

## Ethics and Regulatory Core Consultation Call:

### BeatPain Utah

December 7, 2020

Meeting Participants

Judith Carrithers (Advarra), Julie Fritz (Utah), Andrew Garland (Johns Hopkins), Bryan Gibson (Utah), John Lantos (Children’s Mercy), Martha Matocha (NIH), David Magnus (Stanford), Stephanie Morain (Baylor), Pearl O’Rourke (Retired), Vaso Rahimzadeh (Stanford), Tammy Reece (Duke), Kayte Spector-Bagdady (Michigan), Victor Solis (Utah), Jeremy Sugarman (Johns Hopkins), Kevin Weinfurt (Duke), Dave Wendler (NIH), Ben Wilfond (Washington), Liz Wing (Duke)

AGENDA ITEMS	DISCUSSION	ACTION ITEMS
<p>Overview of Demonstration Project</p>	<ul style="list-style-type: none"> <li>• <b>Overview:</b> BeatPain Utah is an embedded pragmatic clinical trial that will compare the effectiveness of nonpharmacologic intervention strategies for patients with back pain seeking care in 13 federally qualified health centers (FQHCs) throughout Utah. The strategies being evaluated are designed to overcome barriers specific to rural and low-income communities served by FQHC clinics through the innovative use of an electronic referral (through the EHR) and telehealth resources. The intervention consists of counseling, physical therapy (PT), and brief consultation sessions. Referrals will be done through the EHR in the clinics and connect participants with clinicians at the University of Utah.</li> <li>• <b>Collaborative network partners:</b> 13 FQHC clinics overseen by the Association for Utah Community Health</li> <li>• <b>NIH Institute:</b> National Institute of Nursing Research</li> <li>• <b>Study design:</b> BeatPain Utah will evaluate the effectiveness and the implementation of telehealth nonpharmacologic pain treatments delivered as adaptive treatment strategies. In the UG3 phase, the study team will finalize procedures and conduct sociotechnical assessments at implementation sites, including intervention procedures, protocols, e-referral workflow, data</li> </ul>	

AGENDA ITEMS	DISCUSSION	ACTION ITEMS
	<p>collection methods, and training of the FQHC staff. In the UH3 phase, the intervention will individually randomize patients and include:</p> <ul style="list-style-type: none"> <li>○ A telehealth strategy that provides a brief pain teleconsult along with phone-based physical therapy.</li> <li>○ An adaptive strategy that provides the brief pain teleconsult first, followed by phone-based physical therapy among patients who are nonresponsive to treatment.</li> </ul> <ul style="list-style-type: none"> <li>● <b>Outcomes:</b> <ul style="list-style-type: none"> <li>○ Primary: pain interference</li> <li>○ Secondary: opioid use</li> </ul> </li> <li>● <b>Other important notes about the study:</b> BeatPain Utah will also evaluate implementation outcomes to inform future efforts to scale effective strategies into other low-resource health care settings.</li> </ul>	
Status of IRB approval	<ul style="list-style-type: none"> <li>● The study team is still finalizing key components of their IRB submission, with an eye toward harmonizing the HEAL Initiative’s core domain elements (CDE) across the network of participating health clinics.</li> <li>● The University of Utah will be the single IRB of record.</li> </ul>	
Risk classification	<ul style="list-style-type: none"> <li>● The study team anticipates that the intervention will qualify as minimal risk. However, collecting data related to some of the required HEAL domains may alter this assessment.</li> </ul>	Joe Ali will schedule a conversation regarding the required HEAL domains with the study team.
Consent	<ul style="list-style-type: none"> <li>● After a connection is made between a referred patient and a pain teleconsultant, an explanation of the study will be provided to the patient. If the patient is eligible and interested, oral consent will be obtained.</li> <li>● Those on the call agreed that the study would likely qualify for a waiver of documentation of consent.</li> </ul>	
Privacy/HIPAA	<ul style="list-style-type: none"> <li>● The only research data entered in the clinical record is the initial referral. Those on the call discussed potential implications for the Certificate of Confidentiality (see below) related to this.</li> </ul>	

AGENDA ITEMS	DISCUSSION	ACTION ITEMS
Monitoring and oversight	<ul style="list-style-type: none"> <li>• The National Institute of Nursing Research (NINR) requires that the study team set up an external Data and Safety Monitoring Board (DSMB).</li> <li>• Tammy was asked to forward the Collaboratory’s template for a Data Monitoring Committee (DMC) Charter for PCTs to the NIH Project Officer and study team. This document contains helpful guidance for establishing a DSMB/DMC with PCT-specific expertise.</li> <li>• The PI asked if the Collaboratory has suggestions for best practices for safety monitoring for adverse events. It was suggested that during the UG3 phase, the study team could figure out a mechanism for participants to voluntarily report harms.</li> </ul>	<p>Tammy will send the study team and Project Officer the Collaboratory template for Data Monitoring Committees Charter for PCTs and the DSMB article from the special series in <i>Clinical Trials</i>.</p> <p><b>Sent 12/7/20</b></p>
Issues beyond the study	<ul style="list-style-type: none"> <li>• There was a discussion around the telehealth modality, which has raised some unanticipated issues around privacy for virtual medical encounters. The PI said their encounters will be by phone only, without a video or camera component. It was suggested that the study team could provide guidance to the patient about ensuring they are in a private space during the phone calls.</li> <li>• The group discussed the project’s initial plans for data sharing/secondary use of the study data. In particular, what would be permissible uses of the data (including aggregating study data with other data) and plans for minimizing risk of re-identification of study subjects if the data are shared. Since similar issues are being faced across the Demonstration Projects, this issue will be addressed across the Collaboratory.</li> <li>• A Certificate of Confidentiality (CoC) will be automatically provided per NIH policy. This certificate adds provisions for future research uses and confidentiality obligations for future data sharing.</li> </ul>	

## SPECIFIC AIMS

Chronic pain imposes tremendous burden on impacted persons, healthcare systems and society. Back pain is the most common form of chronic pain, with a lifetime prevalence over 80%.<sup>1</sup> Over ¾ of persons whose chronic pain substantially interferes with daily activities (i.e, high impact chronic pain) have back pain.<sup>2</sup> Back pain also plays a sizable role in the opioid epidemic. It is the most common pain diagnosis for which an opioid is prescribed,<sup>3,4</sup> 25-50% of patients newly consulting primary care for back pain receive opioids<sup>5,6</sup> and over 50% of regular opioid users have back pain,<sup>7</sup> despite the lack of evidence supporting opioid use for back pain.<sup>8,9</sup> *Improving back pain care is an essential component of a comprehensive strategy to address the opioid crisis.*

Poverty and rurality are common risk factors for having back pain, being prescribed opioids and progressing to opioid misuse or abuse.<sup>10-12</sup> It is unsurprising that poor and rural communities are disproportionately impacted by the opioid crisis. Individuals in these communities frequently receive care in safety-net settings such as federally qualified health centers (FQHCs). FQHCs are community-based organizations providing primary care in areas with limited healthcare access. In the U.S. about 70% of patients receiving care in FQHCs are at or below the federal poverty level, and half of all FQHC clinics are in rural/frontier communities.<sup>13</sup> FQHCs are at the leading edge of the opioid epidemic, but there is almost no research on non-pharmacologic (NP) pain management alternatives in these settings. *Our project will be conducted in FQHCs at the forefront of the opioid crisis; examining implementation and comparing the effectiveness of efforts to prevent opioid initiation and escalation.*

Evidence-based guidelines are clear that opioids are not first-line care for back pain, and should not be used before NP treatment is provided. Efficacious first-line NP treatments include education to counter maladaptive pain beliefs and promote self-management and exercise provided with cognitive behavioral strategies.<sup>14,15</sup> Limited access and lack of resources are barriers to providing NP care in FQHCs. Telehealth has been used to overcome these barriers for other chronic conditions and has been successful in the Veterans Health system to provide NP pain care. The ongoing COVID pandemic has rapidly accelerated the need for remote solutions to deliver evidence-based care for patients with chronic pain. *This project uses telehealth to overcome barriers to providing NP pain care to patients in FQHC settings, testing a brief pain teleconsult and a phone-based physical therapy program.*

Our goal is to improve pain management and reduce reliance on opioids for patients with back pain in FQHCs in Utah. Our strategy is to compare the effectiveness of first-line NP pain treatments using phone-based telehealth to overcome access barriers. We will use automated EHR reminders for electronic referral to teleconsult services, leveraging widely-adopted health IT standards with high potential scalability. Our project tests adaptive treatments and uses a hybrid type I design - focused on effectiveness outcomes while gathering implementation data to inform future efforts to scale effective strategies. Our project has two Phases:

- 1) Planning Phase to finalize procedures and conduct sociotechnical assessments at implementation sites to design EHR reminders for electronic referral aligned with FQHC clinic work flows. Planning Phase aims are:
  1. Finalize procedures for interventions; develop protocols, procedure manuals and fidelity assessments.
  2. Conduct sociotechnical assessment at FQHC sites to assess current EHR reminder and e-referral workflow
  3. Implement EHR reminders for e-referrals to teleconsult services in the FQHCs.
  4. Finalize study outcomes, data collection methods and data analysis plan.
  5. Train pain teleconsultants and FQHC staff in procedures for the Clinical Trial.
- 2) Clinical Trial Phase comparing the effectiveness and evaluating the implementation of telehealth NP pain treatments delivered as adaptive treatment strategies. Clinical Trial Phase aims are:
  1. Compare effectiveness of a brief pain teleconsult with or without phone-based PT for patients with back pain in FQHCs with pain interference as primary outcome and opioid use as a secondary outcome.
  2. Compare effectiveness of phone-based PT as a first-line strategy vs. a stepped care strategy of phone-based PT as second-line care for patients do not respond to a brief pain teleconsult.
  3. Examine effectiveness results of Aims 1 & 2 in pre-defined patient phenotypes based on gender, presence of HICP and current opioid use.
  4. Explore implementation outcomes for teleconsult services (acceptability, adoption, feasibility and fidelity)

## A. SIGNIFICANCE and SCIENTIFIC PREMISE

**A.1 The Burden of Chronic Back Pain:** One in 3 Americans lives with chronic pain at an estimated annual cost of over \$600 billion.<sup>1</sup> About a third of those with chronic pain experience high-impact chronic pain (HICP) characterized by significant levels of interference in work, social and/or self-care activities.<sup>16</sup> Persons with HICP experience the greatest disablement from pain and account for a large share of the costs attributable to chronic pain.<sup>17</sup> The National Pain Strategy from the Interagency Pain Research Coordinating Committee of the NIH recognizes the need to differentiate chronic pain of moderate impact from HICP.<sup>16</sup>

Back pain is the most prevalent form of chronic pain. Over 75% of those with HICP report lower back and/or neck pain.<sup>2</sup> In 2016, back pain was the costliest medical condition in the U.S. with an estimated \$135 billion in spending, exceeding 153 other conditions including diabetes, heart disease and Alzheimer's.<sup>18</sup> An estimated 2% of the U.S. workforce is compensated for lost time from back pain annually, and back pain is responsible for more disability claims than any other condition.<sup>19</sup> The high impact of back pain on individuals and society is highlighted in the Global Burden of Disease initiative.<sup>20</sup> Of 291 conditions studied, back pain ranked first globally and in the U.S. for associated disability and overall impact in detracting from health.<sup>21</sup> These statistics clearly indicate that *despite intensive and costly efforts, the prevalence of chronic back pain and resultant disability continue to increase, attesting to ineffective health system management.*<sup>22,23</sup>

**A.2 Ineffective Back Pain Management and the Opioid Crisis:** Ineffective back pain management contributes significantly to the opioid epidemic.<sup>24</sup> From 2000-2010 opioid prescribing for non-cancer pain nearly doubled from 11.3% to 19.6% of all physician visits.<sup>25</sup> Back pain accounted for a sizable portion of this increase. Back pain is the most common diagnosis for which opioids are prescribed despite a lack of evidence for any sustained benefit.<sup>26,27</sup> The first recommendation of the CDC Guideline for Prescribing Opioids for Chronic Pain specifies that nonpharmacologic (NP) treatments are preferred to opioids; and if opioids are used it should be in combination with NP treatment.<sup>9</sup> Similarly, evidence-based guidelines advocate NP pain treatments as first-line care for back pain while recognizing that opioids are not a first-line option.<sup>15,28</sup> Despite these recommendations studies find that 30%-50% of back pain visits are associated with an opioid prescription,<sup>29,30</sup> and opioids are often initiated at the first physician encounter.<sup>31</sup> Rates of opioid prescribing for back pain have been declining,<sup>32</sup> yet a recent review found 20.4% of patients with a new back pain consultation filled an opioid prescription within 30 days.<sup>33</sup> The study found considerable variation across states with Utah having the 5<sup>th</sup> highest rate.<sup>33</sup> Based on data from the National Ambulatory Medical Care Survey from 2007-2015, opioids were prescribed at 22% of new consultations for chronic musculoskeletal pain while NP options including physical therapy or other complementary/alternative care were prescribed at 10% and 6% of new consultations respectively.<sup>34</sup> Inappropriate opioid prescribing increases risk for long-term use or misuse, and is associated with prolonged functional recovery, higher health care utilization and increased costs.<sup>35-37</sup>

Various physical, cognitive and behavioral evidence-based NP treatments exist.<sup>38,39</sup> A common goal of these treatments is to facilitate self-management and reduce reliance on health care interventions including medication management.<sup>40</sup> Despite clear and consistent recommendations, persistent overuse of opioids and underuse of NP treatment characterizes back pain care. For example, a review of commercial claims data from 1.6 million individuals receiving care for back pain found 50% received opioids and only 8%-12% received psychological or physical therapies.<sup>29</sup> Increasing the use of effective NP treatment to promote self-management is an opportunity to prevent opioid initiation or escalation, reduce costs, limit transition from acute to HICP, and improve patient-centered outcomes. *The National Pain Strategy highlights the need for broader availability of NP services that can mitigate the impact of pain on daily activities and promote self-management.*<sup>16</sup>

**A.3 Disparities in Pain Management:** Socioeconomic factors are important determinants of health and lead to disparities across numerous conditions including chronic pain.<sup>41</sup> The National Pain Strategy from the NIH Interagency Pain Research Coordinating Committee<sup>16</sup> calls attention to the disparate impact of chronic pain and HICP based on race, ethnicity and socioeconomic status. In 2016, an estimated 20% of the U.S. population experienced chronic pain and 8% experienced HICP. Higher prevalence of chronic pain and HICP was associated with lower household income, less educational attainment, rural communities and public vs. private

insurance.<sup>42,43</sup> For example, the rate of HICP among individuals living in the lowest income quartile in the U.S. was more than double the population average (17% versus 8%).<sup>43</sup>

Residents in low income and rural communities experience higher rates of chronic pain and HICP, as well as disparities in pain management. Disparities in pain management increase the overall burden of chronic pain on individuals and communities. Individuals living in rural communities, particularly those with lower household income, are at increased odds of being prescribed opioids for pain management,<sup>44-46</sup> and are less likely to receive NP care promoting self-management.<sup>47</sup> For example, a study reporting pain management among individuals with a new consultation for back pain in primary care in one large health system reported those with a lower socioeconomic status were 63% more likely to receive an opioid prescription, while NP options such as physical therapy were more frequently offered to people with higher socioeconomic status.<sup>45</sup> A recent CDC report examining opioid prescribing patterns from 2014-2017 reported that individuals in the most rural counties had an 87% higher chance of receiving an opioid prescription in this time period compared with persons in large metropolitan counties.<sup>48</sup>

Pain management disparities are also evident based on race. Turner and colleagues studied individuals of Hispanic ethnicity living in the Southwestern U.S. and found prescription medication was more common for pain management versus exercise or other NP pain treatments, and this discrepancy increased for those with lower income levels.<sup>49</sup> In addition, a survey of U.S. residents of Hispanic ethnicity found many had misperceptions about chronic pain and its management, with sizable proportions overvaluing the benefits of pain medication while under-estimating the associated risks.<sup>50</sup>

Over-representation of HICP and over-utilization of opioids in rural, diverse and low income populations highlight the urgent need to improve pain management in these communities.<sup>42</sup> Realizing the goal of better pain management will require that substantial barriers be confronted and overcome. 85% of rural communities are currently classified as Health Professional Shortage Areas with particularly acute shortages in NP pain providers including behavioral health specialists and physical therapists.<sup>51</sup> Even if NP pain providers are available in a community, financial access barriers can be profound. Rates of uninsured have been increasing in the U.S. since 2016, mostly impacting those with lower household income with disproportionate representation in rural communities and among those of Hispanic ethnicity.<sup>52</sup>

