Received: 8 June 2021 | Revised: 23 August 2021 | Accepted: 12 September 2021

DOI: 10.1002/lrh2.10291

POLICY ANALYSES

Learning Health Systems

Justice and equity in pragmatic clinical trials: Considerations for pain research within integrated health systems

Joseph Ali[1,2] | Alison F. Davis[3] | Diana J. Burgess[4,5] | Daniel I. Rhon[6] | Robert Vining[7] | Stacey Young-McCaughan[8,9] | Sean Green[3] | Robert D. Kerns[10,11]

[1]Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

[2]Johns Hopkins Berman Institute of Bioethics, Baltimore, Maryland, USA

[3]Pain Management Collaboratory, Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut, USA

[4]VA HSR&D Center for Care Delivery and Outcomes Research, Minneapolis VA Medical Center, Minneapolis, Minnesota, USA

[5]Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota, USA

[6]Brooke Army Medical Center and Uniformed Services University of the Health Sciences, Fort Sam Houston, Texas, USA

[7]Palmer Center for Chiropractic Research, Palmer College of Chiropractic, Davenport, Iowa, USA

[8]The University of Texas Health Science Center, Houston, Texas, USA

[9]South Texas Veterans Health Care System, San Antonio, Texas, USA

[10]Departments of Psychiatry, Neurology, and Psychology, Yale University, New Haven, Connecticut, USA

[11]VA Connecticut Healthcare System Pain Research, Informatics, Multimorbidities, and Education (PRIME) Center, West Haven, Connecticut, USA

Correspondence
Joseph Ali, Johns Hopkins Berman Institute of Bioethics, 1809 Ashland Ave, Rm 208, Baltimore, MD, 21205, USA.
Email: jali@jhu.edu

Funding information
Research reported in this publication was made possible by Award No. U24 AT009769 from the U.S. National Institutes of Health (NIH) National Center for Complementary and Integrative Health (NCCIH) and the NIH Office of Behavioral and Social Sciences Research (OBSSR). In addition, some authors were individually supported by NCCIH under awards AT009763 and AT009767; and the Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense, through the Pain Management Collaboratory-Pragmatic Clinical Trials Demonstration Projects under awards W81XWH-18-2-0003 and W81XWH-18-2-0008

Abstract

Introduction: Pragmatic clinical trials (PCTs) can overcome implementation challenges for bringing evidence-based therapies to people living with pain and co-occurring conditions, providing actionable information for patients, providers, health systems, and policy makers. All studies, including those conducted within health systems that have a history of advancing equitable care, should make efforts to address justice and equity.

Methods: Drawing from collective experience within pragmatic pain clinical trials networks, and synthesizing relevant literature, our multidisciplinary working group examined challenges related to integrating justice and equity into pragmatic pain management research conducted in large, integrated health systems. Our analysis draws from military and veteran health system contexts but offers strategies to consider throughout the lifecycle of pragmatic research more widely.

Results: We found that PCTs present a unique opportunity to address major influences on health inequities by occupying a space between research, healthcare delivery, and the complexities of everyday life. We highlight key challenges that require attention to support complementary advancement of justice and equity via pragmatic research, offering several strategies that can be pursued.

Conclusions: Efforts are needed to engage diverse stakeholders broadly and creatively in PCTs, such as through dedicated health equity working groups and other collaborative relationships with stakeholders, to support robust and inclusive approaches to research design and implementation across study settings. These considerations, while essential to pain management research, offer important opportunities toward achieving more equitable healthcare and health systems to benefit people living with pain and co-occurring conditions.

KEYWORDS
equity, ethics, justice, pain management, pragmatic clinical trial

1 | INTRODUCTION

Pain is personal, multidimensional, and often invisible to others—a function of biological (eg, nociception), psychological (eg, cognition and affect), and social (eg, cultural and interpersonal) factors. Chronic pain is a persistent pain experience described variously, including pain intensity and interference with social and emotional functioning.[1] People with chronic pain often report multiple sites of pain and multiple co-occurring pain conditions, alongside other physical and mental health conditions. As such, chronic pain is often difficult to manage, and a growing conceptual and empirical literature supports models of integrated, multimodal pain care that incorporate a range of evidence-based interventions, including nonpharmacological treatments (NPTs).[2-6]

Although many people experience chronic pain, certain populations are at greater risk, including severe, debilitating chronic pain. Military and veteran populations worldwide report particularly high rates of chronic pain and pain interference.[7-9] As such, pain management has become a priority for the U.S. Departments of Defense (DOD) and Veterans Affairs (VA), which have established an integrated stepped care model of pain management with clinical pathways that promote the use of NPTs, including complementary and integrative health approaches.[10] In one successful approach, for example, veterans with preexisting chronic pain and psychological comorbid conditions experienced decreases in pain and pain intensity after receiving auricular acupuncture, a protocolized NPT, in routine clinical settings.[11] Continued support for use of NPTs comes from evidence that active duty military service members with chronic pain who transitioned from DOD to care in VA facilities with prior exposure to NPTs were at significantly lower risk for new-onset alcohol and/or drug use disorder; poisoning with opioids, barbiturates, or sedatives; suicide ideation; and self-inflicted injuries including suicide attempts, compared to those who transitioned without prior exposure to NPTs.[12]

