



**NIH Collaboratory Ethics and Regulatory Core: UG3 Consultation Call**  
**Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (RAMP)**  
**November 13, 2023; 4:00-5:00 pm ET (via Zoom)**

**Attendees:**

- Core, Coordinating Center, and NIH: Joe Ali (Johns Hopkins University), Andrew Garland (Bob Jones University), Karen Kehl (NINR), David Magnus (Stanford University), Kevin McBryde (NCCIH), Kayla Mehl (Johns Hopkins University), MariJo Mencini (Duke University), Stephanie Morain (Johns Hopkins University), Pearl O'Rourke (retired), Caleigh Propes (Johns Hopkins University), Damon Seils (Duke University), Kevin Weinfurt (Duke University)
- Trial team: Lee Cross, Julie Toth

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Brief review of Demonstration Project	<p>Meeting attendees received the Research Strategy and the Resource and Data Sharing Plan for RAMP with the meeting agenda (see supplementary material attached). Pearl O'Rourke facilitated the discussion. Core members, RAMP team members, NIH representatives, and staff from the NIH Pragmatic Trials Collaboratory Coordinating Center introduced themselves. The RAMP team members present included Lee Cross (project manager) and Julie Toth (human research protection program director for the Minneapolis VA Health Care System).</p> <p><b>Project overview:</b> Lee Cross gave an overview of the project. The goal of RAMP is to evaluate the use of a 12-week mind-body skills training program for patients with pain, including a one-on-one session with a "whole health coach" followed by 11 weekly group sessions to include prerecorded expert-led education videos, mind-body skills training and practice, and group discussions.</p> <p><b>Healthcare system partners:</b> Minneapolis VA Health Care System, University of Iowa, and University of Minnesota</p> <p><b>NIH Institute Providing Oversight:</b> National Institute of Nursing Research (NINR)</p>		

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
	<p><b>Study design:</b> In the UG3 planning phase, the study team will conduct stakeholder engagement activities, including identifying and developing new community partnerships and using mixed-methods data collection from patients, community partners, and VA healthcare system leaders and staff to learn about factors that affect long-term adoption. The study team will also conduct a pilot study to assess the feasibility of delivering the intervention. In the UH3 implementation phase, the study will use 1:1 individual randomization of 500 patients to either usual care or the intervention. Potentially eligible patients with chronic pain will be identified via the electronic health record and will then receive an introductory postcard followed by a screening email to confirm eligibility and interest. For patients who are interested in participating, there will be a follow-up phone call describing the project in detail and obtaining oral consent. At the time of this call, individuals will be randomized and details of their participation described.</p> <p><b>Outcomes:</b> The primary effectiveness outcome will be pain interference at 13 and 26 weeks. Secondary outcomes will include opioid use and other outcomes in the NIH HEAL Initiative–recommended domains.</p> <p>Pearl requested more information about randomization (whether 1-to-1 or by cohort) and about whether there will be balancing by patient characteristics. After the meeting, Lee followed up with the study team and confirmed that the trial will use 1-to-1 randomization. The study team is working with the Biostatistics and Study Design Core to explore potential correlation of outcomes between individuals in the intervention arm who participate in the same discussion group. In a prior similar study, such correlation was small and had no impact on the study results.</p>		
Status of IRB approval	<p>The Minneapolis VA Health Care System IRB deemed the UG3 stakeholder engagement activities to be exempt from full IRB review; the research and development committee approved these activities.</p> <p>The study team obtained an exception to the single IRB requirement. The Minneapolis VA Health Care System IRB and the research and development committee provided expedited approval for the UH3 implementation of the trial. The status of IRB review at the University of Iowa and the University of Minnesota is pending.</p>	Provide more information about the engagement of the University of Minnesota and the University of Iowa	<b>Study team</b>

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	Pearl requested more information about the engagement of the University of Minnesota and the University of Iowa and, hence, what activities will be reviewed by an IRB. The study team will provide more information as work with these sites proceeds.		
Risk (Does the project meet regulatory criteria for being considered minimal risk?); and consent (planned processes for relevant subjects)	<p>The study meets the regulatory criteria to be considered minimal risk. The study team has received a waiver of documentation of informed consent from the IRB.</p> <p>David Magnus suggested that it may be appropriate for the control group to receive the unmodified LAMP intervention (pending ongoing analysis to determine the efficacy of LAMP in prior work). This would allow the study team to compare the modified LAMP approach used in RAMP to the unmodified LAMP approach. This proposal was made in light of both ethical and scientific considerations. Lee will share this suggestion with the study team.</p> <p>After the meeting, Lee shared this comment with the study team and reported back that, because there is no plan for the LAMP intervention to become usual care within the VA, the study team believes it is reasonable not to use that intervention as a comparator in the trial.</p>		
Privacy (including HIPAA)	<p>The study team has received a waiver of HIPAA authorization for recruitment purposes only. Participants will need to sign a HIPAA authorization form prior to enrollment. The study team is exploring a VA-approved electronic signature option, likely using either a DocuSign or Qualtrics platform, as these vendors have experience meeting VA security standards.</p> <p>HIPAA authorization forms will be used for both the UG3 stakeholder engagement activities and the UH3 study implementation.</p>		
Monitoring and oversight	<p>The study team has identified members for the data and safety monitoring board and is working on the charter. Pearl referred the study team to the Data and Safety Monitoring chapter of the Living Textbook:  <a href="https://rethinkingclinicaltrials.org/chapters/ethics-and-regulatory/data-and-safety-monitoring/introduction-data-and-safety-monitoring/">https://rethinkingclinicaltrials.org/chapters/ethics-and-regulatory/data-and-safety-monitoring/introduction-data-and-safety-monitoring/</a>.</p>		

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Issues beyond this project (regulatory and ethics concerns raised by the project, if any)	None.		
Other matters	None.		

**SPECIFIC AIMS.** This project addresses the significant challenge of implementing effective, non-opioid interventions for chronic pain management in rural and remote dwelling Veteran patients.<sup>1,2</sup> The Veterans Healthcare Administration (VA) is the nation's largest integrated healthcare system and serves an estimated 2.7 million rural Veterans.<sup>3</sup> Rural Veterans experience a disproportionate share of the national pain burden, with more chronicity, opioid harms, comorbid mental health conditions and substance abuse, compared to non-rural Veterans and non-Veterans.<sup>4,5</sup> Rural Veterans are also less likely to receive comprehensive and specialty pain care,<sup>6,7</sup> are prescribed over 30% more opioids,<sup>8</sup> and are less likely to use self-management interventions for pain than non-rural Veterans.<sup>7,9</sup> Importantly, rural women and minority Veterans living in rural areas experience additional challenges that prevent equitable pain care.<sup>6,10-17</sup>

Pain is a complex biophysical, psychological and social (BPS) condition<sup>10,11</sup> and there is a growing evidence base to support several complementary and integrative health (CIH) approaches to manage chronic pain in a more holistic way.<sup>18-20</sup> While the VA has become a leader in advancing CIH through its Whole Health Initiative, there remain many barriers, especially for rural patients. This includes lack of awareness/knowledge about CIH, shortage of availability and accessibility of CIH/Whole Health pain care services, and absence of the necessary support to successfully engage in CIH self-management.<sup>3,21-24</sup>

**Our long-term objective** is to improve pain management and reduce opioid use among rural patients in the VA. Our multidisciplinary team has co-designed, with multiple-levels of stakeholders, an innovative telehealth intervention that builds upon our team's previous research.<sup>6,25-32</sup> The Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (**RAMP-WH**) project strategically coalesces multiple evidence based CIH self-management strategies to address Veterans' BPS needs and overcome existing barriers. Comprised of mindfulness training, pain education, pain specific exercises, and cognitive behavioral strategies, the program is cohesive and scalable. Designed to be implemented within the VA through its nationwide Whole Health System initiative,<sup>33</sup> RAMP-WH is a 12-week program; it includes a one-to-one session with the WH Coach, followed by 11 group sessions of pre-recorded expert-led education videos, mind-body skills training and practice, and facilitated discussions. To ensure long-term sustainability, we will collaborate with stakeholders including Veteran patients and an established network of VA health system partners including the Office of Rural Health; the Office of Pain Management, Opioid Safety, & Prescription Drug Monitoring (which has been investing in telehealth for pain); and the Office of Patient Centered Care and Cultural Transformation. We will also cultivate new community partnerships with the VA's Community-Based Outpatient Clinics (CBOCs) and local and national Veteran organizations. There are two phases to the project, a UG3 and UH3.

**UG3 Aims (Phase I; Years 1-2):** We will conduct 1) *stakeholder engagement activities* including identifying and developing new community partnerships and using mixed methods data collection from multiple levels of stakeholders (n=35-50 patients, community partners, VA healthcare system leaders and staff), guided by the established RE-AIM/PRISM framework, to learn about key factors that can affect long-term adoption; and 2) conduct a *pilot study* of 40 rural VA patients with chronic pain to assess the feasibility of delivering RAMP-WH (experimental intervention for the UH3 trial) in terms of recruitment and engagement, intervention fidelity and adherence, data collection, and other key metrics.

**UH3 Aims (Phase II; Years 3-5):** We will conduct a *randomized hybrid type 2 effectiveness-implementation pragmatic clinical trial* of RAMP-WH compared to Usual Care, enrolling 500 rural VA patients from the VA healthcare system, oversampling female and racial/ethnic minority patients.

**Aim 1 (EFFECTIVENESS):** To assess the relative effectiveness of RAMP-WH in rural VA patients in terms of pain interference (**primary outcome**) at 13 and 26 weeks and **secondary outcomes** of opioid use and other HEAL recommended outcomes. We will also perform additional exploratory analyses of women and minority Veterans' primary and secondary outcomes.

**Aim 2 (IMPLEMENTATION):** To work iteratively with multiple levels of stakeholders (n=35-50 patients, community partners, VA healthcare system leaders and staff) to evaluate intervention implementation strategies used in the trial and adapt these strategies to scale up RAMP-WH within the national VA healthcare system. This will include:

- Conducting mixed-methods assessments of stakeholder and randomized trial participant views of implementation-related barriers and facilitators, resource needs, and other RE-AIM/PRISM domains.
- Working with stakeholders to co-create additional plausible strategies for overcoming barriers to implementation of RAMP-WH in the national VA healthcare system.
- Conducting budget impact analyses using models informed by stakeholder views to inform future decision making.

This project is innovative in its comprehensive and rigorous assessment of a multi-component CIH telehealth intervention in the nation's largest health system, the VA. Optimized to meet Veterans' BPS needs, we will address critical barriers that currently exist to supporting rural Veterans' pain care. Our approach will not only support larger scale implementation across the VA but will serve as a model for non-VA organizations to integrate novel solutions that promote equitable access to evidence-based non-opioid pain care across rural America.

**Response to Summary Statement for Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (RAMP-WH; 1 UG3 NR020929-01).** We would like to thank the reviewers for their constructive comments. We are confident that the score-driving concerns are addressable and the project will have significant impact. Rural-dwelling Veterans with chronic pain are an understudied, high-needs population who experience significant barriers to accessing chronic pain care that addresses their biopsychosocial needs [1,2,3].

**Concerns for overlap/innovation.** The proposed RAMP-WH intervention is a cohesive multi-modal approach that is significantly different from our previous work. We anticipate it will generate new, scalable knowledge and a reproducible model that can overcome existing barriers, advance pain care and address health disparities experienced by rural Americans. RAMP-WH is a cohesive packaged intervention that is comprised of pain education, mind-body skill training (including mindfulness, pain specific physical movement/exercise) and whole person cognitive behavioral strategies (pacing, guided imagery, relaxed breathing, etc.), intended to target rural Veterans' biopsychosocial pain related needs (pp. 209-210). It differs from our previous LAMP study which examined a mindfulness intervention targeting emotional/stress regulation for pain self-management. While the content and focus of RAMP-WH differs, we will leverage established modes of delivery developed previously by our group (e.g., telehealth, non-clinician led) which proved engaging and satisfactory to Veterans. We will also use the UG3 phase to implement a robust stakeholder engagement plan (pp. 206- 208) to further develop partnerships, learn more about barriers, needs and preferences, and optimize the RAMP-WH intervention. Additionally, a new feature of the RAMP-WH intervention is its greater focus on implementation by embedding it in the nation-wide VA healthcare system. This will be accomplished by using Whole Health Coaches to facilitate RAMP-WH intervention sessions and a broader collaboration with key operational partners (e.g., Office of Rural Health and the VA's Office of Connected Care). This is a critical next step toward the long-term goal of fully integrating evidence based biopsychosocial interventions into clinical care for rural Veterans and making them more accessible.

**Missing details about health coach training, intervention delivery, fidelity, patient experiences, etc.** Our team has substantial experience developing competency-based training programs and supporting resources that have yielded high fidelity rates (>90%). Our proposed strategies for training and fidelity assessment are briefly described on pp. 210-211 and will be further developed during the UG3 phase in partnership with our stakeholders (including the VA Office of Patient Centered Care and Cultural Transformation, which implements Whole Health and CIH within VA) and the lead of the VA's WH coaching (see pp. 206-208). We will measure patient experiences using mixed methods (p. 211).

**Participant burden and secondary outcomes.** Our outcomes have been carefully chosen to address biopsychosocial domains relevant and recommended for research on chronic pain [4,5,6,7,8,9]. Further, we have demonstrated in the previous LAMP study that Veterans are willing and able to complete follow up surveys with a similar number of measures (response rates at 10 weeks: 87.3%, 6 months: 84.2%).

