STUDY PROTOCOL

PARTNERS FOR PAIN & WELLBEING EQUITY: A RANDOMIZED TRIAL OF COMMUNITY SUPPORTED COMPLEMENTARY AND INTEGRATIVE HEALTH SELF-MANAGEMENT FOR BACK PAIN

National Clinical Trial (NCT) Identified Number: NCT05786508

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PROTOCOL REVISION HISTORY

Protocol Version #	Revision Date	Summary of Changes	Protocol Section(s)
2	May 2023	Updated non-key personnel: Removed Jennifer Walter	3. Study Roster
2	May 2023	Clarified study is conducted in English and supplementary materials are available in Spanish for individuals with English as a second language	9.2 Inclusion Criteria
2	May 2023	Added details about the use of TransportationPlus, a rideshare program that will be used to transport participants to study visits to address a potential barrier to participation.	9.4.5 Retention Strategies 9.4.6 Strategies for Addressing Barriers to Recruitment & Retention of Populations Who Experience Health Disparities
2	May 2023	Changed minimum group size from 10 to 7	11.1 Intervention Overview
2	May 2023	Updated screening activities and clarified the timing between randomization and the start of the group interventions is up to 28 days. Also clarified the timing for follow up assessments (Month 2 for the R61 and Months 2, 4, and 6 for the R33) is from the start of the group interventions.	13.2 Screening Assessments 13.3 Intervention Sessions 13.4 Follow up Assessments
2	May 2023	Included video presentation of study and timing for when it would be sent to potential participants	16.1.2 Consent Procedures and Documentation
3	July 2023	Added the following questionnaires: Perceived Discrimination in Healthcare and an adapted version to assess Perceived Discrimination in the P4P Study.	13.1 Schedule of Assessments 13.2.3 Baseline Two Screen 14.2.3 Implementation & Disparity Mitigating Outcomes
3	July 2023	Updated non-key personnel: Added Emma Ward, Shraddha Bika, Jake Kremer, and Erika Kennedy; removed Aditi Das.	3. Study Roster
4	August 2023	Updated sample size (n=30-60) from (n=30-40). Response to recruitment initiatives has gone very well. Study team wanted to provide additional opportunity for underserved participants to be included in the study. Funds and resources are in place for up to 60 participants.	4.1 Synopsis 6 Study Procedures 10.1 Enrollment Procedures 15.2.1 R61 Randomized Pilot Study
4	August 2023	Removed Gaye Adams Massey from External Co-Investigator Consultants (no access to participants or identified data).	3 Study Roster
5	October 2023	Added Carmen Robles, Ivette Izea-Martinez, Jamiela Taylor (no access to participants or identified data). Added section for former team members and listed past project personal: Kari Davis BA, Aditi Das MPH, and Gaye Adams Massey, JD. Updated credentials for project team	3 Study Roster

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TABLES APPEARING IN THE PROTOCOL

ABBREVIATIONS/DEFINITIONS

ADL	Activities of Daily Living
AE	Adverse Event
APEASE	Affordability, Practicality, Effectiveness, Adaptability, Safety, Equity
BL	Baseline
BP	Back pain conditions including back or neck pain
BP-PEHD	Back pain from populations that experience health disparities
BPS	Biophysical, psychological and social
CC	Creative commons
CIH	Complementary and Integrative Healthcare
Co-I	Co-Investigator
CoC	Certificate of Confidentiality
COI	Conflict of Interest
COM-B	Capability, Opportunity, Motivation - Behavior
ConNECT	Integrating **CON**text; Fostering a **N**orm of Inclusion; Ensuring **E**quitable Diffusion of Innovations; Harnessing **C**ommunication Technology; Prioritizing Specialized **T**raining
CRF	Code of Federal Regulations
CRF	Case report form
CV	Curriculum Vitae
DC	Doctor of Chiropractic
DSMP	Data Safety and Monitoring Plan
ETHOS	Ethical Oversight Submission System
FFR	Federal Financial Report
GAD	Generalized Anxiety Disorder
GCP	Good Clinical Practice
HEAL	Helping End Addiction Long Term
HHS	Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HSR	Human Subjects Research
HST	Health Sciences Technology
ICF	Informed Consent Form
ICH	International Council on Harmonization
ID	Identification
IHWRP	Integrative Health and Wellbeing Research Program
IMC	Independent Monitoring Committee
IRB	Institutional Review Board
LAR	Legally Authorized Representative
LBP	Low back Pain
MN	Minnesota
MMSE	Mini-Mental Status Examination
MOP	Manual of Operations
MS	Master of Science
NCCIH	National Center for Complementary and Integrative Health
NCT	National Clinical Trial
NIH	National Institutes of Health
NP	Neck Pain

OHRP	Office for Human Research Protections
OIC	Office of Institutional Compliance
P&A	Professional & Administrative
PEG	Pain, Enjoyment of Life and General Activity
PEHD	Populations Experiencing Health Disparities
PGIC	Patient Global Impression of Change
PhD	Doctor of Philosophy
PHQ-2	Patient Health Questionnaire-2
PI	Principal Investigator
PO	Program Officer
PROMIS	Patient-Reported Outcome Measurement Information System
RE-AIM	Reach, Effectiveness, Adoption, Implementation, Maintenance
REDCap	Research Electronic Data Capture
REPA	Report of External Professional Activities
RNI	Report of New Information
SAE	Serious Adverse Event
SARP	Study Accrual and Retention Plan
SPH	School of Public Health
SRQ	Self-Report Questionnaire
TAPS	Tobacco, Alcohol, Prescription medications and other susbtances
TIDieR	Template for implementation for intervention description and replication
UMN	University of Minnesota
UPIRTSO	Unanticipated Problem Involving Risks to Subjects of Others
UROC	Robert J. Jones Urban Research and Outreach-Engagement Center
USA	United States of America
US	United States
VA	Veterans Administration
YMCA	Young Men’s Christian Association
YWCA	Young Women’s Christian Association

1 STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonization Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

2 INVESTIGATOR SIGNATURES

The signatures below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

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3 STUDY ROSTER

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4 PROTOCOL SUMMARY

4.1 SYNOPSIS

The following provides a synopsis for the **R61 (Phase I)** of the project.

Title	*Phase I (R61): Partners for Pain & Wellbeing Equity: A Randomized Trial of Community Supported Complementary and Integrative Health Self-Management for Back Pain*
Grant Number	1R61AT012309
Study Description	The focus of the R61 project is on developing and optimizing community-based programs for the self-management of back or neck pain for individuals from populations that experience health disparities (BP-PEHD). We will use a community-engaged research approach to conduct quality improvement activities that involves gathering feedback from multiple stakeholders to inform development of the study interventions and materials which will be followed by a randomized pilot study of 30 to 60 participants to evaluate feasibility.
Objectives/Aims	**Aim 1:** We will use mixed methods data collection from multiple levels of stakeholders to assess barriers and facilitators to participating in back pain self-management, and community supported programs. **Aim 2.** Based on information gathered in Aim 1, we will perform participatory intervention mapping to co-develop a community supported CIH self-management intervention program (and control) for BP-PEHD. **Aim 3.** We will conduct a feasibility study (n=30 to 60) to assess essential scientific and feasibility milestones including: a) Finalizing and securing agreements, and regulatory approvals (IRB, NCCIH, IMC) for all required protocols and plans (e.g., clinical protocol, Data Safety and Monitoring Plan, Study Accrual and Retention Plan, etc.) b) Recruiting and enrolling individuals with BP-PEHD and measuring recruitment rates, enrollment rates c) Delivering experimental and control interventions and measuring intervention adherence and fidelity rates d) Data collection by assessing follow up rates of future trial outcome measures as well as the usability and functionality of data collection systems e) Stakeholder views of barriers and facilitators to the above, including affordability, practicality, effectiveness, acceptability, safety, and equity and other factors that could affect the future full scale trial's success
Endpoints	**Aim 1:** Needs and perspectives for addressing barriers and facilitators to back pain management and participation in community supported CIH programs **Aim 2:** Reactions and opinions to Aim 1 findings and planned resources and approaches for the CIH self-management program and feasibility study **Aim 3:** Recruitment feasibility, enrollment feasibility, intervention acceptability and credibility, intervention fidelity, and data collection feasibility
Study Populations	**Aims 1-3:** Community Stakeholders defined as Community Partner Organization leadership members; Community Facilitators; and other Community Members for whom BP-PEHD is relevant

	Aim 3: 30 to 60 adults with chronic neck or back pain from populations that experience health disparities due to race/ethnicity or socioeconomic status
Phase/Design	Mixed methods quality improvement (Aims 1, 2) leading to randomized pilot study (Aim 3)
Sites/Facilities	University of Minnesota; Community Partners include the YMCA of the North and YWCA St. Paul
Study Interventions (experimental, control)	Both intervention programs include nine, 90-minute group sessions that occur weekly. **Experimental:** Partners4Pain is a self-management program of evidence based complementary and integrative health approaches for pain including pain education, mindfulness, cognitive behavioral approaches, and neck/back specific exercises. **Active Control:** Keys to Wellbeing is a general health and wellbeing education program addressing topics such as keeping socially connected, finding meaning and purpose, addressing mental health, and keeping physically fit. The program was designed to control for time, attention, and many other key contextual factors (e.g., program format, materials).
Duration	**Planning, preparation phase (Aims 1, 2):** Nine months **Randomized pilot study (Aim 3):** One year
Participant Duration	**Randomized pilot study:** Three months

The following provides a synopsis for the future **R33 (Phase II)** of the project.

Title	*Phase II (R33): Partners for Pain & Wellbeing Equity: A Randomized Trial of Community Supported Complementary and Integrative Health Self-Management for Back Pain*
Grant Number	TBD
Study Description	The R33 project focuses on assessing the effectiveness of a community-based back or neck pain self-management program, Partners4Pain, relative to an active control for improving important outcomes impacted by chronic pain (Aim 1), and the impact of health disparity factors (Aim 2). The project also focuses on gathering feedback as part of quality improvement activities to gain a better understanding of factors (including those that might mitigate disparities) that could affect the long-term implementation of the community-based self-management programs (Aim 3).
Objectives/Aims	**Aim 1:** To assess the relative effectiveness of Partners4Pain versus Keys to Wellbeing in terms of: a) Primary effectiveness outcomes of pain intensity and interference over 6 months using bi-monthly assessments b) Secondary effectiveness outcomes of pain impact, self-efficacy and other HEAL outcomes **Aim 2:** To assess the impact of health disparity factors on the effectiveness of Partners4Pain for primary and secondary outcomes through subgroup analyses which account for potential complexities between disparity factors **Aim 3:** To describe important disparity mitigating and implementation related measures that can impact and inform sustained translation of the program with community partner organizations
Endpoints	**Aims 1-2:** Pain intensity and interference; pain impact; self-efficacy; life satisfaction; physical functioning; pain catastrophizing; interoceptive awareness; satisfaction;

	improvement; medication use; participation in social roles; healthcare use; CIH self-management; sleep; depression; anxiety; substance use; adverse events **Aim 3:** Views on barriers/facilitators to participation, effectiveness, adoption, maintenance/sustainability, resource needs; Views on affordability, practicality, effectiveness, acceptability, safety, and equity of educational programs; Ability of programs to meet capability, opportunity, and motivational related needs; Views on inclusion and cultural sensitivity; Views on the community-researcher relationship; Views on alignment with organizational mission and business models
Study Populations	**Aims 1-3:** 376 adults with chronic neck or back pain from populations that experience health disparities due to race/ethnicity or socioeconomic status **Aim 3:** Community Stakeholders defined as Community Partner Organization leadership members; Community Facilitators; and other Community Members for whom BP-PEHD is relevant
Phase/Design	Phase II randomized hybrid effectiveness implementation trial using individual level randomization and group treatments (Aims 1, 2); quality improvement activities to gather and account for stakeholder feedback (Aim 3).
Sites/Facilities	University of Minnesota; Community Partners include the YMCA of the North and YWCA St. Paul
Study Interventions (experimental, control)	Both intervention programs include nine, 90-minute group sessions that occur weekly. **Experimental:** Partners4Pain is a self-management program of evidence based complementary and integrative health approaches for pain including pain education, mindfulness, cognitive behavioral approaches, and neck/back specific exercises. **Active Control:** Keys to Wellbeing is a general health and wellbeing education program addressing topics such as keeping socially connected, finding meaning and purpose, addressing mental health, and keeping physically fit. The program was designed to control for time, attention, and other key contextual factors (e.g., program format, materials).
Duration	Three years
Participant Duration	Seven months

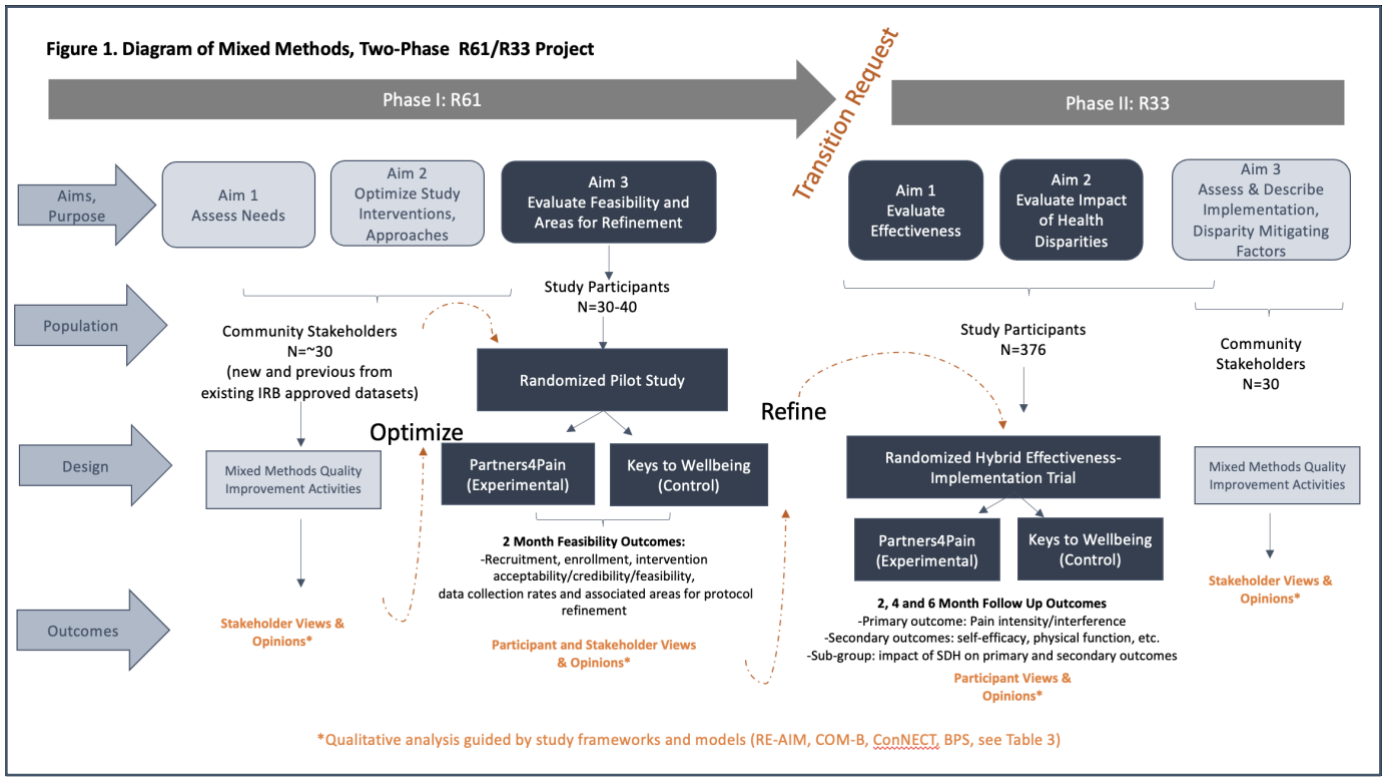
4.2 STUDY OVERVIEW

This research is part of a two-phase project (R61/R33) supported through the National Institutes of Health's Helping to End Addiction Long-term (HEAL) Initiative. The project is summarized below and in Figure 1.