Pragmatic approaches to research have recently gained traction for their ability to address urgent health care problems such as chronic pain, as well as to test the effectiveness and delivery of low-risk pain therapies to counter the nation's opioid epidemic.[13,14] These pragmatic clinical trials (PCTs) are designed to examine the effectiveness of interventions when embedded in healthcare systems with participants representing the population normally seen in clinical practice settings with a range of sociodemographic characteristics, variations of the condition being studied, and co-occurring conditions.[15] Whereas explanatory trials are designed to assess intervention efficacy in an ideal setting, pragmatic trials aim to test intervention effectiveness in a more generalizable setting. Compared to explanatory trial designs, PCTs have broader inclusion criteria and fewer exclusion criteria to allow for more flexible delivery of interventions. PCTs also tend to feature outcomes that are more acceptable and meaningful to participants, the ultimate beneficiaries of the research. These designs allow PCTs to be more likely to provide actionable information for patients, providers, and policy makers about how interventions work within complex care settings.[16] Yet, health systems are prone to disparities in healthcare access and quality that become exacerbated unless proactive steps are taken to address health equity, as has been articulated recently in the context of pragmatic research involving individuals with dementia.[17]

2 | CONTEXTUALIZING INEQUITY AND INJUSTICE TO PAIN PCTs

In pragmatic research, *inequity* results from unfair distribution or realization of benefits and burdens of the research that stem from social conditions and/or structural characteristics of the healthcare systems where PCTs are conducted. Inequities can be described as a form of *injustice*, especially if they arise from the inadvertent neglect of a basic moral, legal, or human right—or from overt or systemic discrimination. People with chronic pain may be vulnerable to experiences of injustice propagated by social factors including poverty, disability, poor social support, homelessness, isolation, and limited access to effective pain care.[5,18] These elements can carry over into the clinical research environment, which is a multidimensional system of influences that can accommodate, ignore, or exacerbate vulnerabilities.[19] Consonant with the biopsychosocial model of pain, which acknowledges its multiple components (biological, psychological, and social influences), these social factors can in turn negatively influence an individual's pain experience.[20] The dynamic interaction of factors within and across the biological, psychological, and social domains of pain therefore draws attention to vulnerabilities across all aspects of life.

It suggests that experiences under any one domain (eg, history of racial or sexual harassment and discrimination) can have broad biological, psychological, and social effects. Inequities arising from health systems and other sources can potentially amplify pre-existing individual vulnerabilities, interfere with the delivery of trial interventions, and delay pain recovery.

Ethical issues arising in PCTs include managing risk, informed consent, blurred distinctions between research and care, stakeholder representation, and collateral findings.[21-30] Because pragmatic research can be integrated deliberately within health systems already challenged by inequities, systematic consideration of the ethical dimensions of justice as applied to pain PCTs is also critical. Given the structural embeddedness of PCTs, the need arises in this context to focus attention on how the principle of justice—a cornerstone of the Belmont Report and other foundational research ethics guidelines—can be operationalized to address issues of *structural injustice* encountered during pragmatic research.[31] This can be facilitated through clear identification of the influences, roles, and responsibilities of all PCT stakeholders, including health providers, research sponsors, regulatory agencies, payers, institutional leadership, as well as advocacy and community organizations.[32,33] In many cases, these gatekeepers will need to be engaged actively to direct their influence towards documenting and rectifying inequities. Here we emphasize that there is an opportunity for pragmatic research itself to provide the knowledge necessary to facilitate this task.

Based on our experience with PCTs in health systems that serve military and veteran populations,[13] we suggest it is particularly important to recognize that: (a) some individuals with chronic pain are vulnerable to injustice, (b) structural and sociocultural challenges that exist within health systems can complicate chronic pain research, and (c) PCTs involving NPTs provide one lens through which injustices may be identified and addressed with the proactive input of a broad range of stakeholders.

3 | CONSIDERING JUSTICE AND EQUITY ACROSS THE LIFE CYCLE OF PRAGMATIC RESEARCH

Comprehensive attention to justice not only has the potential to benefit people living with chronic pain, but also to strengthen the value, quality, and generalizability of pragmatic research. The several approaches described below to address equity within PCTs include targeted interventions at various stages of pragmatic research. Robust stakeholder engagement throughout the lifecycle of research, particularly involving people with lived experience that includes chronic pain and various psycho-social vulnerabilities, is essential to carry out these actions. Examples of these challenges and mitigation strategies are summarized in Table 1.

3.1 | Study context and design

Characteristics of people with chronic pain, of pain researchers, of systems for institutional oversight, and of the environment housing pragmatic research inevitably shape an individual participant's research experience. Funders often support PCT research in major academic health systems, because these systems offer access to relatively large numbers of patients and also tend to employ experienced research teams. However, large academic health systems may not represent environments where many individuals with chronic pain and co-occurring conditions, and who face existing health inequities, receive care. Incentivizing PCT partnerships between academic research institutions and less-resourced or underserved populations (eg, rural and those that serve a high percentage of patients from racial/ethnic minority groups) may support enhanced generalizability, utility, and equity of PCT findings.