Financial barriers are not limited to the uninsured. Many insurance policies do not cover effective NP pain treatments, limit the number of sessions and/or impose high patient co-payment or deductible amounts.<sup>53</sup> State-level Medicaid plans providing coverage for low-income adults often fail to cover NP pain treatments.<sup>54</sup> Strategies to reduce disparities in pain management and decrease opioid over-reliance must overcome limited access due to geographic isolation, provider shortages and financial barriers.<sup>55-57</sup> Pain management disparities are an important component of the opioid crisis in the hardest-hit communities. Over-prescribing not only adversely impacts the individual with pain; but also contributes to overall opioid availability in communities disproportionately impacted by addiction.<sup>58</sup> Disparities in management make strategies to improve pain care in vulnerable communities a high priority. ***Any initiative to reduce the burden of HICP and opioid overuse must overcome barriers to NP pain care for residents in rural and low income communities; yet these settings are rarely included in clinical research and implementation efforts.***

**A.4 The Role of FQHCs in Pain Management for Vulnerable Communities:** Federally qualified health centers (FQHCs) are federally-funded public or private non-profit health care organizations providing comprehensive primary care and preventive services in areas with high prevalence of medically underserved individuals. FQHCs are funded by the Health Resources and Services Administration (HRSA), an agency of the Department of Health and Human Services. FQHCs are health care organizations with a unique mission and structure, providing comprehensive outpatient services in underserved urban and rural communities and include community health centers, migrant health centers, homeless health centers, public housing primary care centers, and programs operated by a tribal organization. FQHCs provide care to all persons regardless of ability to pay.<sup>59</sup>

Although the FQHC program began in 1965, rapid expansion is a more recent phenomenon. The number of FQHC organizations nationwide increased 80% between 2007 and 2014,<sup>60</sup> and the number of patients served has grown by 62%.<sup>13</sup> In 2018 there were 1,382 FQHCs in the U.S. providing care to over 28 million

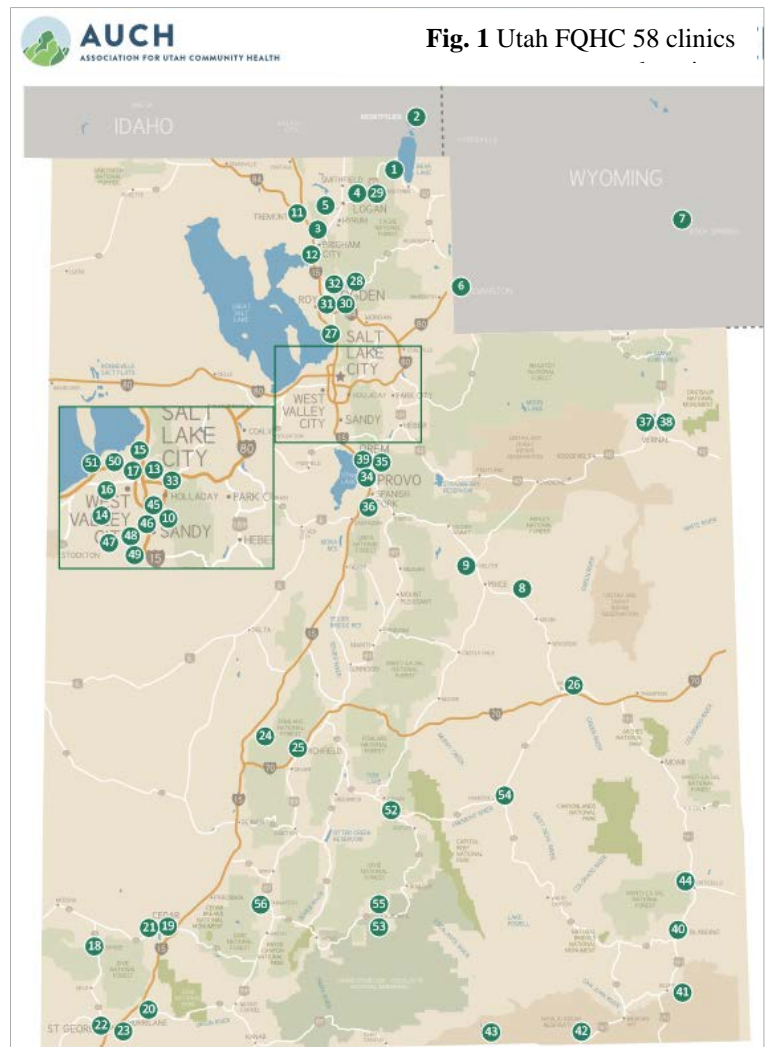
individuals, or about 1 in 12 Americans.<sup>61</sup> About 60% of patients in FQHCs are racial and/or ethnic minorities, and 70% have a household income that is at, or below, the federal poverty level.<sup>62</sup> Almost half (49%) of FQHCs are located in rural or frontier regions of the U.S., and FQHCs provide primary care services to 1 in 5 rural residents nationwide.<sup>61,63</sup>

Considering the patient populations served, it is not surprisingly that chronic pain is highly prevalent in FQHC settings, occurring in 40%-60% of adult patients.<sup>64,65</sup> FQHC primary care providers report low confidence in managing patients with chronic pain, expressing concerns about limited time and limited available resources.<sup>64</sup> Limited time and referral resources for NP pain care contribute to over-reliance on pharmacologic management, including opioids, as the only accessible pain treatment resources. One survey of FQHC patients with chronic pain reported that 57% received medication, while only 17% received education about pain, 14% were referred to physical therapy and 21% to a behavioral health provider.<sup>64</sup>

Research focused on improving primary care pain management and reducing opioid over-prescribing has typically not involved FQHC or similar safety-net settings. Any opioid-related research that has been conducted in FQHCs has concentrated on treatments for substance use disorders.<sup>66,67</sup> While this focus is necessary and understandable, *there is an unmet need to examine the effectiveness and implementation of strategies to prevent inappropriate opioid initiation and escalation in FQHC settings.* This project examines the effectiveness and implementation of scalable interventions conducted in FQHC organizations in Utah focused on increasing use of NP treatments as a strategy to improve patient-centered outcomes and prevent early opioid use and escalation for patients with back pain.

**A.5 FQHCs in Utah and the Association for Utah Community Health (AUCH):** The state of Utah has 13 FQHC organizations who oversee a total of 58 primary care clinics in urban and rural communities throughout the state (Fig. 1). Three out-of-state primary care clinics have special arrangements to receive support from a Utah FQHC organizations based on geographic proximity. Each FQHC organization operates as an independent health care organization with its own executive and board of directors. As with all FQHC organizations, Utah's Health Centers provide primary and preventive health care services regardless of a patient's ability to pay or insurance status. In 2018, Utah's FQHC organizations provided care to over 165,000 persons, 66% of whom were at or below the federal poverty level, and 52% were uninsured. Overall, 47% of Utah FQHC patients are of Hispanic/Latino ethnicity.

The Association for Utah Community Health (AUCH) has represented Utah's FQHC organizations and their patients for the past 20 years. AUCH is designated by the Federal Bureau of Primary Health Care as the state's Primary Care Association (PCA). PCAs are state or regional nonprofit organizations that provide training and technical assistance to safety-net providers. PCAs assist health centers to evaluate and monitor the policy and regulatory environments, and support health centers in adapting to changing demands from an evolving health care environment. As the PCA for Utah's FQHCs, AUCH receives federal program support to develop and enhance services for its member organizations. AUCH provides over



15,000 hours of training and technical assistance, specialized resources and inclusive policy analysis to its 13 member Health Center organizations each year.

**A.6 Strategies to Reduce Disparities in Back Pain Management Using a Stepped Care Approach:** Stepped care is a framework to provide a continuum of evidence-based treatment across stages of pain management, emphasizing an individualized, stepwise approach as patients increase in complexity or fail to respond with less intensive interventions.<sup>68</sup> Stepped care models are attractive because they begin by insuring provision of evidence-based, lower cost, less intensive interventions as the first step for all patients with the target condition. More costly, intensive treatments are used for those who do not respond to these initial efforts. Stepped care has been advocated for conditions such as chronic pain or depression that are highly prevalent and characterized by many patients who are responsive to evidence-based, lower intensity interventions.<sup>69</sup> The stepped care model for pain management is recognized by the National Pain Strategy and endorsed by the American Academy of Pain Medicine, Veterans' Health Administration and U.S. Army Pain Management Task Force<sup>16,70-72</sup> as a framework to improve pain management. In higher-resource health care settings stepped care is often focused on limiting over-utilization and premature use of costly, intensive services such as injection, advanced imaging or surgery.<sup>73</sup> In low resource settings such as FQHCs, the challenge of stepped care is overcoming access barriers to insure consistent provision of first-step, evidence-based care at the primary care level.

For chronic pain conditions, stepped care emphasizes a graduated approach to insure all patients receive effective, nonpharmacologic strategies focused on self-management and activity promotion, with more intensive approaches available for those who do not respond to initial care efforts.<sup>74</sup> Opioid pain management is not a strategy that should be used in the first step of pain management.<sup>9</sup> Insuring broad access to first-line NP care regardless of factors such as geography or socioeconomic status is a substantial challenge for the communities served by FQHCs.<sup>75</sup> A stepped care paradigm for pain management forms the conceptual basis of this project and informs our efforts to develop scalable strategies to overcome access barriers to effective first-step care in rural and low resource communities.

Preliminary work has been done in FQHCs to describe the specific challenges to NP care expressed by FQHC providers and patients.<sup>64,65,76-78</sup> Challenges to providing NP care expressed by FQHC providers including limited access to providers for referral, and concerns about integrating pain management strategies other than prescription medications, such as patient education, into clinical work flows.<sup>76</sup> Primary care providers across practice settings including FQHCs further acknowledge their own limited knowledge for providing pain management to patients with a focus on self-management instead of medication.<sup>64,79</sup> Patients receiving care within FQHC recognize financial and time constraints, concerns about practitioner biases and desire for personalized interactions as concerns related to pain management.<sup>47,77,80</sup> Evidence supports a stepped care framework for pain management.<sup>81</sup> ***Effective strategies to make NP care available as first-step management are a critical, yet under-studied, step towards implementation in low resource settings.***

**A.7 Conceptual Models Informing Nonpharmacologic Treatment for Chronic Back Pain:** The NP treatments tested in this project are informed by two models; a biopsychosocial model of chronic pain<sup>82</sup> and Social Cognitive Theory (SCT) of behavior change.<sup>83</sup> Adoption of a biopsychosocial perspective to understand chronic pain has been an important advance, highlighting the critical role of patients' thoughts, beliefs and environmental circumstances on the pain experience.<sup>84</sup> The biopsychosocial model challenged the traditional, biomedical model of pain as a purely physiologic phenomenon.<sup>82</sup> A biomedical model views all symptoms, including pain, are expressions of a discoverable injury or disease process, and presumes a direct correspondence between the extent of tissue damage and clinical features such as pain intensity or disability.<sup>85</sup> Biomedical perspectives predominate Western medicine, and in the context of chronic back pain have led to overuse of diagnostic testing, invasive procedures and aggressive medication management.<sup>86</sup> The biopsychosocial model recognizes that an individual's pain experience and resultant disability is a multi-dimensional interaction among physiologic, as well as cognitive, emotional, behavioral and social factors, all of which must be considered in effective pain management.<sup>87</sup> The validity of the biopsychosocial model has been consistently upheld as a framework to understand chronic pain and its consequences; clearly demonstrating that patients' attitudes and beliefs about pain and their social circumstances are more predictive of functional



outcomes than any biomedical marker (e.g., imaging finding, etc.) or physiologic measure (e.g., range of motion, strength, etc.).<sup>88,89</sup>

The biopsychosocial model highlights the multi-dimensional nature of chronic pain and the critical role of cognitive, behavioral and environmental factors. SCT specifies how these factors drive human behavior.<sup>90</sup> The SCT applied to chronic pain management (Fig. 2) emphasizes the critical role of self-efficacy, inter-acting with other factors, to facilitate desired behavioral outcomes (increased participation in daily activities, reduced opioid use).<sup>91</sup> Self-efficacy relates to an individual's confidence in his or her skills to manage a behavior and overcome barriers that arise. Pain self-efficacy is supported through positive coping strategies (e.g., physical activity) and by addressing cognitive factors including patients' knowledge about pain and countering negative pain appraisals.<sup>90,92</sup> Positive outcomes of chronic pain management are further influenced by socioeconomic factors including the availability of resources and access to health care, and pain beliefs/expectations which derive from cultural norms, and the pain experiences of the individual and those in their family or community.<sup>93,94</sup>

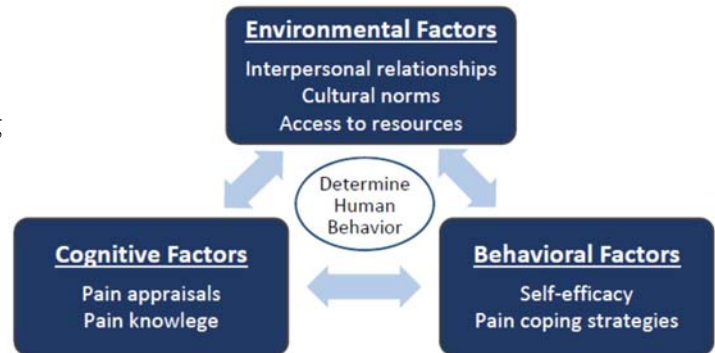


Fig. 2 SCT Model Informing Chronic Pain Interventions

The NP treatments in our project are informed by the biopsychosocial model and SCT; recognizing that the experience of pain is informed by social and economic circumstances, and may elicit powerful psychological responses that modulate pain perceptions including self-efficacy and behavioral response.<sup>95-97</sup> For example, patients making catastrophic appraisals about pain typically have less confidence in their ability to self-manage (i.e., low self-efficacy),<sup>98</sup> promoting fear and heightened attention to perceived pain-related threats; ultimately resulting in reduced physical activity.<sup>99</sup> Activity avoidance may be adaptive for acute pain, but quickly become problematic for those with chronic pain.<sup>100,101</sup> Persistent negative pain appraisals can reduce the ability to regulate pain-related thoughts with higher order coping strategies via descending pathways.<sup>102</sup> Thus, ongoing pain-related catastrophizing can produce a pre-cognitive mental set that primes the person for an exacerbated pain experience<sup>103</sup> which serves to reinforce catastrophic appraisals, low self-efficacy and activity avoidance in a self-perpetuating cycle. This cycle may be further reinforced through maladaptive pain beliefs/expectations held by the individual or those around them, and exacerbated by lack of access to effective NP care. While opioids have limited analgesic effect, opioid use may persist in individuals caught in this cycle as a way to manage adverse pain-related emotions. Thus actual or anticipated pain triggers an automatic reaction (taking opioids), and unconscious habit replaces conscious choice as the primary determinate of opioid use.<sup>104</sup> Residents in low income or rural settings have limited resources to counter this cycle and obtain the desired outcomes of participation in daily activities and pain self-management without opioid reliance.

**A.8 Conceptual Models Informing Implementation of Nonpharmacologic Treatment in FQHC clinics:** The gap between evidence-based interventions and their subsequent use in clinical practice is well-established. To facilitate uptake of evidence-based interventions, experts advise careful consideration of strategies to implement interventions even in research whose primary purpose is examining effectiveness.<sup>105</sup> In this project we will implement NP pain treatment in FQHC clinics using e-referrals generated through clinic EHRs that electronically connect patients with chronic back pain to phone-based pain teleconsults. Implementation will be guided by well-established frameworks and models including; SCT, the Consolidated Framework for Implementation Research (CFIR),<sup>106</sup> Implementation Mapping (IM),<sup>107</sup> and Proctor's taxonomy of Outcomes for Implementation Research.<sup>108</sup> Figure 3 outlines the synergy among these models to form an overall conceptual framework to guide our efforts to implement EHR-based e-referrals for phone-based pain teleconsults.

