Study protocol for the healing opioid misuse and pain through engagement trial: integrated treatment for individuals with co-occurring chronic pain and opioid use disorder

Study Protocol for the Healing Opioid misuse and Pain through Engagement (HOPE) Trial: Integrated Treatment for Individuals with Co-Occurring Chronic Pain and Opioid Use Disorder

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Abstract

Chronic pain and opioid use disorder (OUD) are each public health crises and their co-occurrence has led to further complications and public health impacts. Provision of treatments for comorbid chronic pain and OUD is paramount to address these public health crises. Medications for opioid use disorder (MOUD) are gold standard treatments for OUD that have also demonstrated benefit in pain management. However, clinics that provide MOUD for chronic pain or OUD often lack behavioral treatments to address the challenges experienced by individuals with both conditions. Developing and implementing a behavioral treatment that complements MOUD may better equip clinics to provide comprehensive care to the growing proportion of clients who present with comorbid chronic pain and OUD. In the Healing Opioid misuse and Pain through Engagement (HOPE) Trial, we are using an effectiveness-implementation hybrid design to examine the benefits of an integrated behavioral treatment and to determine the feasibility of implementing the integrated treatment into clinics that provide MOUD. The treatment integrated two evidence-based treatments - Acceptance and Commitment Therapy and Mindfulness-Based Relapse Prevention - to target the emotional, behavioral, and physiological sequelae of OUD and chronic pain. Implementation feasibility will include assessing changes in implementation readiness and identifying facilitators and barriers to implementing the integrated treatment among all personnel employed in clinics that provide MOUD. This commentary offers an overview of the study and design and details adaptations we made to our study protocol, based largely on clinic personnel time constraints and variable clinic procedures during the COVID-19 pandemic.

Keywords: clinical trial protocol, opioid use disorder, chronic pain, behavior treatment

Highlights

- Chronic pain and opioid use disorder are common and often co-occur
- An integrated behavioral treatment can help address both conditions
- Adaptations may be needed to implement the integrated treatment into clinics
- This study protocol will examine the implementation of an integrated treatment

Introduction

Chronic pain and opioid use disorder (OUD) are two public health crises that often co-occur. Chronic pain refers to pain that persists for at least three months[1], and OUD refers to psychological and/or functional impairment from at-risk opioid use (i.e., illicit use, use opioids other than prescribed, use someone else's opioids, or use to get high[2]). In 2019, approximately 50.2 million American adults experienced chronic pain[1] and approximately 7.6 million had past-year OUD[3]. Further, about 12% of individuals with chronic pain engage in at-risk opioid use[4] and 74.7% of individuals with OUD report chronic non-cancer pain[5]. Though medications for OUD (MOUD), particularly buprenorphine and methadone, have shown promise for individuals with OUD or pain[6], pain is a common reason for return to at-risk opioid use (i.e., relapse)[7]. It may be that MOUD alone is insufficient to address the myriad concerns experienced by individuals with both conditions[8]. Consistent with calls from the National Institutes of Health (NIH) Helping to End Addiction Long-term (HEAL) initiative, identifying and offering behavioral treatments that complement pharmacotherapy for OUD can better equip clinics s to provide comprehensive care to the large proportion of their clients who present with comorbid pain and OUD.

The integration of Acceptance and Commitment Therapy (ACT)[9] and Mindfulness-Based Relapse Prevention (MBRP) is one approach to target the emotional, behavioral and physiological sequelae of at-risk opioid use and chronic pain (e.g., craving, pain acceptance)[10]. In a pilot randomized clinical trial of Veterans with chronic pain and at-risk opioid use, a 12-week, group-based integration of ACT and MBRP (ACT+MBRP) was found to improve outcomes (i.e., opioid misuse, pain interference, and pain behavior[11]). This preliminary efficacy of ACT+MBRP warrants examination of its utility in community-based outpatient clinics that provide MOUD.

However, addiction treatment programs and pain management clinics rarely provide services to address both conditions. Identifying the determinants of effective and sustained implementation of ACT+MBRP can help in developing strategies to facilitate its widespread adoption.

Study aims and intervention

Funded by the National Institute of Drug Abuse (NIDA) as part of the Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR) research program, the current study aims to determine whether and how ACT+MBRP translates to community-based outpatient clinics providing MOUD to individuals with both chronic pain and OUD. Specifically, the Healing Opioid misuse and Pain through Engagement (HOPE) trial uses a hybrid effectiveness-implementation type 1 design to determine the clinical effectiveness of ACT+MBRP (aim 1) and the feasibility of implementing ACT+MBRP into standard practice (aim 2) across outpatient clinics that provide MOUD.