#### **Other approach-related concerns**

**Critique 1** (pp. 5-6). We plan to work with the Data Coordinating Center and Clinical Coordinating Center for the final clinical protocol, including the proposed outcome. **Lost to follow-up:** We now plan to explore how lost-to-follow-up patients are different from retained participants. **Accrual concerns:** We have built our planned pace of accrual on LAMP, in which we were able to meet our goals of accruing 750 participants in 19 months. **UG3 recruitment:** We will recruit through the EHR for the UG3 pilot and the UH3 trial as described on p 209 and 2.5 Recruitment & Engagement Plan.

**Fidelity/dose:** Standardized fidelity assessments via videoconference will be performed by an experienced investigator for 30% of intervention sessions in the UG3. Assessment will include evaluation of completion and quality of required session activities. Additionally, 100% of sessions will require documentation by facilitators detailing completion of session activities, factors that may have affected the quality of the session, and rationales for any protocolized activities that were not performed. To measure dose and uptake, we will also measure number of individual and group sessions attended and amount of time individuals self-report engaging in different intervention components using structured surveys. **Aim 2**

**underdeveloped & no rationale for stakeholder sample size:** UG3 Aim 2 is focused on establishing feasibility using appropriate feasibility measures; methods are described on pp 209-211. The total sample size for stakeholders is 35-50, which should be adequate for reaching theme saturation for our qualitative analyses (e.g., the point at which no new themes emerge).

**Critique 2** (pp. 9-10). **Questions about modification of LAMP:** We will use the UG3 phase to modify the original MBI (LAMP) for the trial, including refining protocols for delivering VA-provided tablets to rural participants (pp. 206-211).

**Critique 3** (p. 12). **Effect sizes are modest:** We look forward to drawing from the expertise of the Pragmatic Trials Collaboratory workgroups to address critical issues related to effect sizes.

**Critique 4** (pp 13-14). **Unclear if rural-specific adaptations are needed beyond telehealth delivery:** we anticipate making such adaptations in the UG3 phase, informed by multi-level stakeholder input (pp. 206-208).



## References

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Supplemental  
Material

## A. SIGNIFICANCE

Chronic pain is a pervasive problem in the United States that disproportionately affects Veterans.<sup>4</sup> The Veterans Healthcare Administration (VA) is the nation's largest integrated care system, serving over 9 million Veterans, including 2.7 million rural-dwelling Veterans.<sup>3,34</sup> Two-thirds of all Veterans report chronic pain, resulting in significant functional limitations and high healthcare utilization.<sup>4,35</sup> The most common chronic pain conditions among VA patients are musculoskeletal disorders, with joint pain, back pain and osteoarthritis having the highest prevalence.<sup>36</sup> Despite reductions in overall opioid prescribing across the VA in recent years, there remains a significant subset who continue to receive long-term opioid medications for chronic pain.<sup>37,38</sup> VA patients are more likely than the general population to be treated with opioids,<sup>39</sup> and rural VA patients are disproportionately prescribed these medications.<sup>8</sup> Further, VA patients have nearly twice the rate of accidental fatal poisoning as US adults overall, and opioid analgesics are the drug class most commonly involved in these deaths.<sup>5</sup>

**Pain in Rural America.** Rural-dwelling individuals in the United States have increased prevalence of pain, less access to comprehensive chronic pain care, are more likely to be prescribed opioid medications, and experience greater harms from opioids compared to urban residents.<sup>1,2,7,40-43</sup> Rural VA patients receive over 30% more opioids than urban VA patients,<sup>8</sup> are less likely to receive comprehensive and specialty pain care,<sup>6,7</sup> and are less likely to use self-management interventions for pain.<sup>9</sup> Compared to men, female VA patients have greater rates of pain, are more likely to experience multiple comorbid chronic pain conditions,<sup>10,44</sup> and rural-dwelling female VA patients receive more pharmacologic and less specialty pain care, relative to their urban counterparts.<sup>6</sup>

**The Need for Whole Health Approaches to Pain Management.** Pain, 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.<sup>18,19</sup> Pain is frequently associated with psychological risk factors including poor cognitive and emotional coping strategies, depression, catastrophizing, and fear avoidance behaviors.<sup>45,46</sup> There is also growing evidence that social determinants of health are associated with greater likelihood of chronic pain and poorer outcomes.<sup>47-49</sup> Lack of social support,<sup>50-52</sup> and occupation and related factors such as physical workload, education, injury compensation, and dissatisfaction can also have a negative effect on pain.<sup>43,46</sup> Poor quality relationships, social stressors (e.g., due to racism, ostracism, injustice, invalidation, isolation), and low income and education status also have been shown to contribute to poor outcomes.<sup>43,53,54</sup> Further, there is growing recognition of the important intersections among trauma, violence, substance use, and pain.<sup>55</sup> Veterans in the VA healthcare system are especially impacted by these factors; they have lower levels of income and education and higher levels of trauma exposure compared to non-Veterans and Veterans not enrolled in VA care.<sup>56,57</sup> Compared to men, female VA patients are more likely to report history of interpersonal trauma, military sexual trauma, mood disorders, and anxiety disorders,<sup>10,44</sup> all of which can adversely affect treatment outcomes. Rural-dwelling female VA patients are even more impacted, with a high probability (50%) of interpersonal and/or sexual traumas,<sup>58</sup> high rates of emotional distress, and low levels of social support.<sup>10,11,58</sup>

To reduce the burden of pain, patients require greater access to evidence-based care that addresses their “whole-person” or biopsychosocial needs.<sup>59-61</sup> There has been a growing recognition that pain, like other chronic health conditions, requires ongoing attention to lifestyle factors and engagement in effective self-management.<sup>62,63</sup> While patients recognize the need for self-management strategies, they often need support and validation to initiate and maintain optimal self-care.<sup>64,65</sup>

**The VA and Whole Health:** In response to the opioid crisis which has disproportionately affected Veterans,<sup>4</sup> the VA has adopted policies and devoted resources to replace opioid-centric models of pain management with multi-modal approaches that prioritize evidence-based non-pharmacological pain treatments, including evidence-based complementary and integrative health (CIH) approaches.<sup>66-73</sup> The VA's Office of Patient Centered Care and Cultural Transformation (OPCC&CT) has significantly expanded the provision of CIH services over the last decade, supported by the passage of the Comprehensive Addiction and Recovery Act in 2016.<sup>33,74</sup> Central to this has been the implementation of a Whole Health (WH) model of care which aligns with established BPS models of pain. In the U.S., the VA is recognized as a national leader in Whole Health and nearly one third of VA patients with pain engage in some WH services.<sup>33</sup> Noteworthy is the threefold reduction in opioid use that has been observed among VA patients with chronic pain who engaged WH services compared to those who have not.<sup>33</sup>

A key component of the VA's WH model is the use of WH Coaches to engage in individual and group-based support to complement other healthcare services.<sup>75</sup> The role of the WH Coach is to assist patients in implementing sustainable healthy lifestyle behavior changes to more effectively manage their chronic health conditions. The VA is now hiring dedicated WH Coaches, including those who can support positive pain management behaviors. With training in



motivational communication and behavioral change techniques, WH Coaches are a valuable and affordable resource for implementing clinician recommendations, and increasing the reach of nonpharmacologic self-management approaches to chronic pain treatment, including CIH strategies.<sup>75</sup>

**CIH and Non-Pharmacologic Self-Management Interventions:** There are a range of evidence-based *CIH and non-pharmacologic self-management modalities* for improving pain outcomes,<sup>20,76-81</sup> including psychological strategies (e.g., behavioral or cognitive), mind-body approaches (e.g., mindfulness practices, meditation, relaxation, 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 neuroscience, and pain management tips).<sup>82,83</sup>

Mindfulness-Based Interventions (MBIs) are an especially popular CIH approach and central to the VA's WH model for promoting health.<sup>75</sup> MBIs have been shown to improve chronic pain through multiple pathways<sup>84-86</sup> and have demonstrated effectiveness for improving conditions commonly co-occurring with chronic pain in VA patients, such as PTSD, sleep disorders, depression, and substance abuse.<sup>87-89</sup> MBIs have also demonstrated promise for improving opioid-related outcomes.<sup>90</sup> Preliminary results by our team have found a group telehealth MBI for pain can be safely delivered, and is acceptable and engaging for VA patients (see **C.1 Prior Work**). We have also found a similar group MBI to be significantly more satisfactory and effective in increasing mindfulness and social connectedness than an active control in older adults in a community-based setting (see **C.1 Prior Work**). However, because of the complex biopsychosocial nature of chronic pain, as well as heterogeneous treatment responses and varied preferences and needs, MBIs alone (or any other single approach) are unlikely to meet the chronic pain needs of the majority of VA patients.<sup>22,54</sup> Importantly, VA patients have expressed a desire for more integration of multiple modalities (e.g., mindfulness with more physical movement).<sup>91</sup> Indeed, interventions integrating multiple evidence-based approaches are increasingly advocated to optimize pain management.<sup>22</sup> Multimodal approaches that support patients in better self-managing their emotional reactions, unhelpful coping and thinking patterns, and maladaptive behaviors (e.g., activity avoidance, inactivity, substance over use) are especially promising, particularly for pain sufferers experiencing intersecting biopsychosocial challenges.<sup>61</sup>

**Whole Person CIH Self-Management.** There has been a growing number of multi-modal CIH self-management programs that address pain from a whole-person perspective (i.e., taking into account BPS factors),<sup>92-94</sup> including in our own research.<sup>25</sup> Evidence shows that such programs can lead to improved pain and health behaviors, self-efficacy, and overall health.<sup>92,95-97</sup> In much of the research, however, effect sizes are modest, and the research is limited by inattention to underlying theoretical frameworks that align individuals' specific pain-related needs with appropriate program elements.<sup>63,92,95,98</sup> A major limitation of the existing research of multi-modal CIH self-management programs is that most of the study populations have been mainly White, highly educated, with relatively high levels of self-reported health.<sup>92,95,96,97</sup> This leads to questionable generalizability to Veterans and rural-dwelling populations, including those from racially diverse backgrounds, who are more likely to experience negative social determinants of health and poorer health outcomes.<sup>56,57</sup>

**Barriers to CIH and Whole Health Care:** Although the VA has made great strides in providing CIH approaches to pain, as part of its Whole Health model of care, these approaches remain underutilized,<sup>99</sup> particularly among rural VA patients.

<sup>6,7,9</sup> Studies with VA patients, leadership, and frontline staff managers, including those conducted by our team (see **Section C.1 Prior Work**), have identified key barriers and facilitators to widespread implementation of CIH in the VA,<sup>64,72,73,100-107</sup> including for rural populations.<sup>6,24</sup> Examples include difficulty traveling to the main VA medical centers where CIH services are offered,<sup>24,108</sup> need for a provider referral,<sup>109,110</sup> as well as lack of awareness and knowledge about CIH options for pain.<sup>21-23</sup> Additionally, some female VA patients are reluctant to go to the VA in person due in part to experiences of sexual harassment<sup>111</sup> and history of military sexual trauma.<sup>112</sup>

**Telehealth in the VA:** Telehealth is an evidence-based approach for delivering healthcare, which can reduce some of the barriers to care and improve appointment attendance and patient satisfaction.<sup>113-116</sup> The VA is the largest federal provider of telehealth services,<sup>117</sup> which rapidly expanded with the onset of the COVID-19 pandemic.<sup>118</sup> Last year, more than 2.3 million Veterans used VA telehealth services.<sup>119</sup> Recent studies have demonstrated the effectiveness of telehealth programs for rural Veterans,<sup>113,120,121</sup> including those with chronic pain.<sup>24,108,122</sup> The VA's Office of Connected Care (OCC), which oversees the VA's Telehealth Program, has developed multiple programs to facilitate remote access to telehealth care, in conjunction with the Office of Rural Health (ORH). These efforts include the OCC's work to enhance telehealth options and provide mobile applications to support clinical services and overall patient health, with particular attention to the needs of rural Veterans, who experience greater barriers to accessing telehealth than urban Veterans<sup>118,123</sup>

(see **Letters of Support** from our OCC and ORH partners). The OCC has also developed innovative programs to increase access to telehealth such as the Accessing Telehealth through Local Area Stations (ATLAS) program, which offers convenient locations in communities to access the internet for telehealth services,<sup>124</sup> as well as programs that distribute tablets to VA patients.<sup>125</sup>

## B. INNOVATION

This is an innovative project that will apply rigorous methods to overcome barriers that typically impede the implementation of CIH approaches for pain management for rural patients in the VA healthcare system. It will do so by:

- Using proactive outreach (see **C.3 Recruitment & Enrollment section**), a systems-level model of patient engagement that systematically identifies patients through the electronic health record (EHR) and reaches out to offer them care,<sup>126</sup> overcoming obstacles such as the need for a provider referral and lack of awareness of CIH.<sup>109,110</sup>
- Applying safe and engaging telehealth technology delivery formats to address distance and travel related barriers. These have been developed and previously tested by the investigators to expand reach and accessibility of MBIs and CIH for rural VA patients (see **C.1 Prior Work**); importantly they include options for those who do not have reliable internet access in their home (see **2.5. Recruitment and Retention Plan – Study 1**).
- Utilizing VA WH Coaches to facilitate a contextually relevant program via telehealth. WH Coaches are a valuable yet overlooked resource who understand the more complicated BPS needs of Veterans. They are ideally suited to increase the reach of CIH self-management approaches to chronic pain treatment and are now being used by the VA Office of Pain Management, Opioid Safety, & Prescription Drug Monitoring.<sup>75</sup> By combining WH Coach facilitation with a standardized delivery format using a protocolized curriculum and expert recorded videos tested previously by our team (see **C.1 Prior Work**), we will enhance fidelity, reproducibility and long-term implementation.
- Partnering with Community-Based Outpatient Clinics and non-VA community organizations to increase rural VA patients' access to CIH and other non-drug treatments within the VA and their local communities.
- Applying comprehensive theoretical models (see **C.2 Guiding Theoretical Models**)<sup>54,98,127,128</sup> in intentional ways to address Veterans' pain-related BPS needs, optimize the intervention's effectiveness, and enhance the likelihood of implementation, which is often inadequately addressed in intervention studies, including CIH.<sup>63,82,98</sup> This includes novel application of the established COM-B behavioral model with the BPS model, to ensure RAMP-WH provides rural Veterans' the *opportunities* and resources to enhance their *capabilities* and *motivation* to engage in more adaptive and helpful pain self-management behaviors.<sup>98</sup> We are also guided by the ConNECT Framework to assist our work in addressing health disparities, in partnership with patient, community, and VA stakeholders.<sup>129</sup>
- Measuring essential costs and resource-related data at multiple levels to inform a budget impact analysis that will yield critical information to facilitate policy decisions at the national and local VA levels.