As noted previously, SCT specifies how cognitive, behavioral and environmental factors drive human behavior.<sup>90</sup> The SCT has informed the content of our NP treatments as well as the behavior change necessary for clinic staff to implement the e-referral process and back pain patients to connect with teleconsult interventions. The CFIR compliments SCT by providing a framework to understand the complex contextual factors in participating clinic settings that influence implementation efforts. CFIR has been used widely to guide

the development of tailored implementation strategies for application in real-world clinical settings,<sup>109</sup> and provides a repository of standardized implementation constructs organized in five domains each with various sub-constructs.<sup>110</sup> We identified constructs most relevant to our implementation efforts from the SCT and our prior work in FQHC clinics (*see preliminary work*). The SCT and CFIR models guide efforts to adapt and finalize our strategies to implement the e-referral process and pain teleconsult interventions using IM principles. Implementation mapping uses aspects of implementation science and intervention mapping to outline step-wise tasks for planning an implementation strategy.<sup>107</sup> The five steps in the application of IM integrated into our project are;

- 1) Conducting a needs assessment for implementation in FQHC clinics and with chronic back pain patients using sociotechnical assessments and focus groups respectively, Sociotechnical assessment collects mixed methods data from observations of clinic workflow, identifying barriers that need to be addressed during clinic team training (*see section D.6*). Focus groups will be facilitated by community health workers in settings served by FQHC clinics (*see section D.7*).
- 2) Identifying determinants of change within clinics and with patients based on findings from step 1,
- 3) Selection of theory-driven implementation methods based on SCT and CFIR models informed by findings from steps 1 and 2;
- 4) Establish protocols to implement e-referral and pain teleconsult interventions; and
- 5) Define implementation outcomes to be collected in the Clinical Trial Phase reflecting key implementation domains grounded in Proctor’s taxonomy.<sup>108</sup>

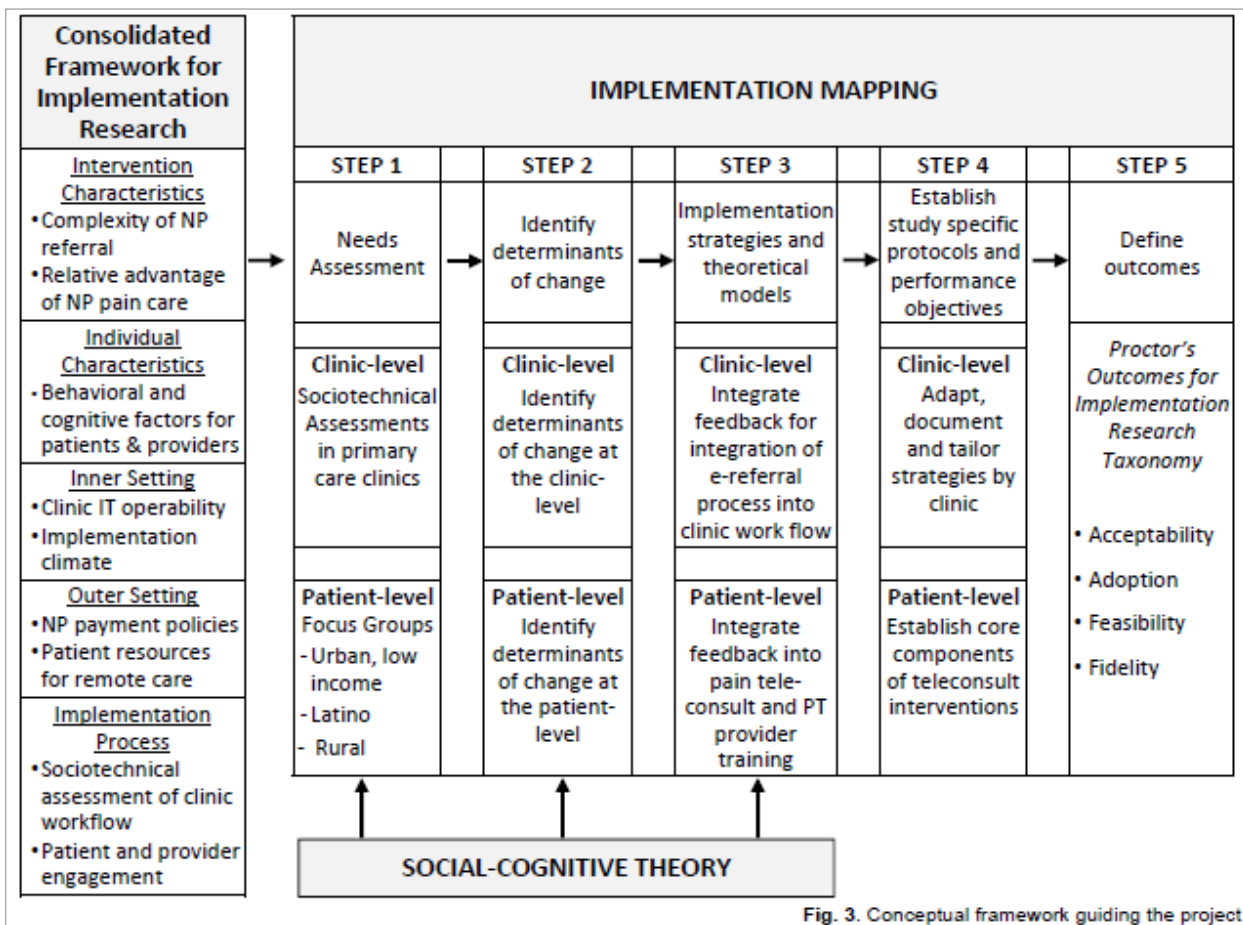


Fig. 3. Conceptual framework guiding the project

**A.9 Evidence for Brief Interventions as NP Treatment for Chronic Back Pain:** Consistent with a biopsychosocial model and SCT, brief cognitive (education and reassurance) and behavioral (physical activity advice) interventions can be efficacious for chronic back pain.<sup>111-114</sup> Brox and colleagues reviewed 12 studies examining brief interventions (4 or fewer contacts) for chronic back pain involving over 3,500 patients collectively.<sup>111</sup> The review found strong evidence of effectiveness on sick leave and short-term disability for

brief interventions compared with usual care.<sup>111</sup> Harris and colleagues studied a brief intervention involving one session provided by a physical therapist that followed a physician visit. The trial randomized patients with chronic back pain who were sick-listed from work to receive the brief intervention alone or accompanied by group physical therapy or cognitive behavioral therapy.<sup>112</sup> All groups demonstrated improvements in disability, work status and coping, with no differences between groups receiving the brief intervention alone versus those receiving the additional intervention.<sup>112</sup>

Evidence supports the use of brief pain interventions as a first-step within a stepped care pain management framework. Effective brief intervention programs for chronic back pain in the studies cited above focused on education about pain to counter negative pain appraisals, advice to be physically active and engage in exercise as positive coping strategies, and reassurance that activity is beneficial and safe to build self-efficacy. These messages and behavioral instruction align well within the conceptual models guiding this project (Fig. 2) as they may benefit patients through disruption of the cycle of negative appraisals of pain and activity avoidance reinforcing disablement and opioid coping strategies. ***Brief pain interventions are evidence-based strategies for chronic pain that may offer a scalable solution to make NP care available in low resource settings.*** Our project examines this hypothesis.

**A.10 Evidence-Based NP Treatment Using Telehealth to Overcome Access Barriers:** Numerous government and health care organizations have used various technologies to remotely providing telehealth interventions for a variety of health conditions.<sup>115</sup> Prior to the COVID-19 pandemic, NP pain care provision using telehealth was limited. Third party payers including Medicare, Medicaid and commercial insurers did not reimburse physical therapy provided via telehealth. In response to COVID-19, most large commercial payers now reimburse telehealth physical therapy visits.<sup>116</sup> The Centers for Medicaid and Medicare Services (CMS) have changed coding rules, making it more likely that they will also provide coverage for physical therapy provided by telehealth.<sup>117</sup> Scalable, effective strategies to provide NP care using remote delivery methods have long been a priority for in low income and rural communities to overcome access barriers, but the COVID-19 crisis has created additional urgency towards developing telehealth solutions. Prior to COVID there was ample evidence highlighting disparities in advanced use of health information technology and uptake of remote, eHealth resources in low income and rural communities.<sup>118,119</sup> Without intentional effort to implement telehealth solutions in these communities, this “digital divide” will be exacerbated as COVID-19 increases focus on telehealth solutions.

Telehealth strategies have employed various technologies such synchronous verbal communication using HIPAA-compliant platforms or telephone-based options, as well as asynchronous non-verbal communication such as text messaging, mobile applications, internet-based programs, e-mails, etc. When developing telehealth strategies for low income communities, it is important not to exacerbate health disparities by requiring technology unavailable in these communities. Recent data indicates that 81% of adults in the U.S. own a smartphone, approximately three-quarters own a desktop or laptop computer, and half own a tablet computer.<sup>120</sup> While laptop and tablet computers are generally prevalent, one in four adults of Hispanic ethnicity,<sup>120</sup> those with incomes below \$30,000,<sup>121</sup> and those living in rural communities<sup>122</sup> are dependent on their smartphone for Internet access. Thus phone-based remote interventions are likely more accessible in these communities than strategies requiring web-based meeting applications (e.g., Skype, Zoom, etc.)

AHRQ has reviewed the evidence for telehealth across health conditions, finding positive outcomes, particularly when telehealth is used for communication and counseling or remote monitoring in chronic conditions.<sup>123</sup> There is some research examining telehealth specifically for chronic musculoskeletal or spinal pain. Results from several studies indicate telephone-based models of care are preferred by patients,<sup>124,125</sup> and phone-based telehealth interventions can reduce pain intensity and disability in patients with osteoarthritis and spinal pain compared to usual care.<sup>126-128</sup> For example, Heapy and colleagues recently reported equivalence in a comparison of phone-based cognitive-behavioral therapy relative to in-person CBT for patients with back pain.<sup>113</sup> Iles and colleagues<sup>129</sup> found a 5-call, phone-based coaching intervention, informed by motivational interviewing, improved self-efficacy, recovery expectations and disability in patients with chronic back pain. Phone-based interventions for chronic pain have been employed successfully to overcome access barriers for Veterans receiving care through the VA Health Care System.<sup>130,131</sup> These findings suggest that phone-based telehealth holds promise for overcoming access barriers, are acceptable to many patients, and can be effective

for improving outcomes. *Our project examines the effectiveness and implementation of phone-based NP pain interventions in FQHC organizations throughout the state of Utah.*

**A.11 Summary of Significance and Scientific Premise:** Our project addresses the ubiquitous problem of back pain, which is responsible for more health care spending, greater diminishment in quality of life and more opioid use than any other health condition. We are conducting our work in FQHC primary care settings that serve the needs of individuals in communities with limited resources due to rurality or low socioeconomic status. Members of these communities experience substantial disparities in chronic pain prevalence and availability of pain management interventions beyond medication. Safety-net settings such as FQHCs are at the front line of the opioid epidemic, but are rarely included in clinical pain research. There is a critical, unmet need to examine strategies to make effective NP pain treatments available and accessible in FQHC settings.

Our study evaluates the effectiveness, and explores implementation, of pragmatic, scalable, point-of-care interventions. Prior studies support the potential of point-of-care health IT strategies to improve health outcomes for a variety of chronic conditions.<sup>132</sup> Our project leverages the EHR at participating health care organizations to connect patients with evidence-based NP pain care. Our pain care strategies are provided using phone-based telehealth approaches to overcome access barriers. As such, our project aligns well with the NIH-wide Research Priorities for Rehabilitation which emphasizes the need for research on telehealth rehabilitation interventions.<sup>133</sup> Our project also embraces recommendations from the NIH Task Force on Research Standards for Chronic Low Back Pain to inform our outcome measures.<sup>134</sup> Our project is highly aligned with the NIH Interagency National Pain Strategy which emphasizes the need to address disparities and promote equitable pain care for vulnerable populations.<sup>16</sup> Finally, our project takes on additional significance in light of the current COVID-19 pandemic. The need for effective telehealth strategies for pain management is urgent. Even when the COVID-19 crisis abates, the need for remote delivery strategies will likely persist as patients may be reluctant to attend in-person health care visits and future waves of COVID infection may require intermittent reinstatement of restrictions.

Our approach to NP care is grounded in a stepped care paradigm which is advocated for pain management by health care organization within the Interagency National Pain Strategy. We will study innovative strategies to overcome access barriers to provide NP pain management as a first-line treatment in a stepped care pain management model for individuals with chronic pain in FQHC settings. Our study design evaluates an adaptive intervention strategy (*see section D.1*), which is aligned with a stepped care model. Specifically, our design allows us to compare the effectiveness of a first-step approach using a brief pain teleconsult combined with phone-based physical therapy, versus an adaptive intervention in which the first-step is a brief pain teleconsult only, with phone-based physical therapy as a second-step intervention for those who are not responders to the brief teleconsult intervention.

The specific NP treatments in this project are based on several key areas of supporting evidence. First, outcomes of telehealth interventions are broadly equivalent to in-person care.<sup>135</sup> Second, telehealth strategies embedded in stepped care models are efficacious for improving pain outcomes in low resource and rural settings.<sup>127,128</sup> Third, phone-based telehealth providing NP care for patients with back pain has preliminary supporting evidence.<sup>126</sup> Finally, evidence-based reviews consistently document the effectiveness of exercise and cognitive interventions provided in-person for patients with chronic back pain.<sup>15,38,39</sup> In particular, interventions that increase patients' pain self-efficacy, or confidence in their ability to self-manage pain, can significantly reduce disablement.<sup>136</sup>

Both the content of our NP care strategies and our strategies to implement them in FQHC settings are grounded in appropriate theoretical frameworks. The content of our NP care strategies are based on biopsychosocial and social cognitive theory frameworks and focus on promoting self-efficacy and reducing problematic pain perceptions through education, reassurance and promotion of physical activity. We will examine the effectiveness of a brief pain teleconsult with or without the addition of a phone-based physical therapy (PT) to further facilitate pain self-management behaviors and promote self-efficacy. We will link patients to these interventions using e-referrals generated through FQHC EHRs. Implementation of the e-referral process and pain teleconsult interventions is guided by the Consolidated Framework for Implementation Research and

Implementation Mapping. *Using telehealth to connect patients to NP pain care resources is a promising strategy to overcome accessibility and affordability barriers in low resource settings such as FQHCs.*<sup>67,137</sup>

**A.12 Alignment of Project with the Purpose of the HEAL PRISM Initiative:** Our project is submitted in response to RFA-AT-20-004 (HEAL Initiative: Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM)). This request encourages phased research projects to conduct “real world” assessments of health care strategies and clinical practices, and procedures in health care systems that may lead to improved pain management along with a reduction in unnecessary opioid prescribing.” The RFA also clarifies that “interventions under study be embedded into health care delivery systems”, and “trials should be conducted across three or more health care systems (HCS) and will become part of and work with the NIH HCS Research Collaboratory.” We recognize that our project engages a group of non-traditional HCS in a more limited geographic distribution than other projects in the PRISM initiative or the HCS Research Collaboratory. We expect our project will be conducted across 8-10 FQHC organizations in the state of Utah. Seven organizations have provided support thus far. Each organization represents a multi-site “system”, as each is an independent entity with its own Director and governing board, and its own IT infrastructure. AUCH represents Utah’s FQHC organizations as the Primary Care Association in the state, and provides training, technical assistance and support to Utah’s autonomous FQHC organizations. Each FQHC organization provides primary and preventive care services in areas where economic, geographic or cultural barriers limit access to affordable health care services, and thus are not integrated systems in the typical sense as they lack inpatient facilities or specialty care services.

Although our trial involves a different type of HCS, we believe inclusion of FQHC organizations within the PRISM initiative and HCS Research Collaboratory will be mutually beneficial. Safety-net settings such as FQHCs are rarely included in clinical and pragmatic research efforts despite the critical needs in these settings. Lack of inclusion in clinical research only exacerbates disparities in care delivery for under-served populations. We are partnering with FQHC organizations in only one state. Although this limits the geographic scope of our project, we believe our results will have broad generalizability and potential scalability. Critical to future scalability is our use of a point-of-care e-referral process outlined in the Approach section that follows a standards-based approach required for EHR certification. In this study, we will implement EHR reminders with e-referrals in two of the most commonly used EHRs in FQHCs nationwide. This approach also allows our e-referral strategy to be integrated with any standards-compliant EHR. Additionally, we are using the e-referral process to connect patients with phone-based NP pain care. Leveraging remote services allows our interventions to be easily replicated with flexibility for adaptations based on local circumstances.

**NOTE regarding the impact of COVID-19:** As noted in our preliminary work (*section C.3*), the research team has a productive, ongoing collaborative relationship with AUCH and member FQHC organizations. The onset of COVID-19 placed extreme demands on the FQHC organizations as it has for all health care systems. Despite the intense efforts to serve their communities in the midst of this pandemic, the AUCH executive director (*see letter of support from Alan Pruhs*) and FQHC organizations remain very supportive of the project. We solicited interest from AUCH and member FQHC organizations before COVID disruptions began, and received very positive responses. COVID preparations rapidly dominated everyone’s time and attention. We have stayed in contact with AUCH and member FQHCs throughout this crisis, and interest remains very strong in this project (*see letters of support from member FQHC organization CEOs*). Based on our history of collaboration with the FQHC member organizations and with enthusiastic support from AUCH, we are confident that FQHC organizations will continue their support for this project and efforts to provide nonpharmacologic care for patients with chronic back pain in their primary care clinics as the intensity of the immediate response to COVID eases. In fact, the opportunity to implement a telehealth infrastructure for pain management is likely to be a high priority as health care organizations seek ways to meet the needs of patients with chronic pain who may have delayed care and to do so in a manner suitable to a post-COVID reality.

