NIH PRAGMATIC TRIALS COLLABORATORY

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NIH Collaboratory Ethics and Regulatory Core: Initial Consultation
Equitable Primary Care for Pain Care (EquiP PC)
January 21, 2026; 2:00-3:00 pm ET (via Zoom)

Attendees:

- Core, Coordinating Center, and NIH: Joe Ali (Johns Hopkins University), Anthony Domenichiello (NINDS), Luke Gelinas (Advarra), Rebecca Hommer (NINDS), Beda Jean-Francois (NCCIH), David Magnus (Stanford University), Kevin McBryde (NCCIH), Stephanie Morain (Johns Hopkins University), Pearl O'Rourke, Caleigh Propes (Johns Hopkins University), Tammy Reece (Duke University), Damon Seils (Duke University), Jeremy Sugarman (Johns Hopkins University), Dave Wendler (NIH Clinical Center), Benjamin Wilfond (University of Washington)
- Study team: Yohali Burrola (University of Washington), Rodger Kessler (DARTNet Institute), Adrienne Meyer (University of Washington), Maria Prado (University of Washington), Kari Stephens (University of Washington), Connie Van Eeghen (University of Vermont)

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Overview of the trial	Meeting attendees received the project's study proposal and data management and sharing plan with the agenda (see supplementary material attached). Jeremy Sugarman facilitated introductions and described the purpose of the consultation. Co–principal investigator Kari Stephens represented the Equip PC team, along with Yohali Burrola (project director, University of Washington), Adrienne Meyer (associate director for reliance at the University of Washington IRB), Maria Prado (research coordinator, University of Washington), and Connie Van Eeghen (University of Vermont). **Project overview**: Kari Stephens gave an overview of the project, which is supported through the NIH HEAL Initiative by a grant from the National Institute of Neurological Disorders and Stroke (NINDS) using a UG3/UH3 award mechanism. EquiP PC will test the effectiveness of an integrated behavioral health (IBH) tool kit to improve chronic pain care. The trial will assess outcomes such as reduced pain interference, improved IBH, implementation success, and access to care with the goal of expanding access to high-quality, team-based chronic pain care in primary care settings.		

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
	Sponsoring institution: University of Washington. **Healthcare system partners**: Duke University's Primary Care Research Consortium (PCRC), the DARTNet Institute and American Academy of Family Medicine's National Research Network (NRN), and the University of Washington Family Medicine (UWM-FM). **NIH Institute Providing Support/Oversight**: National Institute of Neurological Disorders and Stroke (NINDS). **Study design**: The research team plans to conduct a 3-arm, cluster randomized trial to test the effectiveness of an integrated behavioral health (IBH) tool kit to improve chronic pain care. The trial will compare (1) use of the tool kit combined with digital therapeutic apps, (2) use of the tool kit alone, and (3) usual care across 27 primary care practices within healthcare systems and research networks serving underserved populations. The research team will adapt an existing IBH tool kit to train behavioral health providers in cognitive behavioral therapy and exercise therapy and will select and incorporate digital therapeutic apps. The intervention includes a guided approach to engage in a practice-centric effort to target and improve IBH for patients with chronic pain, training behavioral health providers in chronic pain care, selecting evidence-based apps for home use, and engaging a community advisory board of patients, providers, and health system leaders. **Outcomes**: The primary outcome is pain interference as measured using the Pain, Enjoyment of Life, and General Activity (PEG) scale. Secondary outcomes include pain intensity, physical function, quality of life, satisfaction with treatment, substance use screening, depression, and anxiety. The Patient Health Questionnaire (PHQ-9) will also be used. The study will also evaluate the effectiveness of the intervention at the organizational and provider levels. The primary outcome measure for practices is the level of of integration between behavioral health and primary care settings, measured using the Practice Integration Profile (PIP-1), which assesses 6 domains: practice workflow, clinical services, integration methods, case identification, patient engagement, and workspace arrangement. The primary measure for providers is self-efficacy in		

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
	treating chronic pain, as measured through provider ratings. The study will use the PRISM RE-AIM framework to evaluate implementation outcomes.		
Status of IRB approval	The University of Washington will serve as the single IRB for the project. The IRB application has been submitted and has undergone pre-review. The research team is responding to initial requests for additional information from the IRB coordinator.		
Risk (Does the project meet regulatory criteria for being considered minimal risk?); and consent (planned processes for relevant subjects)	Based on the study proposal and initial feedback from the IRB coordinator, the research team anticipates that the trial will meet the criteria for being determined to be minimal risk. The intervention is practice-centric; patients will receive care based on their clinic's workflow rather than at a patient-level. The team should have a plan regarding what information obtained in the PHQ-9 and elsewhere will be acted upon and by whom. The Core offered to discuss this with the team if it would be helpful. The research team plans to use EHR-based queries to identify eligible patients, followed by electronic solicitations. Interested patients will complete an eligibility survey and e-consent via REDCap or can call the study team for more information and/or help. The research team has requested a waiver of consent for the initial recruitment and eligibility screening phases. They will likely seek a waiver of documentation of consent for providers completing surveys. The trial will follow an intent-to-treat design; patients will be asked to provide consent for data collection activities (surveys and EHR data) regardless of the specific care they receive.		
Privacy (including HIPAA)	The research team is requesting a waiver of HIPAA authorization to access EHR data for recruitment and screening. A formal HIPAA authorization form will be part of the e-consent package for all enrolled participants. Only deidentified data will be shared in public repositories after the study's completion.		

AGENDA ITEMS	DISCUSSION	ACTION ITEMS	OWNER
Monitoring and oversight	The research team has submitted a monitoring plan to the IRB. Anthony Domenichiello agreed to double-check NINDS policy to determine if a formal DSMB is required. Members of the Core highlighted available NIH Collaboratory resources for establishing DSMB charters tailored to pragmatic trials.	Double-check NINDS requirements with respect to DSMBs.	**Anthony Domenichiello**
Issues beyond this project (regulatory and ethics concerns raised by the project, if any)	The group discussed the challenge of balancing community-engaged recruitment to achieve a representative sample with the need for standardization across heterogeneous clinic sites. Luke Gelinas noted that using apps as an "object of assessment" could trigger FDA device reviews if the apps are not already fully approved for the specific use case. Adrienne Meyer noted that the University of Washington typically does not require an Investigational Device Exemption (IDE) unless there is a plan to submit data to the FDA. The research team will finalize the framework for selecting digital therapeutics apps in the next 4 to 6 weeks and monitor for any regulatory triggers related to FDA device status. The research team acknowledged potential accessibility issues, including internet access, language barriers (they are currently focusing on English and Spanish), and physical limitations of patients using mobile apps and are working to address these where feasible.		

OMB Number: 4040-0001
Expiration Date: 11/30/2025

Project Summary for Equitable Primary Care for Pain Care (EquiP PC)

Introduction: Based on data showing that 25% of the U.S. population suffers from chronic pain (CP) and that ~1/2 the CP population seek relief in primary care (PC), there is consensus that multidisciplinary coordinated care within PC is critical for treating CP. Integrating behavioral health (IBH) within PC has been shown to improve patient outcomes for mental and chronic physical health conditions but has not been applied to CP management. With PCORI funding, we have developed and tested an IBH Primary Care (IBH-PC) toolkit, which provides a multi-faceted implementation strategy to improve IBH. Given use of the IBH-PC Toolkit has demonstrated improved behavioral health integration, we propose to adapt this toolkit to improve equitable access to CP care, train BHPs in CP care, and augment it with implementation of digital therapeutic app tools for home use, to improve quality of care and ensure sustainability.

Approach: We will conduct a large multi-site pragmatic 3-arm cluster randomized control trial comparing the IBH-PC toolkit + apps vs. IBC-PC toolkit only vs. treatment as usual, and use the ***PRISM RE-AIM*** (**R**each, **E**ffectiveness, **A**doption, **I**mplementation, and **M**aintenance) framework to evaluate implementation outcomes. To address **R**each, we will recruit 2,025 patients with CP and randomize PC practices from partnered practice based research networks and healthcare system (HCS) partners that treat underserved communities including BIPOC (Black, Indigenous and people of color), Hispanic, and people with low socioeconomic status (SES). **In the *UG3 phase, we will convene a Community Advisory Board (CAB) to develop the infrastructure to ensure UH3 RCT success*: AIM 1**: Finalize outcome measures, practice and patient recruitment process, and establish a centralized data coordinating infrastructure. We will incorporate the HEAL Common Data Elements and develop a strategy for participation in the NIH Pragmatic Trials Collaboratory Resource Coordinating Center working groups.. **AIM 2:** Recruit 27 PC practices and create a Community Advisory Board (CAB) from the practices**.** The CAB will be comprised of patients, primary care providers, BHPs, HCS administrators, and practice facilitation experts. **AIM 3:** Refine the IBH-PC Toolkit for CP care, choose DTx apps for homecare use, and adapt the BHP training materials. **In the *UH3 phase, we will execute a 3-arm cluster-randomized pragmatic randomized control trial across 27 PC clinics:* AIM 1:** To determine effectiveness of the adapted (1) IBH-PC Toolkit + apps vs. (2) IBC-PC Toolkit only vs. (3) treatment as usual for improving pain interference and level of integration of IBH. **AIM 2:** Evaluate Implementation of the interventions: IBH-PC Toolkit + apps and IBH Toolkit only. **AIM 3:** Evaluate equity in access and outcomes of CP care in PC.