R61 Overview. The R61 Phase focuses on planning and preparation related 'quality improvement activities' (R61 Aims 1-2) that will assess community stakeholder needs and optimize study interventions and approaches. A randomized pilot study (R61 Aim 3) will evaluate feasibility and provide another opportunity for 'quality improvement' activities and provide refinements in preparation for the R33. The interventions are Partners4Pain (experimental), comprised of evidence based Complementary and Integrative Health (CIH) modalities (e.g., pain education, mindfulness, cognitive behavioral approaches, exercises and physical activity) and an active control, Keys to Wellbeing. Both programs will leverage

assets (e.g., content videos, workbooks, etc.) developed and successfully applied by the investigators in previous studies; these will be used as a starting point to develop and optimize the programs for individuals with BP-PEHD.[1-10] Both intervention programs consist of weekly 90-minute group sessions for 9 weeks that will be offered in-person and via videoconference depending on community partner organization and participant needs.

R33 Overview. The R33 Phase includes a randomized hybrid effectiveness implementation trial (Aims 1 and 2) to evaluate the effectiveness of the Partners4Pain intervention compared to the Key to Wellbeing active control intervention and the impact on health disparities related to pain management. The R33 will also engage study participants and community stakeholders in 'quality improvement activities' (R33 Aim 3) that assess their views of barriers and facilitators to long-term implementation of the Partners4Pain intervention in community-based settings, including those that may help mitigate disparities.



4.3 PARTICIPATING SITES

University of Minnesota Research Sites

The University of Minnesota Twin Cities serves as the primary research site and will assume the following responsibilities:

- Designing and developing the protocol, manual of operations, informed consent and case report forms
- Collecting and maintaining critical regulatory documents from affiliated investigators, e.g., resume/CV, certification of completion of training, signed COI disclosure forms, delegation of authority logs

- Storing and/or managing data, performing data analysis, and data monitoring activities
- Ensuring informed consent is obtained and documented from each subject in compliance with federal regulations
- Recruiting, screening, and enrolling participants
- Delivering study interventions
- Protecting participants' rights
- Providing study specific training to research personnel
- Developing and coordinating randomization scheme and process
- Monitoring compliance with protocol and tracking deviations from the study protocol
- Ensuring the correct versions of the protocol and consent documents are used
- Tracking, reporting, and maintaining documentation of all serious adverse events and unanticipated problems and disseminating the information to appropriate oversight boards
- Providing periodic updates to affiliated investigators on subject enrollment, general study progress, and relevant scientific advances
- Developing the data flow and data management procedures, including data entry, error identification, and correction
- AE monitoring and reporting
- Implementing and monitoring quality control procedures
- Generating and disseminating reports (e.g., enrollment, AEs, participant status, site performance, quality control)
- Comply with necessary protocols and maintain consistency with the HEAL Initiatives Public Access and Data Sharing Policy
- Maintaining documentation of IRB approvals and correspondence and communicating study status changes

Participating University of Minnesota Sites for the R61 are:
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Community Partner Organization Sites: Leaders from the YMCA of the North, the YWCA St. Paul, and the Hue-MAN Partnership serve as consultants on this project. Their role is limited to sharing views and opinions about barriers and facilitators to the study interventions and other processes and procedures, as well as disseminating information about the project through their routine communication channels. Leaders from Community Partner Organizations will facilitate the use of space at their affiliated locations for the University of Minnesota research staff to conduct research procedures (e.g., screening, intervention sessions). None of the Community Partners (including their employees) will take part in study activities involving human subjects nor will they have access to study data.

5 INTRODUCTION

5.1 BACKGROUND

Disease prevalence and impact. Back pain (BP) conditions, including low back and neck pain, are among the most common and disabling chronic pain disorders in the U.S.[11-14] and a leading cause of disability worldwide.[15,16] An estimated 40-80% of adults experience low back pain (LBP) or neck pain (NP), and almost one third of all Americans experience chronic NP or LBP at some point in their lives.[11,17-20] BP is the most common reason for seeking care in the healthcare system[21,22] and the U.S. spends more on BP than any other condition. In 2016, roughly 10% of healthcare expenditures ($134.5 billion) were devoted to the care of BP.[23] BP like most health conditions, has become widely recognized as more than a physical phenomenon; it is a complex condition influenced by interrelated biophysical, psychological, and social (BPS) factors.[24,25]

Population. This study focuses on ***individuals with back pain from populations who experience health disparities (BP-PEHD)***. Overall, there has been relatively little research examining BP-PEHD. While BP prevalence rates are similar between White and Black Americans, Black Americans are more negatively impacted with higher severity and disability.[26]

Current Back Pain Management. While BP has become widely recognized as a biophysical, psychological and social condition, current BP management is still mainly biophysically oriented and the majority of cases remain poorly treated[27,28] with a heavy emphasis on symptom management[29,30] that fails to address sufferers' needs.[24,29-31] The use of epidural injections, opioid prescriptions, and spinal surgeries has increased at alarming rates over the past few decades, with little positive impact on patient outcomes.[32-35] Of particular concern is the overreliance on opioids, which are used by an estimated 30% of chronic LBP patients and 15% of all NP patients.[36,37] While these more aggressive treatments are appropriate for some individuals, the majority of individuals with BP would benefit from less invasive approaches that foster engagement in adaptive pain behaviors, including self-management.[30,38,39]

Disparities in BP care and management are also evident. A study of older U.S. adults seeking care for BP found Blacks and Hispanics used less health care and also had less improvement in clinical outcomes relative to Whites.[40] The opioid epidemic has hit low-income White communities the hardest, where opioid prescriptions and deaths due to overdose are most prevalent.[41] While Black Americans are less likely to be prescribed opioids for BP[42,43] they are also more likely to be under-assessed and under-treated in many areas including screening, diagnostic imaging, use of physical therapy, and surgery.[44] Additionally, adults who are Black, Hispanic, or have lower educational attainment, income, insurance coverage and self-reported health, are less likely to use complementary and integrative health (CIH) approaches, for which there is a growing evidence base.[45]

Socioeconomic Factors and Health Disparities. The relationships between socioeconomic factors and health disparities in the United States are complex due to long-standing institutional discrimination and structural racism.[46,47] There is evidence that socioeconomic factors (e.g., income, employment status, home ownership) are associated with greater likelihood of chronic pain and poorer outcomes.[48-50] Lack of social support[51-53] and work related factors such as physical workload, education, injury compensation, and dissatisfaction can also have a negative effect on BP.[54] Drawing from the larger pain field, poor quality relationships and social stressors (e.g., due to racism, ostracism, injustice, invalidation, isolation, etc.) also contribute to poor outcomes.[55,56] To move the BP-PEHD research field forward, it is imperative that social contexts are more intentionally considered and taken into account in the research process.

Improved Pain Management. To reduce the burden of BP, individuals require greater access to evidence based care that addresses their biopsychosocial needs.[57] There has been a growing recognition that BP,

much like other chronic health conditions, requires ongoing attention to lifestyle factors and engagement in effective self-management.[30,38] While patients recognize the need for self-management strategies, they often need support and validation to initiate and maintain optimal self-care.[58,59] This isn't surprising given that BP is frequently associated with psychological risk factors including poor cognitive and emotional coping strategies, depression, catastrophizing, and fear avoidance beliefs, which can make self-management difficult.[54,60]

Self-Management. While definitions of self-management interventions vary considerably, they can be generally defined as structured or semi-structured instructional programs, which include multiple, distinct modalities aimed at promoting active involvement in managing one's condition.[38,39] Given the symptomatic nature of pain, and the fact that it is encountered throughout the lifespan, *pain self-management* can be viewed as a foundational behavioral skill that all could benefit from. Commonly, self-management approaches help individuals learn and adopt a set of healthy behaviors (e.g., activity versus inactivity, socialization versus isolation, non-drug symptom management versus substance reliance). For BP, there is a range of ***CIH self-management modalities*** including psychological strategies (e.g., behavioral or cognitive); mind-body approaches (including relaxation, meditation or guided imagery); physical activity (e.g., general and rehabilitative exercise, yoga, tai chi); lifestyle advice (e.g., for sleep, daily activities, social support); and pain education (e.g., pain theories, prognosis, and pain management tips).[39,45] Importantly, there is research evidence to support all of these CIH self-management strategies for BP (see **Table 1**).

Table 1. CIH Self-Management Strategies for Back Pain

Strategy	Evidence of effectiveness
Pain education	Small effects on pain and function[61,62]
Cognitive behavioral/coping strategies (including progressive muscle relaxation and guided imagery)	Small effects on pain and function[63]
Mindfulness based interventions	Small effects on pain, small to no effect on function[63-65]
Exercise (back specific and general)	Moderate effects on pain, small effects on function[63,66]

Whole Person CIH Self-Management. There has been a growing number of multi-modality CIH self-management programs that address pain from a whole person perspective (e.g., taking into account BPS factors).[67-69] In our current research, pain sufferers and community stakeholders have expressed an interest in and need for such an approach (R33AT00911, R34AT011209-01S1). One of the most studied existing pain self-management programs is the widely adopted Stanford Program which addresses pain from a more holistic perspective. It is comprised of lay person-led sessions including pain education, effective communication, mind-body approaches (e.g., relaxation), and general exercise for strength, flexibility, etc.[70] Research suggests this program, and those similar to it, can lead to improved pain and health behaviors, self-efficacy, and overall health.[67,71] Effect sizes are modest however, and the research is limited by inattention to underlying theoretical frameworks that align individuals' specific BP related needs with appropriate program elements; further, there has been a lack of consideration of key issues which may contribute to health disparities such as affordability, practicality, acceptability, safety, and equity.[38,67,71,72] A major limitation of the existing research of multi-modality CIH self-management programs is that most of the study populations have been mainly female, White, highly educated, with good self-reported health[67,71] and thus of questionable generalizability to PEHD.

Overcoming Barriers to BP CIH Self-Management. The impact of self-management programs on reducing disparities for pain, including BP, has rarely been addressed[73,74] and much of the CIH self-management research has under-represented individuals who are socio-economically disadvantaged or have a race and ethnicity other than non-Hispanic White.[71,75] There are a range of socioeconomic barriers that prevent individuals with BP-PEHD from receiving and engaging in CIH self-management programs. This includes geography, cost, insurance, time, and other factors.[76-79] Further, there are additional barriers to engaging PEHD in research including fear, distrust, and poorly developed relationships between researchers and communities.[80-82] All of these hurdles, if not addressed, lead to continued unequal access to BP care among marginalized groups, perpetuating health disparities.[73]

Community Based Programs which exist outside the costly and overburdened health care system have the opportunity to overcome many of these barriers, especially if they include delivery formats that are feasible for community organizations to sustain. For example, programs focused on other chronic diseases, like the Diabetes Prevention Program, have demonstrated promise in having lay facilitators implement standardized group programs in community-based settings, including YMCAs.[83] Recent work by the investigators has also demonstrated it is feasible to deliver self-management programs in person or via telehealth (e.g., videoconferencing) with staff facilitators in YMCA and non-clinical VA settings (R33AT00911, NH170001). There is still much work to be done however, including greater community stakeholder involvement - earlier, more frequently, and more collaboratively - throughout the research process,[80] especially in the BP and CIH fields.[10,84] Such efforts, including needs assessment, attention to cultural tailoring, and involvement of community facilitators, have shown promise for improving BP knowledge, self-management skills, and general health.[74] This is consistent with what is advocated in the community engagement research fields[80] and warrants greater attention in future CIH self-management research for BP-PEHD.[10,84,85]

6 STUDY OBJECTIVES

Our broad long-term objective is to bolster the widespread implementation of evidence based CIH approaches for individuals with back pain from populations that experience health disparities (BP-PEHD). The project utilizes mixed methods and will occur over two phases (R61/R33, see Figure 1).

6.1 R61 AIMS & TRANSITION MILESTONES

Phase I (R61). We will conduct the necessary planning and preparations leading to a randomized feasibility study including co-development and assessment of Partners4Pain, a self-management program comprised of evidence based CIH approaches (e.g., pain education, mindfulness, cognitive behavioral/pain coping strategies, back specific exercise) and Keys to Wellbeing (e.g., general health education and exercise).

R61 Aim 1. We will use mixed methods data collection from multiple levels of stakeholders to assess barriers and facilitators to participating in BP self-management and community supported programs. This data collection will augment the existing literature and the results of previous and ongoing studies by the investigators.

R61 Aim 2. Based on information gathered in R61 Aim 1, we will perform participatory intervention mapping to co-develop a community supported CIH self-management intervention program (and control) for BP-PEHD.
R61 Aim 3. We will conduct a feasibility study (n=30 to 60) to assess essential **scientific and feasibility milestones** including:

a. Finalizing and securing agreements and regulatory approvals (IRB, NCCIH, IMC) for all required protocols and plans (e.g., clinical protocol, Data Safety and Monitoring Plan, Study Accrual and Retention Plan, etc.)
b. Recruiting and enrolling individuals with BP-PEHD and measuring recruitment and enrollment rates
c. Delivering experimental and control interventions and measuring intervention adherence and fidelity rates
d. Data collection by assessing follow up rates of future trial outcome measures as well as the usability and functionality of data collection systems
e. Stakeholder views of barriers and facilitators to the above, including affordability, practicality, effectiveness, acceptability, safety, and equity and other factors that could affect the future full scale trial's success

The following specific transition **milestones** have been approved by the funder (NCCIH).