## C. APPROACH

The Reaching Rural Veterans: Applying Mind-Body Skills for Pain Using a Whole Health Telehealth Intervention (**RAMP-WH**) project is comprised of stakeholder engagement activities and a randomized hybrid type 2 effectiveness-implementation trial of an innovative non-opioid approach to chronic pain management. RAMP-WH strategically coalesces multiple evidence-based CIH self-management strategies to address rural VA patients' BPS needs and overcome existing barriers to widespread implementation in the VA healthcare system. RAMP-WH is grounded in mindfulness, and integrates mindfulness practices, pain education, physical and rehabilitative exercise, and cognitive and behavioral strategies into a cohesive, scalable curriculum, designed to be facilitated by VA WH Coaches and implemented within the VA's Whole Health initiative.<sup>33</sup> Importantly, we will collaborate with key stakeholders throughout the life of the project, including rural VA patients, community partners serving diverse Veterans, and the VA healthcare system leadership and staff.

**Design.** This is a two-phase study (see **Figure 1**, also see **C.9 Responsiveness to the RFA**).

**UG3 Phase (Years 1-2)** will prepare for the future UH3 trial. The UG3 aims are as follows:

**UG3 Aim 1** focuses on *stakeholder engagement activities*; this includes identifying and developing new community partnerships and using mixed methods data collection from multiple levels of stakeholders (n=35-50 patients, community partners, healthcare system leaders and staff), guided by the established RE-AIM/PRISM framework, to learn about key factors that can affect long-term adoption and sustainability.

**UG3 Aim 2** will involve a *pilot study* of 40 rural VA patients with chronic pain to assess the feasibility of delivering RAMP-WH (experimental intervention for the UH3 trial) in terms of recruitment and engagement, intervention fidelity and adherence, data collection, and other key metrics.

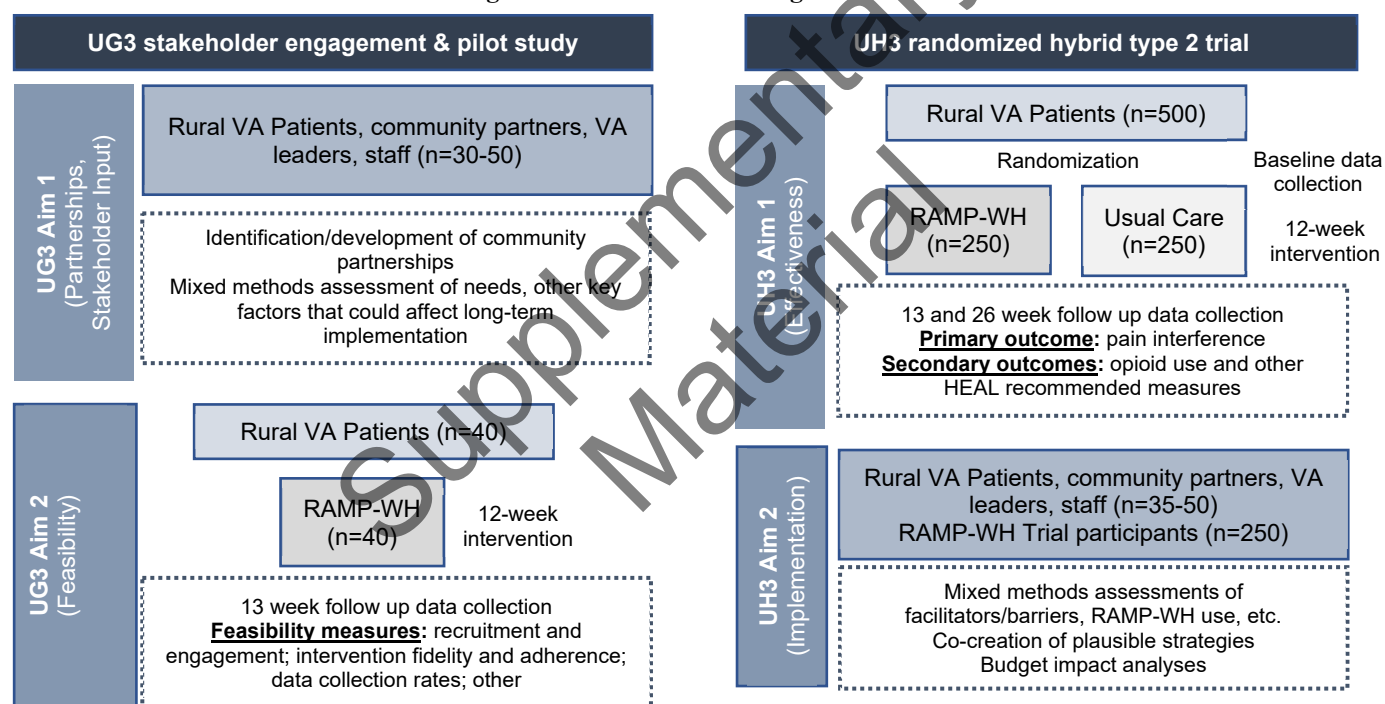
**UH3 Phase (Years 3-5)** consists of a *randomized hybrid type 2 effectiveness-implementation pragmatic clinical trial* of RAMP-WH compared to Usual Care, enrolling 500 rural VA patients from the VA healthcare system, oversampling female and racial/ethnic minority patients.

**UH3 Aim 1 (EFFECTIVENESS)** examines the relative effectiveness of RAMP-WH versus Usual Care in rural VA patients in terms of **primary effectiveness outcome** of pain interference at 13 and 26 weeks and **secondary outcomes** including opioid use and other HEAL recommended outcomes. Additional exploratory analyses of women and minority Veterans' primary and secondary outcomes will also be performed.

**UH3 Aim 2 (IMPLEMENTATION)** will include working iteratively with multiple levels of stakeholders (n=35-50 patients, community partners, VA healthcare system leaders and staff), to evaluate intervention implementation strategies within the trial and adapt these strategies to scale up RAMP-WH within the national VA healthcare system. This will include:

- Conducting mixed-methods assessments of VA stakeholder and randomized trial participant views of implementation related barriers and facilitators, resource needs, and other RE-AIM/PRISM domains.
- Working with VA stakeholders to co-create additional plausible strategies for overcoming barriers to implementation of RAMP-WH, within the national VA healthcare system.
- Conducting budget impact analyses using models informed by stakeholder views to inform future decision making.

Figure 1. UG3 and UH3 Design Overview



We have applied complementary models and frameworks to facilitate the project's long-term objective (see **C.2 Guiding Theoretical Models and Frameworks**).

**RE-AIM/PRISM:** provides overall guidance for improving and measuring Reach, Effectiveness, Adoption, Implementation and Maintenance of the RAMP-WH intervention.

**COM-B Model:** provides guidance for assessing needs, facilitators and barriers and identifying intervention solutions aligned with desired outcomes.

**Dynamic Biopsychosocial (BPS) Model:** provides insight into whole person needs and BPS risk and protective factors, including social determinants of health (SDH)

**ConNECT Framework:** provides guidance for authentically and equitably partnering with stakeholders

**Rationale for design.** Engaging stakeholders is a key element of successful implementation research<sup>22,127</sup> and pilot studies are essential for evaluating feasibility prior to embarking on a larger trial.<sup>130</sup> Hybrid type 2 trials are appropriate when there is a need to focus simultaneously on intervention effectiveness and implementation strategies that are plausible for the intended setting.<sup>131</sup> Importantly, RAMP-WH builds on our team's prior research, including a hybrid type 1 multisite, randomized pragmatic trial of a telehealth mindfulness intervention for pain, which is the precursor of RAMP-WH.<sup>132</sup> This study (which is ongoing) has provided important "implementation momentum,"<sup>133</sup> a robust foundation for the proposed trial, and the design of an intervention that is congruent with VA stakeholder priorities (see **C.1 Prior Work**).<sup>33</sup>

### C.1 Prior work by our study team that supports the proposed project

**Principal Investigators' Prior Work:** The multiple principal investigators (MPIs) have done extensive prior research that supports the proposed project. This includes complex randomized trials, including hybrid type 1 and 2 effectiveness-implementation studies, resulting in high engagement and follow-up rates, including in traditionally underserved and hard-to-reach populations. They have also built strong collaborations with Co-Is who have conducted important research on VA patients' pain-related beliefs and treatment needs, as well addressing barriers and facilitators to CIH implementation in the VA system, including rural VA patients.<sup>8,134,135</sup> The following highlights the most pertinent prior work by our study team that supports the proposed project.

**MPI Burgess** is trained as a social psychologist and has been conducting research on chronic pain for 20 years, with a focus on underserved groups and populations that experience health disparities. Her most recent research focuses on the study of non-pharmacologic treatments for pain and addressing multi-level, implementation barriers impeding their widespread use.

**LAMP (NH170001):** Dr. Burgess currently leads a NIH-DOD-VA Pain Management Collaboratory (PMC) supported

randomized hybrid Type 1 trial (n=811),<sup>132</sup> which has substantially informed the design and development of the proposed randomized hybrid Type 2 trial. LAMP (Learning to Apply Mindfulness to Pain) compares a group telehealth MBI, to an app-only MBI, and Usual Care (control) condition. Dr. Burgess works closely with Co-Is B. Taylor, S. Taylor, Ferguson, and Matthias who have been instrumental in successfully applying an innovative recruitment approach, "proactive outreach" (see **C.3 Recruitment & Enrollment section**), to engage and enroll VA patients. Dr. Burgess has also collaborated with MPI Evans who serves as a Co-I on the LAMP study, and has been responsible with Co-I Haley for applying established behavioral models (COM-B)<sup>98</sup> to design, develop and monitor the LAMP telehealth MBI with consultant Dr. Serpa. Key format features of the LAMP MBI include the use of a standardized curriculum and expert videos to enhance fidelity and potential dissemination and content designed to meet Veteran needs.

Table 1. LAMP Study: Interim RE-AIM Measures	
<b>Reach</b>	<p><b>Patient Characteristics:</b>  811 patients enrolled  38% rural, 48% female, 30% racial/ethnic minorities  Pain: 37% limb/joint pain, 30% back or neck pain, 10% fibromyalgia, 13% other  Mental Health: 37% depression, 24% PTSD, 23% anxiety, 11% stress or trauma</p> <p><b>Recruitment methods:</b>  Email yielded greater response rates than traditional postal recruitment</p>
<b>Effectiveness**</b>	<p><b>Patient Views of LAMP Effectiveness:</b>  75% satisfied  96% would recommend program to another Veteran</p>
<b>Adoption</b>	<p><b>VA Facilitator, Leadership Views:</b>  Recommend use of WH coaches, greater integration with VA WH Initiative to facilitate widespread adoption in VA facilities; additional recommendations made for optimizing program (e.g., longer duration, more focus on pain education, pain related exercises, other options other than mindfulness)</p>
<b>Implementation</b>	<p><b>LAMP group telehealth MBI:</b>  &gt;70% attended 5/8 sessions  &gt;80% of participants report home practice  No serious adverse events of &gt;150 group sessions  &gt;90% of session activities delivered by facilitators as planned</p>
<b>Maintenance**</b>	<p><b>Interviews with VA facilitators/leadership:</b>  Success of LAMP thus far has created interest and momentum; adaptations (see Adoption above) have been recommended and incorporated into RAMP-WH</p>
<p><b>**Effectiveness and maintenance measures are currently being collected as part of the long-term follow up. Current follow up rates are excellent with &gt;80% of participants (experimental and control) having completed 10-week, 6-month, and 12-month assessments.</b></p>	

The LAMP study is currently fully enrolled and collecting final outcomes data. Examples of interim monitoring of key implementation metrics from patient and VA stakeholders using the RE-AIM framework are summarized in **Table 1**.

**ACTION Study (VA HSR&D IIR 13-030-2):** MPI Burgess recently completed a randomized clinical trial of a walking-focused telehealth intervention for Black VA patients with chronic musculoskeletal pain (ACTION), which successfully used proactive outreach to engage underserved patients (many of whom had comorbid mental health conditions) and resulted in shorter-term (3 month) and sustained (6 month) improvements in chronic pain.<sup>109,136,137</sup>



**MPI Evans** is clinically trained as a chiropractor, and scientifically as a clinical trialist with a focus on intervention design; she has been studying a range of non-medication and CIH interventions for pain conditions and overall health for over two decades. Her most recent research emphasizes working with stakeholders at multiple levels and applying theoretical models and frameworks that can facilitate long-term implementation of interventions. She has collaborated with several of the investigators on the proposed project, including Dr. Burgess on the LAMP study (see above). Her current work investigates multi-modal approaches (mindfulness, physical and rehabilitative exercises, cognitive and behavioral strategies) to promote adaptive pain and health behaviors, using in-person and telehealth formats. Her research has included working with patients in out-patient clinical<sup>26,138-140</sup> and community settings (R21/R33AT009110), including those who experience health disparities (R61AT012309). Importantly, her research has resulted in processes and procedures yielding high engagement and follow-up rates, as well as a library of patient centered CIH materials and resources for pain management (e.g., educational and exercise videos, instructional infographic handouts).