This study will test the utility of ACT+MBRP with clients who are currently receiving MOUD for pain and/or at-risk opioid use. Individuals with comorbid chronic pain and OUD experience a myriad of psychological (e.g., self-compassion), emotional (e.g., depression), and physiological (e.g., pain intensity) challenges that MOUD alone may not address. Offering ACT+MBRP as a complement rather than as a substitute to MOUD and to other available services can ensure clinics are meeting the needs of the client holistically. The pilot trial developed the ACT+MBRP treatment manual[11], which serves as the active treatment in the HOPE trial. This 12-week, video conference-delivered ACT+MBRP treatment condition facilitates participants' engagement in exercises and discussions that aim to increase adaptive responsiveness to symptoms of chronic pain and OUD.

Primary and secondary outcomes include assessments of pain interference and at-risk

opioid use (primary outcomes) and other pain-related outcomes (e.g., pain-related anxiety), substance use behaviors (e.g., alcohol use), and other psychosocial factors (e.g., stigma), as well as three theorized mechanisms of action (chronic pain acceptance, engagement in values-based action, and opioid cravings) expected to account for treatment effects on the primary outcomes. Interviewer-led assessments are collected remotely with the participant at baseline, 3-, 9-, and 15-month follow-up assessments, and self-administered assessments are completed weekly throughout the treatment period.

Our second aim is to determine the implementation feasibility and adoption potential of ACT+MBRP across outpatient clinics, based on interviews and assessments of all clinic personnel. Several barriers at the provider and organizational level contribute to suboptimal care for those with co-occurring OUD and pain. For example, providers have limited knowledge and training in both conditions[12], and state and federal regulations around providing MOUD or pain management may limit the time, resources, and funding available for programs to adopt new behavioral interventions[13]. The Consolidated Framework for Implementation Research (CFIR)[14] will guide the implementation of the HOPE trial. The CFIR is a meta-theoretical framework designed to identify determinants of effective, sustained implementation across five broad domains (i.e., intervention characteristics, outer setting, inner setting, characteristics of individuals involved, and implementation process). The current study will administer measures of individual and organizational readiness to change before and after the clinical trial to evaluate changes in clinic personnel perceptions around implementing ACT+MBRP into standard practice. Further, personnel will complete individual interviews, based on CFIR domains after the clinical trial to identify the barriers and facilitators to implementation (see institutional review board approval letter and study protocol in supplemental files).

Developing a hybrid effectiveness-implementation type 1 trial

The HOPE trial is a multi-site study, recruiting from outpatient clinics, that uses a single-blind randomized clinical trial design to examine the clinical effectiveness and a mixed-methods design to examine implementation feasibility of ACT+MBRP. In accordance with recommendations by the CFIR[14] and other implementation models (e.g., Health Equity Implementation Framework[15]), significant time and effort was devoted to the pre-implementation phase of the HOPE trial to maximize the reach, suitability, and translatability of ACT+MBRP in community-based clinics that serve individuals who receive MOUD and tend to report comorbid chronic pain and OUD.

First, we established partnerships with persons with lived experience and other community members (i.e., Collaborative Board), as well as scientific experts in chronic pain, OUD, and/or implementation science (i.e., Scientific Advisory Board) to develop, implement, and evaluate the HOPE trial. The research team meets with each board regularly, and the initial meetings focused on understanding how the proposed intervention fits with the experiences and needs of the individuals and the organizations. Several features of the HOPE trial were based on feedback from these board members as well as from collaborations with the other IMPOWR centers[16], including the appropriate language to include in study materials, the development of the education control condition, the selection of outcome measures to ensure we assessed the *whole* person, stigma, and health disparities affecting this population, and the selection of implementation measures to ensure we assessed the needs and resources of the clinics. For example, we will perform exploratory analyses of several emotional (e.g., depression), social (e.g., perceived social support), and behavioral (e.g., alcohol use) aspects of the whole person that have demonstrated influence on the development and maintenance of chronic pain and

OUD, to fully understand the benefits of the integrated behavioral treatment.

Second, we contacted community-based outpatient clinics that provided MOUD, but differed in the other services that they offer (i.e., addiction, pain management, or primary care services). When, where, and why individuals seek healthcare varies, and evidence indicates that a large proportion of individuals who present to treatment with OUD or chronic pain likely have both conditions. Therefore, limiting the availability of the intervention to certain clinical settings would limit the potential to incorporate ACT+MBRP into the diverse practice settings that serve this population. Finally, our goal was to test an evidence-based intervention that attends to the myriad of challenges faced by individuals with comorbid chronic pain and OUD. Thus, we limited our exclusion criteria to only those individuals with serious mental illness or acute intoxication that may impede one's ability to provide informed consent. Similarly, we defined chronic pain as self-reported experience of pain for more days than not over the past three months. Though we included outcome measures of pain in accordance with the recommended six core domains[17], determining study inclusion with a single, self-report item asking about experience of chronic pain aligns with the inherently subjective nature of pain[18].