- Demonstrate the ability to recruit and retain subjects in the clinical study as follows:
  - Randomize at least 30 participants
  - 75% or more of randomized participants are from NIH-defined racial/ethnic health disparity groups
  - 80% or more of randomized participants are retained for primary outcome measurement at the end of the R61 study (2 month follow up) regardless of adherence to the intervention
- Demonstrate that the delivery of the *intervention(s) and the control intervention(s)* under study can be delivered consistently, as defined by:
  - 85% or more of randomized participants engage in 1 or more sessions
  - 75% or more of randomized participants engage in at least 6 of 9 sessions
- Demonstrate the safety and tolerability of *the intervention(s)* used in the study by:
  - 5% or less of randomized participants experience a severe or serious adverse event related to the intervention(s)
  - 75% or more of randomized participants attend at least 6 of 9 sessions
  - 75% or more of randomized participants are satisfied with assigned program
- Demonstrate the fidelity of *the intervention(s)* used in the study by:
  - Program facilitators deliver 90% of session activities 90% of the time
- Demonstrate the ability to collect study data by:
  - 80% or more of randomized participants complete follow up at 2 months (end of the R61 study)
- Prior to submission of the written R33 transition request, submit R33 clinical study protocols and Data and Safety Monitoring Plan to NCCIH for review and approval
  - Submit the R33 clinical DSMP and SARP by the end of month 20
  - Submit a written R33 Transition Request by the end of month 21

All the above milestones must be reached before requesting transition to the R33 phase.

6.2 R33 AIMS

Phase II (R33). Upon approval by the funder of transition milestones (see above), we will conduct a full-scale multi-level randomized hybrid effectiveness implementation trial (n=376) of the community supported CIH self-management program, Partners4Pain, compared to the active control, Keys to Wellbeing, both of which will have been optimized and feasibility tested in Phase I.

R33 AIM 1. To assess the relative effectiveness of Partners4Pain versus Keys to Wellbeing in terms of:
a. Primary effectiveness outcomes of pain intensity and interference over 6 months using bi-monthly assessments
b. Secondary effectiveness outcomes of pain impact, self-efficacy and other HEAL outcomes.
R33 AIM 2. To assess the impact of health disparity factors on the effectiveness of Partners4Pain for primary and secondary outcomes through subgroup analyses which account for potential complexities between disparity factors
R33 AIM 3. To describe important disparity mitigating and implementation related measures that can impact and inform sustained translation of the program with community partner organizations

7 RISK/BENEFIT ASSESSMENT

7.1 OVERVIEW OF RISK/BENEFIT

The risks differ across study phases and aims; these are summarized in Table 2 and Section 7.3.

Table 2. Risks According to Study Phase and Aims

Study Phase (Aims)	Approach (Population)	Risks	Risk Level
Phase I (R61 Aims 1, 2)	Quality Improvement Activities (Community Stakeholders)	Breach of Confidentiality	Minimal
Phase I (R61 Aim 3)	Randomized Pilot Study (Study Participants with Back Pain)	Breach of Confidentiality Completing Health Surveys Group Based Behavioral Interventions Natural History of Pain	Low
Phase II (R33 Aims 1-3)	Randomized Hybrid Effectiveness-Implementation Trial (Study Participants with Back Pain)	Breach of Confidentiality Completing Health Surveys Group Based Behavioral Interventions Natural History of Pain	Low
Phase II (R33 Aim 3)	Quality Improvement Activities (Community Stakeholders)	Breach of Confidentiality	Minimal

7.2 BENEFITS

7.2.1 QUALITY IMPROVEMENT ACTIVITIES (R61/R33)

The benefits to stakeholders taking part in the Quality Improvement Activities (R61, R33) include experiencing satisfaction in contributing views and opinions that may help individuals with BP-PEHD.

7.2.2 RANDOMIZED PILOT STUDY (R61) & RANDOMIZED TRIAL (R33)

The benefits to participants of the Randomized Pilot Study (R61) and Randomized Trial (R33) include:

- Learning new information about pain and ways to take care of it
- Learning new information about overall health and wellbeing
- Experiencing health benefits, including decreased stress and increased wellbeing
- Experiencing improvement in pain symptoms
- Experiencing improvement in the ability to do daily activities

7.3 RISKS

7.3.1 QUALITY IMPROVEMENT ACTIVITIES (R61, R33)

The risks to stakeholders taking part in the Quality Improvement Activities (R61, R33) are considered minimal.

- **Breach of Confidentiality.**
  - New information will be gathered from stakeholders regarding their views and opinions about the study interventions and approaches. This information is not anticipated to place individuals at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.
  - **Secondary research data** will also be used, including non-identifiable data from previous IRB approved studies**.**

7.3.2 RANDOMIZED PILOT STUDY (R61) & RANDOMIZED TRIAL (R33)

The risks to participants of the Randomized Pilot Study (R61) and Randomized Trial (R33) are considered low.

- **Breach of Confidentiality.**
  - New information will be gathered from participants and is not anticipated to place individuals at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.
- **Completing Health Surveys.** Participants will be asked to complete health surveys as part of the screening and follow up data collection; they may feel uncomfortable answering questions they feel are too personal.
- **Taking Part in Group Based Behavioral Interventions.** Participants will be asked to take part in group behavioral interventions (via Zoom or in-person); the interventions are not physically

invasive, embarrassing, or offensive, and not expected to have adverse lasting impact. Some participants may experience some anxiety or nervousness when participating in group activities.

- **Partners4Pain (Experimental Intervention).** Risks associated with the experimental behavioral intervention may occur in program sessions and practicing on one's own. Expected risks are mild short-lasting physical discomfort (e.g., muscle and joint soreness) as a result of performing short periods of back-specific and general exercises (~5-15 minutes); participants might also feel emotional when doing the brief mind-body practices (~5 minutes) which include mindfulness and behavioral coping strategies (e.g., relaxed breathing, guided imagery, progressive muscle relaxation).
- **Keys to Wellbeing (active control intervention).** Risks associated with the active control intervention may occur in program sessions and practicing on one's own. Expected risks are mild short-lasting physical discomfort (e.g., muscle and joint soreness) as a result of performing short periods of general exercises; participants might also feel emotional when doing the brief workbook exercises (~5 minutes) that ask them to reflect on different areas of their health and wellbeing.

- **Natural History of Pain**. People with back and neck pain that is chronic in nature often experience fluctuations in pain severity, location, character, and quality; such fluctuations may be study related (e.g., due to engaging in exercises) or unrelated (e.g., aggravated by lifting at work or home).

7.4 RISK MITIGATION

The following describes how risks will be minimized.

- **Breach of Confidentiality:** All staff will complete UMN required training on HIPAA, data safety, and the Responsible Conduct of Research prior to working on the project. Data will be stored and accessed following UMN policies for data privacy and confidentiality (SEE SECTION 16.3). Identifiable data will be stored on password protected and HIPAA compliant databases and will only be accessed using HST (Health Sciences Technology) issued and maintained computers. All identifiable data will be removed from datasets used for analysis and all published reports will be summary in nature with no identifiable information for individual participants. Secondary research data from completed and ongoing studies will be limited to summarized findings from reports without identifiable information for individual participants.
- **Completing Health Surveys:** We will provide an explanation for why we are asking questions that may be considered personal and allow participants the ability to not answer any question they don't feel comfortable answering.
- **Taking Part in Group Based Behavioral Interventions:** The behavioral interventions include activities and exercises that are suitable for a range of abilities and preferences. Participants will also have the ability to refrain from participating in activities that feel uncomfortable. Program facilitators will be trained and certified by investigators and monitored for fidelity to ensure they are implementing the interventions in a manner that optimizes patient safety. This will include how to monitor for potential emotional or physical discomfort during session activities and how to implement safety protocols if needed. All participants will be encouraged to contact the project coordinator or an investigator regarding any side effects or adverse events that occur. Participants who experience a potential adverse event will be contacted by a study team member to ensure safety protocols are followed and gather information for adverse event

reporting. Adverse events impacting participant safety may result in withdrawal from the study intervention.

- **Natural History of Pain:** We will provide information to participants about the natural history of pain and how to manage fluctuations. They will also be encouraged to contact their healthcare provider regarding exacerbations in pain they find troubling or hard to manage. Participants will have no restrictions on the care they can receive for their back or neck pain.

8 STUDY DESIGN

8.1 OVERALL DESIGN

This is a two-phase project (see Figure 1).

Phase I (R61) includes mixed methods quality improvement activities and a randomized pilot study. **Phase II (R33)** includes a mixed methods randomized hybrid effectiveness-implementation trial and mixed methods quality improvement activities.

8.2 STUDY RATIONALE

Rationale for Community Engaged Approach:
There are several barriers to participating in research that have been identified in our own and others' work, especially among those from PEHD.[82,86-89] This includes distrust in researchers and the research process, lack of awareness and knowledge of research, and logistical obstacles including time, location, and others.[82,90] Further, while there is evidence to support several CIH self-management approaches for BP, the research to date has rarely taken the needs and preferences of individuals with BP-PEHD into account.[26,91-93] Thus, an important aspect of this project is to use an iterative community engaged and participatory research approach to gather views and opinions from multiple levels of community stakeholders through mixed methods quality improvement processes. This will provide more specific information regarding the needs of individuals with BP-PEHD than what is currently available in the literature and will provide an opportunity to co-develop solutions which is a critical aspect of community engaged research.[80]

Rationale for Experimental Intervention: The Partners4Pain program was chosen as the experimental intervention based on the literature supporting the effectiveness and safety of the individual CIH self-management approaches (see Table 1) of which it is comprised. There has been very little research to date that has investigated the combination of evidence-based CIH approaches, especially in community-based settings and for individuals with BP-PEHD. As a consequence, it is important to assess the feasibility of a combined CIH intervention; the extent to which it meets participants' needs can be implemented within community partner organizations in a fashion that facilitates long term adoption.

Rationale for Control Intervention: The Keys to Wellbeing program controls for contextual factors including time, attention, delivery format, and intervention materials (workbooks, videos). The rationale for the choice of comparison intervention is based on feedback from community partners and our Community Advisory Team. They have expressed a desire for interventions that are useful to participants (versus a no-treatment control), especially given the distrust in research among individuals

with BP-PEHD, noted above. Previous studies conducted by our group have also found the Keys to Wellbeing Program to be satisfying to participants and something they are willing to engage in. We have also observed differences in outcomes between the Keys control intervention and other CIH experimental intervention. We have not assessed it however in populations with BP-PHED. Thus, it is important to assess the feasibility of the control intervention in individuals with BP-PEHD.

8.3 UNDERLYING MODELS & FRAMEWORKS

Engaging communities in CIH research for BP is inherently complex and requires established models and frameworks to guide the work.[24,30,94] Our team has developed a comprehensive conceptual approach for the proposed project based on insights from our community partners, experience of the investigators, and the scientific literature (see Introduction). It is informed by complementary models appropriate for addressing the project goal of developing and implementing evidence based CIH interventions to mitigate BP related health disparities (see Table 3).

Table 3. Models and Frameworks Used in Project

Framework or Model	Rationale for use	Application in Project
RE-AIM Framework[95]	Provides overarching guidance for ensuring relevant contextual factors that can impact study implementation and translation, are considered throughout the project lifespan	Shapes 'quality improvement activities' and 'disparity mitigating' measures of reach, effectiveness, adoption, implementation and maintenance; informs 'quality improvement analyses'
ConNECT Framework[80]	Ensures greater and sustained consideration to how the researchers work with communities who experience health disparities. Includes guiding attention to social contexts; fostering norms of inclusion; ensuring equitable diffusion of innovations; harnessing communication technology; and prioritizing community engagement training for study team members	Shapes conduct of entire project and informs 'quality improvement analyses'
Dynamic Biopsychosocial Model[96]	Facilitates consideration of the complex reciprocal interactions between the evolving biopsychological person with BP and their external, social environment. This is essential for providing insights into pain sufferers' whole-person needs, and BPS risk and protective factors that may serve as barriers and facilitators to BP-PEHD engagement in self-management[72]	Informs the design/development of the intervention and choice of outcome measures; informs 'quality improvement analyses'
COM-B model[72]	A comprehensive behavioral model that provides guidance for assessing and addressing an individual's capability, opportunity, and motivational needs to achieve desired	Informs the 'quality improvement analyses' that help identify individuals' needs; informs the design/

	behavioral outcomes; considers affordability, practicality, effectiveness/cost-effectiveness, acceptability, safety, and equity	development of intervention by matching needs to specific intervention strategies

9 STUDY POPULATION

9.1 STUDY POPULATION DEFINITIONS

Community engaged research and implementation designs require **multiple levels of participation** in a range of study activities (see Figure 1). Study population definitions are summarized below in Table 4.

Table 4. Study Population Definitions and Nature of Participation

Population	Definition	Nature of Participation (e.g. Study Activity, Aim)
Community Stakeholders	Individuals from local communities whose participation is limited to sharing views and opinions of barriers/facilitators to interventions, study approaches INCLUDE: **Community Members**: Individuals from populations who experience health disparities (PEHD) who have experiences dealing with pain themselves or helping others in pain who are from PEHD (e.g., caregivers, clinicians, etc.) **Community Facilitators:** Individuals who currently facilitate or could facilitate similar intervention programs as to what is being examined in the project **Community Partner Organization Leadership**: Individuals in leadership positions at Community Partner Organizations (YMCA of the North, YWCA St. Paul, Hue-MAN Partnership)	R61 Quality Improvement Activities (Aims 1-3) R33 Quality Improvement Activities (Aim 3)
Study Participants	Individuals with back pain from populations who experience health disparities (BP-PEHD) and meet inclusion criteria for Randomized Pilot Study (R61) or future Randomized Hybrid Effectiveness-Implementation Trial	R61 Randomized Pilot Study (Aim 3) R33 Randomized Hybrid Effectiveness Trial (Aims 1-3)

9.2 INCLUSION CRITERIA

The following inclusion criteria apply to the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial.

1. Provide a signed and dated informed consent form
2. State willingness to comply with all study procedures outlined in the consent form
3. Be 18 years of age or older
4. Have self-reported chronic back pain (defined as pain in the low or mid back, or neck pain) which has lasted for 3 months or longer
5. Have a score of 3 or higher on the self-reported Pain, Enjoyment of Life and General Activity (PEG) scale (0 to 10)
6. Be a member of one or more of the following NIH-designated health disparity populations:*
    a. American Indian/Alaska Native
    b. Asian
    c. Black/African American
    d. Hispanic/Latino
    e. Native Hawaiian/Pacific Islanders
    f. Socioeconomically disadvantaged (annual household income less than $50,000)

*This project focuses on back pain in populations that experience health disparities (BP-PEHD). These populations are underrepresented in research studies, have less access to resources for the management of back pain, and have poorer outcomes (see Section 5, Introduction). The study is offered in English, but supplementary materials are available in Spanish for individuals where English is a second language. Supplementary materials may also be offered in other languages.

9.3 EXCLUSION CRITERIA

The following exclusion criteria apply to the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial.

1. Hospitalization for severe mental illness in past six months because the mindfulness and behavioral mind-body practices (e.g., meditation, progressive muscle relaxation, etc.) in the experimental intervention may aggravate symptoms of severe mental illness
2. Active psychotic symptoms, suicidal ideation, or manic episodes in the past three months for the same reasons noted in #1
3. Self-reported cancer with active treatment involving radiation or chemotherapy due to the potential for complications of their back or neck pain and impact on health outcomes
4. Dementia – Mini Mental State Exam score of 23 or lower for those with suspicion of cognitive impairment due to safety risks (e.g., not being able to follow directions for safe physical exercise)
5. Self-reported pregnancy due to the fact that back pain is often associated with pregnancy and differs from non-pregnancy related back pain and thus might have different impacts on health outcomes
6. Children under the age of 18*

*Children under the age of 18 will be excluded from the proposed project consistent with NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects (http://grants.nih.gov/grants/guide/notice-files/not98-024.html). A separate age-appropriate study for children is preferable for several reasons. Most importantly, the self-management education programs are directed toward adults, with content, activities, and exercises that may not be suitable for children. Further, interventions are provided in group settings with facilitated discussions geared towards

challenges faced by adults with back pain. Adapting both the experimental and control interventions for children would require substantial modification, so much so that a separate study is warranted. In addition, many of the biopsychosocial outcome measures proposed for the project were developed specifically for adult populations and have unknown validity or reliability in younger populations.