**Y-U Study (NCCIH R21/R33AT009110):** MPI Evans with Co-Is Leininger and Haley have recently completed a phased pilot study leading to a randomized hybrid type 2 trial (n=182) of a group telehealth MBI versus an active control to increase physical activity in older adults in YMCA settings. The MBI was designed using the COM-B model,<sup>126</sup> and the study used the RE-AIM framework<sup>92</sup> to facilitate future implementation. Participants in the MBI group had consistently greater improvements in accelerometer-based measures compared to the control group, but these were not statistically significant. A significant advantage was observed, however, for the MBI condition in terms of mindfulness, social connectedness and satisfaction. Engagement in both groups was high (95% in intervention group, 89% in control); follow up rates were over 85% in both groups. Home practice rates (use in past week) for the MBI group exceeded 85%. A highlight of the study has been the transfer of the MBI to the YMCA for long-term implementation into its routine programming (done within 6 months of study completion); its first independent cohort is currently underway.

**SUPPORT Trial (NCCIH R34AT011209):** Co-I Leininger recently completed a feasibility study (n=40) examining a multi-modal CIH intervention comprised of exercise and posture techniques and behavioral, sleep, and communication strategies to facilitate engagement in pain self-management behaviors for patients with back-related leg pain (sciatica). The experimental intervention was designed using the COM-B model, which aided in identifying patients' needs;<sup>126</sup> the control intervention was guideline-based medical care. The study had high engagement rates (greater than 90%) in both groups and more than 85% of the CIH intervention group was very satisfied with the different CIH strategies, as well as the supporting resources (e.g., workbook, video recordings, website). An additional associated Administrative Supplement has been completed applying community engagement principles guided by the ConNECT Framework<sup>129</sup> to explore the COM and BPS related needs<sup>93,126</sup> of 28 individuals from traditionally underserved populations (96% minority, 75% low socioeconomic status). Qualitative interviews were conducted and a rapid deductive, content analysis approach was performed guided by the COM and BPS models.<sup>141,142</sup> Preliminary results have revealed a range of important barriers to individuals' specific needs being met (e.g., re-traumatization affecting **psychological motivation** to engage in CIH and other care) as well as facilitators (e.g., **social** factors including positive practitioner/staff-patient relational alliances impacting **motivation**). This information will be matched to appropriate strategies for future intervention development and optimization, including for RAMP-WH.

**PACBACK Study (NCCIH UG3/UH3AT008769):** Drs. Evans and Leininger are Co-Is of a large, randomized hybrid type 2 trial (n=1180), examining a novel multimodal CIH intervention (cognitive behavioral strategies, rehabilitative exercises, and manual therapies) for preventing acute spine pain from progressing to chronic pain. The control intervention is Medical Care (guideline based). Rates of adherence to the intervention sessions have been high (88%), as have follow-up data collection rates (more than 90% for weekly and monthly surveys over 1 year).

**PARTNERS4PAIN Study (NIH HEAL R61AT012309):** Drs. Evans and Leininger are Co-PIs of a recently awarded phased randomized hybrid type 2 community engagement trial. The first phase (R61, n=40) focuses on co-developing a multimodal CIH program for back pain with patients and community organizations and feasibility testing the program; the second phase (R33, n=376), will examine the program's effectiveness and implementation relative to an active control. Informed by the REAIM/PRISM and ConNECT Frameworks,<sup>129,143</sup> and guided by the COM-B model<sup>98</sup> for designing interventions, Partners4Pain seeks to improve equitable access to evidence based CIH approaches for people with pain who experience health disparities. Drs. Burgess, Austin and Mr. Haley are collaborating Co-Is. The investigators have adopted a strong organizational structure and efficient processes to collaborate with stakeholders and co-develop and co-create culturally relevant resources to support pain self-management.

**MPI Hadlandsmyth** is a clinical psychologist and has piloted behavioral pain self-management interventions with both rural VA patients and with women VA patients with chronic pain.<sup>6,30,32</sup> Her research has yielded critical information about

the barriers and facilitators to delivering behavioral pain self-management interventions via telehealth to Veterans in rural settings. This includes the importance of 1) framing pain self-management interventions in ways that lead rural Veterans to being more receptive to trying them, and 2) providing multiple options for telehealth access.

***The Perioperative Pain Self-management (PePS) pilot (ORH 16023):*** Dr Hadlandsmyth recently completed a pilot of a remotely accessible behavioral pain self-management intervention among rural patients undergoing surgery. The objective of the PePS intervention was to enhance pain self-management skills in the pre- and post-operative period to improve long-term pain and opioid use outcomes following surgery. The findings from this pilot (n=110) were promising, with intervention participants having a reduced risk for persistent pain at 3-months post-surgery.<sup>30</sup> Currently, Dr. Hadlandsmyth is conducting a larger multi-site trial of the PePS intervention with Dr. Burgess as the Minneapolis site PI (VA HSR&D IIR 20-115).

***Rural Women with Chronic Pain (ORH 10712):*** Dr. Hadlandsmyth recently completed a needs assessment among rural women patients with chronic pain (N = 153) to identify pain care needs in this population. Findings from this mixed methods needs assessment indicated a desire for greater access to non-pharmacological care, remote access to interventions, and opportunities to receive care with other women with chronic pain. Dr. Hadlandsmyth subsequently developed an intervention and is piloting it in this population (n = 32 to date; target n = 60). Preliminary data indicate high rates of satisfaction with the intervention (92%).

***Co-Investigators' Prior Work:*** The MPIs are supported by an experienced team of co-investigators who have conducted a large body of research that has been pivotal for informing the proposed project. Co-I S. Taylor has led a program of research to understand and address barriers and facilitators to implementation of CIH in the VA. This includes a large-scale multi-level stakeholder qualitative interview study,<sup>100</sup> a national survey of CIH program leads at VA medical centers and CBOCs (289 sites), a large-scale Veteran survey of CIH use and satisfaction,<sup>73</sup> and a project with providers and patients to design and iteratively test patient and provider education materials about CIH therapies.<sup>107</sup> Co-I Matthias has done extensive work examining messages directed toward patients about chronic pain treatment, including treatment decision-making and research addressing patient engagement in pain treatment.<sup>64,105,106,144-149</sup> She and her team (including MPI Burgess) recently completed the COOPERATE trial (VA HSR&D IIR 17-032), a coaching intervention that led to increases in patient activation, communication self-efficacy, and improvements in pain-related outcomes for Black patients.<sup>150,151</sup> Building on COOPERATE, her team (including MPI Burgess and Co-I S. Taylor) have just begun the OPTIONS trial (VA HSR&D SDR 21-012), which focuses on overcoming patient-related barriers to nonpharmacological pain treatments and the EQUIPD trial (NIH HEAL 1R61NS130636), which will test an intervention aimed at Black patients with depression to increase their access to and use of nonpharmacological pain treatments. Co-I Ferguson's research has focused on the equitable delivery of telehealth technology for clinicians, patients, and care partners.<sup>152,153</sup> He also has experience analyzing data collected remotely from VA research participants across a range of geographical areas.<sup>154,155</sup>

## C.2 Guiding Theoretical Models & Frameworks

Our team has developed a comprehensive conceptual approach for the proposed project based on input from our stakeholders, our previous research, and the scientific literature. It is informed by complementary models and frameworks appropriate for addressing the project's aims and objectives of increasing rural VA patients' access to non-pharmacological and CIH approaches for pain. Importantly, the investigators have experience applying these in their previous and ongoing research (see C.1 Prior Work).

Our hybrid effectiveness implementation trial design was informed by the PRECIS tool<sup>156</sup> and maximizes pragmatism, while including several explanatory elements to ensure internal validity. Pragmatic design features include those related to: a) recruitment and b) setting (participants recruited from and study conducted in real-world clinical settings); c) organization (we are using VA Whole Health coaches, a telehealth format consistent with VA healthcare system current initiatives, and are collaborating with community partners (see C.3 UG3 Aim 1)); d) primary outcome (pain interference) and secondary outcomes span biophysical, psychological and social domains highly relevant to patients with chronic pain;<sup>157,158</sup> e) primary analysis (intention-to-treat); and f) eligibility (broad inclusion criteria to maximize diversity, with minimum exclusions based on age, health literacy, expected adherence, or risk/comorbidities). Additionally, g) we do not attempt to control for non-specific effects due to differences in time of and attention to the interventions and h) we use "usual care" as a comparator. More explanatory elements include those related to a) flexibility in delivery (coaches will be delivering a structured program); b) adherence (we will use engagement strategies such as email and text reminders to increase intervention participation); and c) follow-up (we will employ extensive measures to obtain follow-up data from participants at 13- and 26-week time points to ensure high internal validity).



**Guiding Theoretical Models and Frameworks.** We have chosen to use the **RE-AIM/PRISM framework** to provide overarching guidance to ensure relevant contextual factors (e.g., barriers and facilitators, processes of change and related outcomes) from the vantage point of multiple VA stakeholders, which are considered and addressed throughout the project lifespan, enhancing the likelihood of long-term implementation.<sup>22,127</sup> RE-AIM provides the opportunity to iteratively shape and adapt methods and measures by taking into account Reach, Effectiveness, Adoption, Implementation (including fidelity), and Maintenance. PRISM (the Practical Robust Implementation Sustainability Model) is an extension of RE-AIM that pays additional, more nuanced, attention to the internal and external factors affecting the implementing organization.<sup>127</sup>

We are also guided by the **ConNECT Framework** for advancing health equity in behavioral health. This framework provides actionable principles that can be infused throughout the entire research process.<sup>129</sup> Use of ConNECT helps ensure greater and sustained consideration to how the researchers work with communities who experience health disparities, including giving greater attention to social contexts (e.g., socioecological determinants, biological/physical and psychological influences). It also emphasizes processes that foster a norm of inclusion, ensure equitable diffusion of innovations, harness communication technology, and prioritize specialized training for study team members.

The intervention design and development is informed by the **Capabilities, Opportunities, Motivational-Behavioral (COM-B) model**, coupled with the **dynamic biopsychosocial model** of pain, which acknowledges the complex and reciprocal interactions between the evolving biopsychological or “whole” person and their external, social environment.<sup>54,98,128</sup> An advantage of COM-B is that it represents a synthesis of 19 behavioral theoretical frameworks and thus is more comprehensive than a single theory driven model. It posits that to achieve positive or adaptive pain related behaviors (e.g., self-management) an individual’s capabilities, opportunities, and motivations must be addressed. As an example, physical inactivity, poor emotional regulation, and social isolation are common, unhelpful behaviors associated with pain. We hypothesize that by providing rural VA patients’ the *opportunities* and resources through RAMP-WH we can enhance their *capabilities* and *motivation* to engage in more adaptive and helpful pain self-management behaviors.

### C.3. UG3 Activities Preparatory for UH3 Project

**UG3 Milestones.** Essential milestones are presented in **Table 2.** with associated goals and thresholds. They include identifying our specific community partners (see **Stakeholder Engagement Plan** below), finalizing agreements with partners and other stakeholders, securing regulatory approvals; developing recruitment and engagement processes and materials to reach rural VA patients including female and racial/ethnic minority patients, training WH Coach Facilitators and developing processes to encourage intervention fidelity and adherence, and finalizing data collections procedures for effectiveness and implementation related measures.

<b>Table 2. UG3 Milestones*</b>	
<i>Multi-level stakeholder panels established</i>	Community-based partnerships developed; patient, community, and VA stakeholder panels established
<i>Agreements &amp; regulatory approvals</i>	All necessary approvals received (e.g., IRB, NIH DSMB of study protocol, accrual/retention plan, data safety/monitoring plans, etc.)
<i>Recruitment &amp; enrollment (Pilot Study)</i>	40 rural Veterans, at least 35% female, 35% racial/ethnic minorities
<i>Experimental intervention (Pilot Study)</i>	75% satisfied with RAMP-WH program; 75% attend recommended # of sessions (≥ 7/12) WH Coach Facilitators deliver 90% of session activities 90% of the time
<i>Data collection (Pilot Study)</i>	>80% complete post-treatment data collection (at 13 weeks)
<i>Stakeholder views (Stakeholder Engagement)</i>	Multi-level stakeholder perspectives of barriers/facilitators to RAMP-WH implementation, including reach, perceived effectiveness, potential for adoption, implementation, and maintenance (N=35-50; see <b>Stakeholder Engagement Plan</b> and <b>Table 5</b> ).
*Also see <b>5.1.2 Milestone Plan – Study 1</b> for additional details	

### UG3 AIM 1: STAKEHOLDER ENGAGEMENT ACTIVITIES

**UG3 Aim 1** focuses on *stakeholder engagement activities*; this includes identifying and developing new community partnerships and using mixed methods data collection from multiple levels of stakeholders (n=35-50 patients, community partners, healthcare system leaders and staff), guided by the established RE-AIM/PRISM framework, to learn about key factors that can affect long-term adoption and sustainability.

