and opiate misuse		
Principal Investigator:	Wesley Gilliam, Ph.D.	**VAMC:**	New Mexico VA Health Care System

See attached revised consent.

Appendix III
Case Report Form & Site Screening and Enrollment Log

Baseline Assessment

Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid MIsuse

Pt_ID: _____ **Visit Date:** ___ ___ / ___ ___ /

dd mm yyyy

To determine opioid misuse, please check all assessments completed at this visit:**

☐ Current Opioid Misuse Measure (COMM) score of > 12
☐ Structured Clinical Interview for the DSM (SCID; opiate abuse or dependence)

Inclusion Criteria

Participant must:

1. Be between 21 and 65 years old ☐
   Yes ☐ No
2. Have had chronic pain for >6 months in duration ☐
   Yes ☐ No
3. Daily use of prescribed opioids for chronic pain for at least 90 consecutive days preceding assessment ☐
   Yes ☐ No
4. Averaged 4 or greater on a pain intensity scale of 0–10 with medication ☐ Yes ☐ No
5. Identified as having current opioid misuse in initial assessment** ☐ Yes ☐ No
6. Consent to randomization to ACT+MBRP or usual care ☐
   Yes ☐ No
7. Be willing to consent to assessment procedures and to be contacted for the follow-up ☐
   Yes ☐ No
8. The ability to read written English ☐
   Yes ☐ No

NOTE: All inclusion criteria must be answered YES to be included in study.

Exclusion Criteria

Participant cannot:

1. Meet diagnostic criteria for current substance abuse/dependence on a drug other than ☐ Yes ☐ No
2. Meet diagnostic criteria for a current or past DSM diagnosis of schizophrenia, delusional disorder, psychotic or dissociative disorders ☐ Yes ☐ No
3. Be currently taking prescribed medications for opioid addiction (e.g., Buprenorphine/Naloxone/ Suboxone, Methadone) ☐ Yes ☐ No
4. Have a suicide attempt or inpatient hospitalization for suicidal ideation in the past six months ☐ Yes ☐ No

NOTE: All exclusion criteria must be answered NO to participate in the study.

Did the participant meet the eligibility requirements for this study? ☐ Yes ☐ No

Is the participant continuing in the study? ☐ Yes ☐ No

If no, remember to complete a STUDY COMPLETION form.

If yes:

5. Date enrolled (met all eligibility criteria):

__ __ / __ __ __ / __ __ __ __
d d m m m y y y y

6. Date randomized if different from enrolled:

__ __ / __ __ __ / __ __ __ __
d d m m m y y y y

7. Assignment to Condition:

☐ Intervention Group ☐ Control/Standard Care

Comments:

Site Screening and Enrollment Log

Protocol: Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid MIsuse

Subject ID	Date of Consent	Date Screened	Eligible for Enrollment?	Ineligibility Reason (if applicable)

Appendix IV

COMM™

Please answer each question as honestly as possible. Keep in mind that we are only asking about the **past 30 days**. There are no right or wrong answers. If you are unsure about how to answer the question, please give the best answer you can.

Please answer the questions using the following scale:

	Never	**Seldom**	**Sometimes**	**Often**	**Very Often**
	0	1	2	3	4
1. In the past 30 days, how often have you had trouble with thinking clearly or had memory problems?	O	O	O	O	O
2. In the past 30 days, how often do people complain that you are not completing necessary tasks? (i.e., doing things that need to be done, such as going to class, work or appointments)	O	O	O	O	O
3. In the past 30 days, how often have you had to go to someone other than your prescribing physician to get sufficient pain relief from medications? (i.e., another doctor, the Emergency Room, friends, street sources)	O	O	O	O	O
4. In the past 30 days, how often have you taken your medications differently from how they are prescribed?	O	O	O	O	O
5. In the past 30 days, how often have you seriously thought about hurting yourself?	O	O	O	O	O
6. In the past 30 days, how much of your time was spent thinking about opioid medications (having enough, taking them, dosing schedule, etc.)?	O	O	O	O	O
7. In the past 30 days, how often have you been in an argument?	O	O	O	O	O
8. In the past 30 days, how often have you had trouble controlling your anger (e.g., road rage, screaming, etc.)?	O	O	O	O	O
9. In the past 30 days, how often have you needed to take pain medications belonging to someone else?	O	O	O	O	O

Please answer the questions using the following scale:

	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
10. In the past 30 days, how often have you been worried about how you're handling your medications?	O	O	O	O	O
11. In the past 30 days, how often have others been worried about how you're handling your medications?	O	O	O	O	O
12. In the past 30 days, how often have you had to make an emergency phone call or show up at the clinic without an appointment?	O	O	O	O	O
13. In the past 30 days, how often have you gotten angry with people?	O	O	O	O	O
14. In the past 30 days, how often have you had to take more of your medication than prescribed?	O	O	O	O	O
15. In the past 30 days, how often have you borrowed pain medication from someone else?	O	O	O	O	O
16. In the past 30 days, how often have you used your pain medicine for symptoms other than for pain (e.g., to help you sleep, improve your mood, or relieve stress)?	O	O	O	O	O
17. In the past 30 days, how often have you had to visit the Emergency Room?	O	O	O	O	O

Pain Behavior – Calibrated Items

Please respond to each item by marking one box per row.

In the past 7 days....

		Had no Pain	Never	Rarely	Some-times	Often	Always
PAINBE2	When I was in pain I became irritable.....	1	2	3	4	5	6
PAINBE3	When I was in pain I grimaced	1	2	3	4	5	6
PAINBE6	When I was in pain I would lie down	1	2	3	4	5	6
PAINBE8	When I was in pain I moved extremely slowly.....	1	2	3	4	5	6
PAINBE9	When I was in pain I became angry ..	1	2	3	4	5	6
PAINBE11	When I was in pain I clenched my teeth.....	1	2	3	4	5	6
PAINBE13	When I was in pain I tried to stay very still.....	1	2	3	4	5	6
PAINBE16	When I was in pain I appeared upset or sad	1	2	3	4	5	6
PAINBE17	When I was in pain I gasped.....	1	2	3	4	5	6

Pain Interference – Calibrated Items

Please respond to each item by marking one box per row.

In the past 7 days...

		Not at all	A little bit	Some-what	Quite a bit	Very much
PAININ1	How difficult was it for you to take in new information because of pain?	1	2	3	4	5
PAININ3	How much did pain interfere with your enjoyment of life?	1	2	3	4	5
PAININ5	How much did pain interfere with your ability to participate in leisure activities?.....	1	2	3	4	5
PAININ6	How much did pain interfere with your close personal relationships?.....	1	2	3	4	5
PAININ8	How much did pain interfere with your ability to concentrate?.....	1	2	3	4	5
PAININ9	How much did pain interfere with your day to day activities?.....	1	2	3	4	5
PAININ10	How much did pain interfere with your enjoyment of recreational activities?.....	1	2	3	4	5

BC-MDI

The following is a list of symptoms that you may have experienced. Consider your experience with these symptoms over the **past two weeks, including today**. **Please rate each symptom marked in the severity scale (0 – 5).**

0 Not a problem	1 Very Mild Problem	2 Mild Problem	3 Moderate Problem	4 Severe Problem	5 Very Severe Problem

		Severity Rating
1	I feel sad, down in the dumps, or blue (nearly every day).	
2	I lack interest in, or I do not enjoy, most activities (nearly every day)	
3	I have trouble falling asleep or staying asleep (nearly every day).	
4	I sleep much more than in the past (nearly every day).	
5	I feel restless and agitated (nearly every day)	
6	I feel slowed down (for example, I move slowly and think slowly) (nearly every day).	
7	I feel tired and have low energy (nearly every day).	
8	I have a poor appetite (nearly every day).	
9	I have a greater appetite than in the past.	
10	I have lost weight due to poor appetite (in the past 2 weeks).	
11	I have gained weight due to greater appetite (in the past 2 weeks).	
12	I often feel worthless or useless.	
13	I am burdened by guilt (e.g., I feel I have made many mistakes).	
14	I have trouble concentrating, thinking, or solving problems (nearly every day).	
15	I often think about dying (most days).	
16	I think about killing myself.	

*Using the scale below, rate the **impact** that any symptoms and problems have on your life.*

0 No impact on my day-to-day life	1 Mild impact	2 Moderate impact	3 Severe impact	4 Very severe impact on my day-to-day life

		Circle your response				
17	Impact on my ability to be effective at work or in school	0	1	2	3	4
18	(Tick here if the last item is not applicable to your current situation ____)					
19	Impact on my family relationships and responsibilities:	0	1	2	3	4
20	Impact on my social life and recreational activities	0	1	2	3	4

SIP for Chronic Pain

PLEASE RESPOND TO (TICK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH.

SR

2 ☐ I sit during much of the day.

3 ☐ I am sleeping or dozing most of the time - day and night.

4 ☐ I lie down more often during the day in order to rest.

7 ☐ I sleep or nap more during the day.

EB

1 ☐ I say how bad or useless I am, for example, that I am a burden to others.