9.4 RECRUITMENT & RETENTION

Potential Community Stakeholders for the R61 and R33 Quality Improvement Activities will be identified through the routine communication channels of our Community Partnership Organizations (e.g., system-wide emails, newsletters, organizational meetings, presentations, etc.).

Study Participants (See Section 9.1 Study Population Definitions) for the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial will be identified as described below.

9.4.1 RECRUITMENT PROCESS

A range of recruitment strategies will be used to recruit Study Participants; these will be initiated approximately 3-6 months prior to screening activities and will continue until enrollment is complete. These include:

- Dissemination of print and digital recruitment materials via routine communication channels (emails, newsletters, etc.) through our Community Partner Organizations and other Community Members
- Giving study and health related presentations in the community to raise awareness about the study
- Participating in local community events (e.g., health fairs) where dissemination of recruitment materials is encouraged
- Using paid advertising (e.g., digital, print, and radio ads) in local media outlets with reach to PEHD
- Listing study on ResearchMatch, an electronic volunteer recruitment registry
- Distributing print and digital flyers and post-cards on UMN campuses and in the community
- Including information about the study in UMN affiliated newsletters (e.g., The Center for Spirituality & Healing, Office of Public Engagement, the Urban Research and Outreach-Engagement Center (UROC), etc.)
- Posting information about the study on UMN affiliated social media (e.g., The Center for Spirituality & Healing and UROC Facebook and Twitter accounts) and websites (e.g., the School of Nursing, the Center for Spirituality & Healing, as well as a unique study landing page)
- Sharing information about the study with other study investigators who have mechanisms in place to query individuals during the consent process regarding their interest in being contacted about additional studies

9.4.2 SOURCE & IDENTIFICATION OF POTENTIAL PARTICIPANTS

Potential Study Participants will self-identify by responding to recruitment strategies and materials within the general public. We will NOT access private/protected records (e.g., electronic medical records) to identify potential participants.

9.4.3 RECRUITMENT MATERIALS

Recruitment materials will include emails, newsletter study summaries, digital and print media advertisements, radio advertisements, ResearchMatch study description, print and digital flyers, print post cards, social media posts and advertisements, and a website. Copies of these materials will be submitted in ETHOS for approval prior to their use.

9.4.4 PAYMENT

Study Participants in the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial will be provided compensation for their time participating in research activities using a pre-paid debit card called Greenphire ClinCard. Study participants will be compensated for the following study activities:

- $20 for each baseline screening visit attended ($40 total)
- $30 for each of the educational program sessions attended ($270 total)
- $20 for each follow-up assessment completed ($20 total in R61; $60 total in R33)

Total potential compensation for study participants will be $330 during the R61 and $370 during the R33.

Community Stakeholders participating in formal interviews and focus groups will be compensated $30 per event. Community stakeholders named as consultants for the project will be compensated using agreed upon consultancy fees and processes.

9.4.5 RETENTION STRATEGIES

There are many well-recognized barriers to research participation overall including inconvenience, time commitment, geographic location, etc. The investigators have decades of experience successfully addressing these challenges. We will implement the following strategies used in previous studies to facilitate study participant engagement in the interventions and data collection:

- Research staff will routinely track all study visits/time points per participant (screening and intervention session, follow-up) and will work closely with the Community Facilitators and Community Coordinators to devise timely solutions for mitigating retention issues.
- We will offer a range of program session times to accommodate participants' needs; this includes early mornings, day, and evenings. Saturday appointments are also an option, as needed. Programs will be offered in different formats (in-person, videoconference) with our host Community Partner Organizations to accommodate participant preferences and needs.
- If participants need to miss a program session, they will be able to view intervention session educational and skill videos by accessing the study website.
- All participants will be provided reminders of their study related visits.
- Participants will be provided detailed instructions on how to find Community Partner Organization sites for in-person visits; transportation instructions including bus, train, and

interstate routes will be included. Free, easily accessible parking will be made available to study participants.

- Transportation services to and from study visits will be provided to participants, as needed, using Transportation Plus, a Twin Cities based company. The study team will arrange taxi services for the participant. Prior to initiating the ride, participants will provide verbal consent to have their contact information (e.g., name, address, phone number) shared with Transportation Plus. Verbal consent will be captured in the study record. Transportation is paid for by the study; participants will not incur out of pocket costs.
- Participants will receive regular reminders (automated via text, email, or other methods depending on participant preference) to complete self-report questionnaires (SRQs). Study staff will closely monitor completion and contact participants if not completed within designated time frames.
- During screening, study staff will provide a detailed description of the study, including what participants can expect with respect to the commitment necessary to preserve the integrity of the project prior to enrollment. Participants will be given as much time as needed to decide if they want to participate.
- The research team will use patient-centered communication to foster trusting relationships between the study staff and participants. If challenges arise with participants, the study team (e.g., study coordinators) will talk openly with participants about these challenges, without pressure. Further, study staff will make efforts to keep in touch with study participants using participants' preferred contact (e.g., email, phone call), especially after completion of the 9-week intervention phase, to facilitate follow up.

9.4.6 STRATEGIES FOR ADRESSING BARRIERS TO RECRUITMENT & RETENTION OF POPULATIONS WHO EXPERIENCE HEALTH DISPARITIES (PEHD)

- To improve researchers' cultural competency, the research team are provided dedicated professional time to engage in ongoing professional development with Community Partner Organizations, including the YMCA of the North's Equity Innovation Center.
- To address the mistrust individuals from PEHD may have in the research process, we will:
    - Work with Community Partner Organizations and Community Champions to serve as trusted messengers to raise awareness about the project
    - Continue to encourage and support ongoing research staff participation in community volunteer activities and events
    - Hire Community Coordinators in consultation with our Community Partner Organizations to facilitate interfacing with community members
    - Work with an established Community Advisory Team which is guided by a Team Charter, with clearly defined roles and processes for collaborative decision making
    - Provide equitable compensation for Community Advisory Team Members, Community Consultants, Community Coordinators, Community Stakeholders, and Study Participants
- To address logistical issues, including access to technology, we will work with Community Partner Organizations to conduct study activities at sites located in and/or easily accessible to communities of color and lower socioeconomic status. In addition, we will provide access to transportation services for study participants to attend study visits.

- To address the need to be responsive to community needs, we will involve Community Stakeholders, the Community Advisory Team, and our Community Partner Organizations across the research process.

10 ENROLLMENT PROCEDURES

10.1 NUMBER OF STUDY PARTICIPANTS

A total of 30-60 individuals will be enrolled for the R61 Randomized Pilot Study; 376 will be enrolled for the R33 Randomized Hybrid Effectiveness-Implementation Trial.

10.2 SCREENING & ENROLLMENT

Screening and enrollment for the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial will take place over three events. Potential participants will be initially screened for basic eligibility criteria using a web-based survey that can be completed online or over the phone with study staff. Interested and eligible individuals will be invited to a baseline 1 screening visit which will occur face-to-face either in person or using videoconferencing technology. Participants who are eligible will attend a baseline 2 screening visit conducted either face-to-face or over the phone. Eligible participants will be enrolled in the study at the conclusion of baseline 2 (also see Schedule of Assessments and Sections 13.1 to 13.4 for specific details regarding activities at each visit).

10.3 RANDOMIZATION & BLINDING

Eligible individuals will be enrolled and randomized using blocked randomization (with varying block sizes) following stratification for session offerings (e.g., Summer 2023 - Saturday mornings). Computer generated random treatment assignments will be prepared by the independent study statistician and conveyed electronically through REDCap (the electronic study database) at the time of enrollment to preserve allocation concealment. All study staff responsible for screening and enrollment procedures will be blinded to upcoming treatment assignments. The Co-PIs, select Co-Investigators, and the study statistician will be blinded until the study database is locked for analysis. The Co-PIs are authorized to be unblinded when needed for safety-related processes (e.g., decisions to withdraw participants from the intervention following adverse events).

11 INTERVENTIONS

11.1 INTERVENTION OVERVIEW

Both the experimental (Partners4Pain) and active control (Keys to Wellbeing) interventions will be informed by the work conducted in R61 Aims 1 and 2 and research done previously by the investigators (R33AT009110, NH170001, UH3AT008769, R34AT011209).[1-10] The Template for Intervention Description and Replication (TIDieR) checklist has been and will continue to be used to guide the description of the study interventions[97] to facilitate future results interpretation, as well as dissemination and replication. Consistent with the RE-AIM and ConNECT frameworks guiding this project, we anticipate the interventions will be further shaped and adapted based on stakeholder feedback to meet the needs of

community stakeholders and those with BP-PEHD, based on information gathered in R61 Aims 1 and 2.[80,95,98] Elements common to the experimental and control interventions are detailed in Table 5. The investigators have safely and successfully implemented similar group intervention formats in previous studies. Engagement in sessions has been robust (83-92% across in-person and videoconference delivery formats) and no serious adverse events attributable to the interventions have been recorded (n=>500 participants across studies, R33AT009110, NH170001).

Table 5. TIDieR Intervention Elements Common to Both Groups

Intervention Specific Participant Resources	Materials and resources that support specific intervention content (see descriptions for Partners4Pain and Keys to Wellbeing). Includes print and electronic workbooks; access to education and skill training videos via a website for viewing in multiple formats (e.g., cell phone, computer tablet, etc.)
Facilitator Materials	Print and electronic manual with session checklists and safety protocols; Google Slide session presentations with embedded expert-led educational and skill training videos; technology and related peripherals (e.g., headsets) as needed
Facilitator Training	Community Facilitators from our Community Partner Organizations with experience leading group programs; 30 hours of competency-based training by the study investigators and Community Facilitators from previous studies
Procedures	Facilitator-led group sessions; includes viewing of expert-narrated videos specific to each intervention's content, workbook reflection activities, and facilitator-led group discussions Participants are encouraged to practice in between sessions using the provided intervention-specific resources (e.g., workbooks, videos, etc.).
Delivery Format	Sessions offered in-person, via videoconference, or hybrid depending on community partner organization and participant needs. Group sessions with 7-16 participants per group
Location	See participating locations listed in section 4.3
Timing, Schedule	One session per week for 9 weeks 90 minutes per session Similar to other educational programs offered in community partner organizations.
Tailoring	Participants will be encouraged to practice at home, focusing on intervention specific content that meets their needs
Fidelity	10% of the interventions will be monitored by study investigators, either in-person or remotely using a fidelity checklist which will assess completion of required session activities; review of weekly session facilitator documentation in REDCap regarding ability to deliver session activities as planned, including rationale for activities not completed

11.2 EXPERIMENTAL INTERVENTION (PARTNERS4PAIN)

Partners4Pain is informed by the COM-B model for behavioral interventions; it postulates that to achieve desired behavioral outcomes (e.g., engagement in positive self-management behaviors such as increased activity, decreased medication use, etc.), interventions must address an individual's capability, opportunity, and motivational related needs.[72] Application of the COM-B model provides guidance for assessing and addressing needs more specifically (e.g., what knowledge, skills, and resources are needed?) and mapping these to evidence based intervention solutions and formats that are most likely to meet the desired outcomes. Importantly, the COM-B model considers affordability, practicality, effectiveness/cost-effectiveness, acceptability, safety, and equity - all critical considerations for implementation and translation of an intervention over the longer term, particularly for populations experiencing health disparities.[99]

Partners4Pain aims to impact pain and behavioral outcomes by addressing BP-PEHD needs for effective pain self-management behaviors. Content unique to Partners4 Pain includes education, skills training, and support in evidence based CIH strategies, (e.g., pain education; BP specific mobility, strength, and stabilization exercises; mindful movement and meditation; progressive muscle relaxation, guided imagery, etc.) augmented by evidence and theory based behavior change techniques (e.g., action planning, problem solving, graded tasks, social support, etc.) which will be built into the program.[72,100] An important feature of the program will be to provide individuals with resources and support that will empower them to identify what they need (e.g., more information, specific exercises, more or less support from others, etc.) and how to choose which resources are appropriate for them. This approach to self-management is currently being used by the investigators in ongoing studies (R33AT009110, NH170001, UH3AT008769, R34AT011209).

11.3 CONTROL INTERVENTION (KEYS TO WELLBEING)

Keys to Wellbeing is a credible, active comparison for the experimental intervention and will control for contextual factors between groups (See Table 5). It will do so by aiming to impact general health related outcomes by primarily addressing BP-PEHD related capability needs, specifically general knowledge and awareness of health and wellbeing. Topics will include information and tips including keeping socially connected, finding meaning and purpose, sorting health facts from fiction, addressing mental health, and keeping physically fit. This intervention was developed to serve as an active comparison for another CIH self-management study focused on mindfulness (R33AT009110). Adherence and satisfaction rates have been 89% and 79% respectively, indicating its robustness as a credible control.

11.4 INTERVENTION FIDELITY

Intervention fidelity will be assessed by study investigators using fidelity instruments that address whether content elements of intervention sessions were delivered along with facilitator competencies for intervention delivery. At least 10% of the sessions will be assessed either in person or via videoconference. We will use adapted fidelity instruments used in previous studies. Fidelity of intervention delivery will also be assessed by review of session checklists completed by the facilitators.

11.5 INTERVENTION ADHERENCE

Adherence to the experimental and active control interventions is defined as attending six or more of the nine total sessions. During each session, the intervention facilitators will document participant attendance including a checklist of activities covered during the session. Participation in at least 70% of session activities is considered sufficient for attendance. Engagement and satisfaction with study interventions will be queried during the month two assessment.

11.6 CONCOMITANT THERAPY

Participants may continue to use self-management strategies (e.g., over-the-counter medications, exercise) or provider-based interventions such as prescription medications or complementary and integrative therapies (e.g., acupuncture, manual therapy) for the duration of the study. Use of medications, self-management strategies, and provider-based therapies for pain will be assessed and documented in the baseline and follow up surveys.

11.7 RESCUE THERAPY

This project is assessing community-based self-management programs for spinal pain in populations that experience health disparities. Medical providers are not routinely available within community-based self-management programs, thus rescue medication therapy will not be provided by the study. Participants requiring evaluation and provider-based management for back pain will be referred to their health care provider.

12 INTERVENTION DISCONTINUATION & PARTICIPANT WITHDRAWAL

The following describes intervention discontinuation and study participant discontinuation/withdrawal for the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial.