**Stakeholder Engagement Plan.** The objective of our engagement plan is to create a partnership between the research team and important stakeholders characterized by mutual learning. This will maximize our ability to generate trustworthy, internally valid findings, directly relevant to stakeholders, and facilitate the implementation of RAMP-WH to the national VA healthcare system. The Stakeholder Plan will be implemented by the Stakeholder Engagement Team, led by MPI Hadlandsmayth (see **3.5 Structure of the Study Team**), with guidance from stakeholder Dr. Krebs, one of the PIs on the VA HSR&D Pain/Opioid Consortium of Research (CORE) who has extensive experience working with multi-level stakeholders, including as PI of the PCORI-funded VOICE trial (OPD-1511-33052; see **Letter of Support**). Stakeholders will be purposively selected to represent racial, ethnic, gender, and geographic diversity. To facilitate successful collaborations between the stakeholders and researchers, we will develop a formative evaluation strategy for our engagement plan to understand, refine, and continually improve our engagement activities (see **2.5 Recruitment and Retention Plan – Study 3 for Stakeholder Engagement Plan Evaluation**). Dr. Hadlandsmayth will lead this evaluation using methods employed in our LAMP study (see **C.1 Prior Work**). Emerging findings will be frequently reviewed and presented to stakeholders to evaluate if the structure and format of engagement activities matches their preferences and whether they are achieving desired results.

Consistent with the RE-AIM/PRISM and ConNECT Frameworks,<sup>129,143</sup> we have identified three main levels of stakeholders who we will partner with on this study; they are described below in **Table 3** and in the **3.5. Structure of the Study Team document**. We will actively collaborate with our stakeholders, soliciting their views and perspectives on RAMP-WH and considering RE-AIM/PRISM related factors. This will include contextual information collected via mixed methods to provide further insights into issues that could affect the ability to conduct the full-scale UH3 Project, as well as issues that could potentially affect subsequent implementation and translation of RAMP-WH to serve diverse rural VA patients nationwide. Examples of RE-AIM/PRISM related factors relevant to the UG3/UH3 are provided in Table 5.

#### ***Patient Partners (n=15-20).***

In addition to assessing study patient participants views (pilot study and randomized trial), we will also seek input from other rural VA patients with pain.

#### ***RAMP-WH Patient***

#### ***Engagement Panel (PEP)***

***(n=10).*** We will establish a RAMP-WH PEP comprised of rural VA patients with chronic pain from diverse backgrounds (e.g., geography, race/ethnicity, gender, age). The PEP will partner with our team throughout the course of the project, drawing from principles of community-engaged research.<sup>129,143</sup> The PEP will be established in collaboration with the Growing Rural Outreach through Veteran Engagement

(GROVE) Center (see **Letter of Support from Dr. Steffensmeir**) and Veteran leaders Mr. Adam Anicich, Mr. Sean Green and Dr. Vanessa Meade, who are members of our Stakeholder Engagement Panel and have extensive experience partnering with diverse Veteran organizations (see **Letters of Support**). We will use the “community engagement studio” (CE studio) model for working with the PEP,<sup>159</sup> promoted by the VA Health Services Research and Development Veteran Engagement workgroup, and successfully used in the previous LAMP study, to identify and train both stakeholders and researchers in patient engagement. The model will also be used to guide the structure and conduct of meetings to ensure the co-learning experience is successful, focused, and effective.<sup>160</sup> Studios will provide a tailored and creative space to explore study issues with patient partners. Members will be paid for their participation.

**Table 3. Multiple Levels of Stakeholders and Partners**

Stakeholder/Partners (n=35-50)	Description/Specific Focus
<b>Patient Partners (n=15-20)</b>	
RAMP-WH Patient Engagement Panel (PEP; n=10) and other ongoing Veteran Engagement Panels (n=5-10)	Rural VA patients with chronic pain from diverse backgrounds (e.g., geographic, race/ethnicity, gender, age).
<b>Community Partners (n=10-15)</b>	
Non-VA Community Organizations	Organizations serving Veterans in local communities (e.g., VFWs, American Legions) in regions served by VISNs** 7 (Southeast) and 23 (Midwest) and organizations serving diverse Veteran communities (e.g., SWAN: Service Women’s Action Network). Provide guidance on addressing barriers and preferences for rural Veterans from diverse backgrounds and communities.
<b>VA Healthcare System Partners (n=10-15)</b>	
National VA Program Office Leaders*	Sets and oversees VA policy and programs. Guidance on implementing study and on the next stage of integrating RAMP-WH into VA healthcare system nationwide
VA Medical Center Leaders & Staff	“Parent” facilities that provide in person and virtual care resources to affiliated CBOCs*** in VISNs 7 and 23. Co-create plausible strategies for implementing RAMP-WH at local levels
VA CBOCs: Leaders & staff	Clinics in rural locations associated with VA Medical Centers in VISNs 7 and 23. Co-create plausible strategies for implementing RAMP-WH at local level.
*Includes OPCC&CT = Office of Patient Centered Care and Cultural Transformation; PMOP = Pain Management, Opioid Safety, Prescription Drug Monitoring Program; ORH = Office of Rural Health, OCC = Office of Connected Care. Other Potential Program Offices to Involve During UG3 Phase: Primary Care; Women’s Health; Office of Health Equity. **VISN = Veterans Integrated Service Networks. ***CBOC = Community Based Outpatient Clinics.	

**Engagement Format, Frequency:** hybrid (in person and videoconferencing to meet stakeholder preferences) meetings; at least three times per year. These are modeled on the meeting format successfully utilized by Dr. Krebs in her VOICE trial to accelerate stakeholder engagement.

*Other Ongoing Veteran Engagement Panels (n=5-10).* We will also draw on other established Veteran Engagement Panels throughout the project to provide broader perspectives. These include the *Center for Access & Delivery Research and Evaluation (CADRE) Veteran Engagement Panel* comprised of rural VA patients; the *Growing Rural Outreach through Veteran Engagement (GROVE) Center Midwest Veteran Engagement Panel*; and the *Pain/Opioid Care Veteran Engagement Panel*, a diverse panel of patients with chronic pain, who meet regularly to provide feedback to VA research investigators involved in pain and opioid research.

**Engagement Format, Frequency:** hybrid (in person and videoconferencing), at least once per year.

**Community Partners (n=10-15).** As part of the UG3 preparatory activities, we will identify and develop new community partnerships. The RAMP-WH telehealth intervention is intended to reach rural Veterans, who are dispersed throughout different rural communities and receive care at different CBOCs. Because RAMP-WH participants will be dispersed among rural communities in the Midwest and Southeast ((Veterans Integrated Service Networks (VISNs) 7 and 23)), see **Sampling** below), we will identify organizations serving Veterans in local communities in these regions. Examples include local branches of the American Legion and the Veterans of Foreign Wars (VFW). We will also identify organizations serving diverse Veteran communities such as women and racial, ethnic, and sexual minority Veterans, which may be local or national, since those communities may not be represented by local organizations such as the VFW. Recruiting and successfully partnering with such community organizations that specifically serve rural-dwelling patients, will be facilitated via the GROVE center and Mr. Anicich, Mr. Green and Dr. Meade (described in the **Patient Partners** section).

**Engagement Format, Frequency:** hybrid (in person and videoconferencing), at least three times per year.

**VA Healthcare System Partners (n=10-15).** We will partner with leaders from national VA Program Offices who oversee VA policy and programs that will be key to implementing the proposed trial and to integrating RAMP-WH into the VA healthcare system nationwide (Office of Patient Centered Care and Cultural Transformation; Pain Management, Opioid Safety, Prescription Drug Monitoring Program; the Office of Rural Health and the Office of Connected Care; see **Table 3 and Letters of Support** from Drs. Sandbrink, Kligler, Heyworth, and Turvey/Solimeo). We will also work with the VA Community Based Outpatient Clinics (CBOCs), leaders and staff in the Southeast (VISN 7) and the Midwest (VISN 23) and VA Medical Center leaders and staff from “parent” facilities in those regions that provide in-person and virtual clinical care to affiliated, rural CBOCs (e.g., leaders: Pain Committee Lead, Telehealth hub lead, staff: Whole Health coach, WH manager, Whole Health Flagship Site staff, primary care providers, integrative health providers).

**Engagement Format, Frequency:** hybrid (in person and videoconferencing) at least once per year, group and/or individual meetings/communication as needed.

### **Stakeholder Views and Perspectives: Mixed Methods Data Collection and Analyses (UG3 Aim 1)**

We will solicit stakeholder views and perspectives using mixed methods (qualitative and quantitative) to provide further insights into issues that could affect the ability to conduct the full-scale UH3 Project, as well as those that affect eventual adoption of RAMP-WH across the VA nationwide. Examples of our data collection methods include surveys with open-ended response fields and individual and focus group interviews using semi-structured interview guides informed by our study’s conceptual models (see **C.2 Guiding Theoretical Models and Frameworks** and **Table 5**).<sup>141</sup> Interview data will be video and/or audio-recorded and notes documented by interviewers in sessions. Mixed method assessment will be conducted. Quantitative data will be analyzed using descriptive statistics when appropriate (e.g., stakeholder characteristics). For the qualitative analysis, teams of 2-3 will perform rapid deductive, directed content analytic methods to video/audio-recordings and text from open-ended surveys; the coding structure and operational definitions will be guided by the study’s conceptual models<sup>141,142</sup> to provide insights into barriers and facilitators to RAMP-WH’s future implementation.<sup>98,127,128,161</sup> Directed content analyses will also allow for inductive gathering of important themes that might fall outside of our chosen models and frameworks.<sup>142</sup> 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.<sup>141,162</sup> This is in contrast to traditional qualitative methods which rely on resource-heavy methods including transcribing interviews verbatim and in-depth coding of transcripts. The qualitative analyses will be conducted by study team members with qualitative and mixed methods research experience (Evans, Matthias, S. Taylor, Burgess).<sup>106,107,144,145,163,164</sup>

## UG3 AIM 2: PILOT STUDY

**UG3 Aim 2** will involve a *pilot study* of 40 rural VA patients with chronic pain to assess the feasibility of delivering RAMP-WH (experimental intervention for the UH3 trial) in terms of recruitment and engagement, intervention fidelity and adherence, data collection, and other key metrics.

**Sampling.** A total of 40 rural VA patients with chronic pain will be recruited and enrolled to participate in the RAMP-WH intervention. We will draw from an estimated sample of 50,000 rural Veterans from two of the VA's healthcare system's Veterans Integrated Service Networks (VISNs 7 and 23). These VISNs represent the Southeast and Midwest regions of the U.S. and have been chosen for their socio-demographic composition (e.g., race, ethnicity, gender, age). We will oversample female and racial/ethnic minority patients so that we reach milestones of 35% female, and 35% minority VA patients (see **2.4. Inclusion of Women and Minorities – Study 1**).

**Recruitment and Enrollment.** We will identify VA patients from the two VISNs described above using the national VA electronic health record (EHR) and deliver the intervention using telehealth. The sample size for the UG3 has been informed by previous studies by our team who have found this number sufficient for informing the feasibility of larger, randomized clinical trials.<sup>165-167</sup>

We will use a **proactive outreach approach** to recruitment, with tailored engagement materials to raise awareness and generate interest among rural VA patients with chronic pain. Our team has had success using proactive outreach in an ongoing study of mindfulness for VA patients (LAMP; NHI70001) resulting in enrollment of a diverse VA patient population: 48% women (who are an underserved group in VA and are underrepresented in VA studies), 30% from racial/ethnic groups, and 38% rural-dwelling. We will address potential barriers to recruitment including lack of reliable access to a device (e.g., phone, computer) and/or broadband internet service. This includes having study staff connect with individuals on a case-by-case basis to discuss available local options provided by the VA's Office of Connected Care (e.g., ATLAS program, VA provided tablets). Additional details are provided in section **2.7 Recruitment and Retention Plan – Study 1**.

**Screening and Eligibility.** Eligible participants must be rural-dwelling VA patients, using the Health Resources & Services Administration (HRSA) definition of rural. Other eligibility criteria are based on those successfully used in the LAMP trial **described in C.1 Prior Work**.<sup>132</sup> Participants must report pain at least most days in the past 6 months (pain chronicity threshold);<sup>168</sup> have a pain intensity score of  $\geq 4$  on the 0-10 Numeric Rating Scale;<sup>169,170</sup> have an email address in the EHR; and be willing/able to complete study activities including meeting remotely via videoconferencing when RAMP-WH sessions are held (either at home or in a location with internet access). We will exclude patients who have been hospitalized for a severe mental illness-related issue in the past 6 months; have active psychotic symptoms, suicidal ideation, or manic episodes (based on chart review); are currently enrolled in a research study for their pain; or are enrolled in a similar program to RAMP-WH.

**Pilot Study Intervention.** The design of the RAMP-WH multi-modal intervention builds upon the investigators' previous studies of mindfulness, exercise, pain education, and behavioral approaches to chronic pain management (see **C.1 Prior Work**). We developed RAMP-WH with VA Whole Health leadership to ensure that the program meets the criteria for WH coaching programs. Consistent with the VA's Whole Health model, mindfulness plays a central and consistent role in the program; this is also congruent with the approach of several third wave psychotherapies (e.g., Acceptance and Commitment Therapy, mindfulness-based Cognitive Behavioral Therapy), which have incorporated mindfulness.<sup>171</sup> The control condition (Usual Care) for the future UH3 trial will not be feasibility tested in the pilot study since we have already demonstrated our ability to successfully engage Veteran and non-Veteran patients (see **C.1 Prior Work**).