2 ☐ I laugh or cry suddenly.

3 ☐ I often moan and groan in pain or discomfort.

5 ☐ I act nervous or restless.

7 ☐ I act irritable and impatient with myself; for example, I talk badly about myself, swear at myself, and blame myself for things that happen.

9 ☐ I get sudden frights.

BCM

1 ☐ I make difficult moves with help, for example, getting into or out of cars, the bath.

2 ☐ I do not move in or out of a bed or chair by myself but am moved by another person or mechanical aid.

6 ☐ I stand up only with someone's help.

14 ☐ I do not bathe myself completely, for example, I require assistance with bathing

17 ☐ I have trouble getting shoes, socks, stocking on.

19 ☐ I do not fasten my clothing, for example, I require assistance with buttons, zippers, and shoelaces.

23 ☐ I get dressed only with someone's help.

TICK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE

This group of statements is to do with anything you usually do in caring for your home or garden. Considering just those things that you do, please respond by ticking only those statements that you are sure describe you today and are related to your state of health.

M

1 ☐ I am getting around only within one building.

2 ☐ I stay within one room.

4 ☐ I am staying in bed most of the time.

6 ☐ I stay at home most of the time.

8 ☐ I am not going in to town.

SI

3 ☐ I show less interest in other people's problems, for example, I don't listen when they tell me about their problems, I don't offer to help.

4 ☐ I often act irritable to those around me, for example, snap at people, give sharp answers, criticize easily.

5 ☐ I show less affection.

9 ☐ My sexual activity is decreased.

12 ☐ I make many demands, for example, insist that people do things for me, tell them how to do things.

15 ☐ I have frequent outbursts of anger at family members, for example, strike at them, scream, or throw things at them.

20 ☐ I am not joking with my family members as I usually do.

A

2 ☐ I do not walk up or down hills.

3 ☐ I use stairs only with mechanical support, for example, handrails, stick, crutches.

7 ☐ I walk by myself, but with some difficulty, for example, limp, wobble, stumble, have stiff legs.

11 ☐ I get around only by using a walker, crutches, stick, walls, or furniture.

☐ TICK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE

AB

1	☐	I am confused and start several actions at a time.
3	☐	I react slowly to things that are said or done.
4	☐	I do not finish things that I start.
5	☐	I have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things.
8	☐	I do not keep my attention on activities for long.
9	☐	I make more mistakes than usual.
10	☐	I have difficulty doing activities that involve concentration and thinking.

C

1	☐	I am having trouble writing or typing.
2	☐	I communicate mostly by gestures, for example, moving head, pointing, sign language.
4	☐	I often lose control of my voice when I talk; for example, my voice gets louder, or softer, trembles, changes unexpectedly
7	☐	I have difficulty speaking, for example, get stuck, stutter, stammer, slur my words.
8	☐	I am understood with difficulty.
9	☐	I do not speak clearly when I am under stress.

TICK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE

This group of statements is to do with activities that you usually do in your free time.
These activities are things that you might do for relaxation, to pass the time, or for entertainment.
Please tick only those statements that you are sure describe you today and are related to your state of health.

RP

1 ☐ I do my hobbies and recreation activities for shorter periods of time.

2 ☐ I am going out for entertainment less often.

5 ☐ I am doing more inactive pastimes in place of my usual activities.

6 ☐ I am doing fewer community activities.

E

1 ☐ I am eating much less than usual.

5 ☐ I just pick or nibble at my food.

6 ☐ I am drinking less fluids.

7 ☐ I feed myself with help from someone else.

Now can you please review the questions to be certain that you have filled out all the information?
Look at the last tick box on each sheet to make sure that you have not missed a page.

☐ TICK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE

CPAQ

Directions: Below you will find a list of statements. Please rate the truth of each statement as it applies to you by circling a number. Use the following rating scale to make your choices. For instance, if you believe a statement is "Always True", you would circle the 6 next to that statement.

0 Never True	1 Very Rarely True	2 Seldom True	3 Sometimes True	4 Often True	5 Almost Always True	6 Always True

1. I am getting on with the business of living no matter what my level of pain is	0	1	2	3	4	5	6
2. My life is going well, even though I have chronic pain	0	1	2	3	4	5	6
3. It's O.K. to experience pain	0	1	2	3	4	5	6
4. I would gladly sacrifice important things in my life to control this pain better	0	1	2	3	4	5	6
5. It's not necessary for me to control my pain in order to handle my life well	0	1	2	3	4	5	6
6. Although things have changed, I am living a normal life despite my chronic pain	0	1	2	3	4	5	6
7. I need to concentrate on getting rid of my pain	0	1	2	3	4	5	6
8. There are many activities I do when I feel pain	0	1	2	3	4	5	6
9. I lead a full life even though I have chronic pain	0	1	2	3	4	5	6
10. Controlling pain is less important than other goals in my life	0	1	2	3	4	5	6
11. My thoughts and feelings about pain must change before I can take important steps in my life	0	1	2	3	4	5	6
12. Despite the pain, I am now sticking to a certain course in my life	0	1	2	3	4	5	6
13. Keeping my pain level under control takes first priority whenever I am doing something	0	1	2	3	4	5	6
14. Before I can make any serious plans, I have to get some control over my pain	0	1	2	3	4	5	6
15. When my pain increases, I can still take care of my responsibilities	0	1	2	3	4	5	6
16. I will have better control over my life if I can control my negative thoughts about pain	0	1	2	3	4	5	6
17. I avoid putting myself in situations where pain might increase	0	1	2	3	4	5	6
18. My worries and fears about what pain will do to me are true	0	1	2	3	4	5	6
19. It's a relief to realize that I don't have to change my pain to get on with my life	0	1	2	3	4	5	6
20. I have to struggle to do things when I have pain	0	1	2	3	4	5	6

HOW I TYPICALLY ACT TOWARDS MYSELF IN DIFFICULT TIMES

Please read each statement carefully before answering. To the left of each item, indicate how often you behave in the stated manner, using the following scale:

Almost never				Almost always
1	2	3	4	5

_____ 1. I'm disapproving and judgmental about my own flaws and inadequacies.
_____ 2. When I'm feeling down I tend to obsess and fixate on everything that's wrong.
_____ 3. When things are going badly for me, I see the difficulties as part of life that everyone goes through.
_____ 4. When I think about my inadequacies, it tends to make me feel more separate and cut off from the rest of the world.
_____ 5. I try to be loving towards myself when I'm feeling emotional pain.
_____ 6. When I fail at something important to me I become consumed by feelings of inadequacy.
_____ 7. When I'm down and out, I remind myself that there are lots of other people in the world feeling like I am.
_____ 8. When times are really difficult, I tend to be tough on myself.
_____ 9. When something upsets me I try to keep my emotions in balance.
_____ 10. When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people.
_____ 11. I'm intolerant and impatient towards those aspects of my personality I don't like.
_____ 12. When I'm going through a very hard time, I give myself the caring and tenderness I need.
_____ 13. When I'm feeling down, I tend to feel like most other people are probably happier than I am.
_____ 14. When something painful happens I try to take a balanced view of the situation.
_____ 15. I try to see my failings as part of the human condition.
_____ 16. When I see aspects of myself that I don't like, I get down on myself.
_____ 17. When I fail at something important to me I try to keep things in perspective.
_____ 18. When I'm really struggling, I tend to feel like other people must be having an easier time of it.
_____ 19. I'm kind to myself when I'm experiencing suffering.
_____ 20. When something upsets me I get carried away with my feelings.
_____ 21. I can be a bit cold-hearted towards myself when I'm experiencing suffering.
_____ 22. When I'm feeling down I try to approach my feelings with curiosity and openness.
_____ 23. I'm tolerant of my own flaws and inadequacies.
_____ 24. When something painful happens I tend to blow the incident out of proportion.
_____ 25. When I fail at something that's important to me, I tend to feel alone in my failure.
_____ 26. I try to be understanding and patient towards those aspects of my personality I don't like.

PENN ALCOHOL CRAVING SCALE (Modified)

Circle the most appropriate number for each item.