As discussed in detail below, members of our research team have an ongoing PCORI-funded project working with AUCH and 11 FQHC member organizations. This study is focused on implementing EHR-based e-referrals to tobacco quitlines in FQHC primary care clinics. Our group has been discussing a project building on this e-referral infrastructure to address pain management for about a year. Alternatives to opioids and other

medication-focused management strategies for pain is a high priority for these clinics. Disruptions in care for patients with chronic pain due to COVID-19 is likely have adverse impacts on patients with chronic pain, possibly increasing opioid reliance. Availability of non-pharmacologic alternatives as these patients begin to return to clinic visits will be critical. We will use the Planning year to engage with all 13 FQHC organizations and finalize those who will participate in this project.

## **B. INNOVATION**

There is a critical need for comparative effectiveness and implementation research focused on vulnerable populations in low income and rural communities. There have been no prior clinical trials examining the effectiveness or implementation of strategies to provide NP pain care in FQHC clinical settings. Omitting low-resource settings such as FQHCs from effectiveness and implementation research studies exacerbates health disparities. We have conceptualized our project within a stepped care management framework as advocated by the NIH Interagency Pain Strategy. Our project will be the first clinical trial of early stage pain care embedded within a stepped care paradigm conducted in FQHC organizations. Prior studies in these settings have focused on management of substance use disorders resulting in part from inadequate early stage pain management, but have not directly addressed early management.

Our project addresses early stage pain management using strategies targeting access barriers in rural and low income communities. We are combining efficacious NP treatment strategies with telehealth delivery modes that have been tested in patients with back pain and proven effective with other chronic health conditions in low resources settings. In addition, as a result of the COVID-19 pandemic, an increasing number of commercial insurers are reimbursing physical therapy care provided via telehealth, which enhances scalability as the need for remote options for health care delivery becomes more evident.<sup>138</sup>

Our study uses an innovative adaptive research design. An adaptive design uses results from participants in the study to modify the course of treatment received by individual participants based on pre-specified rules.<sup>139</sup> Specifically, our trial tests a strategy of providing brief pain teleconsultation accompanied by phone-based PT to all patients with chronic back pain versus a strategy of first providing the brief pain teleconsultation and waiting to implement phone-based PT until the individual patient's responsiveness to care is evaluated after 12 weeks (*see section D.1, Fig. 4*). This design aligns with a stepped care model and allows us to examine the impact of timing and sequencing of NP strategies on patient outcomes and opioid use; questions rarely addressable in traditional clinical trial designs.

Our proposal is innovative in its explicit attention to implementation alongside a rigorous effectiveness trial. In the Planning Phase we will finalize our procedures based on a conceptual model informed by implementation frameworks (CFIR, Implementation Mapping). The use of IM is innovative and practical systematic process for applying implementation frameworks and behavioral theory to identify effective implementation strategies. An important aspect of our IM strategy are sociotechnical assessments used to gain in-depth understanding of clinic work flows and culture, gather key stakeholder input and finalize procedures to implement EHR-based e-referrals with this critical input. Technical solutions such as our point-of-care e-referral process too often fail when the complex social-technical interactions are not taken into account. In the Clinical Trial Phase we will gather secondary outcomes within an implementation science framework outlined by Proctor whose work defines a core set of implementation outcomes.<sup>108</sup> Our project is thus considered a hybrid type I design, focused on effectiveness outcomes while secondarily collecting implementation information.<sup>105</sup> Using a hybrid study design permits us to investigate how, and to what extent, the e-referral process was adopted in clinical practice and by patients with chronic back pain. Gathering implementation information alongside effectiveness outcomes is increasingly emphasized as an innovation that can accelerate the notoriously slow process from discovery to adoption as routine practice.<sup>105</sup>

## **C. PRELIMINARY WORK**

**C.1 Preliminary Work Training Physical Therapists to Provide Nonpharmacologic Treatments from a Bio-Psychosocial Perspective:** The Principal Investigator (Dr. Fritz) has led or collaborated on several clinical trials demonstrating the benefits of NP care involving physical therapists providing education and exercise instruction

for patients with back pain.<sup>140-143</sup> A key aspect of this work has been training PTs to provide treatment within a biopsychosocial framework and explicitly designed to counter patients' maladaptive beliefs about pain and resultant avoidance behaviors. In a recently completed pilot study funded by a NIH/NICHHD ReACT Center award (NCT03256617) we studied the sustained impact on PTs of 8 hours of training to provide reassurance and education to patients from a biopsychosocial perspective. We found changes in PT beliefs towards a bio-psychosocial focus persisted even 6 months after training, suggesting the effectiveness of the training methods.

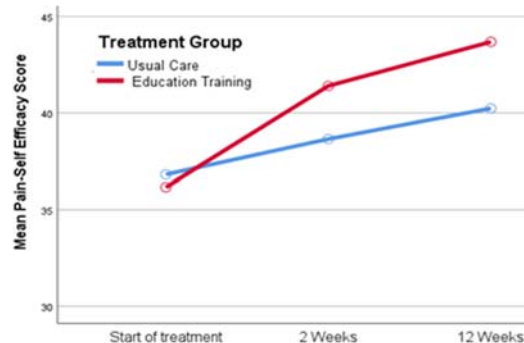


Fig. 4. Change in pain self-efficacy in patients treated by clinicians trained to provide education or not (usual care). Between-group differences = 3.1 and 3.7 points at 2 and 12

We also recently completed a completed a cluster-randomized trial examining outcomes of patients (n=317) with chronic spinal pain treated by physical therapists randomly assigned to receive training in patient education strategies to enhance the understanding of chronic pain from a biopsychosocial perspective, improve expectations for functional improvement, and build confidence in the ability to self-manage pain.<sup>144</sup> Patients treated by trained therapists had significantly greater improvement in pain self-efficacy assessed 2 and 12 weeks after beginning treatment (Fig. 4). Self-efficacy is a mediator of long-term LBP outcomes and thus a key treatment target.<sup>145</sup> ***Our experience training physical therapists to provide biopsychosocial-based NP care will inform training procedures for therapists in this project.***

**C.2 Preliminary Work With Phone-Based Physical Therapy:** The phone-based PT protocol for this project will be based on a recently completed clinical trial by Dr. Adam Goode, a consultant on this project. Dr. Goode completed this work at the Durham VA health system, a setting facing similar access challenges based on serving the needs of patients residing in low resource, rural communities. The trial was a 3-arm pilot randomized trial of a physical activity program designed to improve physical function among n=60 older adults with chronic low back pain, 68% of whom used opioids for pain management.<sup>131</sup> The three arms were a waitlist control group (WL), a physical activity (PA) only group, and a physical activity plus cognitive based therapy for pain group (PA+CB). The PA arm consisted of an initial evaluation by a physical therapist and a home-based exercise program tailored in conjunction with the participant consisting of strengthening, stretching and physical activity. Telephone calls were conducted weekly over the following 12 weeks and consisted of goal setting, exercise progression, pain control with exercise and motivational feedback. The PA+CB group received this exercise instruction and also received education by phone on overcoming pain-related barriers to exercise and managing pain related to participation in activity as well as instruction in CBT skills including activity pacing, breathing relaxation, distraction, progressive muscle relaxation, and cognitive restructuring.

Outcomes from the study most relevant to the current project include measures of physical function, pain interference and intervention adherence. Adherence to the phone-based interventions was good. Of the 40 participants assigned to a phone-based intervention (PA or PA+CB), 88% completed treatment, participating in a mean 10.0 and 8.8 phone sessions (out of 12 possible) for the PA and PA+CB groups respectively. No adverse events were found during the 12-week program. Function was evaluated at

Table 1: Effects of a 12-week, home-based, telephone supported physical activity program for older adults with chronic low back pain.		
Measure	Baseline to 12-Week Differences (95% CI)	Effect Size (Cohen's d)
Roland Morris Disability Questionnaire (range: 0-24, lower scores=less disability)		
WL	0.89 (-1.11, 2.88)	--
PA	-4.10 (-6.85, -1.34)	-0.78
PA + CB	-1.99 (-4.85, 0.86)	-0.38
Health Assessment Questionnaire (range 0-100, lower scores=better function)		
WL	3.21 (-1.61, 8.02)	--
PA	-2.90 (-7.22, 1.43)	-0.64
PA + CB	-0.89 (-6.36, 4.57)	-0.43
PROMIS Pain Interference (raw score range 4-20, lower scores=less activity interference)		
WL	--	
PA	-4.86 (-8.93, -0.79)	-0.42
PA + CB	-5.01 (-9.38, -0.63)	-0.44
WL=waitlist control group, PA=physical activity only group, PA + CB= cognitive-based therapy and physical activity group		

baseline and after 12 weeks with the Health Assessment Questionnaire, a generic measure of the ability to perform daily activities,<sup>146</sup> and the Roland Morris Disability Questionnaire,<sup>147</sup> a measure of back pain-specific function. Effect sizes for the phone-based intervention groups were larger than for the WL control group (Table 1) and generally represented meaningful improvement. Pain interference, or the extent to which pain interferes with daily physical and psychological activities, was assessed with the PROMIS pain interference 4-item short form.<sup>148</sup> The results were similar to those for function across intervention groups (Table 1). Overall, there was no clear benefit to adding the CB component to PA; in fact effect sizes were generally larger for the PA only treatment group.

This pilot trial found that telephone-based physical activity programs were safe, feasible, acceptable and may improve function for patients with chronic back pain. ***Our experience providing phone-based physical activity program provided by physical therapists forms the basis for the protocols we will develop for the populations in the current project.***

**C.3 Preliminary Work with EHR-Based Referral Strategies in Utah FQHCs:** Our team has an ongoing partnership with Utah FQHCs and their state-level Primary Care Association organization (AUCH). A critical service provided by AUCH is technical support to member FQHC organizations. The University of Utah Department of Biomedical Informatics and the Center for Health Outcomes and Population Equity (HOPE), led by members of the research team, has partnered with AUCH to help FQHC organizations optimize the clinical utility of their EHRs while producing generalizable knowledge and scalable solutions through clinical research. Several research projects are underway or under development leveraging this collaboration, including design and implementation of EHR tools for electronic referrals to a tobacco cessation quitline, reminders for HPV immunization, reminders for colorectal cancer screening, and shared-decision making for lung cancer screening.

Most relevant to this application, members of our research team, Drs. Del Fiol, Wetter, Gibson and Greene, are investigators on the ongoing QuitSMART Utah study, with Dr. Wetter serving as the Principal Investigator.<sup>149</sup> QuitSMART Utah is sequential multiple assignment randomized trial (SMART) conducted in 33 primary clinics within 11 of Utah's 13 FQHC organizations. The study tests adaptive tobacco cessation intervention strategies, and uses EHR-based strategies to connect patients within FQHC clinics with a tobacco quitline that offers treatment through a variety of modes, such as phone, text messaging, and Web chat. The study outlined in this proposal builds on our existing partnership with AUCH and its member FQHC organization. Through QuitSMART Utah, we have worked with all of the FQHC clinics that we expect to participate in the project. Thus, we are intimately familiar with the technical capabilities, EHR systems, data reporting, implementation strategies, clinic staff and leadership, etc.; and have built a high degree of mutual trust and respect. We have gained crucial experience developing EHR-based strategies to test adaptive interventions for tobacco cessation. In this application we address another critical health care need of patients in these safety-net settings – access to evidence-based, non-opioid pain management interventions.

As part of the QuitSMART Utah trial funded by PCORI, the informatics team led by Dr. Del Fiol has implemented EHR-based electronic referrals (i.e., e-referrals) to the Utah tobacco quitline (operated by National Jewish Health, one of the largest quitline providers in the US) at the same low income safety net clinics that are part of the current proposal.<sup>149</sup> A key challenge in establishing the e-referral infrastructure was the wide variety of EHR vendors used by Utah's FQHC organizations. E-referrals have been implemented within all three EHR products that are used at Utah FQHCs: e-Clinical Works, Athena Health, and CompuGroup. The technical approach for e-referrals is compliant with national health IT standards that are required for EHR certification which enhances the ability to adapt to varying EHR technical capabilities and likelihood that FQHC organizations may change EHR vendors during the timeframe of the study.

Another aspect of studies of EHR-based referral interventions conducted by the University of Utah Department of Biomedical Informatics is the use of systematic, sociotechnical assessment to facilitate implementation for clinical research and routine practice. The sociotechnical assessment team, led by Dr. Gibson, has expertise in implementation science, cognitive and social psychology, and human factors. Assessments consist of a multi-step process that builds on psychological and informatics design theory to simultaneously meet the goals of: 1) needs assessment and determination of functional requirements; 2) iterative processes of contextually based



design; 3) implementation planning and development of contextually relevant strategies; and 4) evaluation of user satisfaction, quality of user decision-making, workflow efficiency, and institutional population-based levels. Dr. Gibson has been part of sociotechnical teams on several projects using the sociotechnical methods outlined in the current proposal,<sup>150-152</sup> and he leads this effort for the QuitSMART Utah study team. As a part of QuitSMART Utah, Dr. Gibson and his team have conducted onsite workflow observations and interviews at one to two clinics within the FQHC organizations in this proposal. The experience and knowledge gained in this process will be critical in the current proposal.

In summary, the project in this proposal builds on a productive, established, collaborative relationship between FQHC health clinics, their state-wide primary care association (AUCH), and academic researchers with complementary skills in informatics, implementation science and adaptive clinical trial design. This collaborative team has successfully implemented complex, multi-site clinical trials addressing critical health needs of the patients served in low resource settings using scalable strategies. This team is dedicated to approach the problem of opioid over-prescribing with the same collaborative spirit and commitment to optimizing patient health and well-being that is the foundation of all their efforts to-date.

## D. APPROACH

**D1. Summary of Design and Study Organization:** Our goal is to improve patient-centered outcomes and reduce risk of opioid initiation and/or escalation for persons with back pain in FQHC organizations in Utah. We chose to focus on back pain because it is the most prevalent chronic pain condition, a common contributor to HICP, and an important factor in the opioid crisis.<sup>2</sup> Our strategy is to improve stepped care through early access to NP care. Numerous NP treatments are effective for back pain including education, cognitive and behavioral interventions.<sup>38,153</sup> Based on our conceptual frameworks and SCT model (Figs. 2 and 3), we will use a brief pain teleconsult intervention designed to mitigate maladaptive beliefs about pain, build self-efficacy and promote positive pain coping strategies through physical activity. We will compare the effectiveness of this brief teleconsult with or without phone-based, physical therapy (phone-based PT) provided over 12 weeks. Consistent with a stepped care model, our adaptive design also permits comparison of the effectiveness of providing phone-based PT as a first-line therapy versus provision as a second-line treatment for patients who do not adequately respond to a less-intensive initial step (brief pain teleconsult). We are conducting this study in multiple FQHC organizations in Utah. We will evaluate the ability to overcome access barriers in these settings by collecting implementation outcomes in the domains of acceptability, adoption, feasibility and fidelity.