12.1 DISCONTINUATION OF STUDY INTERVENTION

A study participant may discontinue from the experimental or active control interventions, but not from the study overall. In such cases, remaining study procedures will be completed as indicated by the study protocol. If a significant finding (e.g., development of an exclusion criterion) is identified after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new significant findings will be reported as an adverse event (AE).

All efforts will be taken to facilitate study participants' completion of the study interventions. However, participants may be discontinued from their assigned intervention if, for example:

- They develop an exclusion criterion (new or not previously recognized) that would make it unsafe for them to continue
- They exhibit significant study intervention non-compliance (e.g., disruptive or unsafe behavior)
- Any adverse event (AE), medical condition, or other situation occurs such that continued participation in the study would not be in the best interest of the participant

- New evidence emerges which suggests it is unsafe for the participant(s) to proceed with the study
- Participant withdraws consent to continue

The data to be collected at the time of study intervention discontinuation, and for the remainder of the study will include the following:

- Reason for intervention discontinuation and methods for determining the need to discontinue
- Number of completed intervention visits
- AE/SAE information, if indicated
- Self-report surveys will continue to be administered as scheduled, even though the participant has discontinued study interventions

12.2 PARTICIPANT WITHDRAWAL FROM STUDY

A study participant is free to withdraw from participation in the study at any time upon request. An investigator may also discontinue a participant from the study for reasons including, but not limited to, the following:

- Participant develops an exclusion criterion (new or not previously recognized) that would make it unsafe for them to continue
- Participant exhibits significant study intervention non-compliance (e.g., disruptive or unsafe behavior)
- Any adverse event (AE), medical condition, or other situation occurs such that continued participation in the study would not be in the best interest of the participant
- New evidence emerges which suggests it is unsafe for the participant(s) to proceed with the study
- A major change occurs in the participant's life (e.g., incarceration, death)
- Study closure by institute or oversight body
- Participant withdraws consent to continue

The reason for participant discontinuation or withdrawal from the study will be recorded on the Study Completion Case Report Form (CRF) in REDCap and participants will be notified. Subjects who sign the informed consent form and are randomized but do not receive the study intervention will not be replaced. Subjects who sign the informed consent form, are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will not be replaced.

12.3 LOST TO FOLLOW-UP

The R61 pilot study has one follow-up data collection assessment, so criteria for considering a participant lost to follow up to inform further data collection is not required.

For the R33 phase, a participant will be considered lost to follow-up if they fail to complete two consecutive follow up data collection assessments and study staff are unable to contact the participant after at least 3 phone calls (which will be documented in the study record). Further details on processes for enhancing study retention are provided in section 9.4.

13 STUDY ASSESSMENTS & PROCEDURES

The following describes study assessments and procedures for the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial.

13.1 SCHEDULE OF ASSESSMENTS

Table 6 details the schedule of assessments for Study Participants in the R61 Randomized Pilot Study and the R33 Randomized Hybrid Effectiveness-Implementation Trial.

*Table 6. Schedule of Assessments for Study Participants** (R61 Randomized Pilot Study and R33 Randomized Trial)*

	Initial Screen	BL1	BL2	Intervention Sessions 1-9	Month 2 (-21 to +28 days)	R33 Only	
						Month 4 (-21 to +28 days)	Month 6 (-21 to +28 days)
Flow Data for Feasibility Outcomes+							
Feasibility of recruitment, enrollment, intervention, and data collection rates	X	X	X	X	X		
Baseline Assessments							
PhenX toolkit: Demographics & Core SDH Measures	X	X	X				
Informed Consent	X	X	X				
Inclusion/Exclusion Criteria	X	X	X				
Randomization			X				
Intervention Assessments							
Intervention Attendance, Session Activities, Intervention Administration Form				X			
Effectiveness Measures*							
Pain intensity		X	X		X	X	X
Pain interference		X	X		X	X	X
Pain impact and frequency		X	X		X		X
Self-efficacy for managing chronic conditions			X		X	X	X
Domain specific life satisfaction			X		X	X	X
Physical functioning			X		X	X	X
Pain catastrophizing			X		X		X
Interoceptive awareness			X		X	X	X
Satisfaction/Improvement					X	X	X
Medication use (including opioids)			X		X	X	X
Participation in social roles			X		X		X
CIH self-management use			X		X	X	X
Healthcare use			X		X	X	X
Sleep disturbance/duration			X		X		X
Depression			X		X		X
Anxiety			X		X		X
Substance use			X		X		X
Implementation and Disparity Mitigating Measures (guided by RE-AIM, COM, ConNECT)							
Views and opinions related to barriers, facilitators to interventions and study participation (see Table 9, Study Participants for details)	X	X	X		X		
Satisfaction with and use of specific program activities					X	X	X
COM Assessment Survey					X		

	Initial Screen	BL1	BL2	Intervention Sessions 1-9	Month 2 (-21 to +28 days)	R33 Only	
						Month 4 (-21 to +28 days)	Month 6 (-21 to +28 days)
Supportive Environmental and Relational Alliance Survey					X		
Other Measures							
Adverse events/side effects				X	X	X	X
Study Completion Form					X (R61)		X (R33)
**Schedule of quality improvement data collection activities can be found in Table 9 *Effectiveness measures collected in R61 for purpose of assessing data collection feasibility only +Flow data is collected for the purposes of assessing feasibility areas for refinement in the R61 pilot study (including assessing RE-AIM factors)							

13.2 SCREENING ASSESSMENTS

13.2.1 INITIAL SCREEN

Potential participants will be initially screened for eligibility using direct electronic data entry in REDCap administered to the participant either through a web-based survey or a phone screen with trained study staff. Both processes will include an introduction to the study and participants will be required to provide verbal or electronic consent prior to providing information (See section 16.1). Participants will be asked a limited number of questions regarding basic eligibility criteria and demographics to ensure they qualify (e.g., age, race/ethnicity, history of chronic back or neck pain, pregnancy). Study staff will speak with eligible individuals to answer any questions they may have and schedule them for a first baseline screening visit.

13.2.2 BASELINE ONE SCREEN

The first baseline assessment will take place up to 90 days after the initial screen described above. This evaluation will be conducted face-to-face either in person or via videoconference and will included the following activities:

- Trained study staff will perform informed consent (see Consent Procedures in Section 16.1)
- The Folstein Mini-Mental Status Examination (MMSE) will be administered to participants if cognitive impairment is suspected (e.g., repeating questions, unable to respond to/follow basic instructions)
- Participants will complete a self-report web-based survey of questions to assess eligibility and collect baseline assessments for the following:
    - Demographic, occupational, and pain and health-related characteristics, including recommended common data elements for the study of pain[117,130]
    - Self-reported effectiveness and implementation outcome measures detailed in Table 6 (see section 14.2 for detail on individual measures)
- Staff will schedule Baseline Two screening visit

13.2.3 BASELINE TWO SCREEN

A second baseline assessment will take place up to 90 days after BL1. This evaluation may be conducted in-person, via videoconference, or by phone and will include the following activities:

- Trained study staff will confirm consent for participation (See Section 16.1)

- Participants will complete a brief self-report web-based survey to confirm eligibility for exclusion criteria that may have developed after the BL1 evaluation (e.g., pregnancy, cancer treatment)
- Participants will complete baseline assessment for self-reported outcome measures listed in Table 6 (see Section 14.2 for detail on individual measures) and the PhenX toolkit measure for discrimination in healthcare.[101]
- Eligible participants will be enrolled in the study and randomized to either the Partners4Pain or Keys to Wellbeing intervention program.

13.3 INTERVENTION SESSIONS

The group interventions will start within 28 days of randomization. Community Facilitators will document attendance and presence for activities covered during weekly intervention visits using an intervention administration form in REDCap.

13.4 FOLLOW-UP ASSESSMENTS

Follow up assessments of Effectiveness and Implementation/Disparity Mitigating Measures (see Table 6 Schedule of Assessments) will be completed 2 months after the group interventions begin for the R61 Randomized Pilot Study and 2, 4 and 6 months after the group interventions begin for the R33 Randomized Hybrid Effectiveness-Implementation Trial. Details on individual measures are provided in section 14.2.

13.5 ADVERSE EVENTS & SERIOUS ADVERSE EVENTS

13.5.1 DEFINITION OF ADVERSE EVENTS

An adverse event (AE) is any untoward medical occurrence in a subject during participation in the R61 Randomized Pilot Study, the R33 Hybrid Effectiveness-Implementation Trial, or with use of the interventions being studied. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, etc.), or any combination of these regardless of relationship to participation in the study. If there is any doubt as to whether an observation is an AE, the event will be recorded.

13.5.2 DEFINITION OF SERIOUS ADVERSE EVENTS

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect

An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize

the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

13.5.3 CLASSIFICATION OF AN ADVERSE EVENT

The following guidelines will be used to grade the severity of adverse events:

- Mild: no intervention required; no impact on activities of daily living (ADL)
- Moderate: minimal, local, or non-invasive intervention indicated; moderate impact on ADL
- Severe: significant symptoms requiring invasive intervention; subject seeks medical attention, needs major assistance with ADL
- Serious: results in death; life threatening; requires inpatient hospitalization; results in persistent or significant disability; congenital anomaly or birth defect.

13.5.4 RELATIONSHIP TO STUDY PROCEDURES

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by a PI, or designee, on temporal relationship. The degree of certainty about causality will be graded using the categories below (see Table 7).

Table 7. Relationship of Adverse Events to Study Procedures

Relatedness	Definition
Definitely Related	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study procedures administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study procedures should be clinically plausible. The event must be pharmacologically or phenomenologically definitive.
Probably Related	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study procedures, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal.
Potentially Related	There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of study procedures). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
Unlikely to be related	A clinical event, including an abnormal laboratory test result, whose temporal relationship to study procedures administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study procedures) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
Not Related	The AE is completely independent of study procedures administration, and/or evidence exists that the event is related to another etiology. There must be an alternative, definitive etiology documented.

13.5.5 EXPECTEDNESS

The PIs are responsible for determining whether an AE or SAE is expected or unexpected. An adverse event will be considered unexpected if the nature, severity, or frequency of the event is not consistent

with the risk information previously described for the intervention and/or study (e.g., risk information in the consent form, natural history of the condition).

13.5.6 TIME PERIOD & FREQUENCY FOR EVENT ASSESSMENT & FOLLOW-UP

The PI, or designee, will record all reportable events with start dates occurring any time after randomization until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. Study related AE/SAEs will be followed to stabilization/resolution.

13.5.7 ADVERSE EVENT & SERIOUS ADVERSE EVENT REPORTING

Reporting for adverse events, serious adverse events, and other expedited events is summarized in Table 8.

Table 8. Reporting for Adverse events, Serious adverse events, and Other events

Event	**Report to….**	**Reporting Time**
Serious AE or AE – unexpected and **at least probably related** to the research procedures.	UMN IRB	The IRB defines prompt reporting to be within **5 business days**. If an RNI is not filed within 5 business days, explain why the delay in reporting occurred and how prompt reporting will be ensured in the future.
Serious AE – unexpected and related to the intervention	NCCIH PO; IMC	**7 days**
Serious AE – anticipated or unrelated	NCCIH IMC IRB	AE(s) will be summarized in IMC reports. IMC reports will be distributed to the IMC and NCCIH per the guidelines in the IMC Charter and DSMP. IMC reports will be submitted to the IRB as an RNI within 5 business days of the IMC meeting minutes being signed or sent to IMC in lieu of a meeting.
Unexpected Death or life-threatening AE related to the intervention	NCCIH Program Officer, IMC	**3 days of the investigator becoming aware of the event**
Unexpected Death: Unexpected death of a locally enrolled participant whether considered **related to the research or not.** Death is considered unexpected if the risk of death is not listed in the consent form	UMN IRB	The IRB defines prompt reporting to be within **5 business days**. If an RNI is not filed within 5 business days, explain why the delay in reporting occurred, and how prompt reporting will be ensured in the future.
Risk: Information that indicates a new or increased risk, or a safety issue. For example: New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates	UMN IRB	The IRB defines prompt reporting to be within **5 business days**. If an RNI is not filed within 5 business days, explain why the delay in reporting occurred, and how prompt reporting will be ensured in the future.

an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk An adverse event that indicates a potential increase in risk or reduction in benefit (such as those that may prompt a change to the protocol or consent form) Protocol violation that harmed participants or others or that indicates participants or others might be at increased risk of harm Complaint of a participant that indicates participants or others might be at increased risk of harm or at risk of a new harm		
Confidentiality – unauthorized disclosure of confidential information	UMN IRB	The IRB defines prompt reporting to be within **5 business days**. If an RNI is not filed within 5 business days, explain why the delay in reporting occurred, and how prompt reporting will be ensured in the future.
PO: program officer; AE: adverse event; IRB: Institutional Review Board; UMN: University of Minnesota; RNI: Report of New Information; IMC: independent monitoring committee; NCCIH: National Center for Complementary and Integrative Health		

13.5.8 EVENTS OF SPECIAL INTEREST

Reporting of certain events is required by law (e.g., suspected child abuse, vulnerable adult abuse or neglect, excessive use of alcohol or use of controlled substances for non-medical reasons during pregnancy) and may be discovered during the study. If information becomes available that may require mandated reporting, study staff will contact the PIs or Project Coordinators (also see https://mn.gov/dhs/general-public/licensing/maltreatment-investigations/mandated-reporter-resources)

13.5.9 REPORTING OF PREGNANCY

Pregnancy, current or planned, at the point of enrollment is an exclusion criterion for the trial. Enrolled subjects who become pregnant may receive study interventions if there are no increased risks to the pregnant person or fetus. Approval will be sought from the IRB prior to intervention continuation. Such participants will be followed for the remainder of the study for outcome ascertainment. If treatment discontinuation is necessary, the reason for discontinuation will be reported in semi-annual reports to the Independent Monitoring Committee.

13.6 UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

13.6.1 UNANTICIPATED PROBLEMS REPORTING

The PI, or designee, will report Unanticipated Problems (UP) Involving Risks to Subjects or Others (UPIRTSOs) to the IRB within 5 business days of learning of the event. The UP report will include the following information.

- Protocol identifying information: protocol title and number, PI names, and the IRB project number
- A detailed description of the nature and severity of the event and the likely impact of the event on risk to study participants or others
- Date the event occurred; date the study team became aware of the information
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP
- A description of whether the information indicates a new or increased risk, or a safety issue
- A description of any changes to the informed consent documents and plans for notifying participants, if necessary

14 OUTCOMES

The choice of outcomes has been guided by:

- The RE-AIM Framework, to ensure future success of the trial and future long-term translation of the interventions
- The ConNECT Framework, to ensure Community Stakeholders are engaged earlier and more frequently in the research process
- The hybrid effectiveness-implementation trial design, to ensure simultaneous measures of effectiveness and implementation are captured
- The biopsychosocial model, to ensure biophysical, psychological, and social measures relevant to back pain in populations who experience health disparities are addressed
- Alignment with HEAL core and supplementary outcome measures

14.1 R61 OUTCOMES

The purpose of the R61 is to assess needs, optimize study intervention and approaches, and evaluate feasibility of the interventions and study approaches in preparation for the R33 Randomized Hybrid

Effectiveness Trial. This will be accomplished by gathering views and opinions, as well as flow data (see below).

