NON-PHARMACOLOGICAL OPTIONS IN POSTOPERATIVE HOSPITAL-BASED AND REHABILITATION PAIN MANAGEMENT: THE "NOHARM" TRIAL

Principal Investigators:
Andrea Cheville, MD, MSCE

Jon Tilburt, MD
Mayo Clinic, Scottsdale, AZ

Supported by:
The National Institute on Aging
UH3AG067593

IRBe # 20-004839
Protocol Version 6
September 21, 2023

TABLE OF CONTENTS

1 PRÉCIS iv
1.1 Study Title iv
1.2 Objectives iv
1.3 Design and Outcomes iv
1.4 Interventions and Duration iv
1.5 Sample Size and Population iv

2 STUDY TEAM ROSTER 5
2.1 Principal Investigators 5

3 PARTICIPATING STUDY SITES 6

4 STUDY OBJECTIVES 7
4.1 Primary Objective 7
4.2 Secondary Objectives 7

5 BACKGROUND AND RATIONALE 8
5.1 Background on Condition, Disease, or Other Primary Study Focus 8
5.2 Study Rationale 8

6 STUDY DESIGN 9

7 SELECTION AND ENROLLMENT OF PARTICIPANTS 10
7.1 Inclusion Criteria 10
7.2 Exclusion Criteria 10
7.3 Study Enrollment Procedures 10

8 STUDY INTERVENTIONS 12
8.1 Interventions, Administration, and Duration 12
8.2 Handling of Study Interventions 14
8.3 Concomitant Interventions 14
8.4 Adherence Assessment 15

9 STUDY PROCEDURES 16
9.1 Perioperative Care Pathway/NOHARM Touchpoints 16
9.2 Description of Evaluations 16

10 SAFETY ASSESSMENTS 18
10.1 Specification of Safety Parameters 18
10.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters 18
10.3 Adverse Events and Serious Adverse Events 18

10.4 Safety Monitoring 21

11 INTERVENTION DISCONTINUATION 22

12 STATISTICAL CONSIDERATIONS 23

12.1 General Design Issues 23
12.2 Interim analyses and Stopping Rules 24
12.3 Outcomes 24
12.4 Data Analyses 27
12.5 Subgroup analyses 29
12.6 Supplementary Analyses 30

13 DATA COLLECTION AND QUALITY ASSURANCE 31

13.1 Data Collection Forms 31
13.2 Data Management 32
13.3 Quality Assurance 33

14 PARTICIPANT RIGHTS AND CONFIDENTIALITY 35

14.1 Institutional Review Board (IRB) Review 35
14.2 Informed Consent Forms & Authorization Considerations 35
14.3 Participant Confidentiality 35
14.4 Study Discontinuation 35

15 ETHICAL CONSIDERATIONS 36

16 COMMITTEES 37

16.1 Project Workgroups/Responsibilities 37

17 PUBLICATION OF RESEARCH FINDINGS 40

18 REFERENCES 41

19 DESCRIPTION OF SUPPLEMENTS/APPENDICES 43

19.1 Appendix A: Clinician Participants 43
19.2 Appendix B: Resource List ..... **Error! Bookmark not defined.**

1 PRÉCIS

1.1 Study Title

Non-pharmacological **O**ptions in postoperative **H**ospital-based **A**nd **R**ehabilitation pain **M**anagement: the NOHARM trial

1.2 Objectives

The study objectives are 1) to test the impact of the NOHARM intervention on pain interference and physical function at 1, 2, and 3 months following surgery, 2) test the impact of the NOHARM intervention on opioid consumption, anxiety, and health care utilization during the 3 months following surgery.

1.3 Design and Outcomes

This is a pragmatic, embedded clinical trial using a cluster randomized stepped wedge design. Clusters are defined at the level of surgical department or division and qualifying surgical procedures and have been randomized to one of five different sequences to implement the intervention at staggered intervals. (See diagram in section 6 “Study Design”).

1.4 Interventions and Duration

The intervention being tested (i.e. compared to usual care/no intervention) is a multicomponent bundle of a Healing after Surgery Guide; electronic health record (EHR)-based clinical decision support; and resources to support and encourage use of nonpharmacological pain care (NPPC) approaches. Participants undergoing qualifying surgeries at participating sites will be enrolled in the NOHARM trial cohort when their qualifying surgery is scheduled. Participants will remain on the trial until final outcomes are collected at 3 months post-surgery.