This proposal is ***innovative*** as it equitably expands access within existing PC practices through IBH multidisciplinary coordinated care teams, integrates evidence-based apps and is expected to have a ***positive impact*** on transforming PC to equitably treat over half of all patients suffering from CP.

Supplementary Material

Project Narrative for Equitable Primary Care for Pain Care (EquiP PC)

Based on data showing that 25% of the U.S. population suffers from chronic pain and that ~1/2 the chronic pain population seek relief in primary care, there is consensus that multidisciplinary coordinated care within primary care practices is critical for treating chronic pain. We have developed and tested an Integrative Behavioral Health-Primary Care toolkit, which provides an implementation strategy to improve behavioral health integration into primary care, while training Behavioral Health Providers. As this toolkit use has demonstrated improved primary care behavioral health integration, we propose to adapt it to chronic pain multidisciplinary coordinated care and equitable care access, then augment it with implementation of digital therapeutic app tools for home use, to improve equitable access and delivery of chronic pain care and ensure sustainability.

Supplemetary Material

Introduction: In the U.S., 25% of the U.S. population suffers from chronic pain (CP) and ~1/2 of those with CP seek care and relief in primary care (PC), which is driving the critical need for multidisciplinary coordinated care for CP within PC.[1] Integrating behavioral health (IBH) within PC has been shown to improve patient outcomes for mental and chronic physical health conditions, but a successful approach to implement IBH for CP is needed. IBH offers a coordinated care approach in PC that can include cognitive behavioral therapy (CBT) for patients with CP.[2-4] **Our key implementation question is:** ***How effectively can an evidence-based, practice-centric intervention, aimed at adapting IBH to CP, improve equitable access to coordinated multidisciplinary care in primary care?*** Our plan is ***feasible*** because, with Patient Centered Outcomes Research Institute (PCORI) funding, we have developed and tested an IBH Primary Care (IBH-PC) Toolkit. This Toolkit provides a multi-faceted method of organizing the planning, delivery and implementation of IBH services designed to improve organizational and patient outcomes. We studied our IBH-PC Toolkit in a pragmatic cluster randomized controlled trial (RCT) and learned that it increased IBH effectiveness.[5-9] We plan to adapt and improve the IBH-PC Toolkit to specifically target CP outcomes by: 1) targeting IBH services to equitably triage patients with CP to care with behavioral health providers (BHPs) integrated within PC, 2) training BHPs in CP related cognitive behavioral therapy (CBT) and exercise therapy (ET), and 3) target use of evidence-based digital therapeutic (DTx) apps (i.e, approved by the U.S. Food and Drug Association (FDA)) that can improve CP outcomes. BHPs will train patients in home use of DTx apps to sustain delivery of CBT and ET interventions. Our plan is ***sustainable,*** as it will train existing co-located BHPs in PC and improve practice workflow processes for equitable patient access to multidisciplinary coordinated care for CP. The co-location of BHPs includes nearly 50% of Family Medicine board certified physicians and growing[10]; therefore, *by leveraging IBH, training BHPs with CBT and ET skills, and deploying use of DTx apps, we aim in our study to provide* ***Equi****table* ***P****rimary Care for* ***P****ain* ***C****are* ***(EquiP PC)***.

Approach: We will conduct a large multi-site pragmatic 3-arm cluster RCT comparing (1) IBH-PC Toolkit + DTx apps vs. (2) IBC-PC Toolkit only vs. (3) treatment as usual, and use the ***PRISM RE-AIM*** (**R**each, **E**ffectiveness, **A**doption, **I**mplementation, and **M**aintenance) framework[11] to evaluate implementation outcomes. We will recruit patients with CP from PC practices that are part of eight healthcare systems (HCS) partnered with two Practice Based Research Networks (PBRNs) and an academic HCS, that treat high proportions of racial/ethnic minoritized communities and people with low socioeconomic status (SES).

In the ***UG3 phase,*** *we will develop the infrastructure to ensure UH3 RCT success*:

AIM 1: **Finalize outcome measures, practice and patient recruitment process, and establish a centralized data coordinating infrastructure.** We will incorporate the HEAL Common Data Elements and develop a strategy for participation in the NIH Pragmatic Trials Collaboratory Resource Coordinating Center working groups.

AIM 2: **Recruit 27 PC practices and create a Community Advisory Board (CAB) from the practices.** The CAB will be comprised of patients, primary care providers, BHPs, HCS administrators, and practice facilitation experts.

AIM 3: **Refine the IBH-PC Toolkit for CP care, choose DTx apps for homecare use, and adapt the BHP training materials.**

In the ***UH3 phase,*** *we will execute a 3-arm cluster-randomized pragmatic RCT across 27 PC practices****:***

AIM 1: **To determine effectiveness of the adapted (1) IBH-PC Toolkit + apps vs. (2) IBC-PC Toolkit only vs. (3) treatment as usual for improving pain interference and level of integration of IBH.** PC practices across three partners will recruit *N* = 2,025 patients and evaluate outcome measures at baseline, post-intervention and 6-months post-intervention. Outcomes: 1) Patients - primary outcome is pain interference (PEG scale), secondarily pain intensity, physical function, quality of life, satisfaction with treatment, substance use screening, depression and anxiety; 2) Practices - IBH level; and 3) BHPs - treatment self-efficacy.

AIM 2: **Evaluate Implementation of the interventions: IBH-PC Toolkit + apps and IBH Toolkit only*.*** We will use a PRISM RE-AIM framework to assess implementation outcomes.

AIM 3: **Evaluate equity in access and outcomes of CP care in PC.** We will examine variations in race/ethnicity, SES and marginalized subgroups across rates of access to BHP care, engagement in treatment, and heterogeneity of treatment effect across patient outcomes.

This proposal is ***innovative*** as it equitably expands access within existing PC practices through IBH multidisciplinary coordinated care teams, integrates evidence-based apps and is expected to have a ***positive impact*** on transforming PC to equitably treat over half of all patients suffering from CP.

Supplementary Material

RESEARCH STRATEGY

A. SIGNIFICANCE

Definition	Acronym
Behavioral health provider	BHP
Black, Indigenous, or Persons of Color	BIPOC
Chronic pain	CP
Cognitive Behavioral Therapy	CBT
Healthcare System	HSC
Digital therapeutic app	Apps
Exercise therapy	ET
Integrated behavioral health	IBH
Primary care	PC
Primary care providers	PCP

Equitable integrated team-based strategies for chronic pain (CP) treatment within primary care are needed, given: 1) the endemic proportions of CP in the United States (US), ~25% of the US population,[1] 2) the difficulty primary care providers (PCPs) have in adopting non-pharmacologic approaches for CP,[12] 3) the majority of patients with CP seek care in primary care, and 4) equitable access to CP care is lacking for many patients identified as Black, Indigenous, or Persons of Color (BIPOC) and Hispanic, and patients with low socioeconomic status (SES).[13,14] Our team has extensive experience in promoting integrated behavioral health (IBH) in primary care (PC) to improve care for mental and behavioral health related conditions. IBH has been adopted through the growing co-location of behavioral health providers (BHPs) in PC settings nationally,[10] due to its strong evidence base to improve outcomes.[9,15-20]

Cognitive Behavioral Therapy (CBT) and exercise therapy (ET) can specifically target debilitating effects of CP in primary care: CP causes significant suffering and distress leading to interference with daily functions resulting in a national economic burden of ~$560-635B annually.[12] Establishing the biopsychosocial basis for chronic pain has led to the most successful pain management strategies, of which CBT has shown the greatest promise.[26,27] CBT decreases pain chronicity through safe, non-pharmacologic, guided behavioral interventions that have been successfully used by nonspecialist PCPs to manage pain,[3,28] and delivering existing integrated team management approaches has been shown to be successful.[29] In addition to CBT, regular exercise is an essential component of CP treatment as it can reduce pain and improve related challenges in function including sleep, depression, anxiety, and inflammation.[31] Although the specific mechanisms are not known, hypotheses include pain desensitization,[32] endogenous opioid enhancement[33] and exercise-induced hypoalgesia.[34] Although evidence demonstrates both direct and indirect benefit of exercise for CP,[35,36] treatment does not always include ET.[31] In fact, few PCPs deliver CBT and ET as a treatment strategy, as their schedules are typically overbooked and they are inadequately trained.[12] Rather, most PCPs tend to prescribe medications, recommend life-style changes, and refer to behavioral health experts.[1]

Disparities and lack of PCP training and time complicate delivery:[12,37-39] CP tends to be more prevalent and significantly more difficult to treat effectively in BIPOC and Hispanic populations, particularly those with low SES, who experience disparities in treatment.[13,14,40] CP has been primarily studied in adult populations between the ages of 18 and 60[41]; but CP tends to increase with age and the elderly population is particularly vulnerable to disorders of depression and dementia, which are typically addressed in concert with CP.[41] Patients with CP generally tend to seek care and often solely from their PCPs; this is particularly true for low-income BIPOC and Hispanic communities, who seek care at community based primary care practices.[45] The primary challenge for the PCP is that their training in CP treatment is limited[46] in addition to very busy practices.[12] Moreover, evidence has shown that disparate treatment of BIPOC patients with CP increases patient debilitation and distress.[40]

Digital behavioral therapeutics (DTx apps) can help extend and augment access to care:[49-55] The development of smart phone apps for homecare use have increased in popularity since the concerted effort to decrease opioid use for CP,[56-60] particularly during and after the COVID-19 pandemic.[53] Evaluation and testing in randomized control trials (RCTs) has been coincident with this increase in development and use of digital therapeutics by healthcare providers[54] for patient home use.[50] We have reviewed current mobile apps on track for U.S. Food and Drug Administration (FDA) approval and several address ET and CBT.[56-62] Digital therapeutics that include efficacious DTx apps regulated by FDA and wellness apps that promote healthy lifestyle and wellbeing are growing exponentially, creating a need to vet and utilize apps that can extend and augment human and resource constrained primary care settings.