Taken together, the HOPE trial includes aspects of an efficacy trial (e.g., rigorous outcome assessment) and an effectiveness trial (e.g., limited exclusion criteria; recruitment from community-based clinics) that align with the use of a hybrid effectiveness-implementation type 1 trial to acquire information needed for efficient translation of the treatment into practice. As such, all personnel employed at participating clinics will be recruited to complete assessments, as well as an individual interview to gauge their perceptions of individual and organizational readiness to implement the intervention into practice.

Study Adaptations and Future Directions

The practical value of conducting a large, multi-site research trial in real-world treatment settings poses several challenges. Across community-based outpatient clinics, treatment providers have limited time and resources to learn new behavioral treatments, and clinics have standard procedures that may impair efficient adaptations or flexibility to incorporate new treatments into practice[19]. Additionally, the slow transition back to in-person services following the height of the COVID-19 pandemic posed challenges around how clinics could incorporate a new intervention into existing service delivery procedures. Our initial correspondence with three large addiction treatment programs (two in New Mexico; one in Michigan) illuminated these challenges, particularly around executing the HOPE trial on site and asking treatment providers to serve as study therapists. Though all three clinics had the space and resources to provide the intervention on-site, several behavioral services within these clinics were still being offered remotely at the start of the HOPE trial, to limit the potential exposure of clients and personnel to COVID-19. Requiring clients and study personnel to come into the clinic to deliver ACT+MBRP would not only have disrupted service delivery but also may have heightened their risk of contracting COVID-19. To limit barriers to implementing the HOPE trial, the first adaptation that we made was changing the mode of delivery from in-person to remote. Evidence surrounding service delivery during the pandemic suggests this adaptation may hold long-term, practical value. Notably, several telehealth services have demonstrated comparable client outcomes and satisfaction ratings to in-person services.[20] Although the study team will deliver ACT+MBRP for the HOPE trial, we will also provide training in ACT+MBRP to interested personnel from these clinics. Additionally, we have informed administrators of subsequent addiction, pain management, and primary care clinics where we are recruiting clients from that we will train their personnel in ACT+MBRP at the end of the HOPE trial. Training them in the

intervention and assessing their perceptions of the utility and feasibility of incorporating the intervention into standard practice will guide how we can facilitate its future adoption.

We also opted to have licensed clinical psychologists and clinical psychology graduate students previously trained in ACT+MBRP serve as study therapists, rather than clinic staff. Study-specific clinicians allowed us to expand our recruitment and to better utilize clinic staff time for study recruitment. First, having study-affiliated clinicians separate from recruitment clinics allowed us to extend the reach of our project, given the remote delivery of the treatment. We adapted our study protocol to recruit from any clinics or individual prescribers of MOUD in New Mexico and Michigan. We devised a multi-pronged recruitment strategy, including a review of national and state registries to identify providers and clinics that offer MOUD, followed by informational recruitment sessions with clinic administrators and personnel, flyers posted to clinic offices and lobbies, and referrals from other research studies occurring within University of New Mexico and University of Michigan for which the interested participants were screened ineligible. This broadened our recruitment efforts to include more rural areas and patients on MOUD whose prescribers were not originally affiliated with our study sites. Moreover, by having study-affiliated clinicians rather than clinic-affiliated clinicians, we freed up partnered clinic staff availability to review patient medical records for potentially eligible patients.

Taken together, we hope this study and these adaptations will maximize the goals of the HOPE Trial and the IMPOWR program at large: to characterize implementation barriers and solutions, establish community partnerships, and facilitate the incorporation of evidence-based interventions into standard practice. This study has the potential to improve access and quality of treatments for clients. By offering an integrated behavioral treatment in clinics that treat chronic

pain or OUD, clients with both conditions can receive the composition of needed services from *one* clinic. Given that most pain management and addiction treatment clinics comprise of interdisciplinary treatment teams with personnel able to deliver behavioral treatments, clients with different financial, environmental, and functional means to access services can still receive a treatment that addresses both conditions without having to seek treatment at multiple facilities. Identifying the internal and external constraints, and personnel perspectives on implementing the treatment across clinics will help us devise strategies to influence financial and accreditation entities, to adapt organization service delivery, and to raise awareness to address both conditions simultaneously.

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