A combination of factors—including those that are individual, collective, institutional, and structural—influence how data are collected, relevant outcomes are formulated, research-related behaviors are characterized, and findings are interpreted.[34-36] For example, as a structural matter, longstanding sociodemographic categories that are considered important factors in PCTs (eg, race/ethnicity based on administrative or clinical employee observation)[37] have been critiqued and could be supplemented with more current and nuanced patient-reported measures of race, ethnicity, ability, or other characteristics.[38] Similarly, while PCTs strive for efficiency, sometimes by relying on electronic health records or patient portals for data collection, they may inadvertently bias their findings to settings that are well-resourced and comfortable with technology. They may also limit study measures and outcomes to those already integrated into particular systems, regardless of their alignment with the care needs and priorities of traditionally underserved populations. When designing and implementing PCTs, choices about where, when, and how to collect data should be carefully considered early and often, not only as a matter of trial integrity, but also to further goals of broad inclusion.

3.2 | Recruiting participants

Adequate sampling plans designed to engage individuals who are representative of the ultimate beneficiaries of pragmatic research are a prerequisite for ensuring external validity and achieving equitable and just healthcare outcomes. However, selective exclusion of patients still exists,[39] and recruitment can be complicated by variable, overlapping roles of stakeholders.[40] Recruitment of non-representative samples for chronic pain pragmatic trials may be exacerbated, again, by deeply entrenched systemic factors. Most of the nation's healthcare workers (as well as clinical research personnel) are not culturally, racially, or ethnically similar to individuals for whom they provide care.[41] However, overall diversity among research staff may help to build trust in the research process, which can facilitate study recruitment and follow-up. Like with civilian populations, race and gender are risk factors for pain and co-occurring conditions within active duty military and veteran populations.[42-44] In addition, between 15% and 40% of female veterans using VA services have experienced military sexual trauma.[45] Such trauma can contribute to the avoidance of care in an environment perceived as hostile, where many female

TABLE 1 Justice and equity-enhancing strategies for PCTs testing nonpharmacological treatments for chronic pain

Focal area	Examples of challenges	Examples of mitigation strategies
Study context and design	• Potential for biases, prejudices, and inequities to transfer from health systems to PCTs.	• Understand, prospectively, community attitudes and beliefs regarding a health system and how these might transfer to aspects of trial implementation. • Develop, share, and enforce standards for equity and inclusion across the study team and supporting personnel. • Develop and employ innovative tools to prioritize equity on a routine basis across a health system (eg, electronic reminders about common health inequities that affect medical treatment).
	• Limited accessibility to NPTs for some patients due to institutional biases and disincentives against NPTs. • Funding system that prioritizes health systems with strong academic partnerships, leading to the underrepresentation of less resourced health systems.	• Engage with institutional leadership prospectively to identify pathways for integration of pragmatism and NPTs. • Systematically review portfolios and funding strategies with an eye toward health system diversity, including bias education. • Specify and weight criteria that will be applied during grant review processes to achieve more equitable distribution of resources. • Incentivize partnerships between less-resourced health systems with academic research centers.
	• Use of study outcome measures that do not necessarily align with what patients are most interested in, and sociodemographic categories that diverge from how participants view themselves.	• Engage patients/other stakeholders to identify meaningful study outcomes among specific populations. • If needed, supplement existing sociodemographic data with current patient-reported race/ethnicity/ability measures. • Create and include patient engagement groups as part of the research team and invite comments on choice and relevance of study outcomes.
	• Limits on data collection and trial participation due to reliance on digital systems.	• Provide access to technology, through pragmatic means if feasible (eg, leverage existing technology support programs in healthcare systems). • Consider non-EHR based data collection for some populations
Participant recruitment and retention	• Limited participation of some individuals and groups due to diversity-insensitive recruitment approaches and materials.	• Identify potential barriers to trial participation prospectively, including through patient questionnaires designed for this purpose. • Create and include patient engagement groups as part of the research team who can review and offer feedback on recruitment methods and materials. • Include within recruitment materials culturally sensitive and specific images and language that include populations experiencing lower access to care or other known disparities within the study's health system.
	• Limited participation of some individuals and groups by virtue of their transiency or difficulty accessing well-established health systems.	• Tailor recruitment to potentially excluded populations (eg, settings known to care for individuals who are transient or who commonly experience health disparities).
Study interventions	• Inflexible interventions that do not align with contextual needs or strong preference of patient populations.	• Identify multiple strategies (eg, individual and group-delivered interventions; condensed treatment schedules; multi-lingual therapy) to facilitate intervention delivery for different types of patient populations.
Stakeholder engagement	• Limited racial, ethnic, and ability diversity among providers, investigators, and study staff. • Inability to identify and respond to individual and structural barriers to trial participation by marginalized populations.	• Engage with diverse patient groups who can review and offer feedback on study design and implementation choices. • Invite patients who represent a study population formally to be members of the research team. • Offer structural competency and cultural sensitivity training for research and healthcare staff involved in PCTs. • Use known strategies to engage investigators from underrepresented groups (eg, diversity supplements; engage institutions that serve minority populations). • Encourage sharing of diverse perspectives within teams and actively counter microaggressions, rudeness, and harassment.

Abbreviations: EHR, electronic health record; NPT, non-pharmacological treatment; PCT, pragmatic clinical trial.

veterans have reported sexual harassment,[46] sexist treatment, and feeling like they do not belong.[47] As has been noted by others—including the VA Women's Health Practice-Based Research Network[48]—if these issues are not addressed directly as part of a trial's recruitment plan, there will remain a risk of systemic underrepresentation of women veterans in many embedded PCTs.

More broadly, PCTs can promote equitable inclusion by engaging patients with "real-life" co-occurring conditions that interact with the experience of pain, such as alcohol use disorder, who are routinely excluded from efficacy and even many effectiveness trials.[49] Doing so can increase the need for carefully established trial-monitoring plans, but such efforts are important and should be encouraged.