1.5 Sample Size and Population

All Mayo Clinic patients undergoing a qualifying surgical procedure will be enrolled in the NOHARM trial. Based on surgical volumes from 2018 and the number of patients required for sufficient statistical power, we plan to enroll approximately 90,000 patients into the NOHARM trial.

2 STUDY TEAM ROSTER

2.1 Principal Investigators

Andrea Cheville, MD
Mayo Clinic
200 First Street SW, Rochester, MN 55905
cheville.andrea@mayo.edu
Principal Investigator

Jon Tilburt, MD
Mayo Clinic
200 First Street SW, Rochester, MN 55905
tilburt.jon@mayo.edu
Co-Principal Investigator

3 PARTICIPATING STUDY SITES

Mayo Clinic Rochester, Rochester, MN
Site Principal Investigator: Andrea Cheville, MD

Mayo Clinic Arizona, Phoenix, AZ
Site Principal Investigator: Jon Tilburt, MD

Mayo Clinic Florida, Jacksonville, FL
Site Principal Investigator: Cindy Tofthagen, PhD

Mayo Clinic Health System - Mankato, Mankato, MN

Mayo Clinic Health System – Eau Claire, Eau Claire, WI

Mayo Clinic Health System –La Crosse, WI

.

4 STUDY OBJECTIVES

4.1 Primary Objective

To test the impact of a multicomponent NOHARM intervention including a Healing after Surgery Guide, EHR-based clinical decision support, and resources to increase use of NPPC on pain interference and physical function at 1, 2, and 3 months following surgery.

4.2 Secondary Objectives

To test the impact of a multicomponent NOHARM intervention including a Healing after Surgery Guide, EHR-based clinical decision support, and resources to support use of NPPC on opioid use, anxiety, and health care utilization during the 3 months following surgery.

5 BACKGROUND AND RATIONALE

5.1 Background on Condition, Disease, or Other Primary Study Focus

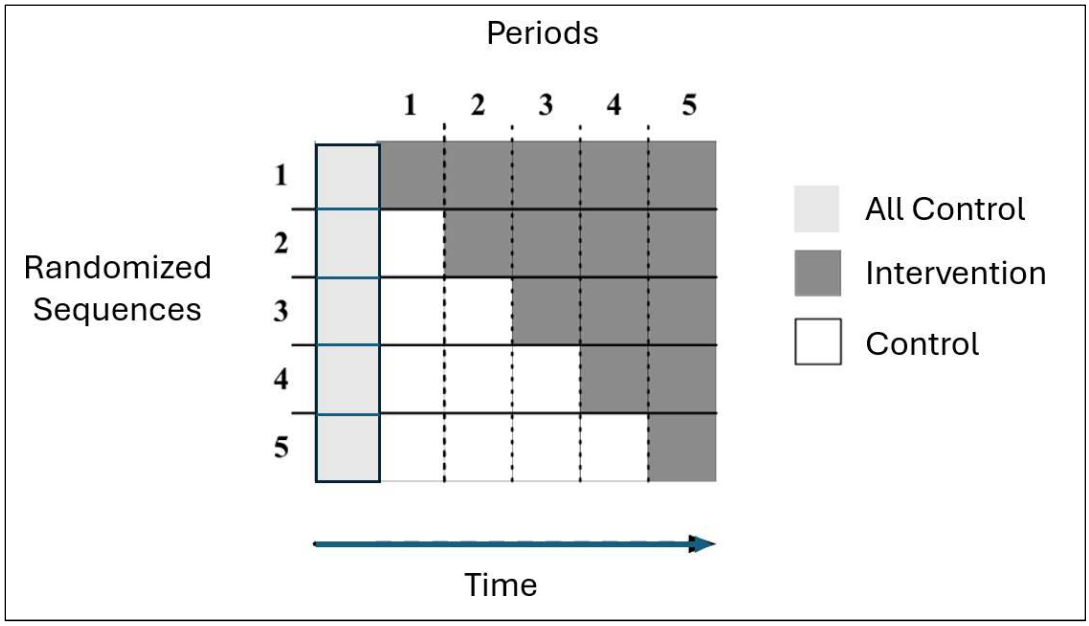
Prescriptions for narcotic pain relief after surgery result in unintended prolonged opioid use for hundreds of thousands of Americans.[1,2] That trend fuels an excess supply of opioids that can lead to dependence, addiction, diversion, and overdoses on a national scale.[3-10] Non-pharmacological pain care (NPPC) is effective and recommended by guidelines for perioperative pain while offering a more favorable risk-to-benefit ratio.[11-14]Additionally, patient and clinician decision support interventions are effective in encouraging patient-centered and guideline-concordant care in many other areas of medicine and hold great promise for promoting and facilitating post-operative non-pharmacologic pain management.[15,16]