14.1.1 VIEWS AND OPINIONS

Community Stakeholder and Study Participant views and opinions will be gathered and used to incorporate non-researcher views into the research process, and contribute to co-learning and co-development, which are important features of community engaged research. Data collection methods will include survey questions (closed- and open-ended), interviews, focus groups, field notes; secondary analyses of previous IRB approved qualitative data will also be used.

The schedule of data collection of Community Stakeholder and Study Participant views and opinions can be found in Table 9. This information will augment the investigators previous and ongoing research and the scientific literature.[10,82,89,90,102]

Table 9. Schedule of Quality Improvement Data Collection

	R61 Phase		R33 Phase	Entire Project
Project Population Level	Assess Needs; Optimize Interventions, Approaches (Pre-Pilot Study, Mixed Methods Quality Improve-ment Activities)	Evaluate Feasibility, Areas for Refinement (Randomized Pilot Study)	Evaluate Effectiveness and Impact of Health Disparities; Assess and Describe Implementation, Disparity Mitigating Factors (Randomized Hybrid Effectiveness-Implementation Trial)	Throughout Project, Time Independent (As they arise)
Community Stakeholders				
Views, opinions re: barriers and facilitators to pain management, self-management identification of capability, opportunity and motivational (COM, BPS), implementation (RE-AIM), and disparity mitigating needs (RE-AIM, ConNECT, COM-APEASE)	X			X
Views, opinions re: solutions to address needs identified above	X			X
Reactions, opinions re: resources and approaches for R61 Pilot Study (e.g., recruitment materials, workbooks, videos, etc.)	X			X
Views and opinions of R61 Pilot Study Results; ideas for optimizing interventions and study approaches for R33 Randomized Trial		X		X
Views and opinions of R33 Randomized Trial Results; ideas for addressing implementation and disparity mitigating needs to prepare for translation to community settings			X	X
Views/opinions re: intervention affordability, practicality, effectiveness, acceptability, safety, and equity; factors that will facilitate adoption, implementation, maintenance (RE-AIM, ConNECT) at community and organizational level			X	X
Study Participants				
Views/opinions re: barriers/facilitators to recruitment, enrollment; reach (RE-AIM)		X	X	

	R61 Phase		R33 Phase	Entire Project
Project Population Level	Assess Needs; Optimize Interventions, Approaches (Pre-Pilot Study, Mixed Methods Quality Improve-ment Activities)	Evaluate Feasibility, Areas for Refinement (Randomized Pilot Study)	Evaluate Effectiveness and Impact of Health Disparities; Assess and Describe Implementation, Disparity Mitigating Factors (Randomized Hybrid Effectiveness-Implementation Trial)	Throughout Project, Time Independent (As they arise)
Views/opinions re: extent to which program met capability, opportunity, motivational (COM) needs; facilitates implementation (RE-AIM)		X	X	
Views/opinions re: intervention affordability, practicality, effectiveness, acceptability, safety, and equity; factors that will facilitate adoption, implementation, maintenance (RE-AIM, ConNECT) at individual level		X	X	
Views/opinions re: ability of the study team to create supportive environment, develop relational alliances that motivate engagement (COM), are inclusive and culturally sensitive (ConNECT); factors that will facilitate adoption, implementation, maintenance at individual level		X	X	
COM=Capability, opportunity, motivation from the COM-B model; RE-AIM=Reach, Effectiveness, Adoption, Implementation, Maintenance as defined by the RE-AIM Framework				

14.1.2 FEASIBILITY OUTCOMES

We will evaluate feasibility outcomes as part of the R61 Randomized Pilot Study by measuring Study Participant flow data, including rates of recruitment, enrollment, intervention acceptability/credibility, intervention fidelity. In addition, as part of determining feasibility, the funder (NCCIH) has approved specific transition milestones that must be met prior to moving forward with the R33 Randomized Trial (see Section 6.1).

Feasibility measures include performance indicators for key study domains that will provide insight into the feasibility of conducting the future R33 Randomized Trial. They will also help us identify areas for refinement.

- **Recruitment feasibility** is an important measure of our ability to ***reach*** individuals with BP-PEHD. Feasibility and areas for refinement will be measured using flow data including the number of participants screened per month; percentage of screened participants from racial/ethnic minority groups; and percentage of screened participants who are socioeconomically disadvantaged. We will also measure the percentage of participants screened per month by recruitment method; percentage of screened participants from racial/ethnic minority groups by recruitment method; and percentage of screened participants who are socioeconomically disadvantaged by recruitment method.

- **Enrollment feasibility** is another important measure of our ability to ***reach*** individuals with BP-PEHD and ensure our study enrollment processes are not providing obstructions to participation. Enrollment feasibility will be measured using flow data including the number of participants enrolled per month; percentage of enrolled participants from racial/ethnic minority groups; percentage of enrolled participants who are socioeconomically disadvantaged. We will also measure the percentage of participants excluded by eligibility criterion; percentage of

participants declining participation; main reasons for declined participation; average time to enrollment from screening visits (e.g., initial screen, baseline 1).

- **Intervention acceptability and credibility feasibility** is an important measure of the potential for the interventions' (experimental and control) ***adoption and implementation***; this will be measured using flow data including the percentage of enrolled participants not attending any sessions; percentage of enrollees attending less than 6 of 9 sessions; percentage satisfied with interventions; and percentage reporting participation in home practice. We will also measure the percentage of enrolled participants withdrawing from interventions and reasons for withdrawal from interventions.

- **Intervention fidelity feasibility** is an important measure of the ability of Community Partner Organizations and Community Facilitators to be able to deliver the interventions as planned and ***adopt*** them over the long term. This will be measured by the percentage of required session activities delivered per session; percentage of intervention activities across intervention programs not performed by facilitator; and frequency of intervention activities not performed by facilitator.

- Data collection feasibility as well as the usability and functionality of our data collection systems are critical measures of our ability to assess the effectiveness and potential implementation of the interventions in the future R33 Randomized Trial. Data collection feasibility will be assessed by the percentage of enrollees completing the month 2 assessment; the percentage of missing variables by data collection instrument; reasons for missed assessments; and average duration of assessments (see also Table 6, Schedule of Assessments).

14.2 R33 RANDOMIZED HYBRID EFFECTIVENESS-IMPLEMENTATION TRIAL

The purpose of the R61 is to evaluate the effectiveness of the interventions and the impact of health disparities. Community Stakeholder and Study Participant views and opinions will also be gathered to facilitate translation of the interventions to community settings.

Data collection methods will include surveys, interviews, focus groups, field notes, and flow data (e.g., screening and enrollment rates, etc.). The assessment schedule is summarized in Table 6 and Table 9.

14.2.1 PRIMARY EFFECTIVENESS OUTCOME

For R33 Aim 1, we will evaluate the ***effectiveness*** the Partners4Pain and Keys to Wellbeing interventions using self-report surveys at 2, 4 and 6 months, measuring the primary outcome.

The primary outcome is pain intensity and interference with life enjoyment and general activity as measured by the Pain, Enjoyment of Life and General Activity (PEG) scale. The PEG is a brief three item scale derived from the Brief Pain Inventory that measures average pain intensity, interference with enjoyment of life, and interference with general activity in the past week. Each item is measured on a 0 (no pain/does not interfere) to 10 numeric rating scale (pain as bad as you can imagine/completely interferes). The overall PEG score provides a single measure of pain intensity and interference and is the average of the individual item scores with a potential range of 0-10. The PEG has been shown to be a

reliable and valid measure in chronic pain populations with responsiveness that is similar to or better than other commonly used pain measures.[103-105]

14.2.2 SECONDARY EFFECTIVENESS OUTCOMES

For R33 Aim 1, we will evaluate the ***effectiveness*** the Partners4Pain and Keys to Wellbeing interventions using self-report surveys at 2, 4 and 6 months, measuring secondary outcomes.

Secondary outcome measures include a range of measures consistent with the Biopsychosocial Model of Pain and are recommended common data elements from the HEAL initiatives core pain domains; in addition, we have included important PROMIS based measures with demonstrated reliability and validity in chronic pain populations.[106]

- Pain impact and frequency over the past 3 months measured using the Graded Chronic Pain Scale-Revised (GCPS-R).[107]
- Physical function using the PROMIS 6-item short form v2.0 which measures difficulty doing household activities and agreement with statements on health limitations in physical activities on a 1 to 5 scale.[108,109]
- Sleep disturbance and duration using the PROMIS 6-item short form v1.0 which measures sleep quality on a 1 to 5 scale from very poor to very good in addition to agreement with statements on sleep quality on a 1 to 5 scale.[108,109] The average amount of sleep per night in the past month will also be obtained.
- Participation in social roles and activities using the PROMIS 4-item short form v2.0 which measures frequency of trouble doing activities for leisure, work, or with family or friends on a 1 to 5 scale.[108,109]
- Anxiety will be measured using the Generalized Anxiety Disorder-2 survey (GAD-2) which includes 2 questions that are summed for a total score that can range from 0 to 6.[110]
- Depression will be measured using the Patient Health Questionnaire-2 (PHQ-2) which includes 2 questions that are summed for a total score that can range from 0 to 6.[110]
- Substance use will be assessed using the Tobacco, Alcohol, Prescription medications, and other Substance (TAPS) survey.[111] The TAPS is comprised of an initial 4-item screen for substance use that may lead to further assessment with substance specific surveys when indicated based on the initial 4-item screen.
- Pain catastrophizing will be assessed using the 6-item short form of the Pain Catastrophizing Scale.[112]
- Self-efficacy for managing chronic conditions will be assessed using the PROMIS 4-item short forms for 1) managing daily activities; 2) managing symptoms; 3) managing emotions; and 4) managing social interactions.[113]
- Interoceptive Awareness will be measured using the Multidimensional Assessment of Interoceptive Awareness survey instrument (V2) using the 1) noticing; 2) attention regulation; 3) emotional awareness; and 4) self-regulation subscales.[114]
- Satisfaction with various domains of life (e.g., education, work, family life) will be assessed using the PROMIS 13-item domain specific life satisfaction measure.[115]
- Self-reported use of CIH self-management strategies, medications (over-the-counter and prescription medications - including opioids), and health care (MRIs, injections, hospitalizations, surgeries, provider visits) for back or neck pain will be measured.
- Participants will be asked to report potential side effects by choosing from a list generated from previous studies of pain self-management programs and known potential risks of exercise and mindfulness interventions (R33AT009110, NH170001, R34AT011209).

- Satisfaction with the interventions will be assessed using a question that has participants rate their overall satisfaction ranging from completely satisfied to completely dissatisfied.[106]
- Overall improvement will be assessed with the Patient Global Impression of Change (PGIC) which has participants rate their overall change from very much worse to very much improved.[106]

For R33 Aim 2, we will evaluate the ***impact of health disparity related factors on the effectiveness*** of Partners4Pain intervention for primary and secondary outcomes described above through subgroup analyses which account for the potential relationships and complexities between disparity factors. See Section 15.4.2.

14.2.3 IMPLEMENTATION & DISPARITY MITIGATING OUTCOMES

For R33 Aim 3, we will assess and describe ***views of factors that could facilitate implementation and mitigate disparities*** to prepare for the long-term translation of the intervention to community partner organizations within and beyond the trial. We will use mixed methods quality improvement data collection of Study Participant and Community Stakeholder views and relevant flow data.

Study Participants will be asked to complete mixed methods surveys collected querying:

- Views on barriers/facilitators to reach and participation
- Perceived effectiveness of the interventions
- Their satisfaction with and use of specific program activities
- The extent to which they felt the program met their capability, opportunity, and motivational (COM) needs[72]
- Their views of the intervention's overall affordability, practicality, effectiveness, acceptability, safety, and equity (APEASE, which is part of the COM model)
- The ability of the study team to create a supportive environment and develop relational alliances that fostered norms of inclusion and cultural sensitivity.[80,93,116-120] This includes a measure detailing perceived discrimination in healthcare that will be adapted to assess perceived discrimination within the study.[101]

Community Stakeholders will also participate in a mixed methods evaluation (e.g., via interviews, focus groups, field notes) of their views of the intervention's APEASE features, the nature and quality of the researcher-community partnership, and other domains that emerge as important for sustainability and translation.[121]

Flow data related to the implementation and disparity mitigating outcomes include:

- Number, proportion, and representative characteristics of Study Participants; reasons for participation or not by social determinants of health factors
- Number, proportion, and representative characteristics of Community Partner Organizations; reasons for participation
- Number, proportion, and representative characteristics of Community Facilitators; reasons for participation

15 STATISTICAL CONSIDERATIONS

15.1 HYPOTHESES

Phase I (R61): No hypotheses have been formulated for the R61 phase of the project given the focus on quality improvement and feasibility.

Phase II (R33):
Aim 1 Hypothesis: The Partners4Pain program will be more effective in reducing the primary outcome of pain intensity and interference, in addition to secondary outcomes relative to the Keys to Wellbeing program (active control).

Aim 2 Hypothesis: Through sub-group analyses accounting for complex relationships between disparity factors and multi-level evaluation of community stakeholders, we will gain insights into the program's ability to mitigate disparities (e.g., by overcoming capability, opportunity, and motivational (COM) barriers, as well as obstacles related to affordability, practicality, effectiveness, acceptability, safety, and equity (APEASE)).

15.2 SAMPLE SIZE

15.2.1 R61 RANDOMIZED PILOT STUDY

A total of 30 to 60 individuals will be enrolled in the R61 Randomized Pilot Study. The sample size has been informed by previous pilot studies by the investigators who have found approximately 15-20 individuals per group sufficient for informing the feasibility of larger, randomized clinical trials.[118,119] We anticipate needing to consent approximately 60 to 80 participants to enroll 30 to 60 individuals into the trial.

15.2.2 R33 RANDOMIZED HYBRID EFFECTIVENESS-IMPLEMENTATION TRIAL

Our sample size for the R33 Randomized Hybrid Effectiveness-Implementation Trial is based on findings from the literature on the PEG instrument (our primary outcome measure), including data on responsiveness and variability.[122,123] We want at least 80% power to detect a group difference of approximately one unit or 10 percentage points on the PEG (0-10 scale) based on the mean of the 2, 4, and 6 month measures. We conducted simulation studies mimicking the structure of our planned study to assess the impact of sample size and group treatment factors (class size and number of classes) on power and detectable group difference. We used data on back pain intensity from the active control intervention (Keys to Wellbeing) in our team's recent trial of physical activity in older adults (R33AT00911) to inform intra-class correlation. We generated normally distributed longitudinal measurements from the 0-10 PEG scale with a moderate intra-individual correlation of 0.25, an intra-class correlation of 0.05, and a residual standard error of 2.5 units.[122,123] The mean response was a function of normally distributed individual- and class-level random effects (with variances chosen to achieve the above correlations) as well as a constant fixed effect of treatment at the 2-, 4-, and 6-month time points. The mean PEG during follow-up was compared between treatment groups using a linear mixed model with fixed effects for treatment and baseline PEG and random effects for individual and class. We carried out simulations across a number of scenarios with class sizes ranging from 10 to 16 participants and a total sample size of 300. In all scenarios, our planned sample size yielded greater than

80% power for a treatment effect of approximately 0.9 units (0-10 scale), corresponding to a standardized between group effect size (mean difference/SD) of 0.36, which we regard as a clinically meaningful difference for pain intensity and interference, and is consistent with recommendations in the literature.[124,125] To account for up to 20% loss to follow up, we plan to enroll a total of 376 participants.