1. *How often have you thought about doing drugs or drinking or about how good that would make you feel during **the past week**?*

Never, that is, 0 times during the past week.	*= 0*
Rarely, that is, 1 to 2 times during the past week.	*= 1*
Occasionally, that is, 3 to 4 during the past week.	*= 2*
Sometimes, that is, 5 to 10 times during the past week or 1 to 2 times a day.	*= 3*
Often, that is, 11 to 20 times during the past week or 2 to three times a day.	*= 4*
Most of the time, that is, 20 to 40 during the past week or 3 to 6 times a day.	*= 5*
Nearly all of the time, that is, more than 40 times during the past week or more than 6 times a day.	*= 6*

2. *At its most severe point, how strong was your craving during **the past week**?*

None at all.	*= 0*
Slight, that is a very mild urge.	*= 1*
Mild urge.	*= 2*
Moderate urge.	*= 3*
Strong urge, but easily controlled.	*= 4*
Strong urge and difficult to control.	*= 5*
Strong urge and would have done drugs or drink alcohol if it were available.	*= 6*

3. *How much time have you spent thinking about doing drugs or drinking or about how that would make you feel during **the past week**?*

None at all	*= 0*
Less than 20 minutes.	*= 1*
21-45 minutes.	*= 2*
46-90 minutes.	*= 3*
90 minutes-3 hours.	*= 4*
Between 3 to 6 hours.	*= 5*
More than 6 hours.	*= 6*

4. *How difficult would it have been to resist doing drugs or drinking during **the past week** if you had known the drugs or alcohol were in your house?*

Not difficult at all.	*= 0*
Very mildly difficult.	*= 1*
Mildly difficult.	*= 2*
Moderately difficult.	*= 3*
Very difficult.	*= 4*
Extremely difficult.	*= 5*
Would not be able to resist.	*= 6*

5. *Keeping in mind your responses to the previous questions, please rate your overall average drug or alcohol craving for the **the past week**.*

Never thought about drugs/drinking and never had the urge to do drugs/drink.	*= 0*
Rarely thought about drugs/drinking and rarely had the urge to do drugs/drink.	*= 1*
Occasionally thought about drinking and occasionally had the urge to do drugs/drink.	*= 2*
Sometimes thought about drinking and sometimes had the urge to do drugs/drink.	*= 3*
Often thought about drinking and often had the urge to do drugs/drink.	*= 4*
Thought about drugs/drinking most of the time and had the urge to do drugs/drink most of the time.	*= 5*
Thought about drugs/drinking nearly all of the time and had the urge to do drugs/drink nearly all the time.	*=6*

Weekly Diary (pg 1)

Wk# _____

1.

Rate how bad your pain was overall in the past week.

None	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Worst Possible

2.

Rate how upset and/or distressed you were overall in the past week.

None	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Worst Possible

3.

Rate how willing were you were to have pain and distress in the past week.

Not Willing at All	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Most Willing

4.

Rate how much effort you put in to making pain or upsetting thoughts, feelings, or memories go away this past week.

None	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Most Effort

5.

Rate how effective you were in taking actions that contributed to a better, more vital, quality of living in the past week.

Not at all	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Most Effective

6.

Rate how effective you were this past week in making progress in the areas of your life that that matter to you.

Not at all	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	Most Effective

Weekly Diary (pg 2)

9. Are you currently taking Buprenorphine, Naloxone, or Suboxone □ **Yes** □ **No**

10. Are you currently in treatment for substance abuse or dependence? □ **Yes** □ **No**

If you checked "Yes", for which drug(s):_____

11. Since your last session with us, have you had any other treatments for pain? □ **Yes** □ **No**

If you checked "Yes", please complete the rest of this form:

Treatments <u>for pain</u> since last session (*check all that apply)*:

_____ Operations (Surgery) (how many?_____)

_____ Alterations or changes in pain medications

_____ Seen a Chiropractor

_____ Stimulator/Pump Implant

____ Psychotherapy or Counselling Sessions

_____ Hypnosis

_____ Injections (how many? ___)

_____ Physical therapy

_____ Osteopathy

_____ TENS Unit

_____ Acupuncture

_____ Hydrotherapy (Pool)

_____ Other _____

Appendix V

Study Completion/Termination

Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid MIsuse

Pt_ID: _____ Visit Date:__ __ / __ __ __ / __ __ __ __

1. Date of final study visit: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y
2. Stage at which participant ended participation:

   _____

3. Primary reason for terminating participation in the study:
   - ☐ Completed study
   - ☐ Participant was determined after enrollment to be ineligible (provide comments): _____
   - ☐ Participant withdrew consent
   - ☐ In the principal investigator's opinion, it was not in the participant's best interest to continue (provide comments): _____
   - ☐ Adverse event (If checked, complete the AE form.)
   - ☐ Death
   - ☐ Lost to follow-up
   - ☐ Other (specify): _____
   - ☐ Unknown

Comments:

_____
_____
_____
_____

PI Signature: _____ Date: _____

Appendix VI
Participant Remuneration Log

Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid Misuse

Pt_ID: _____

1. $60 for completion of the baseline session ☐ Yes ☐ No

   Date of payment: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y

2. $5 per week for completing weekly assessments during active treatment:

WEEK	DATE PAID
1 – ACT	
2 – ACT	
3 – ACT	
4 – ACT	
5 – ACT	
6 – ACT	
7 – ACT	
8 – ACT	
9 – MBSR	
10 – MBSR	
11 – MBSR	
12 – MBSR	

3. $50 for completing the end of treatment assessment (week 13): ☐ Yes ☐ No
   Date of payment: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y
4. $50 for completing the six-month follow-up (week 37): ☐ Yes ☐ No
   Date of payment: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y
5. Did participant complete all assessments? ☐ Yes ☐ No
   If ***yes***, provide $50 bonus payment at the 6-month follow-up.
   Date of payment: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y

Total Remuneration to Participant (*upon completion or termination*): $_____

Comments (e.g. note here if participant terminates prior to receiving full compensation):

_____
_____
_____
_____

Appendix VII
DSMB Biosketches

BIOGRAPHICAL SKETCH

NAME Barbara S. McCrady	POSITION TITLE Distinguished Professor of Psychology and Director, Center on Alcoholism, Substance Abuse, and Addictions, University of New Mexico
eRA COMMONS USER NAME BMcCrady	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Purdue University	B.S.	06/69	Biological Sciences
University of Rhode Island	Ph.D.	08/75	Psychology (Clinical)

A. Personal Statement

I bring specific skills and accomplishments to my role on the: (1) I have conducted NIH- funded clinical trials with substance-abusing populations for 40 years, and have expertise in the design and implementation of rigorous clinical studies; (2) I have conducted clinical research in a range of nontraditional settings, including (a) research on substance-abusing women on temporary assistance to needy families (TANF) seen in inner city welfare offices; (b) screening and brief interventions in inpatient and outpatient hospital settings; (c) current research with opioid-dependent prisoners in the county jail; (3) I have extensive experience the provision of clinical services; (4) I have a strong background in research ethics.

B. Positions and Honors

Positions and Employment:

1974-1975	Clinical Project Evaluator, Butler Hospital
1975-1976	Chief, Psychological Assessment Program, Butler Hospital, Providence, RI
1976-1983	Chief, Problem Drinkers Program, Butler Hospital
1976-1983	Instructor to Associate Professor of Psychiatry and Human Behavior, Brown University, Providence, RI
1990-1992	Acting Director, Center of Alcohol Studies, Rutgers University
1993-2005	Director of Clinical Training, Ph.D. Clinical Psychology Training Program, Rutgers University
1983-2007	Clinical Director, Center of Alcohol Studies, Rutgers University, Piscataway, NJ (since 1983)
1983-2007	Associate Professor to Professor II, Rutgers University
2005-2007	Chair, Department of Psychology, Rutgers University
2007-present	Distinguished Professor of Psychology (since 2008; Professor 2007-2008), University of New Mexico
2007-present	Director, Center on Alcoholism, Substance Abuse, and Addictions, University of New Mexico

Other Experience (selected):

1979-1983	Psychosocial Research Review Committee, NIAAA
1985-1986	Consultant, Sixth Report to Congress on Alcohol and Health, National Institute on Alcohol Abuse and Alcoholism
1987-1989	Member, Institute of Medicine Panel on Research on the Treatment of Alcohol Problems
1989-1992	Member, Extramural Science Advisory Board, NIAAA
1990-1997	Editorial Board, *Journal of Substance Abuse*
1991-2003	Editorial Board, *Journal of Consulting and Clinical Psychology*
1991-1996	Editorial Board, *Alcoholism: Clinical and Experimental Research*

1992-2010	Editorial Board, *Journal of Studies on Alcohol and Drugs*
1993-1995	Member, Fellows Committee, Division 12, American Psychological Association
1994-1996	Member, Panel on Financing and Organization, National Advisory Council on Alcohol Abuse and Alcoholism, Subcommittee on Health Services Research
1995-1998	Secretary-Treasurer, Association for Advancement of Behavior Therapy
1997-2001	Board of Directors, Research Society on Alcoholism
1998-present	*Addiction* (Assistant Editor, 1998-2003; Deputy Regional Editor, 2003-2008; Senior Editor, 2009-present)
2000-2003	President-Elect, President, Past-President, Division 50 (Addictions), American Psychological Association
2002-2007	Board of Directors, Pacific Institute for Research and Evaluation (chair of board, 2004-2005)
2002-present	Editorial Board, *Clinical Psychology: Science and Practice*
2005-2007	Science and Practice Committee, Division 12, American Psychological Association
2011-2014	Vice-President, President, Past-President, Research Society on Alcoholism

Awards and Honors:

1993-present	Fellow, Division 12, American Psychological Association
1994-present	Fellow, Division 50, American Psychological Association
1997	MERIT Award, National Institute on Alcohol Abuse and Alcoholism
1999	Association for Medical Education and Research in Substance Abuse, Betty Ford Lectureship
2007	Association for Cognitive and Behavioral Therapy, Distinguished Service Award
2007	American Psychological Association, Division 50 (Addictions), Distinguished Career Contributions to Education and Training Award