5.2 Study Rationale

Nonpharmacological pain care is rarely used as first or second-line therapy after surgery, despite guidelines to the contrary. [17,18] NPPC offers a more favorable risk-to-benefit ratio than opioid medications which may play a critical role in acute post-operative management but should be tapered in favor of safer and more sustainable analgesic options as patients transition home and gradually resume their life roles. Additionally, patient and clinician support interventions have not been tested pragmatically as a bundle in everyday postoperative care as a means of facilitating the uptake of non-pharmacological pain management strategies in the perioperative setting and in the post-acute recovery timeframe. This study will address this knowledge gap and test the impact of utilizing patient and clinician decision support tools to inform patients and facilitate their preference for non-pharmacological pain management modalities.

6 STUDY DESIGN

This study will utilize a cluster randomized stepped wedge design. Clusters are defined at the level of departments/divisions and qualifying surgical procedures and have been randomized to one of five different sequences to implement the intervention at staggered intervals (one new sequence each wave, see diagram below).



The co-primary outcomes of the trial are PROMIS pain interference and physical function T scores at one to three months post-surgery. This will enable us to determine the effect of the NOHARM intervention on patient-centered outcomes. We hypothesize that increased use of validated NPPC modalities will additionally curb participants' consumption of opioids during the postoperative interval while hospitalized and following hospital discharge without increasing anxiety or health care utilization. Thus, our secondary outcome(s) are opioid use, PROMIS anxiety T scores, and health care utilization (emergency department visits, hospitalizations, and intensive care unit admissions) during the 3 months following the index surgery. This will enable us to understand the impact of our EHR-embedded decision support intervention in an era where opioid prescribing is already being constrained.

All patients receiving common, pre-defined procedures within 7 surgical departments or divisions (e.g., practice areas) at 6 Mayo Clinic locations will receive the trial intervention if their surgery date coincides with the stepped wedge implementation schedule. Study locations include Mayo Clinic Rochester, Mayo Clinic Florida, and Mayo Clinic Arizona, as well as three Mayo Clinic Health System sites (Mankato, MN; La Crosse, WI; and Eau Claire, WI). Participating surgical departments and divisions will include orthopedic surgery, colorectal surgery, gynecological surgery, obstetrics, pulmonary/thoracic/lung surgery, liver and kidney transplant, and cardiac surgery. Due to variable combining of post-op unit care areas, practice size, and related considerations we have formed 22

clusters that will be randomized across 5 sequences.

Enrollment in the intervention arm of the trial will extend from March 2021 to through January 2024.

The intervention consists of enhanced electronic medical record functionality that interfaces with a Healing after Surgery Guide in Epic *MyChart* patient portal. The Healing after Surgery Guide encourages patients to make a plan for post-operative pain management, to understand the risks and benefits of opioids, and to utilize validated NPPC techniques that appeal to them. The intervention also includes EHR tools that remind and prompt clinicians to encourage patients to use their selected NPPC techniques throughout the perioperative period, particularly postoperatively Trial outcomes will be extracted from the EHR. Patient reported outcome measures will include those collected in routine peri-operative care, as well as a limited number specific to the NOHARM trial; self-reported opioid consumption and NPPC modality use after surgery.

SELECTION AND ENROLLMENT OF PARTICIPANTS

6.1 Inclusion Criteria

All patients 18 years of age and older undergoing qualifying surgeries at participating sites will be eligible.

6.2 Exclusion Criteria

None.

6.3 Study Enrollment Procedures

All eligible surgeries at participating sites and within participating departments and divisions will be enrolled in this minimal risk, population-based study. An automated EHR algorithm will identify surgeries meeting inclusion criteria for the NOHARM trial based on age, surgical procedure, clinical department/division, and location.