We have incorporated Veteran, community, and healthcare system-level stakeholder views and applied the **COM-B and biopsychosocial (BPS) pain models** (see **C.2 Guiding Theoretical Models**) to develop the RAMP-WH intervention. COM-B provides guidance for aligning stakeholder needs with appropriate intervention elements. This includes procedures and content that can be delivered with fidelity<sup>172</sup> and meet rural Veterans' BPS and pain related capability, opportunity, and motivational needs, as well as intervention delivery formats and features that can overcome known barriers (see **Significance**).<sup>22,64,102-106</sup>

**Format & Procedures.** Proactive outreach with tailored engagement materials will be used to raise awareness and interest in the program (see **C.3 Recruitment and Enrollment section above**). RAMP-WH consists of 12 sessions, delivered via



telehealth. WH Coaches will serve as an essential form of **support** for VA patients in helping them engage in effective pain self-management;<sup>98,173</sup> coaches will serve a critical function of orienting participants to the program, applying evidence-based communication (e.g., **motivational interviewing**) and behavioral change techniques (e.g., **goal setting, action planning, problem solving, and graded tasks**) through one-on-one and group sessions. These techniques are extensions of the COM-B model, enhancing the likelihood that target capabilities, opportunities, and motivations will be achieved.<sup>33,75</sup> Importantly, they are also congruent with the VA WH Coaching approach.<sup>100,174</sup> The WH Coach will also serve as an important bridge for connecting Veterans to other local and national resources for pain management in the VA and the community (described below).

The first session will be a one-to-one session (60 minutes) with a WH Coach to complete a Personal Health Plan and establish individual goals for pain self-management.<sup>75</sup> This will be followed by 11 weekly group sessions (90 minutes each) facilitated by the WH Coach. In session, group viewing of expert-narrated videos will provide consistent education and training in content (described below) to promote fidelity and reproducibility, which have been limitations of many CIH approaches.<sup>172,175</sup> Videos will be interspersed with workbook reflections and group discussions facilitated by the WH Coach.

**Content.** The content of the intervention will be focused on meeting Veterans' BPS pain-related needs, specifically their capabilities (e.g., knowledge, skills) and motivations (e.g., beliefs). RAMP-WH content will be adapted from resources from the investigators' previous studies of mindfulness, exercise, pain education, and behavioral strategies (R34AT011209, UH3AT008769)<sup>75,132</sup> based on stakeholder input (see **Stakeholder Engagement Activities**). The main content of RAMP-WH includes the following:

- **Pain Education** has been identified as important for patients.<sup>22</sup> Pre-recorded videos by pain experts will provide **information** about causes of pain; how pain is processed in the brain; the importance of the "mind-body connection" for self-managing pain; and the role of mindfulness, exercise, and behavioral approaches.
- **Mind-Body Skill Training** is essential for patients to develop the capabilities for self-managing pain effectively. Skill training will be performed in session using pre-recorded videos by experts in mindfulness, rehabilitation, and psychology; videos will include **demonstration** of a range of mind-body skills which will be **practiced** in session. Patients will also be encouraged to **practice** on their own, using the videos which will be available on a website, or pictures with descriptions in a workbook.
  - **Mindfulness skills** will be trained using guided meditations (5-15 minutes) and mini-mindfulness practices (1-2 minutes), with an emphasis on mindful breathing, body awareness, working with thoughts and emotions, shifting perspectives, and self-compassion.<sup>172,175</sup>
  - **Physical movement and exercise skills** will be trained through focus on simple posture, stretch and strength exercises that have been shown to be effective for pain self-management.<sup>138,140,176-178</sup> Exercises will focus on "core" muscles and joints necessary for daily function and achieving pain relief (e.g., abdominals, back, pelvis, hip, leg, shoulder) and which are suitable for a range of pain conditions. Emphasis will be placed on integrating body-awareness with rehabilitation principles that promote safety and comfort through mindful attention to breathing and being curious about body sensations.<sup>179</sup> Instructions will be provided for appropriate pacing and positioning.
  - **Whole Person Wellbeing Skills** are necessary for patients to effectively address the biopsychosocial impacts of pain. Training will focus on strategies for addressing pain-related stress using pacing, guided imagery, relaxed breathing, and cognitive restructuring; establishing routines for managing sleep disturbances; developing skills to facilitate communication with others related to pain; and addressing physical inactivity.
- **Resources for Pain Management in VA and the Community.** Coaches will provide information about nonpharmacological/CIH pain approaches covered by the VA benefit package and which can be accessed through CBOCs or telehealth within the VA, as well as those available in the community.

**Customizable options and resources** will also be provided to meet patients' preferences, needs, abilities, and resources. This includes different ways of training mindfulness including "mindfulness mini-practices" that are readily accessible and can be easily done anywhere, anytime; varying lengths for guided meditations to encourage practice; mindful exercises suitable for a range of pain conditions, with varied position (e.g., seated, standing) and degree of challenge (easy to more advanced). Downloadable videos will be accessible by mobile phone, tablet, or computer for patients to review and practice independently between sessions. Workbooks including infographics, pictures, and instructions attentive to messaging and which can be removed and put in convenient places to serve as memory aids, will be provided. We also will provide information on locations where patients can access broadband internet, working with programs such as the VA's Accessing Telehealth through Local Area Stations (ATLAS) project, which seeks to expand telehealth by providing internet access to veterans living in rural area in partnership with public and private organizations.<sup>124</sup>

**Fidelity.** A total of 30% of the intervention sessions in the UG3 and 15% in the UH3 will be randomly selected for monitoring by study investigators. These fidelity assessments will be conducted remotely via videoconferencing using a fidelity checklist assessing completion of required session activities adapted from previous studies. WH Coach Facilitators will also document completion of required study activities at each session, and rationales for non-completion.

**Training of WH Facilitators.** Ensuring fidelity of the intervention is an important implementation-related outcome that can affect RAMP-WH's future adoption and success;<sup>131</sup> thus our process for training and support strategies for WH Coach Facilitators is a critical implementation strategy.

Facilitator training and materials will be developed and adapted collaboratively with our stakeholders based on previous studies which found the materials and training to be well received by session facilitators and yielded high fidelity rates (>90%). This includes electronic manuals with checklists for each session's activities, safety protocols, and session slide presentations with embedded expert-narrated videos. We will use a "Train-the-Trainer" model for preparing RAMP-WH Coaches in the UG3 and UH3 to train other RAMP-WH Coaches for future implementation. As part of our previous work, we have developed session facilitation competencies which are based on the COM-B model's theory and evidence informed behavioral strategies.<sup>98,180</sup> Competencies emphasize supporting patients in a manner that is congruent with the educational and skill training content (e.g., consistency with main messages) and ensures safety (e.g., reinforcing instructions for engagement in mind-body skills and recognizing when patients are experiencing difficulty or putting themselves at risk). In preparation for this grant application, we have worked with our VA partners (OPCC&CT) to map these with the principles of Whole Health Coaching in the VA,<sup>75</sup> and found them to be congruent and readily adaptable for the RAMP-WH intervention training.

**Feasibility Study Data Collection (UG3 Aim 2).** We will use electronic data capture through Qualtrics FedRAMP, a secure web application for building and managing online surveys and databases.

- **Recruitment and enrollment** of patients, including those traditionally underrepresented, will be assessed by collecting recruitment and enrollment rates that detail the number, proportion, and characteristics of participants, including reasons for not participating.
- **Experimental intervention delivery** will be assessed by evaluating acceptability of the RAMP-WH intervention (defined by attendance; satisfaction rates with program; and specific elements of the program including facilitators, content, resources, materials, etc.) and fidelity rates (defined by WH Coach Facilitators' ability to deliver required RAMP-WH sessions and activities described in the **Experimental Intervention**).
- **Data collection** will be assessed by follow up rates for the effectiveness outcome measures post-intervention (see **Table 4 for UH3 effectiveness data collection schedule**).
- **Patient views and perspectives** will be assessed using mixed methods including qualitative data collection which is often insufficiently collected in RE-AIM studies; we will include multiple formats to meet patients' needs and include interviews, focus groups and open-ended survey questions (using electronic questionnaires) as well as field notes kept by study staff.<sup>181</sup>

**Feasibility Study Data Analyses.** Mixed method analyses will be conducted. Quantitative data will be analyzed using descriptive statistics (e.g., participant characteristics, satisfaction, fidelity rates, etc.). Qualitative data analyses will use a rapid deductive, content analysis approach (directed and summative) informed by the study's conceptual models and as described previously under **Stakeholder Views and Perspectives: Mixed Methods Data Collection and Analyses (UG3 Aim1)**.

**UG3 Milestones.** Scientific and feasibility milestones for the UG3 research planning phase are described in **Table 2** with additional detail and timelines provided in the **Section 2.7 Study Timeline** and **5.2 Milestone Plan – Study 1**. These are based on our team's previous experience conducting multi-phase studies successfully leading to full-scale randomized trials (1R21AT009110; 1UG3AT008769; NH170001; 1IU1HX002607-01).

#### **C.4. UH3 Randomized Hybrid Effectiveness-Implementation Study**

**UH3 Aims:** We will conduct a randomized hybrid type 2 effectiveness-implementation multi-site pragmatic clinical trial (n=500 rural VA patients with pain) of RAMP-WH compared to Usual Care, oversampling female and racial/ethnic minority patients (see Figure 1).



**Rationale for UH3:** Hybrid type 2 effectiveness-implementation trials are appropriate when there is a need to focus simultaneously on intervention effectiveness and implementation strategies that are plausible for the intended setting. They are ideal for studying modalities that have demonstrated effectiveness in other contexts and settings, and when there is momentum within an organization for implementation.<sup>131</sup> While there is supporting evidence for the individual CIH modalities included as part of RAMP-WH (e.g., mindfulness, exercise, pain education), the effectiveness as a multimodal telehealth intervention informed by the VA's Whole Health System model is not yet known. Further, the implementation processes that will support RAMP-WH adoption over the long-term to serve rural VA patients nationally, as well as suitability for the VA organizational context, require careful assessment and further adaptation and development of strategies for implementing them, taking into consideration the views of all relevant VA stakeholders (see **Stakeholder Engagement Plan**). Interviews conducted by our team (see **C.1 Prior Work**)<sup>132</sup> have yielded important insights into implementation barriers, as well as potential strategies to overcome these barriers. Addressing multiple implementation barriers will be best done using careful application of established implementation frameworks (e.g., RE-AIM/PRISM) to guide the engagement and information gathering from multiple levels of patient, community, and VA stakeholders (see **3.5 Structure of the Study Team – Study 1 and Table 3**).

**UH3 Aim 1 (EFFECTIVENESS):** To assess the relative effectiveness of RAMP-WH versus Usual Care in terms of:

- Primary effectiveness outcome** of pain interference at 13 and 26 weeks.
- Secondary outcomes** including opioid use and other HEAL recommended outcomes.
- Exploratory analyses** among female and racial/ethnic minority VA patients.

**Effectiveness Hypotheses:** We hypothesize that participants in the RAMP-WH intervention will experience a greater reduction in pain interference and opioid use, greater improvement in other secondary outcomes, and greater utilization of CIH and nonpharmacological approaches for pain compared to those in the Usual Care group. Comparisons will be conducted with outcomes repeated at 13 and 26 weeks.

**Recruitment, Enrollment, Screening & Eligibility.** We will use the same methods as described for the UG3 to recruit and screen patients for eligibility for the randomized trial (also see **2.5 Recruitment and Retention Plan – Study 1**). Once eligibility is confirmed, study staff masked to upcoming assignments will randomize patients to one of the 2 study arms (RAMP-WH or UC (1:1)), with 250 participants in each arm.

**Interventions.** The intervention period is 12 weeks. The experimental intervention, RAMP-WH, will be delivered as described for the UG3 (see **Pilot Study Intervention**). The control or comparator group is Usual Care, which is an appropriate choice for a pragmatic trial.<sup>182,183</sup>

Patients in both groups will receive study-related information (e.g., what to expect in terms of data collection), a list of pain management resources for VA patients, and newsletters (used to optimize survey response rates) distributed by email 3 times over 26 weeks (the last data collection point).

**Usual Care Control Group.** The investigators have successfully conducted randomized trials, including Usual Care and similar control groups, with engagement and follow up rates of more than 80% (see **C.1 Prior Work**).

**Format & Procedures.** Usual care will consist of patients continuing with the care they normally engage in for 26 weeks. After the 26 week follow up is completed, patients in Usual Care will receive access to the RAMP-WH intervention website with the same expert narrated videos for pain education and mind-body skill training, as well as resources (e.g., workbook).

**Data Collection.** As with the UG3 portion, we will use electronic data capture through Qualtrics FedRAMP for building and managing online surveys and databases. We will also use VA electronic healthcare records (EHR) to assess measures of chronic pain burden (e.g., changes in medication and healthcare use), using established algorithms. Our study team has developed robust protocols and procedures to facilitate participant retention and follow up (see **2.5 Recruitment & Retention Plan – Study 1**).

**Baseline Measures.** Baseline Measures will include demographic, occupational, and pain- and health-related characteristics, including recommended common data elements for the study of pain.<sup>157,184</sup> We will collect individual and structural level social determinants of health data using the PhenX ToolKit measures (e.g., health services access, income, employment status and prestige, food insecurity, gender identity, social vulnerability)<sup>185</sup> in addition to biopsychosocial outcome measures described below.

**Effectiveness Outcomes (UH3 Aim 1).** We have chosen a range of *biopsychosocial (BPS) outcome measures* relevant to patients, and which are likely to be affected by the intervention, RAMP-WH. They also are recommended for the study of chronic pain by the HEAL initiative.<sup>169,184,186,187</sup> BPS outcome measures will be collected at baseline, 13, and 26 weeks (see **Table 4**).