Team Approaches with BHPs and PCPs can equitably meet treatment needs, but implementation remains a challenge:[45-48] Team management approaches have traditionally involved referral out to CP experts (i.e., pain psychologists or specialized medical providers),[29,47] but IBH approaches can be targeted to address the needs of patients with complex multiple chronic conditions.[48,71] IBH (i.e., the integration of behavioral health

Supplementary Material

in primary care) results in significant improvements in not just mental health outcomes, but also, in a recent review of seven studies, improvement in pain outcomes as well.[9] However, in addition to PCPs, most BHPs also lack training in chronic pain related CBT and ET treatments.

*Summary of Study Premise: We propose to incorporate chronic pain treatment into multidisciplinary coordinated care in existing IBH primary care teams to equitably address the biopsychosocial needs of patients – specifically, we will target our intervention to treat patients with CP within existing IBH teams, train BHPs in chronic pain specific CBT and ET treatments, and integrate evidence-based DTx apps into care, while increasing the overall level of IBH at the practice (see **Figure 1**).*

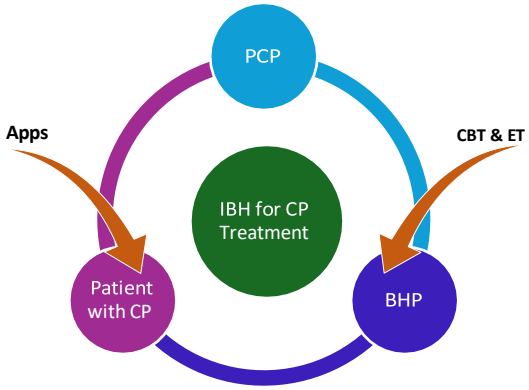

Figure 1: IBH for Chronic Pain in Primary Care

B. INNOVATION

Our proposal is highly innovative for the following reasons. First, ***we will follow the Community of Practice (CoP) Model*[63,64] to adapt our existing evidence-based IBH improvement practice-level intervention,[2,4-8] to improve equitable treatment access and quality of care for patients with chronic pain within primary care settings**. The CoP framework is a powerful tool to bring community members together and has been used by large programs such as the World Bank[65,66] and UC Davis[65,67] for implementing their programs. With PCORI (Patient-Centered Outcomes Research Institute) funding (2016-2022), we developed and tested an Integrated Behavioral Health in Primary Care (IBH-PC) Toolkit in a large pragmatic trial that improved all measured dimensions of IBH[5,6,8] via the Practice Integration Profile (PIP) measure, a psychometrically validated tool to measure IBH developed by Dr. Kessler (co-PI) and colleagues,[21-25] The IBH-PC Toolkit is a multi-faceted implementation strategy to improve integration in a primary care setting with 4 customizable components: 1) an online educational curriculum, 2) a structured set of quality improvement (QI) team workbooks for practice redesign and implementation, 3) an online learning community, and 4) practice facilitation coaching. Namely we propose to adapt the IBH-PC Toolkit to include online educational curriculum for chronic pain treatment specific CBT and ET treatment, address processes and structures related changes to IBH that improve equitable access to BHP care in primary care for patients suffering from CP, deploy an online learning community to support IBH teams to deliver CP treatment, and streamline the toolkit based on our previous study findings to ensure more efficient, rapid use and completion of the quality improvement cycles.

Supplementary Material

Second, ***we will leverage existing IBH teams in primary care practices across eight health care systems (HCSs) via our three partner organizations, while providing a flexible practice-centric intervention*** to allow practices to customize how they approach improving IBH. Our toolkit has already been shown to have high acceptability and adoption by PC practices and IBH teams aiming to target patients with multiple chronic conditions.[5,6,8] We will rapidly develop our final online adapted toolkit materials based on the existing online materials with the help of our Community Advisory Board (CAB) of nine members from the HCSs in collaboration with our investigative team. We have deep commitment from practices within our two partnered practice-based research networks (PBRNs), both of whom Drs. Stephens (PI) and Kessler (Co-PI) have worked extensively with, as well as Dr. Stephens's local HCS. Engagement with the CAB will ensure that the adapted toolkit it optimized to be used by our community of practices and addresses complex equity issues.

Third, ***we will provide efficient and effective CBT and ET trainings for BHPs*** that have been evolved through several efforts led by Dr. Stephens (PI), who has deep expertise in teaching evidence-based behavioral skills and who has developed and delivered trainings to 200+ primary care collaborative care managers and primary care behavioral health providers, including social workers, psychologists, psychiatrists, family medicine physicians, and other licensed behavioral health providers across Washington State and nationally. Trainings for this toolkit will be adapted from an existing *CBT 1-2-3* manual for CP treatment training that Dr. Stephens and colleagues developed in collaboration with Dr. Ehde (Co-I), which has recently successfully been piloted with nurse care managers working in rural primary care settings. This training includes a written manual, online didactic trainings, and an introductory training that can be recorded for repeat administration for any BHP to complete in this study and can be made publicly available going forward.

Finally, ***we will select a set of DTx apps that are on track or have FDA approval to extend and augment evidence-based treatment for CP in primary care.*** We will include materials to enhance our toolkit BHP trainings with instruction on how to integrate DTx apps into BHP care and work with our CAB to ensure apps can be deployed equitably to help extend reach to patients who experience significant barriers to accessing care. We have conducted a review of digital therapeutic apps that can benefit patients with CP and we will work with our CAB to select apps that our practices feel are favorable, are on track or have FDA approval, and offer CBT, ET and other related evidence-based CP related interventions, such as mindfulness.

C. APPROACH

Project Overview: To address providing coordinated care for CP treatment in existing HCSs, we propose a large multi-site pragmatic 3-arm cluster RCT using **PRISM** (Practical, Robust Implementation and Sustainability Model) **RE-AIM** (Reach, Effectiveness, Adoption, Implementation, and Maintenance).[68-70] We plan to capitalize on the existing success of coordinated team-based care successfully used for other conditions, by co-opting IBH in primary care for treatment of CP. Our plan is to adapt our highly successful IBH-PC Toolkit, developed and tested in a PCORI-funded large multi-site pragmatic RCT. We will augment the Toolkit with training in CBT and ET for BHPs, ensure equitable access to treatment for CP and integrate the DTx apps for patients use at home, facilitated by BHPs.

HCS Partners & Sites:

TABLE 1: HCS PARTNERSHIPS, STUDY SITES, & TEAMS

HCS PARTNERSHIPS	# STUDY SITES (CLINICS)	TEAMS
UW MEDICINE FM	31	Kari Stephens London Breedlove
DUKE PCRC	46	Ranee Chatterjee William Yancy
NATIONAL RESEARCH NETWORK (NRN)	38	Christina Hester Rodger Kessler

We are partnering with two PBRNs and one academic HCS, namely, Duke University's Primary Care Research Consortium (PCRC), the DARTNet Institute and American Academy of Family Medicine's National Research Network (NRN), and the University of Washington Family Medicine (UWM-FM), which includes together a total of eight HCSs and 115 primary care practices (see **Table 1)**, from which we will recruit 27 practices and *N* = 2,025 patients from 343,265 patients with documented International Classification of Diseases (ICD) coded CP related diagnoses (see **Table 2)** for the trial. These partners have high proportions of patients identifying as BIPOC, Hispanic and with low SES.

TABLE 2: HEALTH CARE SYSTEMS DEMOGRAPHICS

HCS	# clinics / # of patients with CP	% Female	% White	% Black	% Hispanic / Latinx	% Asian / Pacific Islander	% Other Race &/or Ethnicity
UW MEDICINE FM	31/63,586	60.4%	65.4%	8.8%	7.6%	15.6%	16.0%
DUKE PCRC	46/138,460	61.0%	65.4%	24.8%	4.0%	4.5%	1.2%
NATIONAL RESEARCH NETWORK (NRN) (6 HCSs)	6/709	63.9%	36.5%	5.5%	0.0%	3.0%	55.0%
	5/7,091	64.5%	18.2%	69.1%	0.2%	7.4%	5.1%
	4/7,500	55.3%	13.8%	24.9%	7.6%	27.6%	23.0%
	1/744	41.0%	66.3%	0.5%	13.8%	0.7%	10.6%
	3/33,512	56.4%	65.5%	0.7%	3.3%	0.9%	28.5%
	19/91,663	61.3%	73.8%	9.3%	3.2%	1.1%	10.7%

Key Collaborators:

Overview of Investigative Team: Our key collaborators (see **Table 3)** represent experts in the areas of: implementation science, CBT and ET treatments for CP, IBH, digital behavioral apps, ambulatory primary care, cost estimation and quantitative and qualitative methods. Our team comes from disciplines of psychology, exercise physiology, physical therapy, family medicine, internal medicine, rehabilitation science, biostatistics, economics, pharmacology, and public health, and half are identified as BIPOC and/or Hispanic.

