NIH Collaboratory Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

Ethics and Regulatory Core Consultation Call:

Nonpharmacologic Options in Postoperative Hospital-based and Rehabilitation Pain Management (NOHARM)

Friday, December 20, 2019

Meeting Participants

Joe Ali (Johns Hopkins), Judith Carrithers (Advarra), Andrea Cheville (Mayo Clinic), Jennie Conroy (NIH), John Lantos (Children's Mercy Hospital), David Magnus (Stanford), Stephanie Morain, (Baylor College of Medicine), Pearl O'Rourke (Retired from Partners Health), Marguerite Robinson (Mayo Clinic), Tammy Reece (Duke), Marcel Salive (NIA), Kayte Spector-Bagdady (University of Michigan), Jeremy Sugarman (Johns Hopkins), Jon Tilburt (Mayo Clinic), Wendy Weber (NCCIH), Kevin Weinfurt (Duke), Liz Wing (Duke), Scott Wright (Mayo Clinic)

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020

Overview of Demonstration Project	• **Overview:** The NOHARM study aims to change the postoperative pain care paradigm to help curb the opioid epidemic. The goal is to encourage use of less harmful nonpharmacologic pain care while minimizing symptoms, preserving patient function, honoring patient values, and maintaining availability of opioids as a last resort. The study will use the electronic health record (EHR) to advance a consistent narrative about nonpharmacologic options and promote and honor patient preferences in pain management.
	• **Collaborative network partners:** Four Mayo Clinic–affiliated health systems spanning five states:
	  ○ Rochester, Minnesota (MCR)
	  ○ Florida (MCF)
	  ○ Arizona (MCA)
	  ○ Upper Midwest Health System, Iowa/Wisconsin (MCHS)		

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
	• **NIH Institute:** National Institute on Aging (NIA) • **Study design:** NOHARM is planned as a stepped-wedge, cluster-randomized trial testing a bundled Epic EHR-based intervention (including a conversation guide and clinical decision support) to elicit preferences for, document, and point patients toward evidence-based nonpharmacologic pain care for post-hospital, post-surgical pain. It will be implemented in the largest surgical practice areas within the participating health systems. The team has developed a prototype conversation guide to help facilitate better conversations between providers and patients about chronic pain management in ambulatory settings. In the UG3 phase, the goal is to pilot and confirm the functionality of all NOHARM bundle components, data collection procedures, and analytic strategies. In the UH3 phase, the intervention will be randomized sequentially among 18 practice clusters at 6-month intervals and will enroll up to 140,000 patients. Eligible surgeries include transtibial or transfemoral amputations, ankle or knee disarticulations, knee or hip arthroplasties, scheduled C-sections, gynecological surgeries, and colorectal surgeries. These surgeries were selected based on surgical volume and post-operative pain. The study team noted that they now have additional information on surgical volume and are in the process of modifying the inclusion criteria to ensure sufficient study enrollment.		• There have been no study design changes due to the COVID-19 pandemic. However, the study start will be delayed by 2 months (to March 1, 2021) to minimize the risk of starting and stopping the trial due to the pandemic.

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
	• There was a question on the call about the choice of stepped-wedge design. The study team stated that this design was considered ideal for operational reasons and because multiple practices eventually want access to the intervention. However, after consulting with the Collaboratory's Biostatistics and Study Design Core, the team stated that a phased rollout of a parallel design could be an option, and this is still under consideration. • **Primary and secondary outcomes:** The primary outcome is a composite of pain plus function. The team will measure a broad range of outcomes relevant to diverse decision makers, including opioid use, patient-reported outcome (PRO) measures, nonpharmacologic pain care (NPCC) use, healthcare utilization, and process measures. • The team is not collecting data on nonprescription drug use independent of the EHR. • Those on the call asked about a potential issue concerning the inclusion of research data in the EHR (see Issues beyond the study below).		• The choice of design was fully discussed with the Biostatistics and Study Design Core. Given the study outcomes of pain and function, the pragmatic nature of the trial, and the ability to identify sufficient procedure/practice clusters, the stepped-wedge design is being retained.

Status of IRB approval	• The single IRB of record is the Mayo Clinic IRB for both the UG3 and UH3 phases.
	• The status of phased IRB approvals is:
	  ○ Patient-facing intervention formative data and prototyping activities at the Rochester, MN, site (approved September 2019)
	  ○ Review preparatory to research (approved November 2019)
			The full trial IRB application was submitted in early May 2020 and approved in late May 2020.