**Primary Outcome.** The primary outcome will be the Brief Pain Inventory (BPI) interference score over the 26-week follow-up period, assessed at 13 and 26 weeks.<sup>188-190</sup>

**Secondary Outcomes.** Secondary outcomes will include opioid use (using preestablished algorithms based on EHR data<sup>191</sup> and self-report), PROMIS measures, and other outcomes with demonstrated reliability and validity.<sup>184,186,187</sup> These include measures of pain intensity,<sup>188-190</sup> pain impact,<sup>192</sup> physical function,<sup>193,194</sup> sleep disturbance,<sup>193,194</sup> fatigue,<sup>193,194</sup> anxiety,<sup>193,194</sup> depression,<sup>195</sup> post-traumatic stress disorder,<sup>196</sup> participation in social roles and activities,<sup>193,194</sup> satisfaction and improvement,<sup>186,197</sup> healthcare and medication use from the EHR, non-pharmacological/CIH approaches for pain,<sup>169</sup> and adverse events. In addition, pain catastrophizing,<sup>198</sup> self-efficacy,<sup>199</sup> perceived stress,<sup>200</sup> mindfulness,<sup>201</sup> and body awareness measures<sup>179</sup> will be collected to assess potential mediation effects of RAMP-WH.

We will also include **intervention-related measures** to inform the UH3 effectiveness results and be considered in the UH3 implementation aims (see **C.4 UH3 Aims 2a-c below**). Examples include frequency of use of specific intervention elements (e.g., meditations, mindful exercises, etc.); satisfaction with intervention content and delivery formats; and degree to which patients feel the intervention met their biopsychosocial capability, opportunity, and motivational needs.<sup>98</sup>

**Sample size determination.** Our power calculation uses the Brief Pain Inventory (BPI) interference score as the primary outcome measure. For our primary analysis we estimate up to 20% attrition, so up to 500 people will need to be randomized to obtain a sample of 400 people with complete data; 200 participants in each arm will yield 90% power, with an alpha of 0.05, to reject the null hypothesis of equal means over the repeated follow-up time points (i.e., 13 and 26 weeks) if the arms differ by an effect size of 0.3 or greater. This includes a conservative estimate that the repeated outcome measures are highly correlated ( $r=0.7$ ) and even with only 1 time point there is power to detect effect sizes of 0.32. Analyses that are stratified by subgroups as small as 70 people per arm (i.e., equivalent to restricting to only women or minority patients) would have approximately 90% power to detect differences of 0.50. However, these would only be exploratory in nature and not adjusted for multiple comparisons.

**Analytic Methods (UH3 Aim 1a, 1b).** We will use an intention-to-treat approach. Preliminary descriptive analyses will summarize the distributions of the baseline measures across treatment arms overall and will similarly assess the outcome distributions across assessment time points (i.e., baseline, 13, and 26 weeks). We will summarize the completeness of the self-reported outcome assessments and examine associations between completeness and baseline measures as well as the association with secondary outcome assessments that are collected from the electronic medical record (e.g., medications, healthcare utilization related to pain treatment). Initial analyses will use all available follow-up data and subsequent sensitivity analyses will examine the potential effect of response bias. For analyses of the primary outcome, all repeated measurements of the BPI interference score will be fitted in a mixed model for repeated measures as a function of the group assignment, while controlling for time points and baseline values of the outcome as fixed effects, with participants

<b>Table 4. Data Collection Schedule</b>	<b>BL</b>	<b>13w</b>	<b>26w</b>
Demographic (including core SDH measures)	x		
<b>Primary Outcome</b>			
Pain interference (BPI)	x	x	x
<b>Secondary Outcomes</b>			
Use of opioids (self-report, EHR)	x	x	x
Pain intensity (BPI)	x	x	x
Pain impact (GCPS-R)	x	x	x
Physical function (PROMIS)	x	x	x
Sleep disturbance (PROMIS)	x	x	x
Fatigue (PROMIS)	x	x	x
Anxiety (PROMIS)	x	x	x
Depression (PHQ8)	x	x	x
PTSD (PCL5)	x	x	x
Participation in social roles and activities (PROMIS)	x	x	x
Global improvement and satisfaction		x	x
Healthcare & medication use (EHR)	x	x	x
Use of CIH and non-pharmacological pain management (NSCAP)	x	x	x
Adverse events		x	x
<b>Mediation Measures</b>			
Pain catastrophizing (PCS)	x	x	x
Pain management self-efficacy (PROMIS)	x	x	x
Perceived stress (PSS)	x	x	x
Mindfulness (AMPS)	x	x	x
Body Awareness (MAIA)	x	x	x
<b>Other Measures</b>			
Intervention-related measures*		x	x
BL=baseline; 13w=13 weeks; 26w=26 weeks; SDH=social determinants of health; BPI=brief pain inventory; GCPS-R=graded chronic pain scale-revised; PROMIS=patient-reported outcomes measurement information system; PHQ8=patient health questionnaire depression scale; PCL5=PTSD checklist for DSM-5; EHR=electronic health record; NSCAP=nonpharmacological and self-care approaches for pain; PCS=pain catastrophizing scale; PSS=perceived stress scale; AMPS=applied mindfulness process scale; MAIA=multidimensional assessment of interoceptive awareness; *Intervention related measures are also considered patient-level RE-AIM/PRISM measures (see <b>Table 5</b> ).			

as random effects. Between-group differences over the entire follow-up period will be the primary test of treatment group differences. Between-group differences will be estimated for each of the time points (i.e., baseline, 13, and 26 weeks). Similar to the methods described above for the primary analyses, weighted selection model analyses will examine the sensitivity of the initial results to response biases. To do this, we will fit a series of weighted selection model analyses. Each analysis will use an expectation-maximization algorithm to estimate weights to assign to potential values of the missing outcomes for use in the regression model. The secondary outcomes will be similarly analyzed using the same linear mixed effect models for normal continuous measures and appropriate generalized linear mixed effect models for non-normal measures.

**Exploratory Analysis (UH3 Aim 1c).** Subgroup analyses will explore treatment group effects for individual subgroups (gender, minority groups). Potential interactions by subgroup type will also be explored to see if there is evidence that treatment effects depend on subgroup. Only moderately large subgroup differences would be able to be statistically detected, but exploration of subgroup differences is still important for understanding possible mechanisms and barriers. The models described above for the primary analysis will be modified for looking at these subgroup and interaction effects. Additionally, all of these variables can be explored in multivariable models to look at the relative independent relationships between these factors and the primary and secondary outcomes.

Additional exploratory analyses involve the assessment of the extent to which pain catastrophizing, self-efficacy, perceived stress, mindfulness, and body awareness measures mediate the effects of the intervention. We will use the CAUSALMED procedure in SAS/STAT® 14.3 to estimate mediation effects using a counterfactual framework approach.<sup>202</sup> The overall (total) effect will be decomposed into four component parts. These components include: (i) the effect of the exposure in the absence of the proposed mediators (i.e., controlled direct effect), (ii) the interactive effect when the mediators are left to the levels they would hold in the absence of exposure (i.e., reference interaction), (iii) a mediated interaction, and (iv) a pure indirect (mediated) effect. Four-fold effect decomposition allows for the greatest insight into the causal mechanisms responsible for effect of RAMP-WH on our outcomes by simultaneously assessing the portions of the total effect that are due only to mediation, only to interaction, to both mediation and interaction, and to neither mediation nor interaction. Separate analyses will be conducted pairing each mediator with each outcome.

**UH3 Aim 2 (IMPLEMENTATION).** We will work iteratively with multiple levels of stakeholders (n=35-50 patients, community partners, VA healthcare system leaders and staff), to evaluate intervention implementation strategies within the trial and adapt these strategies to scale up RAMP-WH within the national VA healthcare system. This will include:

- Conducting mixed methods assessments of stakeholder and randomized trial participants' views of implementation related barriers and facilitators, intervention use, resource needs, and other RE-AIM/PRISM domains.
- Working with stakeholders to co-create additional plausible strategies for overcoming barriers to implementation of RAMP-WH nationally.
- Conducting budget impact analyses using models informed by stakeholder views to inform future decision making.

**Implementation Hypotheses:** We hypothesize that, by engaging key stakeholders at multiple levels in iterative data collection and co-development of tailored implementation strategies, we will be successful in achieving key RE-AIM/PRISM implementation outcomes (see **Table 5** for examples) during the hybrid Type 2 trial; these outcomes will inform necessary adaptations for implementation of RAMP-WH for rural patients within the national VA healthcare system.

**Stakeholder Sampling.** We will engage patient- (n=15-20), community- (n=10-15), and VA-level (n=10-15) stakeholders (see **Table 3**). In addition, we will assess study patient participants' views of the RAMP-WH intervention (e.g., those individuals taking part in randomized trial).

### **Implementation Measures and Analyses (UH3 Aim 2).**

**For Aim 2a** we will conduct iterative qualitative assessments of stakeholder perspectives to assess their views of implementation-related barriers and facilitators, costs, resource needs, and other RE-AIM/PRISM domains (**Table 5**) throughout UG3/UH3 (also see **2.7 Study Timeline**). Mixed methods (qualitative and quantitative) data collection and analyses will be performed as described for UG3 Aim 1, by teams of investigators and staff experienced in qualitative methods (see **C.3 UG3 Aim 1 Stakeholder Engagement Activities**). In addition to using rapid qualitative approaches,<sup>142</sup> we will 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.<sup>181,203</sup> 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.<sup>181,204</sup>

**For Aim 2b** we will prepare summaries of the effectiveness and implementation analyses and present them to VA patient, community, and VA stakeholders. This will provide them with the necessary contextual information to meaningfully contribute to participatory research activities focused on problem solving and process mapping,<sup>205</sup> to develop plausible strategies for remaining barriers to implementation of RAMP-WH taking into account internal and external contexts affecting the VA and Whole Health System initiatives at the time.<sup>131</sup> Examples include developing specific facilitation strategies, adapting information and patient-facing resources for particular groups to increase awareness and engagement (i.e., engaging consumers), tailoring intervention process strategies and resources, identifying and preparing champions to lead, support and marketing implementation efforts, and developing training programs.

**For Aim 2c** we will conduct a budget impact analysis synthesizing knowledge gained from stakeholder views/perspectives in Aim 2a, into analytic models that provide viewing of cost implications relevant to particular settings and contexts using recommended methods.<sup>206</sup> This analysis will be performed by investigators with statistical and cost-analyses experience (Leininger and B. Taylor). We will develop models considering both the local

facility and national VA perspectives. Model time horizons will be tailored to stakeholder needs for budget planning. RE-AIM/PRISM data will be used to inform values for model inputs and plausible ranges to consider (e.g., uptake by facilities and patients with chronic pain, training costs, impact on use of other chronic pain interventions, and related costs).<sup>207-209</sup> Scenario analyses altering values of model inputs and model structure will be conducted to allow the consideration of plausible alternative scenarios. Models will be presented to stakeholders while in development to ensure face validity.

**UH3 Milestones.** Annual scientific milestones for the UH3 project phase are provided in **Table 6** and **Section 5.1.2 Milestone Plan**.

Table 5. Examples of RE-AIM/PRISM Data Collection* by Stakeholder Level**	
<b>Reach</b>	<p><b>Patients<sup>+</sup>:</b> Views of how rural VA patients learn about study, including message content, course, importance of peer users, barriers/facilitators to participation; #, proportion and representativeness of participants.</p> <p><b>Community &amp; VA Health System Partners:</b> Views of how rural VA patients learn about RAMP-WH, how to raise awareness of RAMP-WH availability among patients, communities and facilities (message content and mechanism); barriers to participation.</p>
<b>Effectiveness</b>	<p><b>Patients:</b> Views about effectiveness of RAMP-WH in addressing self-management capability and motivational needs,<sup>98</sup> as well as biopsychosocial pain related primary and secondary outcomes (see Table 4); areas for improvement in intervention content, format, and telehealth delivery/internet access.</p> <p><b>Community &amp; VA Health System Partners:</b> Views about effectiveness of RAMP-WH; areas for improvement</p>
<b>Adoption</b>	<p><b>Patients:</b> NA</p> <p><b>Community &amp; VA Health System Partners:</b> #, proportion, characteristics, and representativeness of community partner organizations; views of barriers/facilitators to adoption; assessment of facility capacity, resources, expertise; estimated startup costs</p>
<b>Implementation</b>	<p><b>Patients:</b> Views of barriers/facilitators to engaging; adherence and participation rates; resources required</p> <p><b>Community &amp; VA Health System Partners:</b> Views about barriers/facilitators to delivery of RAMP-WH (e.g., content, mechanisms and formats, future training, administrative codes to account for time, etc.); fidelity rates; costs/resources of implementing RAMP-WH</p>
<b>Maintenance</b>	<p><b>Patients:</b> Use/practice of RAMP-WH at 26 weeks (UH3 only)</p> <p><b>Community &amp; VA Health System Partners:</b> Views about barriers/facilitators to maintaining/sustaining RAMP-WH; identification of needed adaptations for implementation</p>
<p>*RE-AIM/PRISM data collection is an iterative process that occurs through the lifespan of the project (UG3 and UH3); PRISM (the Practical Robust Implementation Sustainability Model) applies more nuanced attention to the internal and external environments that will affect the VA-system and is integrated into the above. **See 3.5 Structure of the Study Team for additional detail regarding stakeholders; + Patients includes patient stakeholders AND study patient participants.</p>	

Table 6. Major UH3 Milestones*	
<i>Recruitment &amp; enrollment</i>	50% of total sample recruited per year (Y3-Y4)
<i>Interventions</i>	50% of participants complete intervention per year (Y3-Y4); Acceptability: 75% satisfied with RAMP-WH program; 75% attend recommended # of group sessions (≥ 7/12) Fidelity: RAMP-WH Coach Facilitators deliver 90% of session activities 90% of the time
<i>Data Collection</i>	>80% trial participants complete post-treatment data collection at 13 and 26 weeks; all multi-level stakeholder data collection complete (Y4)
<i>Data analyses</i>	Mixed methods data analyses complete for UH3 Aims 1, 2 (Y5)
<i>Prepare data summaries; create process plans</i>	Summaries of results to inform the co-creation of process plans for implementing RAMP-WH prepared; process plans completed (Y5)
<i>Experimental intervention Adaptations</i>	Complete necessary intervention adaptations based on results (Y5)
<p>* This table highlights the major milestones for the UH3 trial; also see 2.7 Study Timeline for additional details. UH3 milestones will likely evolve as a result of the UG3 activities; Y=year of project</p>	

## C.6 ANTICIPATED BARRIERS & SOLUTIONS

The **complexity of the VA organizational structure** can pose challenges to sustained implementation of the RAMP-WH intervention. Two of the MPIs (Burgess and Hadlandsmyth) and Co-Is Matthias, B. Taylor, and S. Taylor have substantial experience conducting research at the VA. We have also worked with our VA health system partners prior to the proposal submission to ensure RAMP-WH is congruent with VA priorities and initiatives and meets the needs of rural VA patients. We will also continue to engage VA patient stakeholders and community partners, throughout the life of the project (see **C.3, Community Engagement Activities, 3.5 Structure of the Study Team – Study 1 and Letters of Support**).