Our clinical trial tests adaptive treatment regimens (Fig. 4). All participants receive the brief pain teleconsult as a first-line strategy. We will randomly assign participants with 1:1 distribution to also receive phone-based PT in Phase I treatment or not, permitting a comparative effectiveness evaluation of phone-based PT as a first-line treatment in a Stepped Care model (Aim 1). All participants are re-assessed 12 weeks after randomization. An aspect of the 12-week assessment for all participants is determination of response to initial treatment. Responder status (yes/no) is based on the single-item Patient-Acceptable Symptom State (PASS).<sup>154</sup> For participants not receiving phone-based PT initially, we will base further treatment on responder status at 12 weeks. Non-responders will receive phone-based PT as second-line care. Responders receive no further treatment. Participants randomized to phone-based PT in Phase I receive no further treatment, but will continue with instructions provided during phone-based PT treatment. The primary study outcome is the NIH-PROMIS pain interference (PROMIS-PI) measure, with opioid use as a principal secondary outcome assessed at baseline and after 12, 26 and 52 weeks. This study design permits comparison of the effectiveness of a stepped care approach

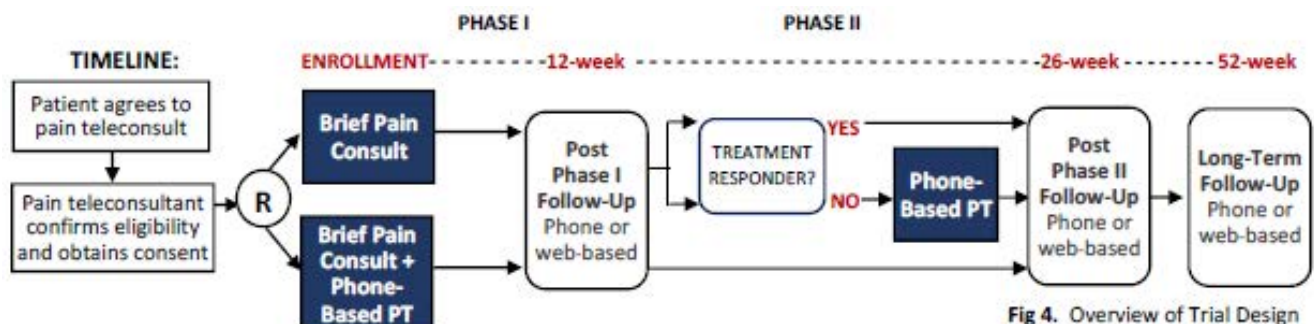


Fig 4. Overview of Trial Design

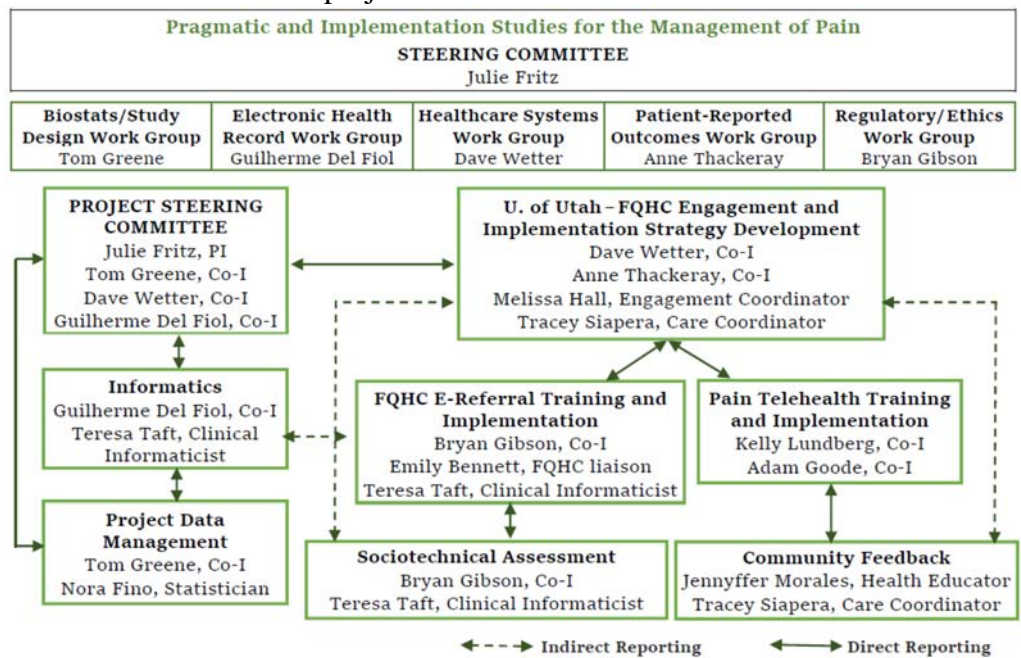
(i.e., phone-based PT initiated only after a less intense option vs. a strategy of phone-based PT as first-line care (Aim 2). We will examine outcomes in pre-specified sub-groups based on baseline variables (gender, HICP, opioid use) to better understand which NP strategies work best for which type of patient (Aim 3).

Our study is a hybrid type I design;<sup>105</sup> prioritizing patient-centered effectiveness outcomes while also gathering data on implementation to inform future studies. Our implementation outcomes collection strategy derives from our overall conceptual framework for implementation (Fig. 3). The specific implementation outcomes to be collected in the clinical trial are based on the framework outlined by Proctor and colleagues<sup>108</sup> that categorizes implementation outcomes that are distinct from service and clinical effectiveness outcomes. We believe our NP care strategies are scalable to other settings and adaptable to other pain conditions; thus we are collecting data to inform and accelerate future implementation efforts. Our project has two Phases; a 1-year Planning Phase and a 4-year Clinical Trial Phase. The Planning Phase will establish procedures, finalize the study design, intervention protocols and strategies to implement the EHR-based e-referral and pain teleconsult processes. Our implementation strategies will be finalized using implementation mapping procedures informed by sociotechnical analysis in participating clinic sites and community-based focus groups in preparation for the Clinical Trial Phase (Fig. 3). The Clinical Trial Phase will be used to conduct the trial examining the effectiveness and implementation outcomes of our NP pain interventions.

**D2. Expertise of Study Team:** Team members from the University of Utah provide complimentary skills necessary to conduct the proposed research and fully engage with work groups across the PRISM Collaboratory. We have developed a study structure (Fig. 5) to organize communication and oversee key components in the Planning and Clinical Trial Phases. We have identified team members with appropriate expertise for participation on PRISM Work Groups. We will finalize Work Group members in the Planning year.

**Dr. Julie Fritz**, is Distinguished Professor in the Department of Physical Therapy and has extensive leadership experience in multi-site clinical trials conducted in healthcare systems focused on patients with chronic back pain<sup>141,142,155</sup> funded through DoD, PCORI, AHRQ and NIH. Several of her previous clinical trials examine adaptive treatment regimens. She is nationally-recognized as a leader in research related to nonpharmacologic pain management strategies and will serve as PI for this project.

**Dr. Tom Greene** directs the Study Design and Biostatistics Center (SDBC) at the Center for Clinical & Translational Science (CCTS). Dr. Greene will serve as a member of the Study Design & Biostatistics Work Group and will oversee data analysis and management for this project. Dr. Greene has 25 years of experience directing statistical design and analysis of multi-site clinical trials<sup>156,157</sup> and has collaborated with Dr. Fritz in the design and analysis of several prior trials.



**Figure 5.** Study structure for internal organization and PRISM participation

**Dr. David Wetter** is the Senior Director for Community Engagement and Cancer Health Equity Research at HCI, Director of the Center for HOPE (Health Outcomes and Population Equity), and Associate Director for Community Engaged Practice at the University of Utah CCTS. Dr. Wetter is the PI of the QuitSMART Utah project and has built a strong collaborative relationship with Utah’s FQHC organizations. He will facilitate

communication between the academic and clinical settings in this proposal and will assist with provider and staff training. Dr. Wetter will represent the project on the Healthcare Systems Work Group.

Dr. Guilherme Del Fiol is part of the ReimagineEHR team in the Department of Biomedical Informatics and a national leader in the development and dissemination of health IT standards for EHR with an exceptional record of dissemination of standards-compliant EHR-based interventions at a variety of settings, including FQHCs in North Carolina and Utah.<sup>158-161</sup> Among other initiatives, the ReimagineEHR team has successfully implemented e-referrals from FQHCs to tobacco quitline through the QuitSMART Utah project. He will lead the EHR-based e-referral strategies and will participate on the EHR Work Group.

Dr. Bryan Gibson is part of the Sociotechnical and Human Factors team in the Department of Biomedical Informatics with expertise in investigation of how humans interact with technology. Dr. Gibson and the Sociotechnical Team have participated in several projects using similar sociotechnical methods as outlined in this proposal,<sup>150-152</sup> including the QuitSMART Utah study which gives him an existing relationship with the FQHC clinics involved in the current study. He will oversee the sociotechnical evaluations and assist with ongoing clinic engagement during the trial. He will represent the project on the Ethics and Regulatory Work Group.

Dr. Anne Thackeray is a Physical Therapist and Research Assistant Professor in the Department of Physical Therapy at the University of Utah with adjunct appointment in the Health System Innovation and Research Division of the Department of Population Health Science. Dr. Thackeray has training in implementation science and implementation mapping. She will oversee the implementation mapping and assist with the development and training of the phone-based PT protocol. She will also serve as the project's representative on the Patient-Reported Outcomes Work Group.

Dr. Kelly Lundberg is Associate Professor (Clinical) in the Department of Psychiatry. She has extensive experience as a clinical psychologist. She is experienced training others from varied professional backgrounds in behavior change interventions using cognitive and behavioral strategies such as motivational interviewing and social cognitive problem-solving. She will oversee training for the and PT providers.

Dr. Adam Goode is Associate Professor in the Departments of Orthopedic Surgery and Population Health Sciences at Duke University; and a core faculty affiliate of the Duke Clinical Research Institute. He is PI on two NIH/NIAMS R01 proposals that focus on understanding the mechanisms of acute and chronic LBP. He has also assisted with the development and successful completion of randomized clinical trials involving telephone-based or internet-assisted exercise programs for patients with chronic musculoskeletal pain conditions.<sup>131,162-164</sup> He will assist with developing and training for the phone-based PT and brief pain consult protocols.

**D3. Approach for UG3 Planning Phase:** In the Planning Phase we will make all necessary preparations for the clinical trial. The Planning Phase aims are listed below and reflect the UG3 milestones outlined in the Human Subjects and Clinical Trials Information section. Subsequent sections outline the approach to accomplish each of these aims:

1. Finalize procedures for interventions; develop protocols, procedure manuals and fidelity assessments.
2. Conduct sociotechnical assessment at FQHC sites to assess current EHR reminder and e-referral workflow
3. Implement EHR reminders for e-referrals to teleconsult services in the FQHCs.
4. Finalize study outcomes, data collection methods and data analysis plan.
5. Train pain teleconsultants and FQHC staff in procedures for the Clinical Trial.

**D4. Summary of Conceptual Framework Guiding the Planning Year:** Activities in the Planning Phase are informed through the integration of implementation frameworks outlined in Fig. 3; 1) Social Cognitive Theory (SCT) to identify determinants of behavior change,<sup>83</sup> 2) the Consolidated Framework for Implementation Research (CFIR) to identify factors across multiple levels that impact implementation,<sup>106</sup> 3) Implementation Mapping through sociotechnical assessment, and 4) Proctor's taxonomy of Outcomes for Implementation Research to define implementation outcomes for the clinical trial.<sup>108</sup> Collectively these models guide activities in the Planning Phase, resulting in finalized strategies to implement the clinic e-referral process and phone-

based teleconsult interventions and methods to evaluate implementation outcomes during the clinical trial consistent with a Hybrid I study design.

**D.5 Procedures for to Finalize Intervention Protocols and Implementation Strategies:** Our phone-based brief pain teleconsult and PT interventions are grounded in biopsychosocial and SCT models (Fig. 2), and focus on building self-efficacy, modifying maladaptive beliefs about pain, promoting positive pain coping strategies, particularly physical activity and stress reduction techniques. Study interventions are designed to overcome barriers to NP care that exacerbate disparities in low resource settings. In Utah FQHC clinics, key obstacles include geographic distance to providers, economic resources and diversity of language and culture. We have three strategies in the Planning year that will help us overcome these barriers.

- 1) We will leverage telehealth technology (e-referral via EHR and phone-based care) common in low income and rural communities. In 2019 over 90% of U.S. households with annual incomes < \$30,000 or located in rural communities owned a cell phone.<sup>120</sup> Phone-based interventions are scalable strategies to provide NP pain care as they are low cost; occur outside the primary clinic work-flow; and can potentially reach a high proportion of patients seeking care in FQHC and other low resource settings. Telehealth strategies for pain care take on an even more critical role due to disruptions related to COVID-19.
- 2) We will conduct sociotechnical assessments in participating FQHC clinics during the Planning year to facilitate implementation of EHR-based e-referral process into the clinic work flow. As outlined in section *D.6*, sociotechnical assessment is a structured process of examining the interplay of new IT-based work processes, existing clinical work flows as well as the social and cultural environment within the clinic setting
- 3) We will gain input from patient communities by conducting focus groups with residents from rural, low income and Hispanic communities. The mobile health program sponsored by the University of Utah Health system have established connections and regular interactions with community members who are also served by several FQHC organizations in Utah. The mobile health program employs community health workers, who are bilingual and well-integrated in the communities they serve, which are majority Hispanic and low income. As outlined in section *D.7*, during the Planning year of the project, we will work with these community health workers to conduct focus groups and seek input from community members regarding our planned telehealth interventions. (see the letter of support from Dr. Robin Marcus, Chief Wellness Officer, University of Utah).

Lessons learned from these strategies will inform our specific implementation strategies for both the EHR-based e-referral process and phone-based pain interventions using implementation mapping principles. Specifically, we are applying two of the five implementation mapping steps in our Planning Year.<sup>107</sup> First, the tasks listed above will provide an assessment of the determinants of use for our interventions including contextual and environmental factors. Second, the implementation methods, messages and materials will be finalized to address the key determinants that are identified. This information will help clarify our implementation strategies and may also prompt modification in the implementation outcomes to be assessed in the Clinical Trial Phase.

Outlined below are the intervention strategies including the conceptual basis and starting point for implementation. We will finalize our protocols with input from the information gathered in the Planning Phase and in consultation with the PRISM program. We will develop our protocols with attention to pragmatism and their ability to be scaled if effective. An important consideration for implementation of evidence-based interventions is an understanding of their core components that need to be delivered with high fidelity, versus those treatment components that can be adapted.<sup>165</sup> We will develop a checklist of core components for each intervention as an aspect of our implementation assessment (Aim 4). The checklist will be completed by project therapists to permit an assessment of fidelity as implementation outcome.

**D.5.1 – Brief Pain Teleconsult:** We will finalize the brief pain teleconsult intervention protocol and implementation methods in the Planning Phase. We will model our protocol off of brief interventions in the literature, particularly the recent trial by Harris and colleagues,<sup>112</sup> as well as our experience with a brief (single session) education intervention we used in a previous trial for patients with back pain.<sup>142</sup> Consistent with the literature, our brief pain teleconsult will focus on pain education from a biopsychosocial approach designed to

address negative pain appraisals, advice to be active and engage in exercise and physical activity, and reassurance that activity is beneficial and safe.

We plan to provide two phone-based pain teleconsult sessions addressing the topics outlined in Table 2. The pain teleconsult sessions will be delivered by physical therapists trained during the Planning year and will include materials about self-management and physical activity provided by mail, e-mail, phone app or text links based on patient preferences. A scripted outline will be developed to guide each call for consistency. Timing of the teleconsult sessions during the day will be flexible to accommodate participants. Sessions will use aspects of motivational interviewing (MI) and basic cognitive behavioral techniques to modify maladaptive thoughts and beliefs about back pain and encourage physical activity.

Two teleconsult sessions will be provided approximately 1 week apart following randomization. Session 1 will provide biopsychosocial education designed to address particularly problematic cognitive pain perceptions identified in the literature including 1) pain intensity is directly related to structural damage to the spine; 2) fear movement and activity will exacerbate pain and damage; and 3) lack of recognition or acceptance of the role of mood, stress, etc. on the pain experience.<sup>88,166,167</sup> During session 1 the teleconsultant will also help patients identify physical activity goals and strategies informed by motivational interviewing (MI) techniques. Session 2 will review physical activity goals and progress towards goals, review educational content from session 1, address questions or concerns, and assist patients in problem-solving identified barriers.

Session	Topics
1	Explain chronic pain from biopsychosocial perspective, explore patient's pain attitudes and beliefs, reassure that activity is safe and beneficial, introduce physical activity and goal setting
2	Review physical activity goals, review education, solicit questions from session 1.

**Table 2.** Topics for teleconsult sessions

Based on our study design (Fig. 4), all participants in the trial will receive the brief pain teleconsult. We anticipate that session 1 will be provided to all participants at the time of enrollment, after consent is provided, but prior to randomization to receive phone-based PT or not. After providing session 1, randomization will determine if the participant will also receive phone-based PT during treatment Phase I. For participants randomized to only brief pain teleconsult in Phase I, session 2 of the brief pain teleconsult will be scheduled for the next week after which participants will be instructed to continue with physical activity goals until the 12 week re-assessment. For participants randomized to receive phone-based PT during treatment Phase I, session 2 of the brief pain teleconsult will be scheduled for the next week after which participants will continue with weekly phone-based PT sessions until the 12-week re-assessment.

***D.5.2 – Phone-Based PT:*** We will finalize the phone-based PT intervention protocol and implementation methods in the Planning Phase. Patients assigned to phone-based PT will receive weekly calls over 10 weeks in either treatment Phase I or II depending on randomization assignment. Phone-based PT will be provided by a physical therapist trained in the Planning year. We will model our phone-based PT protocol off of preliminary work from Dr. Goode. Key components will include reinforcement of biopsychosocial education messages outlined for the brief teleconsult intervention and evidence-based exercise recommendations for back pain<sup>168,169</sup> and physical activity for adults.<sup>170</sup>

The phone-based PT intervention will occur over 10 weekly sessions that include a home-based exercise program, including stretching, strengthening and a general physical activity program (e.g., walking or other regular activity personalized to the individual participant) supplemented with review of biopsychosocial educational messages and pain coping strategies (Table 3). At the first phone-based PT session, the therapist will provide basic information on appropriate exercise techniques and an individualized physical activity program, guided by the physical activity goals set during the brief pain teleconsult. Exercise programs will be based on a core set of strengthening and stretching exercises (in addition to regular aerobic activity), which cover major muscle groups and functional tasks. The physical therapist will provide personalized recommendations from within this set, including specification of specific exercises to perform (e.g., starting with a small number of exercises and focusing on easier options for those with more limited function) and the duration/ number of repetitions for each exercise.