C. Selected peer-reviewed publications (of 240 total publications)

Most relevant to the current application

1. **McCrady, B. S.,** Hayaki, J., Epstein, E. E., & Hirsch, L. S. (2002). Testing hypothesized predictors of change in conjoint behavioral alcoholism treatment for men. *Alcoholism: Clinical and Experimental Research, 26*, 463-470.
2. **McCrady, B. S.,** Epstein, E. E., & Kahler, C. W. (2004). AA and relapse prevention as maintenance strategies after conjoint behavioral alcohol treatment for men: 18 month outcomes. *Journal of Consulting and Clinical Psychology, 72*, 870-878.
3. Epstein, E.E., **McCrady, B.S.,** Morgan, T.J., Cook, S.M., Kugler, G., & Ziedonis, D. (2007). The successive cohort design: A model for developing new behavioral therapies for drug use disorders, and application to behavioral couple treatment. *Addictive Disorders & Their Treatment, 6*, 1-19.
4. Epstein, E.E., **McCrady, B.S.,** Morgan, T.J., Cook, S.M., Kugler, G., & Ziedonis, D. (2007).Couples treatment for drug-dependent males. *Addictive Disorders & Their Treatment*, *6,* 21-37.
5. **McCrady, B. S.,** Epstein, E. E., Cook, S., Jensen, N. K., & Hildebrandt, T. (2009). A randomized trial of individual and couple behavioral alcohol treatment for women. *Journal of Consulting and Clinical Psychology, 77,* 243-256. PMCID19309184

Additional *selected* recent publications of importance to the field (in chronological order)

6. **McCrady, B. S.,** Epstein, E. E., & Hirsch, L. S. (1999). Maintaining change after conjoint behavioral alcohol treatment for men: Outcomes at six months. *Addiction, 94*, 1381-1396.
7. Drapkin, M. L., **McCrady, B. S.,** Swingle, J., Epstein, E. E., & Cook, S. M. (2005). Exploring bidirectional couple violence in a clinical sample of female alcoholics. *Journal of Studies on Alcohol, 66*, 213-219.
8. Morgenstern, J., Blanchard, K. A., Kahler, C., Barbosa, K. M., **McCrady, B. S**., & McVeigh, K. H. (2008). Testing mechanisms of action for intensive case management. *Addiction, 103,* 469-477.

9. Hildebrandt, T., **McCrady, B. S.,** Epstein, E. E., Cook, S., & Jensen, N. (2010). When should clinicians switch treatments?: An application of signal detection theory to two treatments for women with alcohol use disorders. *Behavior Research and Therapy, 48,* 524-530. PMCID2871965
10. Ladd, B. O., **McCrady, B. S.,** Manuel, J. K., & Campbell, W. (2010). Improving the quality of reporting alcohol outcome studies: Effects of the CONSORT statement. *Addictive Behaviors, 35,* 660-666.
11. Hunter Reel, D., **McCrady, B. S.,** Hildebrandt, T., & Epstein, E. E. (2010). The indirect effect of social support for drinking on drinking outcomes: The role of motivation. *Journal of Studies on Alcohol and Drugs, 71*, 930-937. PMCID2965492
12. Cohn, A. M., **McCrady, B. S.,** Epstein, E. E., & Cook, S.M. (2010). Men's avoidance coping and female partner's drinking behavior: A high-risk context for partner violence? *Journal of Family Violence, 25*, 679-687. PMCID3001677
13. **McCrady, B. S.,** Epstein, E. E., Cook, S., Jensen, N. K., & Ladd, B. O. (2011). What do women want? Alcohol treatment choices, treatment entry and retention. *Psychology of Addictive Behaviors, 25,* 521-529. PMCID3178005
14. Manuel, J. K., Austin, J. L., Miller, W. R., **McCrady, B. S.,** Tonigan, J. S., Meyers, R. J., Smith, J. E., & Bogenschutz, M. P. (2012). Community Reinforcement and Family Training: A pilot comparison of group and self-directed delivery. *Journal of Substance Abuse Treatment, 43,* 129-136. PMCID3331969
15. Worden, B. L. & McCrady, B. S. (2013). Effectiveness of a feedback-based brief intervention to reduce alcohol use in community substance use disorders treatment. *Alcoholism Treatment Quarterly, 31*, 186-205. **PMC3686515**

D. Research Support

ONGOING

T32 AA018108-01A1 **McCrady (PI)** **7/1/10-6/30/15**

Alcohol Research Training: Methods & Mechanisms

The central aim of this training program is to provide multidisciplinary pre- and post-doctoral training to prepare future scientists to conduct research to elucidate the processes of change in drinking behavior, develop and test effective methods to effect change through improved approaches to treatment and indicated prevention, and develop and test models of disseminate knowledge of effective interventions to diverse populations.

2U10DA1533-09 **Bogenschutz (PI)** **9/1/10-8/31/15**

Clinical Trials Network: Southwest Node

The major goal of this project is to conduct multiple clinical trials for drug addictions, implemented in community treatment programs and coordinated by the Clinical Trials Network. As a Co-Investigator, Dr. McCrady's role is to contribute to the development and implementation of psychosocial protocols.

Role: Co-Investigator

K01 AA021431 **Houck (PI)** **7/15/13-6/30/18**

Imaging Brain Activity in Substance Use Treatment

The central aim of this grant is to support early career investigator, Dr. Jon Houck, to become an independent scientist whose research addresses the neuroscientific basis of therapeutic mechanisms of behavior change.

Role: Primary Mentor

1U01DA034743-01A1 **Condon (PI)** **3/1/14-4/30/17**

Injectible Pharmacotherapy for Opioid Use Disorders (IPO)

The primary goal of this grant is to test the efficacy of drug education to injectible naltrexone with and without a patient navigator for opioid users who are close to release from jail.

Role: Co-Investigator

F31AA023414A **Owens (PI)** **7/1/14-6/30/16**

Brief Motivational Interventions for Male Drinkers being Released from Jail

The central aim of this predoctoral research fellowship is to support a doctoral student, Ms. Mandy Owens, to further develop her research skills and conduct her dissertation research, a study of a brief motivational to enhance motivation to change drinking and improve social support among inmates close to release from jail.

Role: Primary Mentor

1R34 AA023027-01 **Epstein (PI)** **5/1/14-4/30/17**

Adapting Alcohol Behavioral Couple Therapy for Service Members in Post-Deployment

The primary aim of this study it to modify an existing conjoint treatment model for alcohol use disorders to treat soldiers in the reconstitution stage of service, and develop optional psychoeducation modules to address relevant co-morbid problems and challenges in this population.

Role: Co-Investigator

1R13AA023455-01 **Feldstein-Ewing & Chung (MPIs)** **7/1/14-6/30/17**

Neuroimaging Mechanisms of Change in Psychotherapy for Addictive Behaviors

The conference will facilitate cross-disciplinary collaboration between neuroscientists and clinicians in conducting research on mechanisms of behavior change, and will develop guidelines for integrative (brain/behavior) research that can improve the effectiveness of addictions treatment.Role: Co-Investigator

COMPLETED

R01 AA018376-01A1 **McCrady (PI)** **8/1/10-7/31/14**

Mechanisms of Change: Alcohol Behavioral Couple Therapy

The major goal of this project is to study the mechanisms by which social support effects positive treatment outcomes, specifically by studying within treatment behavior in Alcohol Behavioral Couple Therapy.

R01 AA017163-01A1 **Epstein (PI)** **9/30/08-8/31/14**

Testing CBT models and change mechanisms for Alcohol Dependent Women

The major goal of this grant is to adapt Individual female specific cognitive behavioral therapy (I-FSCBT) to treat women with alcohol dependence in a group approach (GFSCBT).

Role: Co-Investigator

F31 AA021031 **Hallgren (PI)** **12/1/11-6/30/13**

NIH/NIAAA

Targeting Social Networks to Maximize Alcohol Use Disorder Treatment & Prevention

The major goal of this grant is to advance predoctoral training for Mr. Hallgren, a doctoral candidate in clinical psychology. The primary goal of the research project is to conduct simulation studies of drinking in social networks for the purpose of understanding how drinking spreads within a social network.

Role: Primary Mentor

Role: PI

CCN2013-0303 **McCrady (PI)** **4/15/13-12/31/13**

Bernalillo County, NM

An evaluation of the methadone maintenance program at the Bernalillo County Detention Center

The primary goal of this is evaluation project is to examine outcomes in terms of continuity of methadone maintenance treatment, recidivism, and cost-effectiveness of a methadone maintenance program administered in the county jail.

90CU0047 **Spear (PI)** **10/1/07-12/15/10**

Recovering Together Program

The major goal of this program is to test an integrated model of treatment for substance abusing women involved with child protective services. As an Investigator, Dr. McCrady has responsibility for human subjects issues, research design and selection of measures, planning data analyses, interpreting results, and writing research reports.