Organizational culture can also complicate recruitment for PCTs involving integrated models of pain management. For example, within military environments that understandably emphasize hierarchy and service responsibilities, placing a high value on return to duty and battlefield readiness can contribute to stigma for seeking care.[50] Pressure on military commanders for optimal unit readiness may lead to favoring pain treatment modalities that provide rapid, short-term relief over comprehensive care or research participation. Further, by virtue of DOD policies, individuals with persistent symptoms are more likely referred for determination of their ability to continue active military service, making research related to the management of chronic pain conditions very challenging in active duty populations. Finally, the common occurrences of deployment and temporary or permanent changes of station inherent in military systems contribute to substantial transiency, which can disrupt continuity of care and impede the ability to include active duty military populations in PCTs.

Additional hurdles that can disparately affect an individual's research participation in chronic pain PCTs include geographical distance, out-of-pocket and ancillary costs, concerns regarding cultural acceptability of certain NPTs, and discomfort with (or lack of access to) technology used in some PCTs.[51] Lack of NPT providers may also disproportionately affect research participation and care.[52]

3.3 | Interventions

Generally speaking, PCTs grounded in a biopsychosocial pain model may help surface social determinants of health and guide the development of holistic and accessible interventions that promote patient-centered pain outcomes and look to decrease disparities.[53] Introducing some flexibility into intervention delivery, which is a hallmark of many PCTs, can broaden a participant population to meet the needs of diverse patient groups as well as accommodate acute and transient health status changes. For example, to counter some of the pressures of military culture described above, PCTs involving active duty populations might consider implementing intensive or massed treatment approaches. This strategy accelerates delivery of NPTs over a shorter time period, sometimes through group-level interventions, an approach that has been used previously in military populations.[54-56]

In another example of tailoring interventions to stakeholder needs, PCT researchers investigating mindfulness-based interventions for treating chronic pain collaborated with women veteran leaders who had prior exposure to mindfulness treatment to develop a facilitator-training module that addressed specific needs and experiences of female veterans.[57] In this work, all meditations were recorded with both male and female voices, and language in recruitment and course materials were carefully chosen to avoid being potentially disturbing to women. As these examples illustrate, there is a need for conscious and proactive engagement of stakeholders familiar with ability- and access-related challenges of patient beneficiaries of NPTs for managing chronic pain.

3.4 | Stakeholder engagement

Various approaches to engaging people with lived experience and other stakeholders have been applied to the conduct of pragmatic research. These include using qualitative methods during formative phases of research to refine proposed interventions and treatment options, and identifying approaches that optimize recruitment of representative samples to meet the needs of a patient population.[58] The Patient-Centered Outcomes Research Institute has developed an Engagement Rubric to guide stakeholder engagement throughout the research process, from the time a research study is conceived through the dissemination of study findings and beyond.[59] These activities can buffer the impact of potential health inequities in PCT research evaluating pain management.

Effective and equitable stakeholder engagement within pragmatic research should prioritize inclusivity for underrepresented points of view and continue to accept diverse forms of feedback into decision-making throughout the life of a trial. This can be facilitated through intentional efforts to diversify pragmatic trial leadership, which require an explicit attention to systemic biases and other deeply entrenched barriers to engagement and promotion of underrepresented minorities within various scientific and clinical fields. Expanded diversity among scientific review panels and leadership within organizations that sponsor trials is also important. Within PCT networks, designated groups—such as health equity advisory councils—with broad stakeholder representation are also useful to enhance engagement.[17] Indeed, these groups could be designed to include people with chronic pain, co-occurring mental health conditions, substance use disorders, or who have experienced traumatic stress or have other unique healthcare needs. Their input can provide important insights into the effective and ethical design of pragmatic pain management studies.[60-62] In conjunction, stakeholders, and advocates can be afforded an active role on executive committees and as part of research teams, so that their input can be adequately considered and implemented.[63]

4 | EMERGING OPPORTUNITIES TO ADDRESS EQUITY IN PRAGMATIC RESEARCH

Embedded pragmatic research that tests NPTs in integrated pain care pathways provides an avenue to prioritize health equity across the lifecycle of a PCT. Within learning health systems, principles of

continuous learning and feedback to improve care can potentially be put to use not only to secure value in healthcare, but also to support evidence development to guide equitable practice.[64] The opportunity and challenge for pragmatic research aiming to advance safe and effective pain management are to integrate goals of inclusion and equity with the core goals of pragmatic research: namely, testing how to readily integrate interventions into a range of clinical environments (eg, primary care, specialized pain management, military units) and assessing outcomes important to patient populations (eg, pain intensity and interference with functioning) experiencing varying types of pain.[65]

As a treatment class, multimodal approaches to chronic pain management that incorporate NPTs show promise but have not been widely embraced for a range of reasons.[28,66] However, the outcomes of ongoing PCTs evaluating these approaches should be instructive to others. The VA Whole Health Initiative and DOD Move to Health initiative are patient-centered programs that promote the use of complementary and integrative health approaches guided by a personalized health plan.[53] These strategies promote adaptive pain self-management and may offer the opportunity to mitigate system-wide inequities introduced in usual care settings,[67,68] in addition to other pragmatic research efforts, such as the NIH-DOD-VA Pain Management Collaboratory and The NIH Helping to End Addiction Long-term[SM] (HEAL) Initiative. Both are investigating NPTs for pain management.[13,14]