TABLE 3: KEY COLLABORATORS & RELEVANT EXPERIENCE

COLLABORATORS/ROLE ON PROJECT/WORKING GROUP	APPOINTMENTS	RESEARCH EXPERTISE
Kari A. Stephens, PhD Clinical Psychology	• Professor, Vice Chair of Research, & Director of Clinical Research	Advancing data driven care in primary care to address health equity, IBH related mental and behavioral health, chronic pain, PTSD, substance use, cancer, Long COVID, data sharing data science data

Supplementary Material

Contact PI: oversee the project, primary lead of the data core, BHP CBT training and mobile apps WG: EHR, Health Equity	Informatics, Family Medicine, UW SOM • Adjunct Professor in Biomedical Informatics and Medical Education, UW SOM	sharing in primary care settings; clinical expertise in pain and primary care psychology; WA State Bree Collaborative on Chronic Pain in Primary Care Committee Member; Director of the DataQUEST Coordinating Center;
Rodger Kessler, PhD, ABPP Clinical / Health Psychology Co-PI: oversee the project, primary lead of implementation science WG: Implementation Science	• Vice President for Innovation, DARTNet Institute • Senior Scientist, American Academy of Family Physicians' National Research Network (NRN)	Implementation science and large trials to design, implement, and evaluate the effectiveness of IBH in Family Medicine, Internal Medicine, OB-GYN, Neurology, Gastroenterology, Surgery, and Anesthesiology settings; Associate Director for Data Informed Care Transformation; past Director of Collaborative Care Research Network; past Director of Dissemination and Implementation at Arizona State University
Siddhartha Angadi, PhD Exercise Physiology, Nutrition and Wellness Co-I: lead for exercise therapy WG: Patient-Centered Outcomes	• Associate Professor, Kinesiology, University of Virginia	Role of exercise in health, expertise in cardiopulmonary exercise testing for screening and risk stratification across multiple clinical conditions, and assessment of physical activities using triaxial accelerometry and remote monitoring
Yohali Burrola-Mendez, PhD, MS, PT, Rehabilitation Science Physical Therapist Co-I: senior project manager, PT, implementation and engagement WG: Ethics and Regulatory	• Research Scientist, Family Medicine, UW SoM	Rehabilitation science and global health practice and developing, adapting, and implementing toolkits, resources, and training packages aimed at enhancing clinician education across diverse income settings, barriers to accessing training, community engagement and participatory action research
Gary Chan, PhD Biostatistics Co-I: lead biostatistics WG: Biostats & Study Design	• Professor, Biostatistics, Health Systems and Population Health, Affiliate Faculty, eScience Institute, UW	Co-designing and analyzing multiple pragmatic trials, causal inference, missing data & complex outcomes analysis; treatment effect evaluation; pragmatic RCTs; Fellow, American Statistical Association
Ranee Chatterjee, MD, MPH Internal Medicine Co-I: lead Duke PCRC and site engagement	• Associate Professor, Duke University, SoM • Director of Duke's PCRC, Chair of PCRC Research Advisory Board	Recruitment & retention for clinical trials, diabetes prevention research, completed a Duke CTSA KL2 career development award, Site PI experience across multiple trials engaged with PCRC
Dawn Ehde, PhD Clinical Psychology Co-I: CBT BHP training, integrated care, exercise WG: Implementation Science	• Professor, Rehabilitation Medicine, UW SoM • Nancy & Buster Alvord Endowed Professor in Multiple Sclerosis Research	CBT for CP, treating CP, improving the function of persons with Multiple Sclerosis; extensive clinical trial experience with >25 studies addressing CBT, exercise and behavioral treatments for CP
Paul Fishman, PhD Economics Co-I: lead for cost study WG: Implementation Science	• Professor, Health Systems & Population Health, UW • Director, Graduate Program in Health Care Admin	Implementing and evaluating behavioral health interventions as an economist conducting cost effectiveness analyses of implementation costs and examining alternative financial models
Christina M Hester, PhD, MPH Microbiology Co-I: lead AAFP NRN and site engagement WG: Health Care Systems Interactions	• Vice President for Research, DARTNet Institute • Director of the AAFP NRN • Research Associate Professor, University of Kansas Medical Center	Supporting the uptake of evidence-based interventions in primary care practices, leading practice-based research, implementation of behavioral interventions in primary care; recruiting and retaining practices, providers and patients, and engaging in diverse stakeholders
Kris (Pui Kwan) Ma, PhD Clinical-Community Psychology Co-I: lead implementation qualitative study and provide practice facilitation WG: Health Equity	• Assistant Professor, Family Medicine, UW SoM	Qualitative methods and practice-based research in primary care; health disparities and IBH to increase access to evidence-based treatments for mental health and medical conditions; examination of systemic, cultural, and linguistic barriers to care and community-engaged, culturally responsive interventions to improve chronic conditions and dementia in Asian populations with limited English proficiency;
Zsolt Nagykaldi, PhD Pharmacology & Electrophysiology Co-I: co-lead implementation cost study	• Professor, Director of Research, Family & Preventive Medicine, University of Oklahoma Health Sciences Center	Improving quality, safety, cost, and equity of healthcare through translational health services research and patient-centered / community-engaged outcomes research; implementation cost assessment, design and implementation of health innovations
Connie van Eeghan, PhD Public Health Co-I: practice facilitation, toolkit adaptation WG: Implementation Science	• Associate Professor, The Robert Larner, M.D., College of Medicine, University of Vermont	Implementation Science, development of implementation toolkits; healthcare leadership and evaluation of health care organizational change initiatives; patient centered care in health systems; lead designer of the IBH-PC Toolkit
William Yancy, MD, MS Internal Medicine, Health Sciences Site PI: co-lead Duke PCRC and site engagement	• Professor, Interim Chief, General Internal Medicine, Duke University SoM • Associate Director of Duke PCRC	Obesity research and particular expertise in clinical trials of weight loss dietary interventions, weight loss medication, diet and other behavioral lifestyle change interventions, outcomes of weight, body composition, blood pressure, serum lipids, glycemia, pain, sleep, and quality of life

Supplementary Material

Ying Zhang, MD, MPH Family Medicine Co-I: primary care CP treatment WG: Health Care Systems Interactions	• Associate Professor, Family Medicine SoM	Qualitative research exploring individual and collective perspectives on reproductive health topics among immigrant and refugee populations; mobile app for CP and behavioral health treatment in PC

Proposed Collaboration Plan: Drs. Stephens (PI) and Kessler (Co-PI) will co-chair the executive team meetings; subgroup meetings will occur throughout the project (i.e., data analytic team, intervention and practice facilitation team, training team, and community engagement team); the CAB will convene 10 times during the UG3 phase to give key input on the adaptation of the IBH-PC Toolkit and quarterly in the UH3 phase in years 4-5 to give input on interpretation of analyses; and the investigative team will convene in-person, once a year in Seattle at the UW, in addition to monthly meetings throughout the study period.

Preliminary Studies and Relevant Team Experience:

PCORI-funded IBH-PC study.[5,6,8,71-77] *Stephens, Kessler, Chan, Ma, Nagykaldi & van Eeghan.* Our proposed project is conceived as a follow-up to IBH-PC trial, a national large effectiveness RCT that tested a 2-yr practice-change process intervention across 44 PC practices, the IBH-PC Toolkit, a multi-faceted method of organizing the planning, delivery and implementation of IBH services designed to improve organizational and patient outcomes that included: 1) a practice redesign and implementation workbook, 2) remote quality improvement coaching / practice facilitation services, 3) online trainings, and 4) an online learning community. Each practice was required to have a BHP on-site. The intervention was tested in a 2-arm, parallel, superiority, pragmatic, cluster-randomized trial that treated patients as the units of analysis clustered within practices that were the units of intervention. Patients *N* = 2,426 were representative of the general population and had multiple chronic conditions.[76] The ***use of the Toolkit indicated superior integration of the BHP within the practice***.[8,76] Dr. Kessler (co-PI) co-led the study and Dr. Stephens (PI) led recruitment and oversight of 25% of the practices, Dr. van Eeghan (Co-I) was the primary developer of the toolkit, Dr. Ma (Co-I) was a practice facilitator, Dr. Nagykaldi led the cost analysis study, and Dr. Chan was lead methodologist in the recently published study led by Dr. Stephens, that found that the toolkit led to a significant increase in IBH across all dimensions when time and level of toolkit completion were considered.[8] Findings from the main study also indicated that the ***existing toolkit could be streamlined and maximized to target CP*** by simply expanding existing sections focused on CP care and focusing on triage and training BHPs in CP treatment. The median cost was $20,726 per practice for the 2-yr intervention. The cost study aimed to quantify the relative costs associated with integrating behavioral health into primary care and develop a replicable and pragmatic measurement process with flexibility to adapt to emerging developments in each practice environment. ***We will use the methods from this cost study to re-assess cost*** and anticipate finding a reduction in overall median cost in the adaptation of the IBH-PC Toolkit to equitable CP treatment in primary care in this study.