Role: Co-Investigator

BIOGRAPHICAL SKETCH

NAME Yeo, Ronald A.	POSITION TITLE Regents Professor of Psychology
eRA COMMONS USER NAME ronyeo	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Colby College, Waterville, ME	BA	1975	Psychology & Biology
University of Texas at Austin	Ph.D.	1984	Clinical Neuropsychology
Boston VA Medical Center	Internship	1983	Neuropsychology
Boston University Aphasia Research Center	Post-doc		Neuropsychology

A. Personal Statement

I am happy to serve on the Data Safety and Monitoring Board for the project of Dr Vowles. In addition to my familiarity with human subjects research, particularly with complex participants diagnosed with schizophrenia or traumatic brain injury, I serve on the University's Institutional Review Board. I bring with me extensive experience in interdisciplinary work as well. These experiences will allow me to adequately fulfill my role in this project.

B. Positions and Honors

2012 – present: Regents Professor, Department of Psychology, University of New Mexico
2011 – 2012: Principal Investigator coordinator, MIND Research Network, Albuquerque, NM
2010: Earl Walker Award, Outstanding Neuroscience Research, University of New Mexico
2004 - 2008: Chair, Department of Psychology, University of New Mexico.
1998 - 2012: Professor, Department of Psychology, University of New Mexico.
2006: Outstanding Teacher of the Year, University of New Mexico
2000 - 2004: Director of Clinical Training, Department of Psychology, University of New Mexico.
1994 - 1998: Associate Chair for Graduate Studies, Department of Psychology, University of New Mexico.
1983 - 1984: Post-Doctoral fellow in clinical neuropsychology at the Aphasia Research Center, Boston VA Medical Center, funded by National Institute of Health training grant.

C. Selected Peer-reviewed publications (from over 140 publications)

1. Raz, N., Raz, S., Yeo, R. A., Turkheimer, E., Bigler, E. D., & Cullum, C. M. (1986). Relationship between cognitive and morphological asymmetry in dementia of the Alzheimer type: A CT study. International Journal of Neuroscience, 26, 301-309.
2. Yeo, R. A., Turkheimer, E., Raz, N., & Bigler, E. D. (1987). Volumetric asymmetries of the human brain: Intellectual correlates. Brain and Cognition, 6, 15-23.
3. Willis, L., & Yeo, R. A. (1988). Differential declines in cognitive function with aging: The possible role of health status. Developmental Neuropsychology, 4, 23-28.
4. Hunt, A., Orrison, W. W., Yeo, R. A., Haaland, K. Y., Rhyne, R., Garry, P., & Rosenberg, G. A. (1989). Clinical significance of MRI white matter hyperintensities in the elderly. Neurology, 39, 1470-1474.
5. Gennis, V., Garry, P. J., Haaland, K. Y., Yeo, R. A., & Goodwin, J. S. (1991). Hearing and cognition in the elderly. Archives of Internal Medicine, 151, 2259-2265.

6. Burke, H. L., & Yeo, R. (1994). Systematic variations in callosal morphology: The effects of age, gender, hand preference, and anatomic asymmetry. Neuropsychology, 8, 563-571.
7. Yeo, R. A., Gangestad, S. W., Thoma, R. A., Shaw, P., & Repa, K. (1997). Developmental instability and cerebral lateralization. Neuropsychology, 11, 552-561.
8. Yeo, R. A., Hodde-Vargas, J., Hendren, R. L., Vargas, L. A., Brooks, W. M., Ford, C. C., Gangestad, S. W., Hart, B. F. (1997). Brain abnormalities in schizophrenia-spectrum children: Implications for a neurodevelopmental perspective. Psychiatry Research, 76, 1-13.
9. Brooks, W.M., Hodde-Vargas, J., Vargas, L., Yeo, R.A., Ford, C.C., & Hendren, R. Frontal lobe of adolescents with schizotypal signs: A ^{1}H- MRS study. (1998). Biological Psychiatry, 43, 263-269.
10. Friedman, S. D., Brooks, W. M., Jung, R. E., Hart, B. L., & Yeo, R. A. (1998). Proton MR spectroscopic findings correspond to diffuse neuropsychological function in traumatic brain injury. The American Journal of Neuroradiology, 19, 1879-1885.
11. Friedman, S. F., Brooks, W. M., Jung, R. E., Chuilli, S. J., Sloan, J. H., Montoya, B. T., Hart, B. L., & Yeo, R. A. (1999). Quantitative ^{1}H-MRS predicts outcome following traumatic brain injury. Neurology, 52, 1384-1396.
12. Jung, R. E., Brooks, W. M., Yeo, R. A., Weers, D., Hart, B., & Sibbitt, W.L. (1999). Biochemical markers of intelligence: A proton MR spectroscopy study of the normal human brain. Proceedings of the Royal Society B, 266, 1375-1379.
13. Brooks, W. M., Stidely, C. A., Petropoulos, H., Jung, R. E., Weers, D, C., Friedman, S. D., Barlow, M. A., Sibbitt, W. L., & Yeo, R. A. (2000). Metabolic and cognitive response to trumatic brain injury: A proton magnetic resonance study in humans. Journal of Neurotrauma, 17, 629-640.
14. Yeo, R. A., Hill, D. E., Campbell, R. A., Brooks, W. M., Vigil, J., Hart, B., & Zamora, L. (2003). A proton magnetic resonance spectroscopy investigation of the right frontal lobe in children with attention deficit hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 42, 303-310.
15. Driscoll, I. Hamilton, D. A., Petropoulos, H., Yeo, R. A., Brooks, W. M., Baumgartner, R. N., & Sutherland, R. J. (2003). The aging hippocampus: Cognitive, biochemical and structural variations. Cerebral Cortex, 13, 1344-1351.
10. Driscoll, I., Hamilton, D. A., Yeo, R. A., Brooks, W. M., and Sutherland, R. J. (2005). Virtual Navigation in Humans: The Impact of Age, Sex, and Hormones on Place Learning. Hormones and Behavior, 47, 326-335.
16. Rowland, L. M., Bustillo, J. R., Mullins, P. G., Jung, R. E., Lenroot, R., Landgraf, E., Barrow, R., Yeo, R. A., Lauriello, J., Brooks, W. M. (2005). Effects of ketamine on anterior cingulated glutamate metabolism in healthy humans: A 4-T proton MRS study. American Journal of Psychiatry, 162, 394-396.
17. Rowland, L. M., Astur, R. S., Jung, R. E. Bustillo, J. B., Lauriello, J., & Yeo, R. A. (2005). Selective Cognitive Impairments Associated with NMDA Receptor Blockade in Humans. Neuropsychopharmacology, 30, 633-639.
18. Yeo, R. A., Brooks, W. M., Jung, R. E. (2006). NAA and higher cognitive function in humans. Advanced Experimental Medicine and Biology, 576: 215-26, 2006.
19. Yeo, R. A., Hill, D. E., Campbell, R. A., Brooks, W. M., Vigil, J., Hart, B., & Zamora, L. (2003). A proton magnetic resonance spectroscopy investigation of the right frontal lobe in children with attention deficit hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 42, 303-310.
20. Hill, D. E., Yeo, R. A., Campbell, R. A., Hart, B., Vigil, J, & Brooks, W. M. MRI Correlates of Attention Deficit/Hyperactivity Disorder (ADHD) in Children. (2003). Neuropsychology, 17, 491-506.
21. Haier, R. J., Jung, R. E., Yeo, R. A., Head, K., Alkire, M. T. (2004) Structural brain variation and general intelligence. NeuroImage, 23, 425-433.
22. Rowland, L. M., Bustillo, J. R., Mullins, P. G., Jung, R. E., Lenroot, R., Landgraf, E., Barrow, R., Yeo, R. A., Lauriello, J., Brooks, W. M. (2005). Effects of ketamine on anterior cingulate glutamate metabolism in healthy humans: A 4-T proton MRS study. American Journal of Psychiatry, 162, 394-396.