After the first session, weekly calls will be scheduled over the next 9 weeks (10 total sessions). Each call will last approximately 15-20 minutes. All calls will use a semi-structured approach, where the overall content is standardized across participants, but the physical therapist has flexibility to address participant-specific concerns. We will provide participants with resources to facilitate exercise and physical activity. We will make written or video exercise instruction available for viewing or download using a smartphone or other web-based interface. Sessions will use aspects of motivational interviewing (MI). Each follow-up session will include a review of physical activity goals and exercise progression guided by motivational interviewing techniques with provision of positive feedback and reinforcement.

Session	Topics
1	Review physical activity goals from brief teleconsult and discuss any barriers to progress. Identify personalized, home-based exercise program
2	Review biopsychosocial education messages and physical activity goals and exercise program.
3	Introduce pain coping strategies with mindful breathing and progressive muscle relaxation techniques. Review physical activity goals and exercise program.
4, 6, 8	Review of biopsychosocial messages along with physical activity goals and exercise program.
5, 7, 9	Review of pain coping strategies along with physical activity goals and exercise program.
10	Review physical activity goals and coping strategies, transition to self-management plan

**Table 3.** Topics for phone-based PT sessions

Along with physical activity and specific exercise instruction and review, follow-up sessions will reinforce the biopsychosocial education messages introduced in the brief pain teleconsult. Specifically, beginning with the second phone-based PT session and continuing every other session thereafter, phone-based physical therapists will review and expand on the messages designed to overcome maladaptive cognitive and behavioral responses to pain. Examples of specific messages to be used in follow-up sessions are outlined (Table 4). When provided, these messages will be accompanied by solicitation of participant questions or concerns and use of active listening techniques such as repeating patients’ questions or statements, asking for clarifications, etc.

Follow-up phone-based PT sessions will also introduce pain coping strategies beginning on the third session and continuing every other session thereafter. Specific skills on mindful breathing, body scan and progressive muscle relaxation will be provided. These brief mindfulness-based techniques can be helpful strategies to develop conscious, non-judgmental awareness of negative pain appraisals, promote relaxation and provide adaptive coping strategies.<sup>171,172</sup>

Education Element	Specific Message Examples
Biopsychosocial Chronic Pain Perspective	<i>“Pain is not a sign of damage to your spine; hurt does not equal harm”</i> <i>“Pain relies on context. Factors such as mood, anxiety and stress are contributors to persistent pain.”</i>
Importance of Physical Activity and Exercise	<i>“Research has found that being active and exercising is the best approach to recover from an episode of back pain and limit the risk for recurrence.”</i> <i>“Movement and activity can improve your physical health and improve mood, reduce stress and anxiety”</i>
General Expectations for Treatment	<i>“In my experience most people with back pain that I have worked with make important improvements in their pain level and function.”;</i>
General Expectation for Pain Self-Efficacy	<i>“Opioid pain medication is not helpful for most chronic pain conditions, diagnostic tests and imaging is also typically not useful.”</i> <i>“Research shows that the majority of people with back pain can get back to regular activity and will not need surgery”</i>

**Table 4.** Examples of scripted education messages and written material support

A particular challenge for physical activity and exercise programs is adherence. We will explore several strategies to foster adherence that have been beneficial in past studies.<sup>131</sup> We will seek community member feedback on these strategies as part of the development of our implementation plan as described below (section D.7). We plan to have phone-based physical therapists help participants develop goals and action plans that are reasonable to achieve. Specifically, therapists will ask participants to rate their self-efficacy for reaching their goals with a standard question (“How confident are you that you can reach these goals, on a scale of 0-10, with 0 being not at all confident and 10 being very confident?”). If participants rate their self-efficacy lower than 7, the therapist will recommend they revise their plans so they are more confident they will be able to achieve them. This strategy been successful in our prior and ongoing studies,<sup>173,174</sup> helping participants achieve their goals and develop confidence. Lastly, during each telephone call therapists will ask about barriers participants

encountered since the last phone call. This will be in the form of an open-ended question “What barriers did you face to completing your physical activity and exercise plans since we spoke last?” Therapist will then guide participants in a process of problem-solving any barriers noted, and using MI-informed strategies will help the participant incorporate problem-solving strategies into action plans for the next week.

**D6. Sociotechnical Assessments at Clinic Sites:** Implementation of new information technology (IT) can create unanticipated consequences from the interplay of new IT and existing clinic workflows, social interactions, culture and environment.<sup>175</sup> Exploring the complex interactions between social and technical aspects of clinic work processes is an important step to anticipate potential impacts of new IT and inform the design and implementation in a manner facilitating uptake.<sup>176</sup> Sociotechnical analysis is the process of deconstructing the interplay between social (e.g., communication, culture, etc.) and technical (e.g., existing IT use, etc.) contexts of work to inform implementation of new IT.<sup>177</sup> We will conduct structured sociotechnical assessments in FQHC clinic sites in the Planning Phase to inform implementation of EHR-based e-referral for pain teleconsult.

Assessments will use a task-based approach to analyze current clinic workflow around assessing pain, advising patients on pain care and interacting with IT to understand the unique contextual factors that may affect implementing e-referrals for pain teleconsult. We will use a 3-level approach, specifically identifying tasks, responsible agents, and decisions at the individual, event and clinic level.<sup>178</sup> Tasks have attributes including goals, feedback, tools and artefacts to procedurally support the task. Responsible agents are persons with responsibility to move a task forward and have attributes including roles, skills and information needs. A decision point indicates change in a task. A change in the responsible agents constitute a communication event.

Assessments involve qualitative evaluations by the research team including in-clinic observations and short cognitive work analysis interviews<sup>179</sup> with providers and staff at each clinic. We will conduct an assessment in at least one clinic in each participating Utah FQHC organization during the Planning year. Clinics will be selected based on familiarity with e-referral process from other projects with priority given to clinics that have not previously undergone sociotechnical assessment to implement this process.

Clinical providers and staff who are interviewed as part of an assessment are asked to recall a recent back pain patient and provide a summary, timeline and description of the encounter. Interviews are coded through consensus by members of the research team using the attributes listed above. Information gathered from each FQHC by observation and interviews is incorporated into thematic analyses summarizing sociotechnical issues and recommendations for implementation of e-referrals for NP teleconsult. Thematic analyzes and recommendations will be discussed with the investigator team and health system stakeholders including FQHC Directors and staff to finalize design of EHR reminders to optimize integration into clinic workflow. Integration may vary across FQHCs (e.g., when in a visit the reminder is visible to staff). Site-specific adaptations are documented and summarized to inform implementation efforts across clinics as part of implementation mapping.

**D.6.1 – Clinic Sites:** We are partnering with the Association for Utah Community Health (AUCH), the federally designated Primary Care Association representing Utah’s FQHC organizations. The 13 Utah FQHCs operate a total of 58 primary care sites providing high-quality, culturally-competent services regardless of ability to pay. In 2018, Utah’s FQHCs provided care to over 165,000 unique persons; 66% of whom were at or below the federal poverty level, 62% were racial/ethnic minorities and 52% were uninsured. Utah FQHCs serve urban and rural communities. Of Utah’s 29 counties, 24 are designated rural or frontier, and most of these counties are served by FQHC clinics. Eleven of 13 FQHCs have implemented the EHR-based e-referral process for tobacco cessation. We will finalize the number of FQHC organizations for this project during the Planning Phase.

**D.7 Community Member Feedback:** Implementation of our pain teleconsult interventions will be informed by feedback from members of communities served by Utah FQHCs during the Planning year. We will use multiple methods to identify community members due to the diversity of communities served by Utah FQHCs. First, we will work with the University of Utah Wellness and Integrative Health mobile health program community health workers to identify and conduct feedback sessions with members of Hispanic and low income communities served by the program. The mobile health program uses wellness buses to travel to underserved communities and provide chronic disease screening and counseling services. Since its inception in 2017, 67% of community members served by the mobile health program have been uninsured, 67% identify as Hispanic and

57% communicate primarily in Spanish. Community health workers employed by the University of Utah are bilingual and have strong ties in the communities they serve. We will gather two groups of 5-6 community members who have interacted with health care services provided by the Utah mobile health program or in FQHC clinics. One group will be conducted in Spanish, and will review Spanish language intervention procedures and materials. Ms. Jennyffer Morales, Health Educator at the Center for Health Outcomes and Population Equity (HOPE) will facilitate the groups based on her experience with similar tasks at Utah FQHCs in support of the QuitSMART Utah program implementing tobacco cessation strategies.

We will use a different strategy to gain feedback from residents in the rural communities served by Utah's FQHC clinics. We will work with Tracey Siapera, who is a Care Coordinator with AUCH to identify members of rural communities to participate in another feedback group of 5-6 individuals to review implementation procedures for intervention procedures and materials. Feedback groups may be conducted in person or remotely based on the preferences and convenience of community members. Feedback received from all of these groups will be documented and summarized to inform implementation mapping of our pain teleconsult interventions.

**D.8 Design and Implementation of FQHC EHR Reminders and e-Referrals:** Pain teleconsult providers will be based at the University of Utah and will receive e-referrals via Utah's Epic EHR. The University's Department of Biomedical Informatics will design and implement FQHC EHR reminders with pain teleconsult e-referrals between FQHC clinics and the University Epic EHR. We will pursue a standards-based, scalable solution built over widely available capabilities across EHRs. EHR reminders are automated, patient-specific decision support that can increase uptake of recommended care.<sup>180</sup> When clinic staff opens a patient chart, reminders generate automatically if the patient meets certain clinical criteria and present at a specific EHR user interface location. Reminders also provide ways to perform actions, such as launching an e-referral. Both reminders and standards-based e-referrals between EHR systems are required for EHR certification. The most widely adopted standard for e-referrals is the DIRECT protocol, which consists of peer-to-peer, secure e-mail messaging with an attached summary of the patient's record in a format compliant with the Health Level Seven (HL7) Continuity of Care Document (CCD). Implementation of DIRECT involves configuring the sender and recipient EHRs to trust each other's accounts, which will be completed in the Planning Phase.

Two EHR vendors (eClinicalWorks and AthenaHealth) serve 11 of 13 Utah FQHCs and are widely used in FQHCs nationwide. The University of Utah, where pain teleconsult services will be hosted, uses Epic, the lead EHR vendor in academic medical centers. As described in our preliminary work (*see section C.3*), the University's Department of Biomedical Informatics team has enabled tobacco quitline reminders and e-referrals as a part of the PCORI-funded QuitSMART Utah trial. We plan to leverage a similar solution in this project. DIRECT connections between eClinicalWorks, AthenaHealth and Epic have been setup in other states. The University of Utah uses DIRECT for e-referrals to other health care networks in Utah and neighboring states as well as to the Utah quitline. We will follow a similar approach to implement pain teleconsult e-referrals from FQHCs in this project.

**D.9 Study Outcome Measures and Data Collection:** We will finalize the primary and secondary study outcomes in collaboration with the HEAL PRISM program in the Planning year. We will work with the PRISM program to insure that any common data elements of the HEAL initiative are incorporated.

We have developed our expected outcomes and schedule for administration (Table 5) balancing the collection of a broad array of patient-centered measures with a pragmatic study that endeavors to minimize participant burden. We will work with PRISM to harmonize outcomes with other program projects as appropriate. We plan to use pain interference as the primary study outcome because it reflects the degree to which pain interferes with daily activities, which is a hallmark of HICP. Patients with chronic pain often prioritize the functional impact of pain, and this outcome cannot be inferred from pain intensity as correlations are modest.<sup>181</sup> Pain interference is a recommended outcome for chronic pain trials by IMMPACT<sup>182</sup> and specifically for back pain clinical trials by the NIH Task Force on Research Standards for Chronic Low Back Pain.<sup>134</sup> The NIH-funded Patient Reported Outcomes Measurement Information System (PROMIS) developed measures to quantify pain interference with physical, emotional and social activities using robust psychometric methods. We will use a PROMIS pain interference 8-item short form with established reliability, validity and responsiveness equivalent to legacy pain



interference measures (e.g., Brief Pain Inventory, PEG-3 etc.).<sup>183,184</sup> PROMIS measures assess constructs such as pain interference without reference to specific disorders, facilitating comparisons across studies involving different pain conditions or treatments.<sup>185</sup> Spanish-language translations of PROMIS measures including pain interference are available and validated.<sup>186</sup>

For secondary outcomes (Table 5) we plan to include 6 additional domains relevant to patients with chronic pain that can be efficiently assessed with the PROMIS-29 measure (physical function, fatigue, depression, anxiety, ability to participate in social roles and activities, and sleep disturbance). The PROMIS-29 can also be used to calculate a physical and mental health summary score.<sup>187</sup> Because of its role in our conceptual model, we will use the 10-item Pain Self-Efficacy Questionnaire (PSEQ).<sup>188</sup> The PSEQ quantifies an individual's confidence in performing activities despite pain. We will use the Graded Chronic Pain Scale – Revised (GCPS-R) to identify the presence of HICP.<sup>189</sup> The GCPS-R uses 6 items to categorize chronic pain as mild, bothersome, or high impact. High impact chronic pain includes those individuals who report that pain limits life activities or work on most days or every day in the past 3 months. The GCPS-R has been validated as measure to identify persons with HICP. Persons with HICP identified using the GCPS-R are more likely to be receiving long-term opioid therapy.<sup>189</sup>

Effectiveness Outcomes		Baseline	12 weeks	26 weeks	52 weeks
Domain	Measure				
Pain interference	PROMIS 8-item short form*	X	X	X	X
Additional mental and physical health domains	PROMIS-29 v.2**	X	X	X	X
Pain Self-Efficacy	Pain Self-Efficacy Questionnaire	X	X	X	X
High Impact Chronic Pain	Graded Chronic Pain Scale – Revised	X	X	X	X
Treatment Responder Status	Single-item PASS		X	X	X
Opioid Use	Categorization based on EHR data as short-term, episodic or long-term	X^			X
Opioid misuse, abuse, and related events	SR-MAD		X	X	X
Implementation Outcomes (assessed at conclusion of recruitment)					
Acceptability	PATIENT LEVEL - Percentage of individuals with chronic pain asked about a pain teleconsult during a clinic visit who accept the consult.				
Adoption	PROVIDER LEVEL - Percentage of patients asked about a pain teleconsult (i.e., provider asks patient and does not opt out) during a clinic visit out of all back pain patients.				
Feasibility	PATIENT LEVEL – Percentage of brief pain teleconsult and phone-based physical therapy sessions completed out of number specified in intervention protocols,				
Fidelity	PROVIDER LEVEL – Percentage of core treatment components provided at of brief pain teleconsult and phone-based physical therapy sessions out of the total number of sessions provided for each treatment group (brief teleconsult with or without phone-based PT.				

**Table 5.** Outcome variables to evaluate effectiveness and implementation of pain teleconsult interventions. (PROMIS = patient-reported outcome measurement information system, PASS = patient-acceptable symptom state, SR-MAD = self-reported misuse, abuse and diversion; \* indicates primary study outcome, \*\* indicates that redundant pain interference items will be removed, ^ indicates opioid use categorization at baseline will examine use in prior year)

An important secondary outcome will be opioid use. We intend to categorize opioid use based on EHR prescription data in the year before enrollment using previously-defined categories<sup>190</sup> as *none*, *short-term* (total prescribing  $\leq 90$  days), *episodic* (total prescribing 90-120 days with  $<10$  prescriptions) or *long-term* (total prescribing 90-120 days with  $\geq 10$  prescriptions or total prescribing  $>120$  days). We will similarly categorize opioid use in the year post-enrollment. We will assess opioid use events including misuse, abuse and related events (MAREs) with definitions specifically developed for clinical trials.<sup>191</sup> We plan to evaluate MAREs using the 15-item Self-reported Misuse, Abuse and Diversion of Prescription Opioids (SR-MAD) tool with preliminary validation evidence.<sup>192</sup> We will consider other self-report tools for inappropriate opioid use such as the Current Opioid Misuse Measure<sup>193</sup> because psycho-metric properties of these measures are being examined and additional validation or new tools may emerge.<sup>194</sup> Self-reported and EHR-based methods for collecting opioid use outcomes have shortcomings, are susceptible to considerable bias and cannot detect illicit use. While our use of the EHR to categorize opioid use as an outcome will reflect impact of study interventions on the behaviors or FQHC prescribers, it may not accurately capture the impact on participants' opioid use from all

potential sources. We will work with the PRISM team and seek additional input from providers and patients during the Planning year in an effort to capture opioid use outcomes in a manner reflecting the impact of treatments on both the health care systems and individual participants.