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Expertise in Behavioral Health Treatment of CP.[83-88] *Drs. Stephens, Edhe, Kessler & Ma* are Clinical and Health Psychologists, treat patients with CP and study integration of evidence-based behavioral health treatments to improve CP related outcomes. Dr. Stephens (PI) has developed a series of behavioral skills trainings,[83-85] including skills that address patient engagement in opioid tapering, CP self-management, behavioral activation, exposure, distress tolerance, and motivational interviewing. Drs. Stephens (PI) and Edhe (Co-I) co-designed skills trainings for collaborative care care-managers to behaviorally treat CP for the Washington State Department of Labor and Industries based on Dr. Edhe's extensive work on testing CBT for CP.[3-,87-88] These trainings have been adapted into online didactics by Dr. Stephens for broad dissemination with over 66.5k views on YouTube and into multiple trial manuals, including the pilot tested ***CBT 1-2-3 manual, developed for a large pragmatic trial in primary care for nurse care managers treating CP, that will be adapted for this study to streamline BHP trainings as part of the adaptation of the IBH-PC Toolkit***.

Exercise Treatment for CP. [91-94] *Drs. Angadi and Burrola-Mendez* bring expertise in ET as an exercise physiologist and physical therapist with clinical practice ET expertise in treating CP, respectively. Dr. Angadi (Co-I) has published multiple studies involving measuring exercise activity and determining the specificity of the amount of exercise needed to improve health across multiple conditions. ***Measures for capturing***

exercise and related outcomes will be derived from these studies and finalized in the UG3 phase with CAB input to ensure we both target and capture ET related outcomes.

Data Curation and Digital Apps. [49,78-81,82] *Stephens, Ma, Chan, Zhang.* Drs. Stephens (PI) and Kessler (Co-PI) are pioneers in the use of digital tools and therapeutic apps to advance IBH. Dr. Stephens developed and directed the UW Institute for Translational Health Sciences (ITHS) DataQUEST program and Coordinating Center to leverage use of EHR data in clinical research with a network of community based primary care practices,[78-80,96,97] leveraging experience as a professional data design architect and executive steering committee member of the Clinical Translation Science Award (CTSA) funded UW Institute of Translational Health Sciences and Biomedical Informatics Core. Dr. Stephens has partnered DataQUEST research efforts with the DARTNet Institute[95] (partner on this proposal with the NRN, Drs. Kessler (Co-PI) & Hester (Co-I)) in collaborations for over a decade across numerous studies. The ***DataQUEST Coordinating Center will provide all data coordination and analytic support for this project*** and will leverage standard operating procedures to electronically recruit patients across the 27 practices using EHR data.

Drs. Stephens led, in collaboration with Co-I's Drs. Ma, Chan and Zhang, a feasibility RCT to test a ***CBT-ACT digital behavioral app*** developed by 2Morrow, Inc.,[49,81,82] supported by a Phase 2 NIH Fast Track SBIR grant and found that the vast majority of the primary care patients recruited to the study (*N* =108) with CP were willing to use an app to help with CP for up to 90 days; and EHR derived lists of eligible patients was a successful rapid recruitment strategy for enrolling a highly diverse and complete cohort of participants across four HCSs within two months. We also learned from the Phase I that providers and patients were open to mobile app solutions that can deliver CP treatment.

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Practice-based Intervention: IBH-PC Toolkit for CP and Digital Therapeutics (Apps)

Overview of Interventions – Adapted IBH-PC Toolkit: Both intervention arms will include our proposed 12-month practice-centric intervention, which is based on an adapted version of the IBH-PC Toolkit that is a multi-faceted implementation strategy that supports complex change in a primary care setting to move practices toward greater behavioral health integration through four components: (1) a structured, team-based, practice redesign and implementation set of workbooks to guide a quality improvement (QI) team and facilitator through a step-wise series of activities in distinct project stages (planning, redesign of workflows, and implementation of practice changes) and sub-stages that will be *adapted to streamline tactics and focus on a patients with CP*; (2) online educational curriculum that will be *streamlined to include online trainings for BHPs that teach CBT and ET treatment skills* adapted from the pilot tested CBT 1-2-3 training manual, recorded didactics, and patient worksheets (see **Figure 2**); (3) remote QI coaching / practice facilitation services, providing practice-specific support for a QI team and facilitator by experts in IBH, QI and workflow redesign; and 4) an online learning community that will be *adapted to support BHPs in learning and sustaining CBT CP skills*. The BHP trainings will be based on "CBT 1-2-3 - Empowering Chronic Pain Self-Management: Cognitive behavioral strategies for care managers" manual developed by Dr. Stephens (PI) and colleagues. The goals of CBT 1-2-3 are to reduce impact / interference of pain in daily life, improve physical and emotional functioning, increase effective coping skills, and reduce pain intensity.

Adapted IBH-PC Toolkit + Digital Therapeutics (DTx) Apps: The second intervention arm will additionally include training for BHPs to offer DTx apps (i.e., software-enabled solutions that deliver treatment direct to patients). The FDA is growing in the number of approvals of DTx each year, with about 25 approved as of 2023, of which 16 were mobile apps.[116] We conducted a review of current FDA approved DTx that have potential to extend CP care and they include: 1) RelievRx, CBT based virtual reality solution for improving chronic pain, 2) Hinge Health and Kaia Health, both apps for

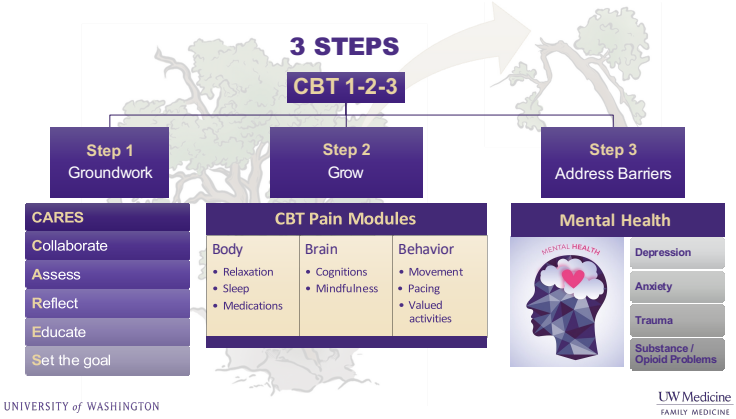

Figure 2: CBT 1-2-3 Training Steps

delivering physical therapy for joint / musculoskeletal pain; 3) Calm, an app for mindfulness, stress and anxiety, 4) Mindfulness, an app for meditation and sleep; 5) Rejoyn, trains the brain to activate centers that improve depression, and 6) reSET, an app for substance use disorder and reSETO, an app for opioid use disorder, both delivering self-guided CBT. Apps that address both CBT and ET will be chosen from an up-to-date review of available DTx apps. BHPs will be trained to offer them to patients at no cost as part of CP care.

UG3 Phase – Planning and IBH-PC Toolkit Adaptation:

Overview of UG3 Phase: In the UG3 phase, we will use a Communities of Practice (CoP) Method,[63,98-101] to create cross-organization collaboration between the CAB members (Community), to focus on helping us achieve equity in CP care in PC (Domain), to work on adaptation of the IBH-PC Toolkit and processes for recruitment (Practice). We will form our CAB with members comprised of patients, providers and administrators from the HCSs, including at least three members drawn from each of the three partners organizations. Our CAB will also include Dr. Jill Vanwyk, family medicine physician who leads a behavioral health forward chronic pain service to provide safer opioid prescribing at University of Colorado in Family Medicine; Dr. Joey Nelson, family medicine physician, Director of Diversity, Equity and Inclusion for UW Family Medicine Residency, and an enrolled member of the Confederated Tribes and Bands of the Yakama Nation; and Dr. London Breedlove, psychologist and Director of Behavioral Health at UW Family Medicine). The CAB will meet 10 times over the UG3 Phase and work together with the investigative team to advise on the adaptation of the IBH-PC Toolkit, processes related to recruitment and retention, and outcomes. The following milestones include Go/No-Go criteria for the UH3 phase:

AIM 1: Finalize outcome measures, practice and patient recruitment processes, and establish a centralized data coordinating infrastructure.

1.1 Establish participation in NIH Collaboratory Working groups. Drs. Stephens and Kessler (PIs) will work with the NIH Collaboratory Coordinating Center to orient the investigative team and project staff to the working groups. See **Table 3** for designations of which study team members will attend the six working groups. We have designated key collaborators to ensure that we have participation in all working groups.

1.2 Obtain IRB approval across sites. Drs. Stephens and Kessler will finalize the single Internal Review Board (IRB) approval through the University of Washington IRB and facilitate through the Site PIs within the NRN and PCRC HCSs that IRB reliance agreements or the equivalent are executed.

1.3 Finalize outcome measures. Dr. Stephens and Kessler will work with the investigative team, the CAB, and the NIH PRISM Collaboratory and working groups to review and finalize all outcome measures in addition to the chosen HEAL CDE's outlined in **Table 5.** The CAB's input on the RE-AIM measures will be refined based on feedback from CAB members about important implementation outcomes that would facilitate discovery and dissemination success.