23. Edgar, C., Yeo, R. A., Canive, J., Miller, G. Reduced auditory M100. (2006). Asymmetry in schizophrenia and dyslexia: Applying a developmental instability approach to assess atypical brain asymmetry. Neuropsychologia, 44, 289-299.
24. Thoma, R. J., Yeo, R. A., Gangestad, S. W., Halgren, E., Davis, J., Paulson, K. M., & Lewine, J. D. (2006). Developmental instability and the neural dynamics of the speed-intelligence relationship. NeuroImage, 32(3), 1456-1464.
25. Yeo, R. A., Phillips., J. P., Jung, R. E., Brown,. A. J., Campbell, R. C., & Brooks, W. M. (2006). Magnetic resonance spectroscopy detects brain injury and predicts cognitive functioning in children with brain injuries. Journal of Neurotrauma, 23 (10), 1427-1435.
26. Yeo, R. A., Gangestad, S. G., & Thoma, R. J. (2007). Developmental instability and individual variation in brain development: Implications for the etiology of neurodevelopmental disorders. Current Directions in Psychological Science, 16, 245-249.
27. Gasparovic, C., Yeo, R. A., Mannell, M., Elgie, R., Phillips, J. P., Dozema, D., & Mayer, A. R. (2009). Neurometabolite Concentrations in Gray and White Matter in Mild Traumatic Brain Injury: A ^{1}H–Magnetic Resonance Spectroscopy Study. Journal of Neurotrauma, 26, 1635-1643.
28. Mayer, A. M., Mannell, M. V., Ling, J., Elgie, R., Gasparovic, C., Phillips, J. P., Dozema, D., & Yeo, R. A. (2009). Auditory orienting and inhibition of return in mild traumatic brain injury: A fMRI study. Human Brain Mapping, 30, 1652-1666.
29. Mayer, A. R., Ling, J., Mannell, M. V., Gasparovic, C., Phillips, J. P., Doezema, D., Reichard, R., & Yeo, R. A. (2010). A Prospective Diffusion Tensor Imaging Study in Mild Traumatic Brain Injury. Neurology, 74, 643-650.
30. Thoma, R. J., Monnig, M. A., Ruhl, D. A., Lysne, P., Pommy, J., Bogenschutz, M., Tonigan, S., Yeo, R. A. (2011). Substance abuse in adolescence: The effects of alcohol, marijuana, tobacco, and risk status on neuropsychological performance. Alcoholism: Clinical and Experimental Research, 35, 1-8.
31. Yeo, R. A., Gasparovic, C., Merideth, F., Ruhl, D., Doezema, D., & Mayer, A. R. (2011). A Longitudinal proton magnetic resonance spectroscopy study of mild traumatic brain injury. Journal of Neurotrauma, 28, 1-11.
32. Yeo, R. A., Gangestad, S. W., Liu, J., Calhoun, V. D., Hutchison, K. (2011). Rare copy number deletions predicts individual variation in intelligence. Public Library of Science One.
33. Yeo, R. A., Arden, R., & Jung, R. E. (2011). Alzheimer's disease and intelligence. Current Alzheimer Research, 8(4), 345-353.
34. Yeo, R. A., Gangestad. S. W., Gasparovic, C., Liu, J., Calhoun, V. D. Thoma, R. J., Mayer, A. R., Kalnayam, R., & Hutchison, K. E. (2011). Rare copy number deletions predict individual variation in human brain metabolite concentrations in individuals with alcohol use disorders. Biological Psychiatry, 70(6), 537-544.
35. Mayer, A. M., Ling, J., Mannell, M., Gasparovic, C., Yeo, R. A. (2011). Default mode network activity on mild traumatic brain injury: A fMRI study. Human Brain Mapping, 32: 1825- 1835.
36. Ling, J., Pena, A., Yeo, R. A., Merideth, F., Klimaj, S., Gasparovic, C., & Mayer, A. R. (2012). An examination of diffusion anisotropy in replication and longitudinal samples of Mild Traumatic Brain Injury. Brain, 135, 1281-1292.
37. Monnig, M. A., Tonigan, J. S., Yeo, R. A., Thoma, R. J., & McCrady, B. S. (2012). Review and meta-analysis of white matter volume in alcohol use disorders. Addictions Biology, 17, 1369-1375.
38. Mayer, A. R., Yang, Z., Yeo, R. A., Pena, A., Ling, J., Mannell, M. V. & Gasparovic, C. (2012). A fMRI study of multimodal selective attention following mild Traumatic Brain Injury. Brain Imaging and Behavior, 6, 343-354.
39. Yang, Z., Yeo, R. A., Pena, A., Ling, J. M., Klimaj, S., Campbell, R. A., Doezema, D., & Mayer, A. R. (2012). A fMRI study of auditory orienting and inhibition of return in pediatric mild traumatic brain injury. Journal of Neurotrauma, 29, 2109-2123.
40. Mayer, A. R., Ling, J., Yang, Z., Pena, A., Yeo, R. A., & Klimaj, S. (2012). Diffusion Abnormalities in Pediatric Mild Traumatic Brain Injury. Journal of Neuroscience, 32, 17961-17969.
41. Yeo, R. A., Thoma, R. J., Gasparovic, C., Monnig, M., Harlaar, N., Calhoun, V. D., Kalyanam, R., Durazzo, T. C., & Hutchison, K. E. (2013). Neurometabolite concentration and clinical features of alcohol use disorders: A proton magnetic resonance spectroscopy study. Psychiatry Research Neuroimaging, 211, 141-147.

42. Monnig, M., Caprihan, A., Yeo, R. A., Gasparovic, C., Ruhl, D., Lysne, P., Tonigan, S., Bogenschutz, M., Hutchison, K., Thoma, R. J. (2013). Diffusion tensor imaging of white matter networks in individuals with current and remitted alcohol use disorders and comorbid conditions. Psychology of Addictive Behaviors.
43. Liu, J., Ulloa, A., Perrone-Bizzozero, N., Yeo, R. A., Calhoun, V. C. (2012). Collective effects of 22q13.31 deletions on gray matter concentration in schizophrenia. Public Library of Science One,10.1371/journal.pone.0052865.
44. Yeo, R. A., Thoma, R. J., Gasparovic, C., Monnig, M., Harlaar, N., Calhoun, V. D., Kalyanam, R., Durazzo, T. C., & Hutchison, K. E. (2013). Neurometabolite concentration and clinical features of alcohol use disorders: A proton magnetic resonance spectroscopy study. Psychiatry Research Neuroimaging, 211, 141 -147.
45. Yeo, R. A., Gangestad, S. W., Liu, J., Thoma, R. J., Pommy, J., Mayer, A. R., Schulz, S. C., Ehrlich, S., Wassink, T., Morrow, E., Bustillo, J., Ho, B-C., Calhoun, V. D. (2013). The impact of copy number deletions on general cognitive ability and ventricle size in patients with schizophrenia and healthy controls. Biological Psychiatry, 73: 540-545.
46. Yeo, R. A., Martinez, D., Pommy, J. M., Ehrlich, S., Schulz, S. C., Ho, B.-C., Bustillo, J. R., & Calhoun, V. D. (2013, online). The impact of parent socioeconomic status on executive functioning and cortical morphology in individuals with schizophrenia and healthy controls. Psychological Medicine. DOI: 10.1017/S0033291713001608.
47. Monnig, M. A., Caprihan, A., Yeo, R. A., Bryan, A. Claus, E. D., Calhoun, V. D., Thoma, R. J., & Hutchison, K. E. (2013). Alcohol abuse is associated with white matter variation in reward and self-regulation networks: A DTI-BOLD study. Brain and Behavior, 4, 158-170.
48. Yeo, R. A., Martinez, D., Pommy, J. M., Ehrlich, S., Schulz, S. C., Ho, B.-C., Bustillo, J. R., & Calhoun, V. D. (2014). The impact of parent socioeconomic status on executive functioning and cortical morphology in individuals with schizophrenia and healthy controls. Psychological Medicine, 44, 1257-1265.
49. Yeo, R. A., Gangestad, S. W., Walton, E., Ehrlich, S., Pommy, J., Turner, J. A., Liu, J., Mayer, A. R., Schulz, S. C., Ho, B. C., Bustillo, J. R., Wassink, T. H., Sponheim, S. R., & Calhoun, V. D. (2014). Genetic influences on cognitive endophenotypes in schizophrenia. Schizophrenia Research, 156, 71-75.
50. Ryman, S. G., van den Heuvel, M., Yeo, R. A., Vakhtin, A. A., Carrassco, J., Flores, A. A., Wertz, C., & Jung, R. E. (2014). Sex differences in the relationship between complex connectivity and creativity. NeuroImage, 101, 380-389.

Ongoing Research Support

Principal Investigator: Robin Ohls, MD, Co-Investigator: Ronald A. Yeo, Ph.D.
Title: Brain Imaging and developmental follow-up of infants treated with Erythropoietin
Agency: National Institutes of Health, Developmental brain disorders study section
Type: R01, Period 6/1/10 – 5/31/15.
This study will utilize multimodal neuroimaging (MRI, DTI, MRS) and neurocognitive assessment to evaluate the impact of treatment of very low birth weight infants with recombinant erythropoietin, which stimulates red blood cell production and may serve as a neuroprotective agent.

Principal Investigator: Andrew Mayer, Ph.D., Co-Investigator: Ronald A. Yeo, Ph.D.
Title: A Multidimensional Approach for Understanding Cognitive Control Deficits in Psychopathology
Agency: NIH
Type: RO1
This study is investigating multimodal cognitive control using fMRI and genetics in a population of individuals with psychotic disorders.