**Recruitment, engagement, and adherence** are well-recognized barriers in randomized trials. We have developed a thorough **Recruitment and Retention Plan** (see Section **2.5 – Study 1**) that addresses the unique barriers faced by rural VA patients with pain, especially among those who are traditionally underrepresented in the VA (women and those from racial/ethnic minority groups). Additionally, the iterative nature of the project and repeated measuring and monitoring of important contextual factors (see **Table 5**) will allow us to adjust our processes, and address challenges as they arise. Achieving sufficient data collection follow-up rates is another challenge in studies such as this; our team will use established protocols and procedures that have yielded excellent follow up in ongoing and previous studies with similar numbers of outcome measures (see **C.1 Prior Work**).

## C.7 EXPERTISE OF THE STUDY TEAM

Our multidisciplinary team is ideally suited to conduct the proposed project (also see **C.1 Prior Work**). We represent a breadth of clinical and scientific disciplines (social and health psychology, chiropractic, nursing, clinical trials, health economics, biostatistics and study design, implementation science, and health equity) and have extensive experience managing and studying pain using the evidence-based approaches included in the proposed RAMP-WH intervention (mindfulness, cognitive and behavioral approaches, exercise and rehabilitation), and conducting research within the VA healthcare system.

Our team has led large scale pragmatic trials related to pain, including hybrid effectiveness-implementation studies guided by established theoretical models and frameworks and we have a strong background in qualitative and quantitative research methods engaging multiple levels of stakeholders. Further, we are adept at developing and adapting technology to meet user needs and ensure patient safety. The organizational structure for the proposed project is detailed in **3.5 Structure of the Study Team – Study 1**.

## C.9 RESPONSIVENESS TO THE RFA

The proposed project includes a randomized type 2 hybrid effectiveness-implementation trial and meets all the required criteria as outlined in RFA-NR-23-001 (see **Table 7**).

**Table 7. Responsiveness to RFA Required Criteria**

Intervention must apply broadly to pain patient populations, and can be implemented in rural and remote areas, with the broad goal of determining whether the intervention(s) improves pain outcomes/management and adds value to the utilization of the nation's health care resources.	<b>Responsiveness [relevant proposal section]</b>
The results of the question being tested will have a significant impact on pain management in rural and/or remote populations at the individual or systems level.	Inclusion criteria is broad [C.3 UG3 Aim 2: Pilot Study Screening and Eligibility]; intervention format is appropriate for implementation in rural and remote areas [C.3 UG3 Aim 2: Pilot Study Intervention]; UH3 trial addresses effectiveness for pain related outcomes (pain interference and others) and HEAL outcomes [Table 4 Data Collection Schedule]; project will add value through its focus on Veterans who are disproportionately affected by pain, and the VA, the nation's largest healthcare system [A. Significance].
The intervention(s) must be well-characterized and available such that it could be reliably delivered by clinical providers and/or HCS.	Rural-dwelling VA patients are greatly affected by pain, opioid use, etc.; the results have the potential to significantly impact individual VA patients by increasing access to non-pharmacologic CIH resources; through the use of a standardized delivery format designed for integration into the VA's nationwide Whole Health Initiative, the results also have the opportunity to impact the entire VA healthcare system by providing a widely accessible pain self-management program [A. Significance, B. Innovation].
	The RAMP-WH intervention is well characterized and informed by an evidence-based behavioral change model [C.2 Guiding Theoretical Models, C.3 UG3 Aim 2: Pilot Study Intervention]; the format of delivery is appropriate for widespread delivery in the VA healthcare system [C.3 UG3 Aim 2: Pilot Study Intervention].

The intervention(s) must be reasonably simple and not require a complex structure for implementation or monitoring.	The RAMP-WH intervention has been designed to ensure ease of implementation; it includes a protocolized curriculum with pre-recorded expert videos for delivery by an existing VA healthcare system resource (WH Coaches); a previous study by our team demonstrated high levels of fidelity and patient engagement using a similar format [C.3 UG3 Aim 2: Pilot Study Intervention, C.1 Prior Work].
As in routine practice, the project must allow for interventions to be implemented with flexibility and by appropriate practitioners.	The RAMP-WH intervention has been designed to ensure flexibility for meeting individual VA patients' needs; it is also appropriate for any VA practitioner to suggest for their patients; VA patients can also self-select into the program without a practitioner referral. Further, the protocolized curriculum allows for practitioners other than WH coaches to deliver the intervention, should that be desired by the VA healthcare system [C.3 UG3 Aim 2: Pilot Study Intervention].
The project outcome measure(s) must be clinically meaningful and important to stakeholders including patients, providers, health care systems, and policy makers. Clinical outcome measures must be defined at the patient, provider, and/or system level. Additional outcome measures, such as use of health care services or medications and other resources may be included.	We have chosen a range of <b>biopsychosocial (BPS) outcome measures</b> relevant to VA patients. They are also important to providers, the VA healthcare system and its policy makers and are recommended for the study of chronic pain by the HEAL initiative [Table 4 Data Collection Schedule].
The project design must incorporate rigorous controls, prospectively identified, preferably by randomization. The design may incorporate alternative randomization approaches, such as by cluster or timing of implementation.	For the UH3, will use randomization to allocate VA patients to the experimental intervention (RAMP-WH) and control group (Usual Care) [C.4 UH3 Aim 1]; importantly, previous studies by our team have demonstrated VA patients are willing to be randomized and engage similar conditions [C.1 Prior Work]. The VA healthcare system is the largest in the nation; it is anticipated that it will be sufficient for enrolling sufficient numbers of patients [C.3 UG3 Aim 2 Pilot Study Sampling].
Proposed analytic plans for projects that proposed cluster-randomized trials must address adequacy of sample size and study power and employ analytic strategies relevant for such pragmatic trial designs.	We are not proposing a cluster-randomized trial. However, we have addressed sample size and study power [C.4 UH3 Aim 1 Sample Size Determination].
The project must enroll patients based on broad eligibility criteria to maximize diversity and minimize intentional or unintentional exclusions based on risk, age, health literacy, demographics, or expected adherence. Projects with a focus on NIH-designated disparity populations in rural and remote areas are encouraged.	We propose to use broad eligibility criteria which have been successfully applied in previous pain studies by our group we will also oversample for minority and female VA patients (populations who experience health disparities in the VA) [C.1 Prior Work, 2.5 Recruitment and Retention Plan – Study 1].



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## Resource and Data Sharing Plan

The resource sharing plan or data management and sharing plan will comply with the HEAL Initiative Public Access and Data Sharing Policy, the HEAL PRISM (Pragmatic and Implementation Studies to Improve the management of Pain and Reduce Opioid Prescribing) Program's Data Sharing Policy; and will also comply with local institutional policies and local, state and federal laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) Privacy and Security Rules.

This resource sharing plan refers to both Phase 1 (UG3) and Phase II (UH3) of the proposed project. It is consistent with the FAIR (Findable, Accessible, Interoperable, and Reusable) data principles in accordance with the NIH, HEAL Initiative, and PRISM Program,

## Release of Publications and Data

Publications from this research will be made available to the public through the National Library of Medicine PubMed Central website within one year after the date of publication. Final data sets underlying all publications resulting from the proposed research will be shared outside VA. The data sets will include research involving human subjects. Where practicable, Limited Datasets (LDSs) will be created and shared pursuant to a Data Use Agreement (DUA) appropriately limiting use of the dataset and prohibiting the recipient from identifying or re-identifying (or taking steps to identify or re-identify) any individual whose data are included in the dataset. Final deidentified, anonymized datasets in machine-readable format may be created and shared via PubMed Central (and similar) sites with care taken to ensure that the individuals cannot be reidentified using other publicly available information.

## Data Type

Data generated by this research is derived from UG3 (N=40) and UH3 (N=500) participants and associated activities. Data will include participant-reported outcome measures including recommended common data elements (CDEs) from the HEAL initiatives core pain domains in addition to baseline demographic, occupational, health characteristics including PhenX ToolKit social determinants of health measures (see **Research Strategy** for all measures). VA PHI and VA sensitive data will be securely stored on a VA Research network drive behind the VA firewall or secured file cabinet. No PHI or VA sensitive data will be shared, unless approved by VA Privacy Officers. Only authorized research personnel as approved by the ACOS in agreement with the PI, will have access to individually identifiable data.

The research project team and PRISM/Collaboratory Program Coordinating Center will work together in order to offer deidentified or limited data sets that will be available to the public. Case-report forms will be submitted to the HEAL Clinical Data Elements (CDE) Program to ensure standardized variable names, responses, coding, and other information. We understand that formatting the case-report forms will be done in a such a standardized way that is compliant with accessibility standards under Section 508 of the Rehabilitation Act of 1973, which "requires Federal agencies to make their electronic and information technology accessible to people with disabilities".

The study team will obtain licenses for all copyrighted questionnaires prior to initiating data collection. Licenses will be shared with the HEAL CDE team and the program officer prior to use of copyrighted materials. Study protocols, data collection instruments, and data dictionaries will be made available to facilitate interpretation of publicly available data sets.

## Related Tools, Software and/or Code

This project does not intend to develop any standalone software packages so there are no timelines for making full software packages available to be shared outside of the research team.

However, this project's research team is expert in the use and development of code for extraction of data from VA electronic data systems. Our team intends to be a very active participant on the PRISM/Collaboratory Program Coordinating Center's Work Groups. The Center for Care Delivery and Outcomes Research (CCDOR) has a data team, led by Co-Investigator Dr. Brent Taylor, which creates customized research applications based on the needs of each research project. These applications allow project staff to recruit, enroll, randomize participants to the study, and complete follow-up assessments of study outcomes. These customized applications operate behind the VA firewall in order to protect participant data and they are developed in such a way that they cannot be easily transferred to other research settings. So, while the code for these applications would not be terribly useful for other research groups because it is highly customized for CCDOR systems, the general concepts underlying these applications is able to be shared. Also, in working with other members of the PRISM/Collaboratory Program, we might be able to come up with sections of code that can help improve the workflow for other research teams.

The program assets created by the study team and used during this research project will potentially be made available for other platforms to incorporate. If shown to be successful, the goal would be for the key components of this content to be widely disseminated. This project will work closely with the Coordinating Center to disseminate these research findings and content.

Aside from the software code that is developed by CCDOR programmers for the day-to-day work of running the research study, this project will also be contracting with Qualtrics FedRAMP, a survey and communications vendor. Initial screening and survey data will be securely stored on Qualtrics FedRAMP VA cloud servers that are approved and fully compliant to house VA research data.

### **Standards**

The research project team will work closely with the PRISM/Collaboratory Program Coordinating Center to provide deidentified or limited data sets that will be available to the public. The MPIs (Multiple Principal Investigators) (or designee) will ensure all data will be kept in consistent standardized data formats throughout the duration of the study. Data will be collected, processed, archived and shared in accordance with guidelines from the HEAL Data Ecosystem. We anticipate that the PRISM/Collaboratory Program Coordinating Center will develop infrastructure to allow independent research groups to request access to view relevant data from this project in order to evaluate the extent that data support conclusions made by authors in published studies as well as view supplemental details that might not be included in publications.

### **Data Preservation, Access and Associated Timelines**

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 and PRISM Program.

### **Access, Distribution or Reuse Considerations**

*Informed consent.* Potential risks associated with data sharing include a breach of confidentiality. This will be minimized as all identifiable data will be kept within the VA firewall and even within the VA firewall analytical datasets will be assigned a unique study specific identifier such that participant identifiers (e.g., name, SSN, addresses, medical numbers, etc.) can be separated from study variables. Prior to the start of the study, the PIs and local IRB will assess informed consent materials to determine whether the Underlying Primary Data may be shared as contemplated in this Policy and make adjustments as needed to conform to this data

sharing policy. To the extent possible, broad data sharing, data access, and reuse requirements will be integrated into informed consent and/or information sheet forms, as guided by HEAL.

*Privacy and confidentiality protections.* Scientific data that is shared will be aggregated when possible and any individual level data will be deidentified (e.g., no participant identifying information). VA Privacy Officers will review and approve the release of any individual data to insure the protection of VA patient data. The MPIs (or designee) will ensure all data will be kept in consistent standardized data formats throughout the duration of the study. Data will be collected, processed, archived and shared in accordance with VA guidelines.

#### **Oversight of Data Management and Sharing**

Oversight and compliance with the proposed resource sharing plan will be monitored on a routine basis (monthly to quarterly depending on need and phase of the project) by the PIs and Data & Technology Team (see **Section 3.5 Structure of the Study Team**).

Supplementary  
Material