However, increasing awareness about the value of NPTs, and access to them, is an ongoing issue beyond the confines of pragmatic research. Payer-based restrictions impose significant barriers to patient access to NPTs,[69] and although virtual delivery of NPTs for pain management (including through PCTs) rose significantly during the COVID-19 pandemic and is likely to remain in widespread use, equity-related issues have arisen from this adaptation,[70] for example ready access to high-speed internet. On the other hand, use of virtual delivery of pain care may find increased appeal from individuals who are members of groups that have historically faced challenges with accessing facility-based NPTs, or those who have encountered discrimination when seeking pharmacological pain treatments in person[71]—a phenomenon documented in both VA[72] and civilian healthcare settings.[73] More extensive study of virtual care delivery of NPTs within PCTs that include equity-oriented outcome measures would be of particular value.

5 | CONCLUSIONS

PCTs can help address health inequities by occupying a unique space between research, healthcare delivery, and the complexities of everyday life. Although informed pragmatic research teams have an opportunity to address health inequities in pain management, unintentional blind spots to equity often remain. We have observed that learning organizations, such as our Pain Management Collaboratory and others like it that create frequent opportunities for acquiring and disseminating knowledge and best practices, benefit from collaborative relationships with stakeholders including research participants, health systems leadership, and funders. Additional efforts are needed to engage stakeholders of pragmatic research more broadly and creatively, such as through a dedicated health equity working group[17] within a PCT network, or via other approaches. Future research to further develop measures and evidence that advance equity-sensitive pain PCTs is needed. A range of interventional strategies might also be developed and tested to address some of the psychological and social factors that may bridge both the experience of pain and the experience of inequity. We believe the considerations articulate herein, while essential to pain management research, also extend broadly to other areas of healthcare and offer important opportunities toward achieving more equitable healthcare and health systems.

ACKNOWLEDGMENT

The NIH-DOD-VA Pain Management Collaboratory operates a Coordinating Center that is supported by the U.S. National Institutes of Health (NIH) National Center for Complementary and Integrative Health (NCCIH) and the NIH Office of Behavioral and Social Sciences Research (OBSSR). Projects are individually supported by multiple U. S. government agencies and entities, including NIH (NCCIH, National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Drug Abuse (NIDA), National Institute of Alcohol Abuse and Alcoholism (NIAAA), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Office of Research on Women's Health (ORWH), and National Institute of Nursing Research (NINR)); Department of Defense (DOD) (Clinical and Rehabilitative Medicine Research Program (CRMRP), Military Operational Medicine Research Program (MOMRP)); the Uniformed Services University of the Health Sciences (USU); and Department of Veterans Affairs (VA) Health Services Research & Development (HSR&D) Service of the Office of Research and Development.

Research reported in this publication was made possible by Award No. U24 AT009769 from NCCIH and OBSSR. In addition, some authors were individually supported by NCCIH under awards AT009763 and AT009767; and the Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense, through the Pain Management Collaboratory-Pragmatic Clinical Trials Demonstration Projects under awards W81XWH-18-2-0003 and W81XWH-18-2-0008.

The content of this publication is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Department of Defense, the U.S. Department of Veterans Affairs or the United States Government.

For more information about the NIH-DOD-VA Pain Management Collaboratory, visit https://painmanagementcollaboratory.org/.

CONFLICTS OF INTEREST

The authors declares no conflicts of interest.