BIOGRAPHICAL SKETCH

NAME J. Scott Tonigan, Ph.D.	POSITION TITLE Research Professor
eRA COMMONS USER NAME jtonigan	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
The University of New Mexico, Albuquerque, NM	B.A.	1977	History/Economics
The University of New Mexico, Albuquerque, NM	M.A.	1982	Educational Psychology
The University of New Mexico, Albuquerque, NM	Ph.D.	1989	Educational Psychology

A. Personal Statement

I am an applied statistician trained in the tradition of NIH funded RCT's investigating addiction-focused interventions. I also have a long-standing commitment to the formal psychometric development of self-report questionnaires and semi-structured interviews in addictions research. Since 1993 I have served as an NIH measurement consultant, work that has contributed to the dissemination of two clinician-based assessment reference/training manuals. I also serve as the chair of the main campus Institutional Review Board for the University of New Mexico. I am facile in the application of the proposed analytic methods described in this application, and I have published extensively in the areas of moderated and mediated effects within the context of psychosocial interventions for substance abuse. I have substantial experience working with data safety and monitoring and am well-qualified to serve in this capacity on this project.

Positions and Honors.

1993-95	Research Assistant Professor of Psychology, UNM
1994-present	National Institute on Alcoholism and Alcohol Abuse (NIAAA) Assessment Consultant
1995-01	Research Associate Professor of Psychology, UNM
2001-present	Research Professor of Psychology, UNM
2002-2002	Consulting Editor, Journal of Consulting and Clinical Psychology
2003	Co-Director, Center of Alcoholism, Substance Abuse, and Addictions (CASAA), UNM
2003-2007	Member, Clinical and treatment subcommittee (NIAAA) initial review group (AA-3)
2008-2010	Chair, Clinical, Treatment and Health Services Research Review Subcommittee, NIAAA
2004-present	Editorial Review Board: Journal of Substance Abuse Treatment; Alcoholism Treatment Quarterly; Psychology of Addictive Behavior; Journal of Behavioral Medicine
2007-present	Chair, Main Campus University of New Mexico Institutional Review Board
2009-present	Associate Editor, Psychology of Addictive Behaviors
2010-2011	Associate Editor, Journal of Behavioral Health

B. Selected peer-reviewed publications most relevant to current application

Miller, W. R., & Tonigan, J. S. (1996). Assessing drinkers motivation for change: The Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES), *Psychology of Addictive Behaviors*. 10, 81-89.

Tonigan, J. S., Miller, W. R., & Brown, J. M. (1997). The reliability of Form 90: An instrument for assessing alcohol treatment outcome*, Journal of Studies on Alcohol* 58, 358-364.

Westerberg, V. S., Miller, W. R., & Tonigan, J. S. (1999). Reliability of Form 90D: An instrument for quantifying drug use, *Substance Abuse,* 19, 4, p. 179-189.

Tonigan, J. S., & Miller, W. R. (2002). The Inventory of Drug Use Consequences (InDuC): Test-retest Stability and sensitivity to Detect Change*. Psychology of Addictive Behaviors*, 16(2):165-168.

Slesnick, N. & Tonigan, J. S. (2004). Assessment of alcohol and other drug use by runaway youths: A test-retest study of the Form 90, *Alcoholism Treatment Quarterly,* 22, 2

Freyer, J., Tonigan, J. S., Keller, S., Rumpf, H.-J., John U., Hapke, U. (2005). Readiness for change and readiness for help-seeking: A composite assessment of client motivation, *Alcohol and Alcoholism*, 40 (6), 540-544.

Tonigan, J. S. (2007). Statistical Considerations in Identifying Mechanisms of Change*, Alcoholism: Clinical and Experimental Research*, 31, S3.

Forcehimes, A.A., Tonigan, J.S., Miller, W.R., Kenna, G.A. & Baer, J.S. (2007). Psychometrics of the Drinker Inventory of Consequences (DrInC). *Addictive Behaviors,* 32, 1699-1704.

Huebner, R., & Tonigan, J.S. (2007). The search for mechanisms of behavior change in evidence-based behavioral treatments for alcohol use disorders: Overview. *Alcoholism: Clinical and Experimental Research*, *31*(Suppl 3), 1S-3S.

Hettema, J. E., Miller, W. R., Tonigan, J. S., & Delaney, H. (2008). The reliability of the Form 90-DWI: An instrument for assessing intoxicated drivers. *Psychology of Addictive Behaviors*, 22, 1, p 117-121

Bogenschutz, M. P. , Tonigan, J. S., & Pettinati, H. M., (2009). Effects of alcoholism typology on response to naltrexone in the COMBINE trial*, Alcoholism: Clinical and Experimental Research.33, 1,p 10-18.*

Freyer-Adam J, Coder B, Ottersbach C, Tonigan J S, Rumpf H-J, John U Hapke U (2009). The Performance of Two Motivation Measures and Outcome after Alcohol Detoxification, *Alcohol and Alcoholism*, 44(1): 77-83.

Bogenschutz, M. P., Abbott, P.J. Kushner, R., Tonigan, J. S., & Woody, G. E. (2010). Effects of buprenorphine and hepitis C on liver enzymes in adolescents and young adults. *Journal of Addiction Medicine*, 4, 4, 211-216.

Tonigan, J. S. & Rynes, K. N. (in press). Do changes in selfishness explain 12-step benefit? : A prospective lagged meditational analysis. *Substance Abuse*.

Rynes, K. N, & Tonigan, J. S. (in press) Do Social Networks Explain 12-Step Sponsorship Effects? A Prospective Lagged Mediation Analysis. *Psychology of Addictive Behaviors*.

C. Ongoing Research Support

R21 AA020242-01 Tonigan (PI)
NIH/NIAAA
Review of the AA Literature: Clinical and Research Implications.
This review is applying meta-analytic techniques to summarize the AA literature 1993-2010. Initial efforts to identify relevant articles are now in progress. Analyses will first focus on the associations between AA attendance, drinking, and secondary outcomes. The review will also report the magnitude of associations for mediation pathways in MOC research on AA, e.g. spirituality and social support. The moderating effects of study and sample characteristics will be reported, e.g., dual diagnosis, and the relative effectiveness of different therapeutic approaches to facilitate 12-step attendance will be documented.

R01 AA018376-01 McCrady (PI) 08/10/10-07/31/13
NIH/NIAAA
Mechanisms of Change: Alcohol Behavioral Couple Therapy
This study will identify if spousal behavior in couples therapy in the first therapy session predicts later drinking. Other aims will test if couple interactions change through the course of therapy, how such changes may predict drinking, and how pretreatment couple characteristics moderate relationships of interest. Existing audiotapes of 186 first session and 136 mid- treatment sessions from four randomized clinical trials of ABCT will be coded. Dr. Tonigan is a Co-I on this project and is responsible for the primary data analyses.

U10DA1533 Southwest Clinical Trials Network Node Bogenschutz (PI) 09/01/10-08/31/15
NIH/NIDA

This multisite cooperative agreement is intended to partner with community-based treatment providers to assess the efficacy and effectiveness of various pharmacotherapy and psychosocial treatments for substance abuse. Dr. Tonigan is Co-I for the Albuquerque node.

Templeton Foundation, Pagano, (PI) 04/01/09-03/31/12
Helping Others and Long-term Outcomes among Youth with Substance Use Disorders.
This is a naturalistic follow-up study of adolescents with substance abuse problems. The project has three primary aims: (1) to validate the "Helping Others" questionnaire, (2) to investigate faith-based mechanisms for sustaining service over time, and (3) to examine health and social outcomes in relation to youth involvement in service. Administered by Case Western University, Dr. Tonigan is a consultant on the project.

Completed Research Support

R01-AA014197-01A1-08 Tonigan (PI) 04/15/05-09/29/11
NIH/NIAAA
A Transtheoretical Model of AA-related Behavior Change
This single-group longitudinal study recruited 253 AA-exposed adults from community-based AA and outpatient treatment. Prospective hypotheses about the relative importance of change readiness, self-efficacy, perceived social group dynamics, and AA-specific change mechanisms, e.g., spirituality, have been tested with preliminary reports provided at RSA in 2009 and 2010. Several papers are now under review reporting findings out to the 24 month follow-up. An extended 5 year follow-up is currently in progess.

K02-AA00326-10, Tonigan (PI) 09/01/06- 08/27/11
NIH/ NIAAA
The Social Context for AA-related Behavior Change
This award is focused on the acquisition of analytic skills and knowledge gains in social psychology necessary to model AA-related behavior change in a dynamic social context. To achieve these objectives Dr. Tonigan's career plan included didactic coursework, statistical workshops, coordination of MOC-based workshops at RSA, and structured consultations. The K02 award fully supports Dr. Tonigan's research efforts.

R21AA 017313-02, Thoma (PI) 09/30/07-08/31/11
NIH/NIAAA
Adolescent Neurodevelopment and Alcohol.
This study is investigating the effect of adolescent alcohol abuse on brain development. We have collected intake, 1 and 6-month measures including neuropsychological variables, self-reported drinking measures, magnetic resonance spectroscopy, diffusion tensor imaging, morphometric assessment, EEG, and MEG data. Three groups were recruited: (1) a control group of non-drinking,

but high-risk participants (N = 10), a healthy, normal control (HC; N = 10), and adolescents entering treatment for chronic alcohol abuse (CAA N = 20). Preliminary analyses are underway. We are currently in the data analysis phase, and Dr. Tonigan is a Co-I on the project.

