NIH Collaboratory Ethics and Regulatory Core: UG3 Consultation Call
Hybrid Effectiveness-Implementation Trial of Guided Relaxation and Acupuncture for Chronic Sickle Cell Disease Pain (GRACE)
December 10, 2020

Attendees: 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	CURRENT STATUS As of March 18, 2022
Overview of Demonstration Project	**Overview**: 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. **Collaborative network partners**: • University of Illinois Hospital and Health Sciences System • University of Florida Health	The project team will consider whether to add apheresis to the exclusion criteria for the study.	The Demonstration Project is being implemented as described. Participation in a chronic transfusion/exchange program has been added to the exclusion criteria.

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	• Duke University Health System **NIH institute**: National Center for Complementary and Integrative Health (NCCIH) **Study design**: 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. **Outcomes**: • Primary: pain • Secondary: mental and physical well-being and satisfaction with care **Other important notes about the study**: • The trial will use the Consolidated Framework for Implementation Research (CFIR) to plan, execute, and evaluate the associated implementation processes. • 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		

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	may be worth considering whether to add it to the exclusion criteria.		
Status of IRB approval	The University of Illinois-Chicago (UIC) will be the single IRB of record. The SMART IRB platform will be used. 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.		All of the reliance agreements have been completed. The IRB protocol has been approved by the single IRB.
Risk classification	The study team anticipates that the intervention will qualify as minimal risk. 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. Similarly, responses to suicidal ideation by the patients would need to be considered by the IRB before a determination of minimal risk is granted.		The IRB determined that the study is minimal risk.
Consent	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. 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.	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.	Plans for consent and recruitment have not changed since they were discussed during the December 10, 2020, consultation. Obtaining data about patients' expectations regarding care were not part of the planned data collection in the UG3 phase, and there are no longer plans to place research information in the EHR; therefore, these data were not collected.

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	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.		
Privacy/HIPAA	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."		All PHI will be collected in REDCap, which is password-protected and secure.
Monitoring and oversight	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.		The DSMB is in place and has met twice.
Issues beyond the study	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. 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.		The study team is not currently placing any information in the EHR. However, an important aim of this study is to have relevant study information incorporated into clinical care. Ideally it would be possible for patient-reported outcomes (PROs) to be directly added to the electronic health record (EHR) through the

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	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. 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.		patient portal (MyChart). However, none of the healthcare systems will be fully capturing all 8 PROs through Epic at the start of the study. As a short-term solution, at the initiation of the UH3 implementation phase of the study, GRACE has moved forward at all 3 study sites collecting data in REDCap. At this point in time, we have not yet determined how we will communicate study findings to clinicians. As PROs start to be captured in REDCap, we will develop a clinician communication plan.
Additional follow-up information			The study team has not encountered any additional regulatory or ethics issues since the December 10, 2020, consultation.