ORCID

Joseph Ali https://orcid.org/0000-0002-4767-2512

REFERENCES

1. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007;133(4):581-624. https://doi.org/10.1037/0033-2909.133.4.581
2. Beehler GP, Murphy JL, King PR, et al. Brief cognitive behavioral therapy for chronic pain: results from a clinical demonstration project in primary care behavioral health. *Clin J Pain*. 2019;35(10):809-817. https://doi.org/10.1097/AJP.0000000000000747
3. Skelly AC, Chou R, Dettori JR, et al. Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review. Rockville (MD): Agency for Healthcare Research and Quality (US); June 2018.
4. Chou R, Deyo R, Friedly J, et al. Nonpharmacologic therapies for low Back pain: a systematic review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med*. 2017;166(7):493-505. https://doi.org/10.7326/M16-2459
5. Dale R, Stacey B. Multimodal treatment of chronic pain. *Med Clin North Am*. 2016;100(1):55-64. https://doi.org/10.1016/j.mcna.2015.08.012
6. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain-United States, 2016. *JAMA*. 2016;315(15):1624-1645. https://doi.org/10.1001/jama.2016.1464
7. Wayne J, Francis O, Patricia D, Macedonia C. Military Medicine. Volume 175, August 2010, Supplement. Total Force Fitness for the 21st Century A New Paradigm; 2010.
8. Kerns RD, Heapy A, Kerns RD, Heapy AA. Advances in pain management for Veterans: current status of research and future directions. *J Rehabil Res Dev*. 2016;53(1):7-10. https://doi.org/10.1682/JRRD.2015.10.0196
9. Van Den Kerkhof EG, Van Til L, Thompson JM, et al. Pain in Canadian veterans: analysis of data from the survey on transition to civilian life. *Pain Res Manag*. 2015;20(2):89-95. https://doi.org/10.1155/2015/763768
10. Malecki HL, Gollie JM, Scholten J. Physical activity, exercise, whole health, and integrative health coaching. *Phys Med Rehabil Clin N Am*. 2020;31(4):649-663. https://doi.org/10.1016/j.pmr.2020.06.001
11. Zeliadt SB, Thomas ER, Olson J, et al. Patient feedback on the effectiveness of auricular acupuncture on pain in routine clinical care: the experience of 11,406 veterans. *Med Care*. 2020;58(9 Suppl):S101-S107. https://doi.org/10.1097/MLR.0000000000001368
12. Meerwijk EL, Larson MJ, Schmidt EM, et al. Nonpharmacological treatment of Army Service members with chronic pain is associated with fewer adverse outcomes after transition to the veterans health administration. *J Gen Intern Med*. 2020;35(3):775-783. https://doi.org/10.1007/s11606-019-05450-4
13. Kerns RD, Brandt CA, Peduzzi P. NIH-DoD-VA pain management Collaboratory. *Pain Med*. 2019;20(12):2336-2345. https://doi.org/10.1093/pm/pnz186
14. Pragmatic and implementation studies for the management of pain to reduce opioid prescribing (PRISM). https://heal.nih.gov/research/clinical-research/prism. Accessed June 7, 2021.
15. Rowbotham MC, Gilron I, Glazer C, et al. Can pragmatic trials help us better understand chronic pain and improve treatment? *Pain*. 2013;154(5):643-646. https://doi.org/10.1016/j.pain.2013.02.034
16. Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA*. 2003;290(12):1624-1632. https://doi.org/10.1001/jama.290.12.1624
17. Quiñones AR, Mitchell SL, Jackson JD, et al. Achieving health equity in embedded pragmatic trials for people living with dementia and their family caregivers. *J Am Geriatr Soc*. 2020;68(Suppl 2):S8-S13. https://doi.org/10.1111/jgs.16614
18. MMWR. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults-United States, 2016. *Morb Mortal Wkly Rep*. 2018;67(36):1001-1006.
19. Tait RC. Vulnerability in clinical research with patients in pain: a risk analysis. *J Law Med Ethics*. 2009;37(1):59-72. https://doi.org/10.1111/j.1748-720X.2009.00351.x
20. Darnall BD, Carr DB, Schatman ME. Pain psychology and the biopsychosocial model of pain treatment: ethical imperatives and social responsibility. *Pain Med*. 2017;18(8):1413-1415. https://doi.org/10.1093/pm/pnw166
21. Lantos JD, Wendler D, Septimus E, Wahba S, Madigan R, Bliss G. Considerations in the evaluation and determination of minimal risk in pragmatic clinical trials. *Clin Trials*. 2015;12(5):485-493. https://doi.org/10.1177/1740774515597687
22. O'Rourke PP, Carrithers J, Patrick-Lake B, et al. Harmonization and streamlining of research oversight for pragmatic clinical trials. *Clin Trials*. 2015;12(5):449-456. https://doi.org/10.1177/1740774515597685
23. Anderson ML, Griffin J, Goldkind SF, et al. The food and drug administration and pragmatic clinical trials of marketed medical products. *Clin Trials*. 2015;12(5):511-519. https://doi.org/10.1177/1740774515597700
24. Basic HHS. Policy for Protection of Human Research Subjects Section 46.116—General requirements for informed consent. 56 FR 28012, 28022; June 18, 1991, as amended at 70 FR 36328; June 23, 2005. Available from https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML. Accessed June 7, 2021.
25. Kim SY, Miller FG. Informed consent for pragmatic trials-the integrated consent model. *N Engl J Med*. 2014;370(8):769-772. https://doi.org/10.1056/NEJMhle1312508
26. McGraw D, Greene SM, Miner CS, Staman KL, Welch MJ, Rubel A. Privacy and confidentiality in pragmatic clinical trials. *Clin Trials*. 2015;12(5):520-529. https://doi.org/10.1177/1740774515597677
27. McKinney RE Jr, Beskow LM, Ford DE, et al. Use of altered informed consent in pragmatic clinical research. *Clin Trials*. 2015;12(5):494-502. https://doi.org/10.1177/1740774515597688
28. Foster NE, Anema JR, Cherkin D, et al. Prevention and treatment of low back pain: evidence, challenges, and promising directions. *Lancet*. 2018;391(10137):2368-2383. https://doi.org/10.1016/S0140-6736(18)30489-6
29. Morain SR, Weinfurt K, Bollinger J, Geller G, Mathews DJ, Sugarman J. Ethics and collateral findings in pragmatic clinical trials. *Am J Bioeth*. 2020;20(1):6-18. https://doi.org/10.1080/15265161.2020.1689031
30. Smalley JB, Merritt MW, Al-Khatib SM, McCall D, Staman KL, Stepnowsky C. Ethical responsibilities toward indirect and collateral participants in pragmatic clinical trials. *Clin Trials*. 2015;12(5):476-484. https://doi.org/10.1177/1740774515597698
31. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Bethesda, MD: The Commission; 1978.
32. Nicholls SG, Carroll K, Zwarenstein M, et al. The ethical challenges raised in the design and conduct of pragmatic trials: an interview study with key stakeholders. *Trials*. 2019;20(1):765. https://doi.org/10.1186/s13063-019-3899-x
33. Whicher DM, Miller JE, Dunham KM, Joffe S. Gatekeepers for pragmatic clinical trials. *Clin Trials*. 2015;12(5):442-448. https://doi.org/10.1177/1740774515597699
34. Levine C, Faden R, Grady C, et al. The limitations of "vulnerability" as a protection for human research participants. *Am J Bioeth*. 2004;4(3):44-49. https://doi.org/10.1080/15265160490497083
35. Shivas T. Contextualizing the vulnerability standard. *Am J Bioeth*. 2004;4(3):84-W32. https://doi.org/10.1080/15265160490497137
36. Welch MJ, Lally R, Miller JE, et al. The ethics and regulatory landscape of including vulnerable populations in pragmatic clinical trials. *Clin Trials*. 2015;12(5):503-510. https://doi.org/10.1177/1740774515597701
37. Sohn MW, Zhang H, Arnold N, et al. Transition to the new race/ethnicity data collection standards in the Department of Veterans Affairs. *Popul Health Metr*. 2006;4:7. https://doi.org/10.1186/1478-7954-4-7

