

**Ethics and Regulatory Core Consultation Call:**

**Hybrid Effectiveness-Implementation Trial of Guided Relaxation and Acupuncture for Chronic Sickle Cell Disease Pain (GRACE)**

**December 10, 2020  
Meeting Participants**

Joe Ali (Johns Hopkins), Cheryl Boyce (NIH), Andrew Boyd (University of Illinois-Chicago), Judith Carrithers (Advarra), Tory DeMartelly (University of Illinois-Chicago), Ardith Doorenbos (University of Illinois-Chicago), Brandi Drumgole (University of Illinois-Chicago), Elaine Fluder (University of Illinois-Chicago), Andrew Garland (Johns Hopkins), John Lantos (Children’s Mercy Hospital), David Magnus (Stanford), MariJo Mencini (Duke), Bob Molokie (University of Illinois-Chicago), Stephanie Morain (Baylor), Pearl O’Rourke (Retired), Tammy Reece (Duke), Alison Santiago (University of Illinois-Chicago), Judith Schlaeger (University of Illinois-Chicago), Jeremy Sugarman (Johns Hopkins), Wendy Weber (NIH), Kevin Weinfurt (Duke), Dave Wendler (NIH), Ben Wilfond (Washington), Liz Wing (Duke)

AGENDA ITEMS	DISCUSSION	ACTION ITEMS
Overview of Demonstration Project	<ul style="list-style-type: none"> <li>● <b>Overview:</b> GRACE is a pragmatic, hybrid type 1 effectiveness-implementation trial that will be conducted across three large health systems. The trial will assess guided relaxation and acupuncture treatments, compared with usual care, for improving pain control in adults with sickle cell disease (SCD). The two treatments are widely used by patients, and there is an evidence base that the therapies are safe and effective for reducing pain. However, they have not been studied in this patient population nor across multiple health systems. The study also aims to determine the most appropriate and effective treatment sequence for any given patient based on their unique characteristics, and to describe the processes and structures required to implement guided relaxation and acupuncture within healthcare systems.</li> <li>● <b>Collaborative network partners:</b> <ul style="list-style-type: none"> <li>○ University of Illinois Hospital and Health Sciences System</li> <li>○ University of Florida Health</li> <li>○ Duke University Health System</li> </ul> </li> <li>● <b>NIH institute:</b> National Center for Complementary and Integrative Health (NCCIH)</li> </ul>	The project team will consider whether to add apheresis to the exclusion criteria for the study.

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	<ul style="list-style-type: none"> <li>• <b>Study design:</b> The UH3 implementation phase will randomly assign participants to one of three arms: guided relaxation (a mind-based therapy) versus acupuncture (a body-based therapy) versus usual care. The intervention will follow an adaptive design that responds to patients’ characteristics and evolving pain status. The adaptive intervention sequence consists of (1) initiate guided relaxation and either continue guided relaxation or switch to acupuncture for nonresponders at midpoint or (2) initiate acupuncture and either continue acupuncture or switch to guided relaxation for nonresponders at midpoint. The acupuncture intervention is two treatments per week for 5 weeks. The guided relaxation videos are delivered via a tablet device, used daily for 2 weeks and then any time the patient experiences pain.</li> <li>• <b>Outcomes:</b> <ul style="list-style-type: none"> <li>○ Primary: pain</li> <li>○ Secondary: mental and physical well-being and satisfaction with care</li> </ul> </li> <li>• <b>Other important notes about the study:</b> <ul style="list-style-type: none"> <li>○ The trial will use the Consolidated Framework for Implementation Research (CFIR) to plan, execute, and evaluate the associated implementation processes.</li> <li>○ There was a question about whether the timing of patients receiving apheresis would affect the pain outcome measures and whether that factor would be monitored. The study team said it is not an exclusion criterion; however, given that pain in SCD is complex, it may be worth considering whether to add it to the exclusion criteria.</li> </ul> </li> </ul>	
Status of IRB approval	<ul style="list-style-type: none"> <li>• The University of Illinois-Chicago (UIC) will be the single IRB of record. The SMART IRB platform will be used.</li> <li>• The team has approval from the IRB for the current UG3 phase, but the protocol for the UH3 phase has not yet been submitted. The UIC IRB must approve the protocol first, followed by the completion of reliance agreements from Florida and Duke.</li> </ul>	
Risk classification	<ul style="list-style-type: none"> <li>• The study team anticipates that the intervention will qualify as minimal risk.</li> </ul>	

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	<ul style="list-style-type: none"> <li>• There was discussion on the call about how this determination may relate to the possibility that the interviews may uncover potentially stigmatizing information such as opioid use disorder.</li> <li>• Similarly, responses to suicidal ideation by the patients would need to be considered by the IRB before a determination of minimal risk is granted.</li> </ul>	
Consent	<ul style="list-style-type: none"> <li>• Patients who are 18 years of age and older will be recruited from partner healthcare systems during a routine clinic visit, admission to the hospital, or in response to an IRB-approved flyer or social media invitation. Participants who meet all the inclusion criteria and none of the exclusion criteria will be asked to participate.</li> <li>• The trial will implement a full informed consent process for eligible participants. Consent will be written or electronic. Consent will be obtained separately from the providers who are participating in the focus groups being done as part of the implementation assessment.</li> <li>• There was discussion on the call about what the expectation of patients would be for receiving care since information obtained as part of the research will be placed in the electronic health record (EHR). It was suggested that, during the UG3 phase, the study team attempt to understand these issues.</li> </ul>	During the UG3 phase, the study team should attempt to understand what the expectation of patients would be for receiving care since information obtained as part of the research will be placed in the EHR.
Privacy/HIPAA	<ul style="list-style-type: none"> <li>• From the study protocol (attachment): “While PHI is necessary to initially identify patients with SCD, data will be stored on password-protected computers in locked offices at each site. To prevent any data breaches, we will follow the HIPAA Safe Harbor Standard for de-identification of all datasets. Study participants will not be personally identified in any publication about this research study. The information obtained because of participation in this research will not be included in medical records.”</li> </ul>	
Monitoring and oversight	<ul style="list-style-type: none"> <li>• NCCIH has its own requirement for establishing the DSMB. The NCCIH is currently reviewing names for the DSMB, and there are no concerns at this point.</li> </ul>	

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Issues beyond the study	<ul style="list-style-type: none"> <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> <li>• Those on the call discussed the implications of the CoC for safeguards and downstream protections in pragmatic trials in which data used for research is recorded in the EHR.</li> <li>• In the patient-reported outcome (PRO) consent form, the participant is informed that their data is shared in the EHR and becomes part of clinical care.</li> <li>• The study team said that, for this study, sharing PRO data with the clinical care team is essential for demonstrating to the clinicians that the intervention is effective.</li> </ul>	

# Study Protocol

[View the published protocol for the GRACE Demonstration Project.](#)

Citation: Doorenbos AZ, Schlaeger JM, deMartelly VA, et al. Hybrid effectiveness-implementation trial of guided relaxation and acupuncture for chronic sickle cell disease pain (GRACE): A protocol. *Contemp Clin Trials Commun.* 2023 Jan 18;32:101076. doi: 10.1016/j.conctc.2023.101076. PMID: 36852100.