Consistent with a hybrid I design, we will collect implementation outcomes grounded in Proctor's taxonomy and designated as relevant to early stage implementation efforts.<sup>108</sup> We will evaluate implementation domains of *Acceptability* of pain teleconsult e-referral as a point-of-care strategy to connect patients to NP care by examining the percentage of patients accepting the consult when offered in the clinic setting. *Adoption* of teleconsult e-referral by FQHC staff will be evaluated as the percentage of patients offered the consult relative to the total number of patients with back pain based on EHR data from participating FQHC clinics. *Feasibility* will be evaluated as the number of treatment sessions attended relative to the intended number specified by study protocols. We will evaluate *Fidelity* for each using the core component checklists developed for each study intervention (Brief Pain Teleconsult with or without Phone-Based PT). Core component checklists will be reported by study intervention providers in the project's RedCap data collection platform.

**D.10 Training Study Providers and FQHC Staff:** Training for FQHC clinic providers and staff including medical assistants, physicians, nurse practitioners and physician assistants; and for providers of pain teleconsult interventions, will be provided in the Planning year. Training procedures are outlined below and will be adapted based on feedback from the sociotechnical assessments and implementation mapping procedures.

**D.10.1 – FQHC Staff Training:** Training provided to FQHC clinic providers and staff will be led by research team members from the Center for Health Outcomes & Equity (HOPE) (Drs. Wetter and Hall) in collaboration with Emily Bennett, Behavioral Health Integration Coordinator for AUCH, and research team members from the University of Utah Department of Biomedical Informatics team (Drs. Del Fiol, Taft and Gibson). A core mission of AUCH is to provide regular training to staff and providers working in Utah's FQHCs. The Center for HOPE and the University's informatics team have established relationships with FQHC clinic personnel through ongoing work implementing e-referral procedures for other remote health care services (*see preliminary work section C.3*).

Research team members in the University's Department of Biomedical Informatics will implement pain teleconsult EHR referral infrastructure in FQHC clinics following a standards-based approach. This approach allows pain teleconsult infrastructure to be integrated not only with EHRs in the study FQHC clinics, but with any standards-compliant EHR nationwide. We plan to use an opt-out (instead of opt-in) policy, which our team has implemented within the participating FQHC clinics for an ongoing project connecting patients who smoke to quitline resources.<sup>149</sup> In the opt-out approach, the EHR requires clinical staff to advise individuals with chronic back pain that phone-based resources are a preferable and more effective than medication management, and offer a connection to the Pain Teleconsult prior to moving forward or to opt-out. Opting out is simple and generally requires only one keystroke. *See section D.11 for further details.*

Implementation of e-referral for pain teleconsult in participating FQHC sites will begin after the sociotechnical assessments. We will then provide a brief (30-minute) in-person training for each site's practice team (e.g., nurses, medical assistants, physicians). Training will be led by the sociotechnical assessment team headed by Dr. Gibson, and will include evidence-based information on guidelines for chronic pain management from the CDC and other organizations. We will provide practical training on how to present the pain teleconsult to patients as an alternative to medication management and how to use the EHR e-referral linking the patient with teleconsult service. We anticipate in-person training sessions at each FQHC site in the Planning Phase with intermittent information and reminders during the Clinical Trial Phase to maintain engagement and account for turnover. The teleconsult resource will be implemented across participating clinics. By not randomizing the teleconsult we will be able to examine implementation outcomes for the e-referral process at all sites and create a sustainable infrastructure that can endure beyond the project support period.

**D.10.2 – Pain Teleconsult Provider Training:** Pain teleconsult providers will be licensed physical therapists who will provide both the brief pain teleconsult and phone-based PT. Three physical therapists will be hired for the project during the Planning year, at least two will be bilingual. Training for these providers will be led by research team members with expertise in MI and behavior change counseling for providers working with

underserved populations including both English- and Spanish-speaking community members (Drs. Wetter and Lundberg) and members of the study team with expertise in physical therapy (Drs. Goode and Fritz). Training will be informed by input from the sociotechnical assessments and community member focus groups. Training for all providers will include procedures related to human subjects' research including Good Clinical Practice certification, HIPAA privacy protections and procedures for adverse event reporting.

Training will involve about 40 hours of instruction including strategies to provide key messages about back pain from a biopsychosocial perspective and countering maladaptive beliefs. Training will be provided in basic MI techniques of reflective listening, summarizing, communicating empathy and optimism, avoiding argumentation, developing discrepancy and soliciting change language. Self-efficacy enhancement instruction will include cognitive behavioral strategies around goal-setting, identifying barriers and problem-solving solutions and positive reinforcement for attainment.

Additional training topics are specific to the protocol for phone-base PT and include:

- 1) pain education using evidence-based approaches grounded in a biopsychosocial model. Evidence-based pain education emphasizing the importance of physical activity, the unhelpfulness of pain medication and imaging procedures towards improving function, and reinforcing the ability to self-manage pain.<sup>195</sup> Education with this approach helps patients re-conceptualize pain in a biopsychosocial context, increase function, decrease catastrophizing, negative pain appraisals.<sup>196-198</sup> We have trained PTs in this approach in past studies.<sup>144</sup>
- 2) pain coping strategies including relaxation and distraction techniques (e.g., progressive muscle relaxation, mindful breathing) as well as activity pacing strategies.<sup>199</sup> Physical therapists can provide these interventions effectively when appropriately trained.<sup>200</sup>
- 3) efficacious exercises<sup>201</sup> for back pain and a general physical activity program provided using an MI-informed goal-setting approach with positive reinforcement to enhance self-efficacy. Physical therapists will provide instruction in back exercises to improve strength, flexibility, balance and endurance. Systematic reviews indicate that while exercise is beneficial for chronic back pain, there is little difference among different forms of exercise,<sup>39</sup> thus the emphasis will be on helping participants select exercise and general physical activity modalities that fit into their lifestyle and preferences.

**D.11 *Data Management and Quality Control:*** Data management will be overseen by the University of Utah Study Design and Biostatistics Center (SDBC) at the University's Center for Clinical and Translational Science in collaboration with the PRISM Study Design and Biostatistics Work Group and Steering committees. The study database will be maintained on secure servers supplied by University of Utah Health Sciences. The SDBC, directed by co-investigator Dr. Greene, will develop a plan to monitor progress, including rates of recruitment, retention and adherence to study protocols. The SDBC and Dr. Greene have extensive experience providing data management and quality control procedures for multi-site clinical trials.

Sources of study data are anticipated to include patient self-report and EHR data. We plan to collect self-report data via RedCap, an NIH-supported, web-based service<sup>202</sup> for direct data input from any browser. A mobile app allows input from smart phones and provides a tool for offline input in places with poor internet connection.<sup>203</sup> We anticipate that data will be collected by blinded research assistants by phone and input directly into RedCap. Additional data will be extracted administratively from site EHRs. This will include patient-level opioid prescribing data and age, sex, race/ethnicity, co-morbidity and insurance information.

Quality control procedures will also be finalized in the Planning Phase. Study data entry in RedCap will be subject to verification checks. Missing data or data anomalies will be communicated to the investigators for clarification/resolution. Compliance checks will also be conducted periodically on EHR data. The PI and Dr. Greene will be responsible for ensuring all project data are securely stored, that storage is in compliance with University and federal regulations and that no unauthorized persons have access to identifiable data. All HIPAA regulations and guidelines will be followed. All study staff must complete approved human subjects and HIPAA training programs. The PIs will hold regular meetings with study team and review documentation, the number and type of enrolled patients, reasons for exclusions and data completeness. Should excessive risk to

participants be determined or data security or loss of patient confidentiality be identified the study will be stopped and patients notified in a manner appropriate to the risk.

**D12. Ethical and Regulatory Oversight:** Study personnel will be trained in Ethical Conduct for Human Subjects Research, Good Research Practices, HIPAA protections and computer security using resources from NIH and the University of Utah IRB. Research personnel will be uniformly trained in data collection and management and will participate in regular conference calls to evaluate recruitment and enrollment activities and address issues surrounding IRB regulatory compliance and data monitoring. Clinical trial data will be stored at the SDBC. SDBC datasets will not include patient identifying information. Patients will instead be assigned a unique study identification number. At the end of the trial, de-identified study datasets will be archived. We will work with the PRISM program to comply with data sharing procedures.

**D.13 Timeline and Key Milestones for UG3 Phase:** Milestones for the 1-year UG3 Planning Phase represent quantifiable and scientifically justified achievements required to proceed to the UH3 Phase of the Project. Key Milestones for the UG3 Phase will establish the necessary study infrastructure and regulatory compliance required before transition to the Clinical Trial UH3 Phase. The UG3 milestones are summarized below followed by a timeline for the UG3 period. *Further detail on Study Milestones is provided in the Milestone Plan Attachment included with the Other Clinical Trial-related Attachments.*

UG3 Phase Milestone	Definition of Completion
Finalize statistical analysis plan and sample size in collaboration with the HEAL PRISM Study Design and Biostatistics Work Group	Statistical analysis plan completed addressing all Aims of the UH3 clinical trial. Sample size for the UH3 clinical trial finalized.
IRB submission	Submission to the University of Utah IRB which will serve as the sIRB for the UH3 clinical trial
Finalize FQHC clinical sites for the UH3 clinical trial	Finalize list of participating FQHC clinical sites. Consideration of adding sites if feasibility for obtaining necessary sample size is deemed inadequate.
Finalize clinical trial protocol including training procedures, data management, team roles and responsibilities	Protocol document completed in consultation with the HEAL PRISM and CCC. The protocol will follow International Conference on Harmonization E6 Good Clinical Practice Consolidated Guidance, and formatted based on standard interventional protocol template to be provided by the HEAL PRISM program.
Register UH3 trial with clinicaltrials.gov	NCT number assigned to the trial from clinicaltrials.gov
Complete sociotechnical assessments	Sociotechnical assessments completed at representative FQHC clinics
Complete training of FQHC staff and Intervention Providers	Research team members complete training of FQHC clinic staff and providers of clinical trial interventions based on the training plan established
Finalize Manual of Procedures in collaboration with HEAL PRISM Coordinating Center	Using an NIH template, finalize the MOP document including detailed descriptions of all study procedures and finalization of all documents necessary to implement the UH3 clinical trial.
Finalize transition request for UH3 phase	Submission of complete transition request to the NIH

The chart below provides a timeline by month for the 1-year UG3 Planning Phase.

MONTH	1	2	3	4	5	6	7	8	9	10	11	12
Finalize roles of research team members in conjunction with PRISM program work groups												
Finalize outcome measures and data elements for UH3 clinical trial												
Finalize statistical analysis plan and sample size												
Conduct sociotechnical assessments at FQHC clinic sites												
Conduct community member focus groups												
Finalize FQHC clinic sites for UH3 clinical trial												
Submit protocol to University of Utah IRB												
Finalize clinical trial protocol												

MONTH	1	2	3	4	5	6	7	8	9	10	11	12
Train phone-base PT and teleconsult providers												
Train FQHC clinic staff at participating sites												
Register UH3 trial with clinicaltrials.gov												
Finalize Manual of Procedures in collaboration with Heal PRISM Coordinating Center												
Finalize transition request for UH3 phase												

**D.14 Approach for the UH3 Clinical Trial Phase:** Goals for the UH3 Phase are to conduct the comparative effectiveness clinical trial outlined in Fig. 4. Our design aligns with a stepped care model of pain management and is intended to test scalable interventions. The Clinical Trial Phase has 4 Specific Aims listed below which reflect the UH3 milestones outlined in the Human Subjects and Clinical Trials Information section. Subsequent sections outline the approach to accomplish these Aims:

1. Compare effectiveness of a brief pain teleconsult with or without phone-based PT for patients with back pain in FQHCs with pain interference as primary outcome and opioid use as a secondary outcome.
2. Compare effectiveness of phone-based PT as a first-line strategy vs. a stepped care strategy of phone-based PT as second-line care for patients do not respond to a brief pain teleconsult.
3. Examine effectiveness results of Aims 1 & 2 in pre-defined patient phenotypes based on gender, presence of HICP and current opioid use.
4. Explore implementation outcomes for teleconsult services (acceptability, adoption, feasibility and fidelity).

**D.15 Patient Recruitment and Eligibility:** Recruitment for the UH3 clinical trial will use an EHR-based approach to recruitment that we have used to streamline and facilitate enrollment in evidence-based tobacco treatment in primary care settings including FQHC clinics.<sup>204,205</sup> The strategy consists of reminders for medical assistants to ask patients about their interest in support for their chronic back pain (“Ask”); recommend the pain teleconsult intervention as an opportunity for support (“Advise”); and submit an e-referral for teleconsult for interested individuals (“Connect”).<sup>206</sup> This EHR-based e-referral strategy has proven effective at connecting more patients in safety-net clinics to treatment than traditional passive referrals that rely on patients to initiate care.<sup>205,207</sup> We will leverage our established e-referral infrastructure to connect patients with pain teleconsult. The process is outlined in Fig. 5. Patients are identified at the point-of-care in the FQHC clinic. Clinic staff is alerted via the EHR of the opportunity for referral. Staff asks if the patient has back pain that interferes with activity, advises that pain teleconsult may be beneficial and connects the patient to the service via e-referral. Staff may opt-out of the process at any step with one keystroke. E-referrals are sent to teleconsultants at the University of Utah via the University’s Epic EHR. Consultants proactively reach out to the patient by phone, also offering the opportunity to participate in the study. Patients who wish to participate will begin the informed consent process. Those who do not wish to participate receive the teleconsult but are not randomized or asked to provide project data. In either circumstance feedback is sent to the FQHC clinic.

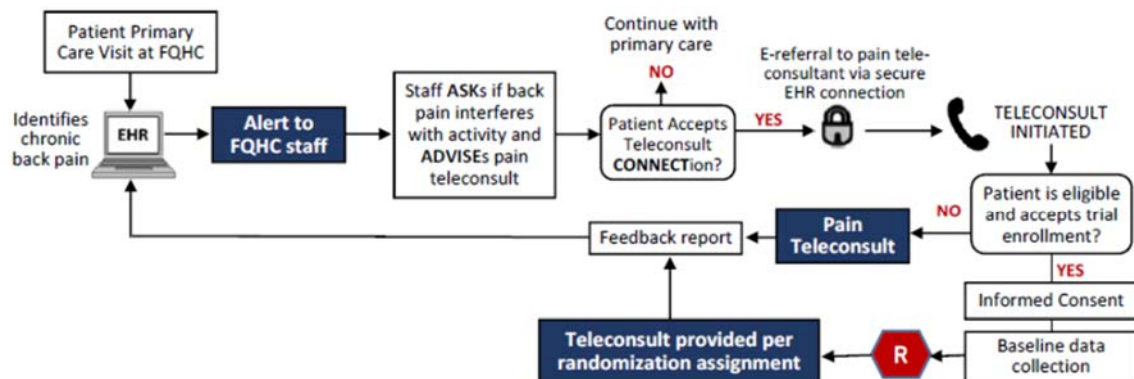


Fig. 5 E-referral and recruitment procedures

Eligibility criteria will be finalized in the Planning Phase. Consistent with a pragmatic design we will use broad eligibility criteria. We anticipate recruiting adults age 18-70, English or Spanish-speaking, seeking care in a participating FQHC for back pain. Back pain, defined as pain in the lumbar, thoracic or sacral region may be identified by chief complaint or from diagnostic codes in the EHR associated with visits in the past 6 months. Patient identification procedures will be finalized and tested in the Planning Phase. We will use the NIH Back Pain Task Force definition of chronic back pain.<sup>134</sup> We will exclude anyone with active substance use disorder, diagnoses associated with non-musculoskeletal causes for back pain (e.g., spinal tumor, kidney stone, etc.) or significant mobility limitation restricting physical activity (e.g., wheelchair dependent, etc.). We will exclude women who know they are pregnant at the time of enrollment because pregnancy-related back pain may require different care. Current opioid use will be recorded but is not required or disallowed for eligibility.

**D.16 Randomization and Data Collection:** Once a connection is made between a referred patient and a pain teleconsult an explanation of the study will be provided. If the patient is eligible and interested he or she will be consented using oral consent procedures. After informed consent, baseline data will be collected using the options outlined below. Baseline data will include patient-reported outcomes and demographic information not obtainable from the EHR. After collecting baseline data all participants will receive the first session of the Brief Pain Teleconsult; after which randomization to a Phase I intervention arm will occur to avoid bias in presenting the first session of the Brief Teleconsult intervention.

After completing the initial brief pain teleconsult session all participants will be scheduled for a follow-up phone session after about 1 week. For those randomized to only the Brief Pain Teleconsult the second session will include only the activities outlined in Table 2. After completion of the second session individuals in the Brief Teleconsult only treatment arm will be instructed to continue with their physical activity program and consult primary care provider as needed. For participants randomized to Phone-Based PT, the second session will include the activities listed in Table 2 for the second teleconsult session and then will transition to the 10-week phone-based PT protocol (Table 3). All participants will be followed-up at 12 weeks post-enrollment, coinciding with the conclusion of the first treatment phase (Fig.4).

Randomization will be administered in RedCap randomization module using schedules developed in the Planning year. We will stratify randomization based on pre-specified sub-grouping variables opioid use, gender, presence of HICP; and we may consider other stratification variables such as site during the Planning year.