38. Hughes JL, Camden AA, Yangchen T. Rethinking and updating demographic questions: guidance to improve descriptions of research samples [editorial]. *Psi Chi J Psychol Res*. 2016;21:138-151.
39. Lidz CW, Benedicto CM, Albert K, Appelbaum PS, Dunn LB. Clinical concerns and the validity of clinical trials. *AJOB Prim Res*. 2013;4:26-38.
40. Donovan JL, Paramasivan S, de Salis I, Toerien M. Clear obstacles and hidden challenges: understanding recruiter perspectives in six pragmatic randomised controlled trials. *Trials*. 2014;15:5. https://doi.org/10.1186/1745-6215-15-5
41. Valantine HA, Davis AF. Workforce diversity and capacity building to address health disparities. *The Science of Health Disparities Research*. Dordrecht: Springer; 2021:445-454.
42. Blakey SM, Wagner HR, Naylor J, et al. Chronic pain, TBI, and PTSD in military veterans: a link to suicidal ideation and violent impulses? *J Pain*. 2018;19(7):797-806. https://doi.org/10.1016/j.jpain.2018.02.012
43. Higgins DM, Kerns RD, Brandt CA, et al. Persistent pain and comorbidity among operation enduring freedom/operation Iraqi freedom/operation new Dawn veterans. *Pain Med*. 2014;15(5):782-790. https://doi.org/10.1111/pme.12388
44. Knox JB, Orchowski JR, Owens B. Racial differences in the incidence of acute low back pain in United States military service members. *Spine*. 2012;37(19):1688-1692. https://doi.org/10.1097/BRS.0b013e318255a07b
45. Klap R, Darling JE, Hamilton AB, et al. Prevalence of stranger harassment of women veterans at veterans affairs medical centers and impacts on delayed and missed care. *Womens Health Issues*. 2019;29(2):107-115. https://doi.org/10.1016/j.whi.2018.12.002
46. Stander VA, Thomsen CJ. Sexual harassment and assault in the U.S. military: a review of policy and research trends. *Mil Med*. 2016;181(1 Suppl):20-27. https://doi.org/10.7205/MILMED-D-15-00336
47. Treated Like a 'Piece of Meat': Female Veterans Endure Harassment at the V.A. New York Times, March 12, 2019. Available from https://www.nytimes.com/2019/03/12/us/politics/women-veterans-harassment.html. Accessed June 7, 2021.
48. Pomernacki A, Carney DV, Kimerling R, et al. Lessons from initiating the first veterans health administration (VA) Women's health practice-based research network (WH-PBRN) study. *J Am Board Fam Med*. 2015;28(5):649-657. https://doi.org/10.3122/jabfm.2015.05.150029
49. Heapy AA, Driscoll MA, Buta E, et al. Co-operative pain education and self-management (COPES) expanding treatment for real-world access (ExTRA): pragmatic trial protocol. *Pain Med*. 2020;21(12 Suppl 2):S21-S28. https://doi.org/10.1093/pm/pnaa365
50. Adirim T. A military health system for the twenty-first century. *Health Aff*. 2019;38(8):1268-1273. https://doi.org/10.1377/hlthaff.2019.00302
51. Ali J, Andrews JE, Somkin CP, Rabinovich CE. Harms, benefits, and the nature of interventions in pragmatic clinical trials. *Clin Trials*. 2015;12(5):467-475. https://doi.org/10.1177/1740774515597686
52. Green BN, Johnson CD, Daniels CJ, Napuli JG, Gliedt JA, Paris DJ. Integration of chiropractic Services in Military and Veteran Health Care Facilities: a systematic review of the literature. *J Evid Based Complementary Altern Med*. 2016;21(2):115-130. https://doi.org/10.1177/2156587215621461
53. Special focus issue on multimodal approaches in integrative health: whole persons, whole practices, whole systems. *J Altern Comp Med*. 2019;25:S1-S6.
54. Foa EB, McLean CP, Zang Y, et al. Effect of prolonged exposure therapy delivered over 2 weeks vs 8 weeks vs present-centered therapy on PTSD symptom severity in military personnel: a randomized clinical trial [published correction appears in JAMA. 2018 Aug 21;320(7):724]. *JAMA*. 2018;319(4):354-364. https://doi.org/10.1001/jama.2017.21242
55. Peterson AL, Foa EB, Blount TH, et al. Intensive prolonged exposure therapy for combat-related posttraumatic stress disorder: design and methodology of a randomized clinical trial. *Contemp Clin Trials*. 2018;72:126-136. https://doi.org/10.1016/j.cct.2018.07.016
56. Sloan DM, Marx BP, Resick PA, et al. Study design comparing written exposure therapy to cognitive processing therapy for PTSD among military service members: a noninferiority trial. *Contemp Clin Trials Commun*. 2019;17:100507. https://doi.org/10.1016/j.conctc.2019.100507
57. Burgess DJ, Evans R, Allen KD, et al. Learning to apply mindfulness to pain (LAMP): design for a Pragmatic Clinical Trial of two mindfulness-based interventions for chronic pain. *Pain Med*. 2020;21(Suppl 2):S29-S36. https://doi.org/10.1093/pm/pnaa337
58. Bastian LA, Cohen SP, Katsovich L, et al. Stakeholder engagement in pragmatic clinical trials: emphasizing relationships to improve pain management delivery and outcomes. *Pain Med*. 2020;21(Suppl 2):S13-S20. https://doi.org/10.1093/pm/pnaa333
59. Sheridan S, Schrandt S, Forsythe L, Hilliard TS. Paez KA; advisory panel on patient engagement (2013 inaugural panel). The PCORI engagement rubric: promising practices for partnering in research. *Ann Fam Med*. 2017;15(2):165-170. https://doi.org/10.1370/afm.2042
60. Becker WC, Mattocks KM, Frank JW, et al. Mixed methods formative evaluation of a collaborative care program to decrease risky opioid prescribing and increase non-pharmacologic approaches to pain management. *Addict Behav*. 2018;86:138-145. https://doi.org/10.1016/j.addbeh.2018.03.009
61. Mattocks K, Rosen MI, Sellinger J, et al. Pain Care in the Department of veterans affairs: understanding how a cultural shift in pain care impacts provider decisions and collaboration. *Pain Med*. 2020;21(5):970-977. https://doi.org/10.1093/pm/pnz341
62. Tegethoff M, Belardi A, Stalujanis E, Meinlschmidt G. Comorbidity of mental disorders and chronic pain: chronology of onset in adolescents of a National Representative Cohort. *J Pain*. 2015;16(10):1054-1064. https://doi.org/10.1016/j.jpain.2015.06.009
63. Young-McCaughan S, Rich IM, Lindsay GC, Bertram KA. The Department of Defense Congressionally Directed Medical Research Program: innovations in the federal funding of biomedical research. *Clin Cancer Res*. 2002;8(4):957-962.
64. Faden RR, Beauchamp TL, Kass NE. Learning health care systems and justice. *Hast Cent Rep*. 2011;41(4):3.
65. Jong MC, Boers I, van Wietmarschen HA, et al. Hypnotherapy or transcendental meditation versus progressive muscle relaxation exercises in the treatment of children with primary headaches: a multi-Centre, pragmatic, randomised clinical study. *Eur J Pediatr*. 2019;178(2):147-154. https://doi.org/10.1007/s00431-018-3270-3
66. Goertz CM, George SZ. Insurer coverage of nonpharmacological treatments for low Back pain-time for a change. *JAMA Netw Open*. 2018;1(6):e183037. https://doi.org/10.1001/jamanetworkopen.2018.3037
67. Seal KH, Becker WC, Murphy JL, et al. Whole health options and pain education (wHOPE): a pragmatic trial comparing whole health team vs primary care group education to promote nonpharmacological strategies to improve pain, functioning, and quality of life in veterans-rationale, methods, and implementation. *Pain Med*. 2020;21(Suppl 2):S91-S99. https://doi.org/10.1093/pm/pnaa366
68. Teyhen DSUSA, Robbins D, Ryan BA. Promoting and sustaining positive personal health behaviors-putting the person first. *Mil Med*. 2018;183(suppl_3):213-219. https://doi.org/10.1093/milmed/usy212
69. Heyward J, Jones CM, Compton WM, et al. Coverage of nonpharmacologic treatments for low Back pain among US public and private insurers. *JAMA Netw Open*. 2018;1(6):e183044. https://doi.org/10.1001/jamanetworkopen.2018.3044