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
	○ The team expects to submit a prospective intervention pilot at multiple sites to the IRB in mid-February ○ Plan to submit full multisite trial to the IRB in May 2020		
Risk classification	• There are burdens associated with eliciting and documenting patient preferences about nonpharmacologic care. • With respect to risk, there was discussion about the effects of the intervention in reducing opioid prescribing. • Those on the call thought that the NOHARM intervention would be deemed minimal risk because its purpose is to change physician behavior toward guideline-concordant practice. The intervention is not testing the guidelines, but rather whether following the guidelines reduces opioid prescribing while maintaining postoperative function and mitigating pain. • It was pointed out that guidelines from the National Academy of Medicine and the CDC (and others) indicate that opioids should be the last resort for pain, including postoperative acute pain. Guideline-concordant care should be a realistic option within existing delivery systems.		
Consent	• The approach to consent or other approaches to notification and authorization has not been decided yet by the study team. • There was discussion regarding that patient receptivity to the NPPC modality may be different		• Waiver of patient consent was determined to be permissible. After further deliberations with IRB leadership, a robust practice group authorization is also being

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
	after opioids are withdrawn and they are seeking care options. • This is a population-based study, and the study team hopes to have all eligible patients (who have qualifying surgeries) enrolled. The study team does not want patients to opt out before engaging in conversation as specified in the guide because they will not necessarily have the opportunity to communicate their preferred NPPC modality. • Those on the call discussed that the study team might be able to make the case for a waiver of consent because the study appears to be minimal risk and consent would be impracticable to obtain given the stepped-wedge design if it is selected and the nature of the intervention. The study team was encouraged to think about it more and can engage the Core again for further guidance. • There was a suggestion that the team should consider whether the clinicians are participants, because the study will collect information on clinician opioid-prescribing. The study team mentioned that they believed that the care team will not be at risk and can choose not to engage with the intervention. • The Mayo Clinic health system in Rochester, MN, has a special opt-out policy. Based on the Minnesota statute requiring research authorization: Data collected from patients who have not given permission for use of their EHR data for research		included. Specifically, in advance of each step, we will seek and document explicit endorsement for the trial from each involved practice group. • Mayo Clinic is an organization steeped in due process and group decision making. In this context, a practice-level endorsement model honors the agency of individuals and groups in the practice. In addition, proactive involvement of nursing leaders in the intervention build mitigated concerns about disruptiveness of the intervention to nursing workflows. In the end, clinicians will be able choose to engage the interventions to the degree they desire, as can patients (e.g., they are not required to fill out the fields of the conversation guide component of our bundled intervention prior to surgery).

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
	will not be utilized in the NOHARM trial analyses, reported on, or transferred to the PRISM Centers or outside institutions.		
Privacy/HIPAA	• From the team's supplementary material: Delivery of the intervention will include pain and anxiety monitoring via secure mechanisms and involvement of the study participant's surgical team. All exchanges of clinical information will comply with HIPAA standards of patient privacy, and all data collected, transferred, and stored for research purposes will be done in a manner to assure confidentiality.	Tammy sent the link for the HEAL Initiative's data sharing policy to those on the call (completed December 20, 2019): NIH HEAL Initiative Public Access and Data Sharing Policy: https://heal.nih.gov/about/public-access-data	
Monitoring and oversight	• To be determined. The NIA policy requires a 3-5 member DSMB to review the protocol up front and to review progress and safety issues periodically. The study team will confer with NIA to meet the requirements for monitoring and oversight. • DSMBs may still be used when the intervention is minimal risk, especially for large trials.		The study has a data and safety monitoring plan (DSMP), and a full DSMB will monitor and oversee the trial per NIA policy.
Issues beyond the study	• A certificate of confidentiality will be automatically provided per recent NIH policy. This certificate adds provisions for future research uses and confidentiality obligations for future data sharing. • The certificate has implications for sharing the dataset later if research data is added to the clinical record because the clinical record may then be considered as part of the research record.		

AGENDA ITEMS	DISCUSSION December 20, 2019	ACTION ITEMS December 20, 2019	CURRENT STATUS As of November 10, 2020
Additional follow-up information			• There was further discussion between the study team and a subset of Ethics and Regulatory Core members about what the investigator's obligations are regarding the collection of sensitive information, how to manage the identification of outlier patient reported outcomes, even in the aggregate, and when and how to give feedback to the healthcare system. • The DSMP outlines steps to monitor/audit for pain-related readmissions in the unlikely event that the intervention inadvertently constrained opioid prescribing. As the trial is initiated, if patterns of pain readmission are identified, or anecdotally noticed patterns of pain management that are contrary to the intentions of the trial, they will be discussed with the DSMB, and if relevant will be reported as an "adverse event" as outlined in the study's IRB application.