R21DA025241-02, Geppert (PI) 08/01/09-07/31/11
NIH/NIDA
A Survey Study of Informed Consent Processes in Addiction Treatment
The study surveyed 1,500 clinicians from treatment programs of the NIDA Clinical Trials Network (CTN) via an Internet web-based platform. The survey instrument focused on knowledge of clinical ethics concerning the informed consent process, consent practices, and attitudes toward informed consent situations. Participating sites include 16 CTN nodes each linked with five to ten or more Community-based Programs. Preliminary findings are reported in this application, *Training in the Responsible Conduct of Research.*

R01 AA015419-05 Bogenschutz (PI) **0**9/01/05-05/31/11
NIH/NIAAA
12-step Facilitation Adapted for the Dually Diagnosed
This study adapted the 12-step manual developed for Project MATCH for use with dually diagnosed clients (N = 121). The primary objective of this adapted manual was to facilitate attendance in Double Trouble (DT), a mutual-help program for dually diagnosed substance abusers. Follow-up was done at 3, 6, 9, and 12 months, and attendance and commitment to DT and AA was closely monitored and documented. The project is now in the data analysis phase. Dr. Tonigan is a Co-I on this project.

R21AA016974-03 Tonigan (PI) 08/31/07-07/30/10

NIH/NIAAA

Therapeutic Mechanisms in AA

This study investigated the plausibility that causal mechanisms identified in the core AA literature accounted for AA-related benefit, i.e., reduced anger and selfishness and increased spirituality. We recruited 130 alcohol dependent adults from community-based AA and outpatient treatment with limited treatment and AA histories and interviewed them at intake, 3, 6, and 9-months. Preliminary results have been reported at RSA in 2010 and several papers are now under peer-review.

R21 AA 016762-03 Kelly (PI) 05/01/08-03/29/10
NIH/NIAAA
Mechanisms and Moderators of Behavior Change in Alcoholics Anonymous
This study conducted secondary analyses on the Project MATCH data set with special attention paid to identifying change mechanism in AA and how such benefit is moderated by static and dynamic client characteristics. Dr. Tonigan served as a co-investigator on this project and has co-authored four papers with the investigative team.

R21AA13073-01 Tonigan (PI) 10/01/00-09/30/03
NIH/NIAAA
Spirituality and AA practices: 10 year MATCH follow-up.
This study examined the temporal relationships between prescribed AA-related behaviors, spiritual development, and drinking by conducting a 10-year follow-up of the Project MATCH sample (N = 122) recruited at the Albuquerque clinical research unit.

Appendix VIII
Protocol Deviation Tracking Log

Protocol ID/Number:					**Site Name/Number:**		**VA Medical Center, Albuquerque, NM**		
Protocol Title (Abbreviated):			**Combined Treatment for Chronic Pain and Opioid MIsuse**						
Principal Investigator:					**Page number [1]:**				
Ref No.	**Subject ID**	**Date of Deviation**	**Date Identified**	**Deviation Description**	**Dev. Type [2]**	**Resulted in AE?**	**Did Subject Continue in Study?**	**Meets IRB Reporting Req. (Yes/No)**	**IRB Reporting Date**
1									
2									
3									
4									
5									
6									
7									

Investigator Signature: _____ **Date:** _____

Form Instructions:

[1] Each page should be separately numbered to allow cross-referencing (e.g., deviation #2 on p. 7)
[2] Deviation Type: (A-J) See codes below—enter the appropriate deviation code from the list.

Protocol Deviation Codes:

A – Consent Procedures
B – Inclusion/Exclusion Criteria
C – Concomitant Medication/Therapy
D – Laboratory Assessments/Procedures
E – Study Procedures
F – Serious Adverse Event Reporting/Unanticipated Adverse Device Effect
G – Randomization Procedures/Study Drug Dosing
H – Visit Schedule/Interval
I – Efficacy Ratings
J – Other

Adverse Event Form

Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid Misuse

Pt_ID:_____	**This form is cumulative and captures adverse events of a single participant throughout the study.**

Severity	**Study Event Relationship**	**Action Taken Regarding Study Intervention**	***Outcome of AE***	**Expected**	**Serious Adverse Event (SAE)**
1 = Mild 2 = Moderate 3 = Severe 4 = Life-Threatening	0 = Not related 1 = Unlikely related 2 = Possibly related 3 = Probably related 4 = Definitely related	0 = None 1 = Dose modification 2 = Medical Intervention 3 = Hospitalization 4 = Intervention discontinued 5 = Other	1 = Resolved 2 = Recovered with minor sequelae 3 = Recovered with major sequelae 4 = Ongoing/Continuing treatment 5 = Condition worsening 6 = Death 7 = Unknown	1 = Yes 2 = No	1 = Yes 2 = No (if yes, complete SAE form)

At end of study only: Check this box if participant had no adverse events ☐ **None**

Adverse Event	Start Date	Stop Date	Severity	Relation-ship	Action Taken	Outcome of AE	Expected?	SAE?

Serious Adverse Event (SAE)
Report Form

Pilot Study of Combined Treatment for Veterans with Chronic Pain and Opioid MIsuse

Pt ID:_____

Date Participant Reported:

__ __ / __ __ __ / __ __ __ __
d d m m m y y y y

1. SAE onset date: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
   d d m m m y y y y
2. SAE stop date: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
   d d m m m y y y y
3. Location of SAE:_____
4. Was this an unexpected adverse event? ☐ Yes ☐ No
5. Brief description of participants with no personal identifiers:
   Sex: ☐ F ☐ M Age: _____
   Diagnosis for study participation:_____
   _____
6. Brief description of the nature of the SAE (attach description if more space is needed):
   _____
   _____
7. Category of the SAE:
   - ☐ Date of death ___/_____/_____ (dd/mmm/yyyy)
   - ☐ Life threatening
   - ☐ Hospitalization – initial or prolonged
   - ☐ Disability/incapacity
   - ☐ Congenital anomaly/birth defect
   - ☐ Required intervention to prevent permanent impairment
   - ☐ Other:_____

8. Intervention type:
   ☐ Behavioral/lifestyle (specify): Psychosocial intervention: Combined ACT and MBSR

9. Relationship of event to intervention:
   ☐ Unrelated (clearly not related to the intervention)
   ☐ Possible (may be related to intervention)
   ☐ Definite (clearly related to intervention)

10. Was study intervention discontinued due to event? ☐ Yes ☐ No

11. What medications or other steps were taken to treat the SAE?

    _____

12. List any relevant tests, laboratory data, and history, including preexisting medical conditions:

    _____

13. Type of report:
    ☐ Initial
    ☐ Follow-up
    ☐ Final

Signature of principal investigator: _____ Date: _____

Appendix IX

Data and Safety Monitoring Log

Table 1. Enrollment by Month of Study

Month	# Expected	# Screened	# Enrolled or Randomized	# Withdrawn	# Actual (# Enrolled - # Withdrawn)	# Cumulative (Sum of # Actual by Month)

*Enrollment can also be displayed graphically in a Figure, with cumulative subject accrual plotted over time.

Table 2. Demographics

Characteristics	**N**	**N%**
Gender		
Female		
Male		
Ethnicity		
Hispanic or Latino		
Not Hispanic or Latino		
Unknown		
Age Mean (SE)		
Race		
AIAN		
Asian		
Nat Hawaiian/Other Pac Islander		
Black or African American		
White		
Other		
More than one race		
Unknown		

Table 3. Subject Status

Pt Identifier	Date Enrolled	Date Completed Study	Study Status	Reason for Withdrawal	% Adherence to Intervention	Intervention Duration (Weeks)

Status:
A = Active
C = Completed
W = Withdrew
L = Lost to followup

% Compliance to Intervention:
(# tablets taken/total # per protocol)*100
or
(# classes taken/total # of sessions should have attended per protocol)*100

Table 4. Adverse Events

Pt Identifier	AE Onset	AE End	AE Code (MedRA, CTCAE)	Severity	SAE? (Y/N)	Related-ness	Action Taken	Outcome	Comments

Severity of AE:
1 = Mild
2 = Moderate
3 = Severe
4 = Life threatening or disabling

Relatedness to Intervention:
0 = Definitely unrelated
1 = Unlikely
2 = Possibly related
3 = Probably related
4 = Definitely related

Action Taken:
0 = None
1 = Dose modification
2 = Medical intervention (specify in comments)
3 = Hospitalization
4 = Intervention discontinued
5 = Other

Outcome:
1 = Resolved
2 = Recovered with minor sequelae
3 = Recovered with major sequelae
4 = Continuing treatment
5 = Condition worsening
6 = Patient death**

**Provide further details regarding all reported serious AEs and deaths in the SAE and Subject Deaths tables listed at the end of this section.

Table 5. Serious Adverse Events

Pt Identifier	Age	Treatment Date	SAE	SAE Date	Related to Intervention	Description of Actions and Outcomes (e.g., hospitalization, withdrawn from study)

Table 6. Subject Deaths

Pt Identifier	DOB	Date Enrolled	Treatment Date	Cause of Death	Date of Death	Comments