70. Fritz JM, Davis AF, Burgess DJ, et al. Pivoting to virtual delivery for managing chronic pain with nonpharmacological treatments: implications for pragmatic research. *Pain*. 2021;162(6):1591-1596. https://doi.org/10.1097/j.pain.0000000000002139
71. Shippee TP, Schafer MH, Ferraro KF. Beyond the barriers: racial discrimination and use of complementary and alternative medicine among Black Americans. *Soc Sci Med*. 2012;74(8):1155-1162. https://doi.org/10.1016/j.socscimed.2012.01.003
72. Burgess DJ, Nelson DB, Gravely AA, et al. Racial differences in prescription of opioid analgesics for chronic noncancer pain in a national sample of veterans. *J Pain*. 2014;15(4):447-455. https://doi.org/10.1016/j.jpain.2013.12.010
73. Pletcher MJ, Kertesz SG, Kohn MA, Gonzales R. Trends in opioid prescribing by race/ethnicity for patients seeking care in US emergency departments. *JAMA*. 2008;299(1):70-78. https://doi.org/10.1001/jama.2007.64

How to cite this article: Ali J, Davis AF, Burgess DJ, et al. Justice and equity in pragmatic clinical trials: Considerations for pain research within integrated health systems. *Learn Health Sys*. 2022;6(2):e10291. doi:10.1002/lrh2.10291