1.4 Finalize patient recruitment strategies across HCSs and practices. Drs. Stephens and Kessler will work with Drs. Breedlove, Hester, Montgomery, and Yancy, as well as HCS champions to define the best way to create EHR derived eligible cohorts to drive study recruitment solicitations. Details will also be determined on the best way to send messages to patients, including best processes for how to send solicitations (i.e., via from EHR MyChart portals, emails, letters, REDCap etc.). Oversampling methods will be refined to ensure samples recruited and consented include at least 50% identified as BIPOC or Hispanic.

1.5 Develop data collection processes and infrastructure (i.e., EHR extraction specifications, survey builds). A data dictionary, data coordination infrastructure of file structures and databases will be established for tracking enrollment and survey, EHR, study notes and interview data over time. EHR data extraction specifications and case report forms for patient and practice surveys will be completed. REDCap enrolment, e-consent, and survey project builds will be completed.

AIM 2: Recruit 27 PC practices and create a Community Advisory Board (CAB) from the practices.

2.1 Assess practices for feasibility to participate (i.e., clinic characteristics, readiness for intervention). An assessment questionnaire and clinic characteristics survey will be designed and collected across the three partners' HSCs to identify eligible clinics.

2.2 Recruit and randomize 27 practices across 3 partners. Drs. Stephens and Kessler will work with site champions to finalize recruitment of 9 practices per partner for a total of 27 practices. Diversity of patient population served and diversity of practice characteristics will be prioritized. Site champions will return practice

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surveys and agreements to participate to the UW research team to trigger randomization. Each partner is expected to recruit 9 practices randomized evenly across 3 arms to ensure we have a spread across all arms and across all 3 partners.

2.3 Establish CAB membership. Site champions will work to identify at least 3 CAB members that represent people from each of the target groups. Dr. Stephens will work with site champions to introduce and prep all new CAB members before the first large group CAB meeting. Ensure payments are made to CAB members for their participation in the meetings.

2.4 Conduct CAB meetings. The CAB will meet in months 3-12 over the course of 10 monthly meetings Co-Chaired by Drs. Stephens (PI) and Ma (Co-I) using a CoP method to garner input from the CAB about key decisions, adaptations, and approaches needed to adapt the IBH-PC Toolkit, ensure focus on equity in access to and delivery of CP care.

AIM 3: Refine the IBH-PC Toolkit for CP care, choose DTx apps for homecare use, and adapt the BHP training materials.

3.1 Finalize adaptations to the IBH-PC Toolkit. Drs. Stephens and van Eeghen will ensure adaptations to all four components of the original IBH-PC Toolkit will be adapted to ensure streamlining content and processes based on the PCORI study learnings, aiming the purpose of the Toolkit to increase IBH care for CP equitably.

3.2 Finalize digital therapeutics / apps and contracts. A review of current FDA approved DTx's or apps on track to be approved by FDA will be conducted. DTx app options will be reviewed with the CAB to facilitate decision making on which apps to choose for inclusion in the IBH-PC Toolkit + app intervention arm. Vendor contracts for the chosen apps will be executed, including data specifications on what usage companies will send to the study team.

3.3 Refine and finalize BHP training materials for CBT and ET for chronic pain. Drs. Stephens and Ehde will collaborate with Drs. Angadi and Burrola-Mendez to adapt the CBT 1-2-3 training materials to include ET approaches as part of the focus on movement and how to introduce digital therapeutics into care and follow-up on use. All materials for trainings will be finalized, including instructions for BHPs on how to complete training.

3.4 Finalize website and digital resources for adapted IBH-PC Toolkit and trainings. A website will be created to deliver the content for the new adapted IBH-PC Toolkit with accompanying trainings so that practice champions and BHPs randomized to the intervention arms are ready to begin engagement at the start of UH3.

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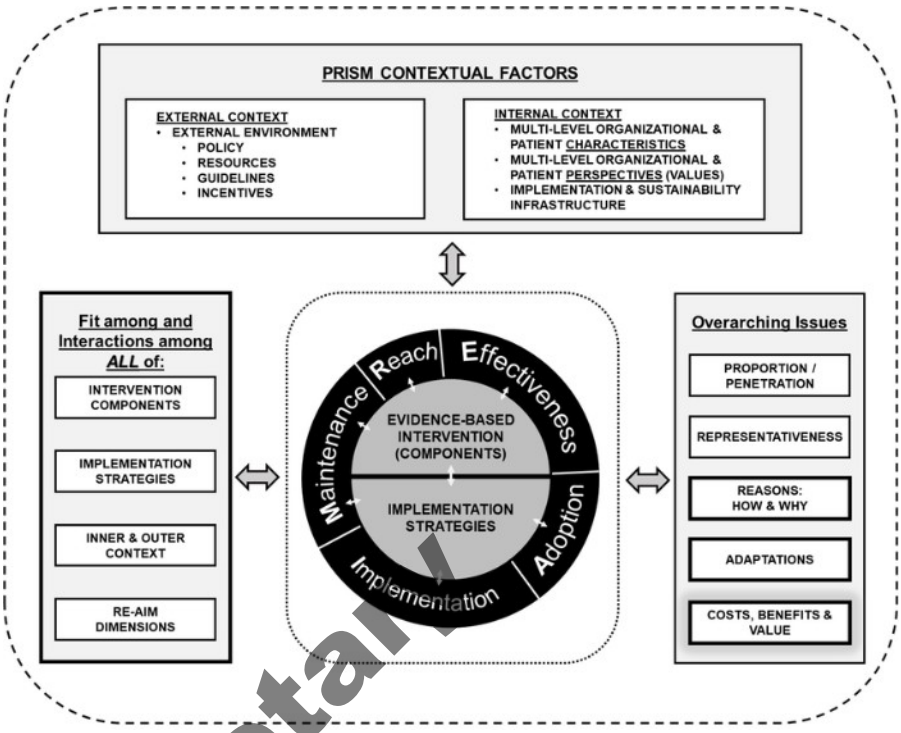
Table 4: UG3 Milestones	FY1											
Month	1	2	3	4	5	6	7	8	9	10	11	12
AIM 1: *Finalize outcome measures, practice and patient recruitment processes, and establish a centralized data coordinating infrastructure.*												
1.1 Establish participation in NIH Collaboratory Workgroups	X	X	X	X	X	X	X	X	X	X	X	X
1.2 Obtain IRB approval across sites	X	X	X	X	X	X						
1.3 Finalize outcome measures				X	X	X	X	X				
1.4 Finalize patient recruitment strategies across HCSs and practices							X	X	X	X		
1.5 Develop data collection processes and infrastructure (i.e., EHR extraction specifications, survey builds)							X	X	X	X	X	X
AIM 2: *Recruit 27 practices and create a Community Advisory Board (CAB) from the practices.*												
2.1 Assess practices for feasibility to participate (i.e., clinic characteristics, readiness for intervention)				X	X	X	X	X				
2.2 Recruit and randomize 27 practices across 3 partners							X	X	X	X	X	X
2.3 Establish CAB membership	X	X										
2.4 Conduct CAB meetings			X	X	X	X	X	X	X	X	X	X
AIM 3: *Refine the IBH-PC Toolkit for CP care, choose digital therapeutics/apps for CP homecare use, and adapt the BHP training materials.*												
3.1 Finalize adaptations to the IBH-PC Toolkit		X	X	X	X	X	X	X	X	X	X	X
3.2 Finalize digital therapeutics / apps and contracts				X	X	X	X					
3.3 Refine and finalize BHP training materials for CBT and ET for chronic pain				X	X	X	X	X	X	X	X	X
3.4 Finalize website and digital resources for adapted IBH-PC Toolkit and trainings										X	X	X

UH3 Phase – Implementation Trial:

Overview of UH3 Phase: In the UH3 phase, we propose a 3-arm cluster-randomized pragmatic RCT across 27 practices and *N* = 2,025 patients with CP to test our adapted IBH-PC intervention developed in the UG3 Phase and with and without the use of digital therapeutics to improve equity and quality of CP care.

Implementation Model: For UH3 we plan to use the **PRISM RE-AIM Implementation Model** (see **Figure 3**).[11] Over a period of 20 years, RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance)[102] evolved into PRISM, the Pragmatic Robust Implementation and Sustainability Model, as the translational component that is easily applied to implementation, evaluation, and dissemination.[11]

Figure 3: PRISM RE-AIM Model



Sampling and Power Analysis: To evaluate the effectiveness of the IBH-PC Toolkits, we will conduct a pragmatic cluster randomized trial with three treatment arms. We plan to recruit 27 practices and randomly assign 9 to each treatment arm, and to recruit 2,025 patients with CP with the listed eligibility criteria (75 patients from each practice). Assuming a two-sided type I error of 0.05, a conservative estimate of 25% dropout proportion of practices and patients, and an intraclass correlation of 6-9% of PEG outcome within a practice, the study has 81%-92% power to detect a small standardized effect size of *d*=0.35 between the intervention groups and the control group. Using a conservative Bonferroni correction, the study has >80% power to detect standardized effect *d*=0.4 or greater for the secondary individual-level health outcomes, and *d*=0.75 or greater for secondary practice-level outcomes.