15.3 POPULATIONS FOR ANALYSES & GENERAL APPROACH (R33)

The primary analysis for the R33 Randomized Hybrid Effectiveness-Implementation Trial will use an intent-to-treat (ITT) approach[126] with all enrolled subjects included in the analysis. Per-protocol analysis including only participants compliant with study protocols will be conducted as a secondary analysis. Secondary analyses are exploratory and will not be corrected for multiple comparisons. We will use hierarchical linear mixed model regression analyses to account for repeated measures within trial participants (the unit of randomization) in addition to the clustering of individuals within classes when receiving the experimental or control interventions.[127] Missing data analyses will be informed by the pattern and reasons for missing data and will include multiple imputation (data missing at random) and sensitivity analyses using pattern mixture models (data not missing at random), if appropriate.[128,129] This approach has been applied in previous trials by the investigators and highlighted as an exemplar in Annals of Internal Medicine.[130]

15.4 DATA ANALYSES

15.4.1 R61 PHASE

Aims 1 & 2: Mixed method assessment will be conducted. Quantitative data will be analyzed using descriptive statistics when appropriate. For the qualitative analysis, experienced members of the study team will apply rapid deductive, directed content analytic methods of individual and group interviews in real-time, audio-recordings of interviews, and text from open-ended surveys. The coding structure and operational definitions will be guided by the study's conceptual models[131,132] to provide insights into barriers and facilitators to future implementation.[72,96,133,134] Directed content analyses will also allow for inductive gathering of important themes that might fall outside of our chosen models and frameworks.[132] Rapid approaches have been advocated for implementation research as they balance rigor with efficiency, yielding timely and meaningful evaluation of stakeholder needs and perspectives that can be more quickly matched to solutions.[131,135] This is in contrast to traditional qualitative methods which rely on resource-heavy methods including transcribing interviews verbatim and in-depth coding of transcripts which take more time. Given the short time frame between the R61 and future R33 study, a rapid analytic approach is most appropriate.

In addition to using rapid qualitative approaches,[132] we may also apply traditional qualitative methods when more nuanced information would be helpful. In these instances, we will use semi-structured interview guides for individual stakeholder interviews and focus groups which will be recorded and transcribed verbatim. Teams of 2-3 will perform in-depth, directed content analyses of the transcripts applying a codebook in NVivo qualitative software.[136,137] We will use deductive approaches aligned with the study's models and frameworks, as well as inductive thematic coding to document other important information that falls outside the coding structure. Representative quotations will be identified; when

useful (e.g., to gain insight as to theme importance) we will also quantify themes by categorizing them as present or absent for each case, and presented descriptively as frequencies.[136,137]

Aim 3: Mixed method analyses will be conducted.[136] Quantitative data will be presented using descriptive statistics (e.g. means, percentages). No between group statistical comparisons are planned for the R61 Randomized Pilot Study due to the small sample size and focus on feasibility. Qualitative data will be analyzed using the methods described above for Aims 1 and 2.

15.4.2 R33 RANDOMIZED HYBRID EFFECTIVENESS-IMPLEMENTATION TRIAL

Primary Analysis

For the primary analysis, we will use mean PEG during follow-up (at 2, 4, and 6 months) as the outcome. The effect of treatment will be assessed using a hierarchical linear mixed model with fixed effects for treatment and baseline PEG and random effects for individual and class. In addition, we will test for evidence of an interaction between time and treatment by fitting a mixed model with an interaction between the treatment group indicator and follow-up time (viewed as a categorical random variable) and using a likelihood ratio test to assess whether the interaction terms are jointly significant. The results of this analysis will inform the interpretation of the primary analysis and guide secondary analyses. Analyses will be carried out using the statistical software R.

Secondary Analyses

Responder Analyses: We will derive responder categories for our primary outcome of pain intensity and interference (PEG) at 2, 4, and 6 months corresponding to reductions from baseline of 30% (minimal improvement), 50% (moderate improvement), 75% and 100% (substantial improvement). Then, we will fit proportional odds models to assess the effect of treatment on the probability of falling into each of these categories. In addition, we will conduct cumulative responder analyses to assess the proportion of responders for all possible levels of pain intensity and interference reduction (0 to 100% reduction).[138]

Secondary Outcomes: Secondary numerical outcome measures (e.g., self-efficacy, life satisfaction, physical functioning) will be analyzed similarly to the primary PEG outcome. Generalized linear mixed models will be used for binary and count outcomes.

Longitudinal Analyses: Systematic reviews and meta-analyses of interventions for chronic pain and chronic back pain commonly use short-, medium-, and long-term treatment effects for analysis. Therefore, in addition to the analyses of primary and secondary outcomes which provide a measure of cumulative burden over the six-month study period, we will conduct longitudinal analyses with time coded as a categorical variable to quantify group differences in primary and secondary outcomes at 2, 4, and 6 months. Differences in numerical outcomes will be assessed using linear mixed models as described above. Differences in categorical outcomes (e.g., Graded Chronic Pain Scale, health care use) will be assessed using multi-level mixed effects generalized linear models.

Effect Heterogeneity Analyses: While it remains important to estimate the overall (mean) effect of an intervention, analyses of intervention studies have increasingly focused on characterizing how population subgroups experience differential treatment effects.[139-141] Here, we will employ modern statistical machine learning methods (including some co-developed by co-I Wolfson[142]) to describe how disparity factors (i.e. race, ethnicity, income, wealth, education, health care access) interact to influence how responsive individuals are to treatment. These flexible methods combining matching techniques

with decision trees will allow us to carry out a formal statistical test for effect heterogeneity, and (in the presence of heterogeneity) also yield simple classification rules that partition the population according to their expected treatment effect. In previous work, we have successfully applied these techniques to randomized trials with fewer participants (n=180) than we will have in this study (n=376) so we anticipate that we will have an adequate sample size to achieve meaningful results. For these analyses, we will use a limited set of outcomes (e.g., PEG, self-efficacy) at 2, 4, and 6 months to characterize the treatment effect. All analyses are exploratory and will not be corrected for multiple comparisons.

Mediation Analyses: In addition to characterizing how treatment effects vary across individuals, we will also explore the potential mechanisms driving these treatment effects via mediation analysis. Specifically, we will apply established methods[143] to characterize the proportion of treatment effect for changes in pain intensity and interference at months 4 and 6 that can be explained by changes in self-efficacy, interoceptive awareness, and domain-specific life satisfaction measured in prior months. Mediation models will be estimated using the *mediation* package in R.[144] Further, we will apply decomposition methods[145] to understand whether the relationship between treatment effects and self-efficacy/life satisfaction is driven by mediation, moderation, or moderated mediation.

Comparisons to Back Pain Populations with Low Health Disparities: To assess the impact of Partners4Pain on mitigating disparities in pain self-management, we will compare findings to results from studies assessing self-management programs for chronic back pain with low PEHD representation, including studies from the HEAL initiative.[67,71] This includes studies by our team assessing the impact of self-management for chronic neck and back pain.[3,4,6,8] We will assess the similarity of mean outcome levels at baseline, treatment effects, drivers of effect heterogeneity, and mediating variables. Where possible, we will combine individual-level data (from previous studies conducted by our team) to formally test differences across studies.

Implementation and Disparity Mitigating Outcome Analyses: Qualitative measures will be analyzed using methods described previously (see R61 Aims 1 & 2). Quantitative measures will be summarized and compared between treatment groups using two-sample t-tests (for continuous measures) and chi-square tests (for categorical measures). Exploratory analyses will employ regression and decision tree models to investigate the impact of disparity factors (i.e., race, ethnicity, income, wealth, education, health care access) on measures of program implementation.

16 REGULATORY, ETHICAL, & STUDY OVERSIGHT

16.1 INFORMED CONSENT

16.1.1 CONSENT & OTHER INFORMATIONAL DOCUMENTS

Community Stakeholder Information Sheet

Community Stakeholders (see Table 4) will be provided with an informational sheet prior to sharing their views and opinions. The information sheet details the names of the researchers, an explanation of what the community stakeholders will be expected to do and any risks associated with their involvement, and contact information for the IRB office and University of Minnesota in case of questions or concerns.

Informed Consent Form (Study Participants)
The consent form will include, but is not limited to, the following: information regarding the study purpose and research design, study procedures, potential risks and benefits, alternatives to participation, voluntary nature of participation, privacy and confidentiality, research-related injury, disclosure of new information regarding participation, and who to contact outside the study in case of issues. Contact information for the PIs and project coordinator(s) will also be provided. Participants, study staff, and an impartial witness, as needed, will sign and date the consent form.

Changes to the Informed Consent Form
In the event the informed consent form changes, following necessary IRB approvals, study staff will meet with the PI or designee and review changes to the form prior to conducting consent with new study participants. If existing study participants need to be informed of specific changes in the risks or benefits of study participation, an addendum consent will be used. This addendum will be used to, for example, inform enrolled participants about significant new findings that may have a bearing on their willingness to continue participation in the study. The addendum consent will be given to the participant at a study visit, emailed, or mailed to the participant's home.

16.1.2 CONSENT PROCEDURES & DOCUMENTATION

Consent & Human Subjects Training
All research staff obtaining informed consent are required to undergo project specific human subjects training that addresses the essential components to the informed consent process. Staff responsible for consenting participants will be documented in the study's Delegation of Authority Log and in Ethos. In addition, staff will complete human subjects training in accordance with the UMN's human subjects and HIPAA training requirements.

This procedure establishes the process to obtain informed consent from participants. The process begins when an individual identifies as a potential candidate for the study and will continue throughout the duration of the study. The process ends when a participant declines consent to participate (e.g., prior to signing the consent, withdrawing consent) or when study completion occurs. Participants must demonstrate the ability to autonomously provide written or electronic consent. A Legally Authorized Representative (LAR) will not be used. The Principal Investigators are responsible for ensuring these procedures are carried out.

Potential participants will consent at 3 different time points: during a brief initial screening survey and at each of the two baseline screening appointments.

Initial Screening Survey/Pre-Baseline Screening Visit
Interested individuals are initially screened using a web-based screening survey that can be completed independently online or over the phone with study staff. An overview of the study will be provided during the web-screen, and electronic consent secured prior to collecting preliminary information on eligibility (e.g., age, presence of chronic back or neck pain). Following the web-based screening, potential participants will be sent an informational video describing the study in more detail and will be contacted by study staff to answer any preliminary questions they may have (e.g., purpose of the study, interventions, time commitment) and schedule the first baseline screening appointment.

Baseline 1 Screening Visit

This appointment can take place virtually or in-person at a participating study location. Prior to this appointment, participants will be given a copy of the consent document to review on their own. Study staff will verify the most current IRB-approved version of the consent form is used. Easy to understand, IRB pre-approved, electronic and print informational materials, including visual media, will be used to facilitate understanding of study procedures. As part of the informed consent process, potential research participants will be made aware of financial or business interests that may affect their decision to participate. None are anticipated; see Conflict of Interest Policy if a change in circumstance occurs. Study staff will review the consent form with the participants, section by section. This may be done one-on-one or in a group setting with other potential participants. Following review of the consent form, participants will be invited to ask questions one-on-one with study staff in a private and quiet space. Research staff will assess comprehension and understanding of information presented in the consent form using a series of open-ended questions (e.g., study purpose, interventions, risks). Participants will be encouraged to discuss taking part in the research study with family members, friends and/or healthcare providers, as appropriate. Participants are encouraged to think about study participation and will not be coerced or pressured into deciding to participate before they are ready. Written or electronic consent will be obtained from each study candidate. Only individuals who demonstrate comprehension will be considered eligible to participate. If the participant cannot read, an impartial witness can be used. The impartial witness must:

- Be present during the entire consent discussion to attest to the adequacy of the consent process and to the participant's voluntary consent. The witness must be present during the entire consent conversation, not just for signing the document(s).
- The witness may be a family member, friend, caregiver etc. The witness may not be a person involved in the design, conduct, or reporting of the research study.

All participants will be given a copy of the signed consent form for their personal records. Original signed paper consent forms will be secured in the respective participant's research file. Signed e-consent forms will be maintained in REDCap.

Baseline 2 Screening Visit

At the second baseline screening visit, research staff will review the study purpose and procedures (e.g., study visits, data collection) and confirm continued consent to participate.

To complete the informed consent process at the end of study participation, study staff will inform the subject when their participation has ended and will document the discussion in the study record.

16.2 STUDY DISCONTINUATION & CLOSURE

The study may be temporarily suspended or prematurely closed if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided to study participants, investigators and study collaborators, funding agency, and regulatory authorities, including the UMN IRB, by the PIs or designee. In the event of any type of closure, the PIs, or designee, will promptly inform ongoing study participants, the IRB, and sponsor/funding agency and provide the reason(s) for the termination or temporary suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants

- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Major difficulties with study recruitment or retention
- Natural disaster, public health crisis

The study may resume once concerns about safety, protocol compliance, and data quality are addressed and satisfy regulatory bodies (e.g., funding agency, IRB, IMC).

STUDY CLOSURE

The Principal Investigators, or their designee, have the responsibility of informing the IRB, and other regulatory bodies, when a protocol has been completed. A protocol is considered to be open and active until the investigator has notified the IRB the study has been completed.

Study Close Out Procedures are as follows:

- Confirm a signed ICF is on file for each participant
- All CRFs for each participant are complete or closed; all other data entry is complete
- Status of all outstanding data edits, queries, or missing data is known and there is a timeline for their resolution
- Procedures for locking the database are complete or in progress
- All regulatory and other pertinent study documents for the protocol are current, complete, and on file (e.g., IRB approvals, consent documents, current CRFs)
- Inform IRB of study closure status or identify plans to this, per IRB reporting requirements
- Notify monitoring committee of study closure status
- Update clinicaltrials.gov
- Update Study Closure Status
- Post the study Informed Consent Form to clinicaltrials.gov
- Study results will be submitted to clinicaltrials.gov no later than 12 months after the primary completion date)
- Following publication of study findings, de-identified and non-traceable data generated by the project will be submitted to study-appropriate repositories in consultation with the HEAL Data Stewardship Group to ensure the data is accessible via the HEAL Initiative Data Ecosystem.

16.3 CONFIDENTIALITY & PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the IMC, and the funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team.

Authorized representatives of the funding agency, representatives of the Institutional Review Board (IRB), and other regulatory agencies may inspect all documents and records required to be maintained by the investigator for the participants in this study.

The study participant's contact information will be securely stored for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as

dictated by the reviewing IRB, Institutional policies, or funding agency requirements. We will permit access to such records.