**D.16.1 – Data Collection:** Consistent with a pragmatic study we have kept the number of assessments low which will facilitate phone-based data collection. We anticipate this will be our primary means of data collection. Research assistants will enter participant responses into a project platform in RedCap. We will finalize data collection and management plans in collaboration with the HEAL PRISM Data Coordinating Center. We will assess treatment fidelity to the brief pain teleconsult and phone-based PT using self-report checklists completed by the pain teleconsultants at each session recording core components of each intervention arm as detailed in our finalized study protocol.

Data extracted administratively will be obtained through AUCH and the FQHC EHRs. From AUCH we will collect clinic-level data including numbers of patients served with back pain over defined time periods, numbers of patients potentially eligible for participation, and those offered pain teleconsult. Data gathered from EHRs will include patient-level opioid prescribing data and age, sex, race/ethnicity, co-morbidity and health insurance information. Data extracted administratively will be integrated with the patient-reported data recorded in RedCap by the SDBC statistical team at the University of Utah CCTS. Once merged, personally identifiable information will be removed and final datasets will meet requirements to be considered de-identified. Data analyses for the UH3 clinical trial will occur using de-identified datasets.

**D.16.2 – Follow-Up:** Follow-ups will be conducted using the methods described above. We anticipate follow-ups will be done by phone. Follow-up assessments will be overseen by a research assistant blind to participants' treatment group and will occur 12-, 26- and 52-weeks after randomization.

**D.16.3 – Responder Determination:** The NIH Task Force on Research Standards for Chronic Low Back Pain recommends a binary responder analysis accompanying other outcomes in clinical trials.<sup>134</sup> We will conduct a

responder analysis at each follow-up. At the 12-week follow-up responder status is used to determine if patients assigned to the brief pain teleconsult intervention only in treatment Phase I should receive phone-based PT in treatment Phase II consistent with our adaptive treatment regimens (Fig. 4). We will define a “responder” based on our conceptual model (Fig. 2) which seeks to promote self-management of back pain. We may use a single-item self-rating, such as the Patient Acceptable Symptom State (PASS), which evaluates if a patient has passed a self-defined threshold such that they consider themselves well.<sup>208</sup> The PASS asks, “Taking into account all the activities you have during your daily life, your ability to function and your level of pain, do you consider that your current state is satisfactory?” Those answering “yes” are considered a responder. Alternatively we may use a minimum level of change in the primary outcome (PROMIS-PI) to define a responder. We prefer the single-item approach because it would be more readily implemented in routine practice if it facilitates decision-making versus achieving a threshold level of change as the latter approach requires having access to both scores and the computation for the change score, which may not be feasible in a routine clinic work flow. We will finalize our responder determination during the Planning year with input from other stakeholders.

**D.17 Timeline and Key Milestones for UH3 Phase:** Milestones for the 4-year UH3 Phase represent quantifiable and scientifically justified achievements to meet the Aims of the clinical trial. Annual milestones for the UH3 phase are presented, but may evolve based on determinations made in the UG3 Phase. The UH3 milestones are summarized below followed by a timeline for the UH3 period. *Further detail on Study Milestones is provided in the Milestone Plan Attachment included with the Other Clinical Trial-related Attachments.*

Project Year	Annual Milestones
1	<ul style="list-style-type: none"> <li>a. Activate teleconsult process and participant recruitment across all participating FOHC clinic sites</li> <li>b. Publish study protocol in open access, peer-review scientific journal</li> <li>c. Enroll the first participant at each participating FOHC clinic site</li> </ul>
2	<ul style="list-style-type: none"> <li>a. Continue participant enrollment at each performance site</li> <li>b. Recruit 50% of total sample size by the end of the 3<sup>rd</sup> quarter of year 2</li> </ul>
3	<ul style="list-style-type: none"> <li>a. Complete participant recruitment by the end of the 3<sup>rd</sup> quarter of year 3</li> <li>b. Begin interim dataset extraction and transfer procedures as participants reach 1-year follow-up.</li> </ul>
4	<ul style="list-style-type: none"> <li>a. Complete 1-year follow-up on all participants</li> <li>b. Finalize and close the database</li> <li>c. Complete pre-planned data analyses of primary and secondary aims in accordance with study protocol</li> <li>d. Completion of final study reports</li> <li>e. Reporting results in ClinicalTrials.gov</li> <li>f. Disseminate results according to Dissemination Plan</li> </ul>

The chart provides a timeline by quarter for the 4-year UH3 Clinical Trial Demonstration Phase.

Year	1				2				3				4				
	Quarter	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Finalize IRB Approval																	
Participant Recruitment across Sites (projected accrual to meet sample size target ~ 75 participants per quarter)																	
Publish trial protocol																	
Complete all follow-up assessments																	
Conduct data analyses																	
Disseminate study findings																	
Report results in Clinicaltrials.gov																	

**D.18 Data Analysis and Sample Size Considerations:** We will finalize our outcome measures, statistical analysis plan and power calculations in the Planning year. Below we provide an overview of our planned analytic framework and provide a preliminary sample size calculation to insure the proposed clinical trial is feasible given the resources available within FQHC health care organizations. ***Additional details are provided in the Statistical Analysis Plan (SAP) of this application.***

***D.18.1 General Considerations.*** Our data analyses will address the four aims defined in Section D.12. Aims 1 and 2 constitute the co-primary aims for comparison of effectiveness of the experimental interventions in the study. Aim 3 constitutes exploratory comparisons of effectiveness of the interventions in pre-specified subgroups, and Aim 4 addresses descriptive summaries of implementation outcomes. We anticipate using the PROMIS pain interference (PROMIS-PI) as the primary outcome for comparisons of effectiveness (*see Section D.9*), with key secondary outcomes including additional PROMIS domains and opioid use (Table 5). Aims 1-3 addressing the effectiveness of study interventions will follow the intention-to-treat principle, with all patients analyzed according to their randomized treatment assignment irrespective of adherence; exploratory analyses will summarize the association of outcomes with implementation and adherence measures. Aim 4 will use primarily descriptive statistics to examine implementation outcomes.

While one of our treatment strategies constitutes an adaptive intervention whose 2nd treatment phase is modified based on phase 1 response, our design has a single randomization and intention-to-treat comparisons of the two randomized groups compare the average effectiveness of initial assignment to the two different regimens (brief pain teleconsult only vs. brief pain teleconsult + phone-based PT). Aim 1 analyses compare outcomes at 12 weeks to compare the effectiveness of Phase I treatment – A) brief pain teleconsult alone, or B) brief pain teleconsult with phone-based PT as first line therapy. Aim 2 analyses compare long-term outcomes (52 weeks as primary comparison) between the same 2 regimens to compare effectiveness of a strategy in which phone-based PT is provided as first-line therapy vs. an adaptive strategy in which phone-based PT is added only for patients who fail to respond to initial treatment of brief pain teleconsult only. Because Aims 1 and 2 will be considered co-primary and address fundamentally distinct issues concerning the intervention regimens, we do not plan to use multiple comparison adjustment of our type I error rate ( $p < 0.05$ ) across the two aims.<sup>209</sup>

***Co-Primary Analyses of Aims 1 and 2:*** Reflecting the longitudinal design, the co-primary analyses of Aims 1 and 2 will use longitudinal mixed effect analyses<sup>210</sup> of the primary effectiveness outcome scores (PROMIS-PI) at baseline, and across the 12-, 26-, and 52-week follow-ups, while assuming equal baseline mean PI scores across randomized groups to optimize statistical power.<sup>211,212</sup> Linear contrasts will compare outcomes between randomized groups at 12 weeks to address Aim 1, and at 26 and 52 weeks (primary comparison) for Aim 2. Analogous linear mixed models or generalized estimating equations under general linear models<sup>213</sup> will compare other secondary outcomes between the randomized groups.

Under assumptions that include 80% retention, a standard deviation (SD) for the PROMIS-PI of 8.0 T-score points in back pain cohorts,<sup>183,214</sup> a serial correlation between repeated assessments  $\geq 0.35$ , and a MCID range for the PROMIS-PI of 2.0 - 3.5 T-score points for back pain.<sup>183,184,214</sup> we tentatively estimate a sample size of 300 in each group (total 600 participants). This sample size provides  $> 90\%$  power with 2-sided significance in Aims 1 and 2 to detect differences in mean PROMIS-PI scores of 2.7 T-score points. This sample size will retain adequate power if retention rates are lower than anticipated, or if variability in PROMIS-PI scores is greater than anticipated. This sample size also retains 80% power to detect at least a difference of at least 3.3 T-score points for exploratory sub-group analyses described under Aim 3 for sub-groups with a prevalence of 50%. *See the SAP for additional details.*

***Secondary Sub-group Analyses (Aim 3):*** Sub-group analyses will be achieved by repeating the longitudinal analyses described for Aims 1 and 2 with the addition of a main effect term for the sub-group factor, and an interaction term between treatment and the sub-group factor, to the mixed effects models to estimate treatment effects within each sub-group and test interactions between treatment and the sub-group factor. Results will be interpreted as exploratory and displayed as forest plots with point estimates and 95% confidence intervals for each treatment comparisons provided for each subgroup.



We will finalize the sub-grouping variables to be tested in the project Planning year. We plan to explore heterogeneity for the primary and select secondary outcomes based on gender, the presence of HICP, and current opioid use at the time of enrollment into the study. The presence of HICP is based on the GCPS-R which categorizes the impact of a person's chronic pain mild, bothersome or high impact. Current opioid use at baseline is categorized as short-term, episodic or long-term. For sub-group analysis we expect to examine long-term opioid users relative to those who are not long-term users. *See section D.9 for further details on baseline measurement procedures.*

***Implementation Outcomes (Aim 4):*** Consistent with a hybrid type I study design we will evaluate selected implementation outcomes as an aspect of our trial. (*see section D.9 for further details on implementation outcome measures*). In general, implementation outcomes will be examined descriptively with frequencies and percents for categorical outcomes and summary statistics including means, standard deviations, and relevant percentiles for numeric outcomes, with supplemental graphical displays using box plots, histograms and overlaid kernel density curves. We will also compute 95% confidence intervals for binary outcomes such as the percentage of patients asked about a pain teleconsult in clinics (*adoption*) and the percentage of patients accepting the consultation (*acceptability*), and for the cumulative percentages of treatment sessions attended (*feasibility*) and the cumulative percentage of core treatment components provided (*fidelity*) relative to the intended numbers specified by study protocols for the brief pain teleconsult and phone-based IT interventions. We may use linear mixed models or generalized estimating equations under general linear models as appropriate to provide complimentary assessments of differences in implementation outcomes between treatment groups.

***D.18.2 Missing Data:*** Fully sequential multiple imputation will be used for missing data.<sup>215</sup> The imputation models will include all variables in the respective outcome models plus additional variables identified as likely related to the risk of missingness or the values of the variables being imputed. In particular, any non-missing baseline, 12 or 26 week or 1 year measurements for a given outcome will be included in imputation models for that outcome. The application of multiple imputation will assure that statistical inferences are approximately unbiased so long as the mechanism of missingness follows a missing at random [MAR] structure after accounting for both the analysis variables and additional auxiliary variables included in the imputation models.

***D.19 Adequacy of Clinic Sites:*** We are confident that our sample size can be obtained from FQHC organizations in Utah. Eleven FQHC organizations are working with the University of Utah research team on EHR-based e-referral. Seven of these organizations have provided support for this project (*see letters of support*). These 7 organizations operate a total of 34 primary care clinics serving 72,440 unique adults in 2018. Chronic pain is diagnosed in at least 40% of adults in FQHCs,<sup>64,65</sup> or about 29,000 in these sites. If 1 in 4 of these adults have back pain and 10% consented to the project, this would result in about 724 annual participants. In the UG3 Phase we will confirm participation and further examine the adequacy of our recruitment projections. If necessary, we will work with AUCH to add more Utah FQHC organizations.

***D.20 Potential Challenges and Contingencies:*** Our approach offers many strengths with respect to scientific premise and innovation. There is a robust body of literature supporting the effectiveness and importance of providing nonpharmacologic pain interventions as a strategy to mitigate over-reliance on opioid therapy and improve functional outcomes. Although nonpharmacologic interventions are evidence-based and benefit many people, it is important to note that effect sizes among heterogeneous samples in pragmatic studies are often modest. Therefore, our clinical trial may produce effects that have a meaningful impact, yet are small in magnitude. We considered alternative designs to mitigate this concern. We considered comparing active treatments to a control group, but decided pain management disparities and opioid concerns argue against a wait-list, or usual care control group. We considered a factorial design to evaluate treatment combinations. We decided instead to test an adaptive treatment regimen because this allows us to examine a question related to treatment sequencing. Sequencing is a key concept of a stepped care model which is advocated by the National Pain Strategy and informs our study.

We decided not to randomize patients to the brief pain teleconsult intervention. We consider the infrastructure for connecting patients with telehealth resources as a necessary foundational step in FQHCs to overcome access

barriers. The e-referral infrastructure is sustainable beyond the study as it builds on similar processes connecting patients to outside resources through EHR-based e-referrals. Regardless of which treatment arm is more effective, the e-referral platform will be a valuable resource in participating FQHC organizations. Implementing the e-referral process across organizations participating in the project for all patients also allows us to gather implementation outcomes for this process step separated from implementation outcomes related to specific intervention strategies.

We considered strategies to provide in-person, nonpharmacologic pain care instead of relying on phone-based delivery. Although in-person care could offer advantages in terms of developing strong working alliance between therapists and patients with chronic pain, the resources required to provide in-person care would not be sustainable and scalable in low resource and rural settings. The need to develop technology-based, telehealth strategies to provide these treatments remotely is critical to overcome access barriers in low resource and rural communities; and even more essential in light of the ongoing COVID-19 pandemic.

There are many challenges that may occur in the course of our project. As with all clinical trials, adequate recruitment may prove challenging. In the Planning Phase we will confirm participating organization and continue to assess the adequacy of our clinical sites to meet accrual goals. We will consider more sites if needed. The completion of follow-up assessments can be challenging, particularly in low resource settings. We will gather data on preferred communication methods from community members in the Planning Phase and may use several options during the Clinical Trial Phase. Many individuals receiving service in Utah FQHC organizations communicate primarily in Spanish, requiring bilingual providers and adaptations for our interventions and data collection. Utah has an unprecedented number of bilingual residents of all ages, facilitating hiring. University of Utah Health and the Center for Health Outcomes and Population Equity (HOPE) are experienced in meeting the needs of Spanish-speaking community members. We will use prescribing data from FQHC EHRs and are considering self-report questionnaires to evaluate opioid use in our clinical trial. There are several shortcomings of this approach including accuracy in reporting, the inability to collect information on non-prescription opioid and prescription use that occurs outside of the FQHC clinic. We considered using Utah's All-Payers Claims Database to offset some of these concerns, however the high rates of uninsured patients in Utah's FQHCs limit the usefulness of this approach.

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## **RESOURCE SHARING PLAN**

We are committed to open and timely dissemination of research outcomes of our study and study data with appropriate privacy and confidentiality protections to facilitate further research, reuse of data, and replication. Sharing of data generated by this project will be an important part of the proposed activities of this research and will be carried out in several ways. All research resources developed in this project (manuals, policies, protocols, etc.) will be made readily available to the scientific community for non-profit research purposes. All investigators in this proposal will abide by the principles for sharing research resources, as described by NIH in “Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Programs” All data and resources will be shared consistent with the guidelines and policies of the NIH, the NIH HEAL Initiative and as developed by the Steering Committee of the PRISM Program.

## **DATA SHARING PLAN**

Sharing data generated by this project will be carried out in several ways. Data generated will be presented at national or international conferences and published in the scientific literature in a timely fashion. All final peer-reviewed manuscripts that arise from this project will be submitted to the digital archive PubMed Central. We will make our data available to the community of scientists interested in implementing strategies to enhance the uptake of evidence-based practices and to improve outcomes for patients with low back pain. We will comply with the Data Sharing Policy developed by the Health Care Systems Collaboratory Steering Committee ([https://www.nihcollaboratory.org/Products/Collaboratory.DataSharingPolicy\\_June232014.pdf](https://www.nihcollaboratory.org/Products/Collaboratory.DataSharingPolicy_June232014.pdf)) and as specified in the NIH HEAL Initiative Public Access and Data Sharing requirements (<https://heal.nih.gov/about/public-access-data>).

Any data shared upon request will be de-identified and released only after documentation (e.g., data sharing agreements) as appropriate is completed by the relevant entities. Users must agree to the conditions of use governing access to the public release data, including restrictions against attempting to identify study participants, destruction of the data after analyses are completed, reporting responsibilities, restrictions on redistribution of the data to 3rd parties, proper acknowledgement of the data resource, information provided to users will not be used for commercial purposes, and will not be redistributed to third parties.