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Patient Recruitment & Eligibility: We will recruit 75 patients from each of the 27 practices based on the following eligibility criteria: adult patients (i.e., aged >=18 years), chronic non-cancer related pain current and present for >=3 months, documentation of at least one International Classification of Diseases (ICD) code of a common pain related conditions, >=2 primary care visits within the last 12 months at the time of recruitment, significant levels of self-reported pain interference (i.e., PEG>=4), no dementia, and not in palliative/hospice care or living in a controlled setting (i.e., nursing home, group home, rehabilitation facility). We will use an established protocol to recruit patients electronically established by the DataQUEST Coordinating Center that identifies patients with eligible criteria, using electronic health record (EHR) data extracted from each HCS. From the generated patient lists, random cohorts are selected for recruitment through a series of electronic (i.e., email or patient portal) blasts until 75 patients are recruited from each practice through digital e-consent in REDCap. Oversampling of racial and ethnic minority patients will be added to the recruitment blasts; and non-Hispanic White patients will become ineligible to enroll once 50% consent per practice, to ensure oversampling of racial and ethnic minority identified participants. Electronic solicitations will contain a link to an interest survey with three options: 1) proceed to the study eligibility survey, 2) request a call back from a study coordinator for further discussion, or 3) opt out of the study. Patients who proceed to the eligibility survey will be informed at the end of the survey of their study eligibility. A study coordinator will follow up with any call requests and if needed, assist with the consent over the phone.

Randomization: Practices will be randomized to one of three arms: IBH-PC Toolkit only vs. IBH-PC Toolkit + apps vs. treatment as usual. Participants will be assigned to a condition based on the practice randomization and recruited to stratify by age and gender, ensuring distribution of participants equally across practices. This stratified allocation will be implemented in the REDCap randomization module.

Data Collection: ***EHR*** – We will work with the participating PBRNs, Data QUEST, and the DARTNet Institute to complete electronic health record (EHR) data extractions to support recruitment efforts, post-intervention and 6-month post intervention outcome evaluations. Contact information, patient demographics, social determinants of health, service utilization patterns, and diagnoses will be extracted from the EHR. ***Patient surveys*** – REDCap will be used to capture patient reported outcomes, service utilization and app usage. ***Coaching/practice facilitation notes*** – Practice facilitators will use a template to collect note from interactions with practice champions as they support intervention practices throughout the use of the Toolkit. ***Training***

reports – The study team will capture which BHPs have engaged trainings and level of completion of training activities. ***Practice champion surveys*** – REDCap will be used to capture practice characteristics, Toolkit tactics used and stages completed, and time-cost estimations from practice champions (i.e, practice leads who are designated as the point person to invoke use of the IBH-PC Toolkit). ***BHP surveys*** – REDCap will be used to capture ratings of self-efficacy for using CBT 1-2-3 skills and DTx apps in practice, and fidelity measures of BHP treatment. ***DTx App usage*** – App vendors will provide usage outcome data for the apps that participants engage in for use during the study period. ***Key informant interviews*** – Transcriptions from *N* = 36 qualitative interviews across BHPs and practice champions after intervention across the 18 intervention practices will capture IBH processes and structures targeted for change, implementation challenges and adjustments made to the intervention during implementation.

AIM 1: To determine effectiveness of the adapted (1) IBH-PC Toolkit + apps vs. (2) IBC-PC Toolkit only vs. (3) treatment as usual (TAU) for improving pain interference and level of integration of IBH. *We hypothesize that the interventions arms will improve outcomes better than TAU.*

PRISM RE-AIM *Effectiveness.* Patient Outcome Measures: Our primary outcome measure will be patient pain interference (PEG scale[103,104]) and secondary outcome measures will include: pain intensity (PEG scale), physical function (PROMIS short form 6b[104]), quality of life (QoL; WHOQOL-2[105]), satisfaction with treatment (PGIC[106]), substance use screening (TAPS 1[107]), depression (PHQ-9[108]) and anxiety (GAD-7[109]). BHP Outcome Measure: BHP's self-efficacy treating CP will be measured using a BHP provider rating based on the BHP report. Practice Outcome Measures: Level of IBH will be measured by the Practice Integration Profile 1 (PIP-1), which was developed to operationalize the lexicon for Behavioral Health and Primary Care Integration.[21,110] The PIP has been shown to discriminate differing levels of integrated care processes and differences in type of practice across six domains: practice workflow, clinical services, integration methods, case identification, patient engagement, and workspace arrangement and infrastructure.[21,23,25] The PIP will be administered to at least four people at each practice (i.e., a medical primary care provider (PCP), BHP, an administrator such as a practice/clinic manager, and a provider or staff of the practice's choice) to create an average composite score.

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Analytic Plan: The primary evaluation for Aim 1 will utilize linear mixed models with random effect at practice level to compare individual PEG scores post-randomization at 9 months after baseline (post-intervention) between practices that are assigned to different intervention groups. We will employ an intention to treat (ITT) approach regardless of the level of implementation of the IBH-PC among the practices that receive interventions. Individual and practice-level precision variables such as baseline PEG scores will be included in the model, together with indicator variables for the treatment arms. Treatment effect estimates, two-sided 95% confidence intervals, and the joint significance test of a null treatment effect at 5% significance level will be reported. We will also test whether the mean PEG score is different between any 2 of the 3 treatment arms, using a conservative 1.7% significance level to correct for multiple comparisons. For BHP, practice level, and secondary patient outcomes measured at post-intervention, we will use generalized linear mixed models with identity, logit and logarithm links for continuous, binary and count outcomes. We will use the Bonforroni and the Benjamini-Hochberg procedure to correct for multiple comparisons. We will conduct a secondary analysis for longitudinally collected outcomes to study the potential change of treatment effects over time. To handle missing data, we will use multiple imputation which is recommended for trials.[111] Missing data will be imputed 10 times, the statistical analyses will be repeated on each of the 10 datasets and combined using the Rubin's rule.[112]

AIM 2: Evaluate implementation of the interventions: IBH-PC Toolkit + mobile apps and IBH Toolkit only.

Analytic Plan: PRISM RE-AIM Framework will be used to define implementation outcomes (see **Table 5**).
Reach: We will measure the proportion of patients who we reach out to, who agree to participate in our study, and who receive services from the BHP and / or PCP.
Effectiveness. See Aim 1.
Adoption: We will: 1) compute the proportion of practices we reach out to and proportion who agree to participate, 2) describe the type of personnel at the practices who engage in the toolkit, 3) compute the

proportion of BHPs who engage in the trainings, 4) compute the proportion of patients who engage in at least 1 and >1 BHP visit, 5) compute the proportion of patients who use a DTx app that were offered one and describe usage rates of the apps, and 6) describe the type and total tactics used from the Toolkit.

Implementation: Feasibility related descriptive statistics will be used to describe total Toolkit stages completed across practice sites, rates of BHP training completion, rates of BHP use of CBT 1-2-3 skills in visits, and rates of BHP recommending use of DTx apps. Practice changes targeted and completed will be documented and summarized. Implementation costs will be quantified by close estimates of time-effort related to implementing the adapted IBH-PC Toolkit, using the analytic approach published in the IBH-PC cost study led by Dr. Nagykaldi (Co-I).[72] Descriptions of challenges and adjustments made during implementation will be described.

Maintenance. We will determine maintenance of change at 6-months post-intervention in our effectiveness outcomes in which significant change was found, based on the analytic approach detailed in Aim 1. We will describe which changes practices made to IBH that remained in place 6-months post-intervention.

Key informant interview analyses. Interview transcripts will be analyzed using content analysis approach,[113,114] which is a systematic, replicable technique for compressing many words of text into fewer content categories based on explicit rules of coding and will be conducted by two coders led by Dr. Ma (Co-I).

TABLE 5: IMPLEMENTATION OUTCOMES FOR UH3 EQUIP CP STUDY

PRISM RE-AIM IMPLEMENTATION	OUTCOMES	MEASURE	DATA SOURCE
Reach	Patients approached	Proportion of patients eligible and enrolled	Enrollment data
	Patients treated by BHP and PCP	Proportion of patients seen by BHP and PCP	Patient report / EHR data
Effectiveness & Maintenance	**Patient Outcomes**		
	Pain interference	PEG	Patient report
	Pain intensity	PEG	Patient report
	Physical function	PROMIS Physical Functioning Short Form 6b	Patient report
	Quality of life	WHOQOL-2	Patient report
	Satisfaction with treatment	PGIC	Patient report
	Substance use screening	TAPS-1	Patient report
	Depression	PHQ-9	Patient report
	Anxiety	GAD-7	Patient report
	BHP Provider Outcomes		
	Self-efficacy treating chronic pain	BHP rating	BHP report
	Practice Outcomes		
	Level of integrated behavioral health	PIP	Practice report
	What will persist after the study	Processes and structures changed	Practice champion interview
Adoption	Practice engagement	Proportion of practices engaged in the study; descriptives of personnel engaged in the toolkit use	Practice characteristics
	Staff/provider engagement	Proportion of BHPs engaged in trainings	BHP training report
	Patient engagement in BHP care and app use	Proportion of patients engaged in BHP and apps	BHP report; Patient report
	Toolkit tactics used	Individual and total tactics used in intervention toolkit	Practice champion interview; practice champion survey; coaching notes
Implementation	Feasibility: intervention toolkit completion rate	Stages completed	Practice champion interview, coaching notes, practice champion survey
	Feasibility: BHP training completion rate	Completion rates for training modules and attendance	Training tracking report
	Fidelity: BHP clinical delivery	Proportion of visits BHP used CBT or ET	BHP report
	Fidelity: BHP delivery of apps	Proportion of patients recommended to use an app	BHP report
	Fidelity: planned vs executed changes	Fidelity practice survey	Practice champion report
	Cost	Time and financial cost estimates of intervention	Practice champion report
	Adaptations: Implementation challenges, adjustments made	Qualitative interview	Practice champion interview

Supplemetary Material

AIM 3: Evaluate equity in access and outcomes of CP care in PC.