The study will primarily capture data electronically, back up paper files will only be used when electronic data systems are unavailable. Electronic data will be housed on password protected; HIPAA compliant databases stored on secure servers also operated by the UMN Health Sciences Technology (HST). The servers are in a physically secure location on campus and are backed up nightly, with the backups stored in accordance with the HST. Hard-copy participant research files, with identifiable information, will be secured in a locked file cabinet, in a locked office, with no public access at the University of Minnesota (UMN). Further, study participants will be assigned a unique ID number. This ID number will be used in lieu of using identifiable information whenever possible. Identifiable information will be accessible to study-related personnel who have met the UMN's training requirements for the Responsible Conduct of Research, HIPAA, and data security.

Routine communication with study participants regarding scheduling and reminders for study visits will occur by phone or email. Authorization for email communication regarding scheduling and reminders for study visits will be obtained from participants.

All published reports will be of summary nature and no individual subjects will be identified beyond the investigative staff involved in the project.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

16.4 KEY ROLES & STUDY GOVERNANCE

The structure and organization of the study team is summarized in Table 10 and is based on the investigators' previous work successfully conducting complex milestone driven projects.

Members of the study team represent a professionally diverse group of individuals from scientific and community settings and are at various stages of their research and professional careers. They have been strategically brought together based on their skills and experience which will enhance the likelihood of the project's success.

Due to the project's complexity, there are two Principal Investigators (PIs).

Table 10. Key Roles and Study Governance

Study Committee/Team/Hub	Roles & Responsibilities
Steering Committee (Comprised of PIs and Co-Is, Community Partner Organization Leadership Members as Co-I Consultants)	• Provide guidance to the PIs related to the overall scientific agenda, decision making, monitoring of study progress and the dissemination and implementation plan • Facilitates relationships between researchers and Community Partner Organizations
Management Team (Comprised of Co-I Hub Leads, PIs, Project Coordinators)	• Oversees study development and implementation • Supports and monitors Individual Team Hub Progress • Develops/maintains Overall Study Team Charter • Maintains regular communication with Community Partner Organizations regarding study status and collaboration • Develops and routinely reviews protocol • Conducts regular review of study progress, timelines, budget, payment of consultants, etc.
Project Coordination Hub (Comprised of Project Coordinators, PIs)	• Coordinates research activities across hubs • Standardizes processes for priorities work-flow management using project management tools (e.g., ClickUp) • Identifies and brings attention to barriers obstructing timeline completion of milestones, time sensitive issues • Assembles and maintains entire study MOP; initiates timely review of MOP sections • Maintains Project Coordination MOP Sections

Regulatory Hub*	• Coordinates, develops, maintains, ensures compliance regarding:
	  • IRB submissions
	  • Protocol
	  • AE/UPIRTSO reporting
	  • Regulatory Binder
	  • Delegation of Authority Logs
	• Coordinates, trains staff and ensures compliance re: Informed Consent Activities
	• Coordinates, ensures documentation and compliance of Human Subjects Training of study staff
	• Coordinates meetings, preparation of reports and responses related to Independent Monitoring Committee
	• Maintains timely reporting on Clinicaltrials.gov
	• Maintains Regulatory MOP Sections

Data Collection and Management Hub*	• Coordinates development of study CRFs • Develops and maintains study databases/management systems (REDCap) • Coordinates randomization system • Trains staff in data collection/management activities • Stores and manages all study related data • Prepares data for data analysis • Oversees quality assurance and quality control of data collection and data management • Prepares monitoring reports for internal and external reporting purposes • Maintains Data Collection and Management MOP Sections
Intervention Hub*	• Develops the intervention curricula for experimental and control

	• Designs, develops, and produces intervention assets; seeks input from Community Stakeholders with the assistance of the Data Management Hub • Works with the Delivery Platforms, Technology Hub to produce website related content • Hires, trains, and managements Community Facilitators • Designs, develops intervention training materials for Study Staff and Community Facilitators • Designs, develops, and implements intervention CRFs, fidelity assessments in coordination with the Data Management Hub • Maintains Intervention MOP Sections
Delivery Platforms, Technology Hub*	• Assesses and makes recommendations for delivery platforms and technology to support participant facing activities • Develops and trains staff in the use of associated delivery platforms and technology • Coordinates the design, development and maintenance of the study related website Partners4Pain.org • Maintains Delivery Platforms, Technology MOP Sections
Community Engagement and Recruitment Hub*	• Develops and implements the recruitment plan • Develops and implements the engagement plan • Coordinates convening of Community Advisory Team • Works with the Data Management Hub to coordinate Community Stakeholder Quality Improvement Data Collection • Maintains Community Engagement and Recruitment Hub MOP Sections
Communications, Public Relations Hub*	• Develops and implements communications and public relations plans • Designs, develops, and produces communication assets (e.g., brand kit, press releases, newsletters, etc.) • Works with the Delivery Platforms, Technology Hub to produce website related content • Maintains Communications, Public Relations Hub MOP Sections

Participant Coordination Hub*	• Coordinates activities with Data Collection/Management and Community Engagement Hubs
	• Responsible for overseeing the implementation of all activities at a participant level; includes:
	  • Reminder emails (sessions, follow up)
	  • Scheduling visits
	  • Monitoring communication systems
	  • Troubleshooting and assisting participants as needed
	• Maintains Participant Coordination Hub MOP Sections

Community Advisory Team (Comprised of Community Members and Leadership from Community Partner Organizations Serving in Consultant Roles)	Works in partnership with researchers to • Advise researchers on how to overcome barriers to engaging diverse populations in research participation • Connect researchers to other community organizations and community leaders to encourage community member participation in a range of research-related activities • Co-facilitate community talks and other conversations • Contribute to study conceptualization, design, development, implementation, results interpretation, and dissemination • Co-create and co-develop culturally sensitive research processes and materials • Contribute to decisions regarding new and ongoing projects upon researcher request • Expand reach to involve more communities in the research process • Disseminate recruitment materials through routine communication channels
Community Champions (Comprised of individuals from varied organizational domains including health care professionals, faith-based leaders, charitable organizations, neighborhood associations, senior communities, etc.)	• Disseminate recruitment materials through routine communication channels
*Hubs (with the exception of the Project Coordination Hub) are comprised of at least one PI, at least one Co-I with subject matter expertise, and at least one Project Coordinator MOP=Manual of Operations	

16.5 SAFETY OVERSIGHT

Safety oversight for the study will be under the direction of an Independent Monitoring Committee, composed of 4 individuals with the appropriate expertise and experience in clinical trial monitoring, including safety monitoring. The IMC was chosen by the study team and approved by NCCIH.

The DSMP and IMC Charter provide specific details regarding IMC membership, responsibilities, meeting and report frequency, and more. This committee is independent from the study conduct and free of conflicts of interest.

16.6 CLINICAL MONITORING

Study monitoring will be conducted internally by the study team to ensure that the rights and wellbeing of trial participants are protected; that the reported trial data are accurate, complete, and verifiable; and the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Council on Harmonization Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s). Self-monitoring activities are described in Section 16.7, Quality Assurance and Quality Control.

16.7 QUALITY ASSURANCE & QUALITY CONTROL

We will perform internal quality management of study conduct, data collection, documentation, and completion.

Quality assurance and control procedures will be implemented as follows:

Research staff will undergo project-specific training in informed consent, screening and enrollment procedures, data collection, safety assessment, and adverse event protocols prior to study enrollment. Study intervention facilitators will undergo project-specific training in screening and enrollment procedures, their respective interventions, and safety assessment and adverse event protocols prior to study enrollment. Certification by a principal investigator (or designee) requires adherence to standard operating procedures outlined in the manual of operations. Training and certification will be logged.

Informed consent — Study staff will review both the documentation of the consenting process as well as completed consent documents for enrolled participants. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Outcome data collection — The primary method of data collection for participant self-reported outcomes will be direct electronic entry through a survey interface with REDCap. Logic rules specifying the type and range of acceptable responses will be programmed into REDCap. Participants will receive an error message if they enter an invalid response. The PIs will review reports on data capture and quality on a monthly basis. Missing data reporting and other customized reports will be developed in order to facilitate efficient workflow and high-quality data capture. Data collection instrument specific follow-up rates will be tabulated and reviewed during meetings between the PIs and study staff. Additional training will be provided as needed based on the findings.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in Section 11.4.

Protocol Deviations — The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

16.8 DATA HANDLING & RECORD KEEPING

16.8.1 DATA COLLECTION & MANAGEMENT RESPONSIBILITIES

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the investigators. All source documents will be reviewed by the study team and data entry staff, who will ensure that they are accurate and complete. Unanticipated problems and adverse events will be reviewed by the investigator or designee.

Data collection for the study will be primarily web-based. Initial screening is conducted via a web-based form completed either directly by the subject or by study staff conducting an interview over the phone. Baseline screening and intervention-related data acquisition will be primarily direct-electronic entry but may include a small number of handwritten forms that are later keyed by study staff if electronic data systems are unavailable. Outcomes will be obtained primarily through web-based forms completed directly by subjects. In some instances, responses may be obtained through phone interviews by study staff or paper surveys mailed to subjects. These responses are then data-entered study staff.

All handwritten data forms for enrolled patients will be scanned and uploaded to the data management system for review. A history of CRFs and all fielded versions will be maintained. CRFs will be implemented as web-based eCRFs including checks for valid entry and incomplete responses.

Database Protection
Data for this study will be entered into a REDCap database, which uses a MySQL database via a secure web interface with data checks used during data entry to ensure data quality. REDCap includes a complete suite of features to support HIPAA compliance, including a full audit trail, user-based privileges, and integration with the institutional LDAP server. The MySQL database and the web server will both be housed on secure servers operated by the University of Minnesota HST. The servers are in a physically secure location on campus and are backed up nightly, with the backups stored in accordance with the HST retention schedule of daily, weekly, and monthly tapes retained for 1 month, 3 months, and 6 months, respectively. Weekly backup tapes are stored offsite. The HST servers provide a stable, secure, well-maintained, and high-capacity data storage environment, and both REDCap and MySQL are widely used, powerful, reliable, well-supported systems. Access to the study's data in REDCap will be restricted to the members of the study team by username and password. The database incorporates an electronic audit trail to show change(s) to data after original entry including the date/time and user making the change. Electronic communication with outside collaborators will involve only non-identifiable information.

Source Document Protection
Electronic source documents will be stored on a password protected computers supported and maintained by the UMN HST. Participant ID numbers will be used to protect participants' confidentiality. All paper source documents will be stored in a locked file cabinet, in a locked office at the University of Minnesota with no public access.

16.8.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years from the date of Federal Financial Report (FFR) submission. Documents may be retained for a longer period, if required by local regulations.

16.9 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the study team and implemented promptly, as required. It is the responsibility of investigators and research staff to follow the written protocol approved by the IRB.

Protocol deviations include, but are not limited to the following:

- Failure to keep IRB approval up to date
- Implementing protocol modifications without obtaining prospective IRB approval
- Conducting research during a lapse in IRB approval
- Enrolling more subjects than what is approved in the protocol
- Performing research procedures outside the protocol specified window
- Failure on the part of any individual involved in research review or oversight to abide by applicable laws or regulations, or the University of Minnesota IRB policies
- Randomization of an ineligible participant; not-adhering to inclusion/exclusion criteria
- Failure to obtain Informed Consent or altering from the informed consent process as described in the IRB approved protocol, including obtaining consent using an outdated consent form
- Failure to report an SAE, Breach of Confidentiality, Unanticipated Problem
- Failure to report an event that requires expedited reporting to the IRB (e.g., unexpected death, participant becomes incarcerated)
- Wrong intervention administered to a participant

Documenting and Reporting Requirements
All protocol deviations, violations and research failures will be documented in REDCap by study staff. Deviations, violations, and research failures that are also SAEs, UPIRTSOs, or result in harm to the participant may have different, or additional, reporting requirements. See Sections 13.5 to 13.6 of this study protocol for more information.

Protocol deviations and violations will be reported to regulatory agencies as required (e.g., IMC reports per reporting requirements outlined in the DSMP and/or Charter; per the UMN IRB and funding agency requirements).

16.10 PUBLICATION & DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication. Electronic copies of publications will be deposited within four weeks of acceptance by a journal in PubMed Central with proper metadata to be made discoverable and accessible upon publication. Publications will be made publicly available immediately without any embargo period and will be published under the Creative Commons Attribution 4.0 Generic License (CC BY 4.0) or an equivalent license or otherwise dedicated to the public domain (e.g., Creative Commons public domain tool, CC0).

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data generated by the project will be submitted to study-appropriate repositories in

consultation with the HEAL Data Stewardship Group to ensure the data is accessible via the HEAL Initiative Data Ecosystem. To the extent feasible, underlying primary data will be shared simultaneously with publications and made immediately accessible through release under the CC BY 4.0 or an equivalent license or otherwise dedicated to the public domain (e.g., Creative Commons public domain tool, CC0). Considerations for ensuring confidentiality of these shared data are described in Section 16.12.

16.11 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The University of Minnesota has established policies and procedures for all study group members to disclose all potential conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

UMN researchers must adhere to Board of Regents and Administrative conflict of interest policies that require the timely disclosure of financial and business interests relating to the researcher's University responsibilities and expertise. Disclosure of these interests is required annually and within 30 days of a "change in circumstances" using the Report of External Professional Activities (REPA). Current REPA reports are maintained for study staff (paid faculty, P&A employees and other individuals designated by a senior UMN leader or designate) with study regulatory documents. Covered individuals must complete the University's conflict of interest course when filing the REPA for the first time, and every four years thereafter. University investigators must disclose all reportable conflicts to the University's Office of Institutional Compliance (OIC).

The existence of financial and/or business interests related to the research study will be disclosed in the New Study and Continuing Review forms in ETHOS for all study personnel. Any conflict not previously disclosed to the IRB will be reported via the Reportable New Information SmartForm in ETHOS. The investigators will also submit a modification in ETHOS to address any revisions to the study if required.

The following strategies may be employed when COIs or potential COIs are identified. The strategies below are organized from minimal to more restrictive management and are not an exhaustive list. Management plans will be submitted to the IRB for approval and other regulatory bodies will be notified per their respective policies (e.g., IMC, NIH).

- Disclose (if legally permissible) the conflict in the informed consent form and in any publications or presentations related to the research
- Restrict the conflicted person's access to identifiable data
- Restrict the conflicted person's ability to determine eligibility status of prospective participants.
- Restrict the conflicted person from obtaining informed consent
- Restrict the conflicted person from adjudicating adverse events, serious adverse events and/or unanticipated problems
- Restrict the conflicted person's participation in data analysis and interpretation

- Remove conflicted person from involvement in the conduct of the study. This is a last resort consideration that may require regulatory approval (e.g, sponsor approval, steering committee approval).

16.12 FUTURE USE OF DATA

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PIs will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). The study is funded by the NIH's Helping End Addiction Long-term (HEAL) initiative and will comply with the HEAL Initiative's Public Access and Data Sharing Policy (*https://heal.nih.gov/about/public-access-data*). This includes submitting de-identified and non-traceable data generated by the project to study-appropriate repositories in consultation with the HEAL Data Stewardship Group to ensure the data is accessible via the HEAL Initiative Data Ecosystem. Plans for sharing data for future use will be disclosed to study participants during informed consent.

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