We will evaluate variations in rates of access to BHP care and engagement in treatment and heterogeneity of treatment effect across outcomes for subgroups of patient. Completion of this aim will inform our level of success in achieving our primary goal of ensuring BIPOC, Hispanic and low SES communities have equitable access to CP treatment in PC. Two sets of analyses will be conducted: **1) Examine demographic data to determine equity in access and rates of access to CP care by BHPs in PC.** Factors will include age, sex at

birth, gender identity, race/ethnicity, highest level of education, employment status, relationship status, and annual household income. T-tests or ANOVA will be used to assess whether the access is the same across levels in each factor. **2) Analyze the outcomes data to determine equity in CP care by BHPs in PC by examining heterogeneity of treatment effect across patient primary and secondary outcomes.** Subgroup analyses will be considered exploratory to study the heterogeneity of treatment effect (HTE) using features and patient characteristics (X) at baseline (e.g. race/ethnicity, gender identity, comorbidities, degree of rurality, and insurance status). HTE will be assessed through both a traditional regression approach testing interactions one-modifier at a time, and a contemporary nonparametric estimation of the CATE (conditional average treatment effect) using honest causal forest,[115] which is an ensemble method that contains honest causal trees using random re-samples of observations for each tree that maximize HTE effects across nodes/variables and uses cross-fitting for controlling overfitting of effect estimates.

Timeline. Data collection, analyses and dissemination activities are illustrated below (see **Table 6**). Practices will be staggered to start baseline measures and intervention activities every two months across the UH3 Phase in sync with the treatment as usual clinics to ensure baseline measures are taken at the same time across arms (see the Milestones attachment for illustration of the staggering of practices across the 3-arms).

Table 6: UH3 Milestones

	FY2												FY3												FY4												FY5											
Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
DATA COLLECTION																																															
Patient data collection for times T0 (baseline), T1 (post intervention), and T2 (maintenance)	T0: baseline												T1: post-intervention												T2: maintenance 6-month post-intervention																						
EHR data for enrollment	T0 timepoints foreach practice																																														
BHP care delivery fidelity surveys													T1 timepoints foreach practice																																		
Practice champion cost and toolkit use surveys																																														
Qualitative key informant interviews																																														
EHR data for outcomes																									T2 timepoints foreach practice																						
Practice champion Maintenance survey																																														
App usage data																																														
Coaching / facilitation notes					Intervention practices are using the Toolkit																																											
BHP training survey						Month post BHPs complete training																																											
ANALYSES																																														
Complete Aim 1 effectivness analyses																																			Aim 1: Effectiveness											
Complete Aim 2 implementation analyses																													Aim 2: Reach, Adoption, Implementation, Maintenance																	
Complete Aim 3 subgroup/equity analyses																																					Aim 3: Equityin acesss & outcomes										
DISSEMINATION																																														
Manuscript submissions	UG3 manuscripts																				UH3 manuscripts																								
Website development and release																																										Study/Toolkit website						
Data dissemination - upload public dataset																																													upload	

Supplemetary Material

D. SUSTAINABILITY

We have embedded sustainability tools that will be developed in UG3 and implemented in UH3. These include:

Continued BHP Co-location in PC: The basis of sustainability for this program are the embedded BHPs co-located with in PC practices. Given the co-location of BHPs has been successful in these practices, continues to grow nationally, and that the practices already financially sustain the BHPs, we believe improvements to IBH made during the study period will remain in place after the study ends.

Adapted IBH-PC Toolkit: The Toolkit with BHP trainings will easily accessible to the public on a ***newly developed up-to-date website*** built during the UH3 Phase. Training recordings and adapted Toolkit materials will be presented on the new user friendly, easy to access unique website that will be hosted on the UW Family Medicine website. New and future BHPs will be able to access trainings at any time after the study ends.

DTx Apps for Continued BHP Training & Patient Home Use: Practices and HSCs will be encouraged to continue access to DTx apps for patients as part of their continued CP care. FDA approval allows these apps to be prescribed by providers and potentially covered by insurance. We will work with the practices to document resources they may be able to use to facilitate insurance reimbursement for their patients that will be added to the website.

Creation of a BHP for CP Online Forum: BHPs will be encouraged to set up a chatroom where they can share experiences, challenges, and comment on their continued treatment of CP patients. They will also be invited to participate in the UW TelePain, a free weekly service funded by Washington State Legislature ECHO program, free to providers treating patients with chronic pain to increase knowledge and confidence.

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DATA MANAGEMENT AND SHARING PLAN

Element 1: Data Type

A. Types and amount of scientific data expected to be generated in the project:

Types of data will include: 1) Participant surveys (at baseline, post-intervention, and 6-months post-intervention), 2) EHR data to facilitate recruitment (i.e., patient contact information and demographics) and outcome evaluation data (i.e., patient demographics, social determinants of health, service utilization patterns, and diagnoses), 3) practice champion and behavioral health provider (BHP) surveys (i.e., measures of behavioral health provider self-efficacy for delivering treatment for chronic pain, engagement throughout the intervention, elements of the intervention used, cost survey, and anticipated maintenance of practice changes), 4) post-intervention key informant interview data, and 5) mobile app usage data.

Estimated amount of data will include: 1) EHR data for recruitment will be across all eligible patients with rolling recruitment per practice until 75 are recruited from each of the 27 practices; therefore total number of patients is TBD but will likely be thousands to reach the goal of N = 2,030; 2) 2,030 participants for EHR and patient survey data; 3) practice champions and (BHP) surveys will be collected across all 27 practices; 4) interviews will be conducted with N = 36 participants (2 from each of the 18 intervention practices); and 5) mobile app usage data will be from no more than 1,350 participants who participate in the intervention arms.

B. Scientific data that will be preserved and shared, and the rationale for doing so:

The final research dataset will include a compilation of: 1) participant data from the EHR and surveys, 2) practice surveys from champions and BHPs, 3) mobile app usage data from intervention arm participants. Data will be prepared into a final research dataset to conduct study aims related analyses and shared and structured to maximize future scientific value while protecting patient and health system privacy.

C. Metadata, other relevant data, and associated documentation:

A comprehensive data dictionary will provide definitions for all data variables, as well as a detailed study protocol that includes measure definitions and references, to support data usage.

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Element 2: Related Tools, Software and/or Code: N/A

Element 3: Standards: Standards from the Heal Initiative Common Data Elements (CDEs) will be used, along with standard EHR related codes (e.g., ICD codes for diagnoses) and summary totals computed for published measures used in surveys.

Element 4: Data Preservation, Access, and Associated Timelines

A. Repository where scientific data and metadata will be archived:

Inter-university Consortium for Political and Social Research (ICPSR)
https://www.icpsr.umich.edu/web/pages/about/

B. How scientific data will be findable and identifiable:

We will use the native ICPSR search features and include published works that will be uploaded and associated with the dataset in ICPSR. We will also include a link to this repository from our research group's main webpage that will have a description of the study posted once completed.

C. When and how long the scientific data will be made available:

Data will be made available after the primary outcomes of the trial are published and will remain available for at least 7 years.

Element 5: Access, Distribution, or Reuse Considerations

A. **Factors affecting subsequent access, distribution, or reuse of scientific data:**

Only patient participant de-identified data will be shared with all practice location data removed to protect patient confidentiality.

B. **Whether access to scientific data will be controlled:**

Data will be made available by the above stated data repository based on dated permission specifications submitted at time of deposit of data. Data will be freely available via the associated repository's public website.

C. Protections for privacy, rights, and confidentiality of human research participants:

All patients' protected health information (based on HIPAA identifiers) will be removed, only age will be included at time of baseline, all geographic location information will be removed and only quantitative survey and EHR related data will be shared that include only summary data of service utilization to ensure all service dates can be removed. All IRB and certificates of confidentiality will be honored.

Element 6: Oversight of Data Management and Sharing:

Administrative PI, Dr. Kari Stephens, Professor at University of Washington Family Medicine, will ensure that data are monitored and uploaded for sharing based on FAIR principles to the above noted repository, based on details in this plan and in compliance with the repository's processes and in accordance with all data sharing governance requirements to protect participant confidentiality. Data will be monitored by Dr. Stephens and the appointed research team members, including the senior project manager, who have been delegated data coordination responsibilities regularly throughout the study's active period. All members of the research team will review this plan and coordinate to ensure compliance with this stated plan.

Supplementary Material