During usual care periods, patients will receive usual perioperative pain care; data collected during these periods will serve as “control” data in this stepped wedge study.

During intervention periods, patients scheduled for qualifying surgeries; as well as their surgical care teams, physical and occupational therapists, and unit nurses will be exposed to the intervention per the randomization scheme. Because the intervention is embedded in the EHR, patients who are unable to interact with the portal-based Healing After Surgery Guide will not be able to enter their NPPC selections which are needed to drive the EHR-based algorithms and clinical decision support tools. However, patients may receive a printed version of the Healing After Surgery Guide during Pre-procedural Evaluation Clinic visits. Additionally, the patients who do not interact with the Healing after Surgery Guide via the EHR patient portal prior to their hospital admission` will have the opportunity to select NPPC modalities during their hospitalization, both pre- and post-operatively. By communicating their NPPC selections to their unit nurses,

their preferences will be entered into the EHR via flowsheets. Subsequently, all EHR clinical decision support functionalities to encourage NPPC use will be operational for these patients. Cognitive limitations, lack of English fluency, or psychiatric illness may result in an inability to use the Healing After Surgery Guide which may also result in reduced exposure to the intervention.

7 STUDY INTERVENTIONS

7.1 Interventions, Administration, and Duration

Once the NOHARM intervention is activated in a cluster, patients undergoing qualifying surgical procedures will be exposed to the NOHARM intervention.

The intervention includes:

Healing after Surgery Guide:

The Healing after Surgery Guide (HAS) is an interactive module in the Mayo Clinic patient portal (MyChart). Scheduling of an eligible surgery will trigger an EHR algorithm to automatically send a message to the patient's portal describing the need for an "individualized pain management plan to promote healing after surgery." The portal message will provide a link allowing patients to access and engage with the HAS Guide before their surgery. The HAS Guide will encourage realistic expectations about post-surgical pain, educate patients on thirteen evidence-based, non-pharmacological pain management strategies (all robustly validated and endorsed in clinical guidelines), and encourage patients to select the NPPC modalities that appeal to them in managing post-acute pain during the months following their discharge. Supported NOHARM NPPC modalities will include yoga, tai chi, walking, guided imagery, music listening, progressive muscle relaxation, relaxed breathing, meditation, aromatherapy, transcutaneous electrical nerve stimulation (TENS), massage, acupressure, and heat or cold. Patient selections elicited via the Healing After Surgery Guide will prompt a follow-up portal message, acknowledging the patient's NPPC selections and extending the opportunity for them to receive a printed Healing After Surgery workbook if they request that such resources be mailed to them. Patients will have the opportunity to receive portal messages based on their responses to the Healing After Surgery Guide, as well as based on the length of time from surgery. These messages will include directions on how they can access the website, join Zoom support calls if desired or contact the NOHARM team. Section 8.1.1 gives a breakdown of the possible portal messages. The Zoom support calls referenced in the portal messages are to assist patients with their selected modalities if they so wish. Patients will log into these calls anonymously and PHI will not be discussed. There will be calls that center around specific modalities as well as open Q&A style.

EHR-based Clinical Decision Support:
The NPPC selections will be stored in the EHR and used to prompt perioperative clinician interactions, direct education delivered by unit nurses, inform modality choices during physical and occupational therapy sessions, and populate patients' pain management plans for controlling pain following hospital discharge. Their NPPC selections will additionally determine the content that will auto populate their discharge summaries. The NPPC-specific discharge summary content will assist participants in using their preferred modalities in their home environments and to effectively identify and pursue local resources, e.g., certified medically specialized masseuses. Additionally, patients' NPPC selection will be visible to

clinical providers on the Epic inpatient Summary view. These components align with standard of care.

Mayo Education Material:

A suite of self-management educational materials will be available to support patients' use of NPPC modalities and to help them trouble shoot and refine the use of their selected modalities. These print materials and videos provide information and instruction on the safe and appropriate use of NPPC strategies for addressing post-surgical, post-acute pain. The materials additionally clarify how patients may adapt NPPC modalities to derive optimal benefit given their unique requirements and post-surgical precautions. All education materials have been developed, vetted and approved through Mayo Clinic's Office of Patient Education processes and reflect existing standard of care for patient education. These materials will be available to patients via the Healing After Surgery website (healingaftersurgery.mayoclinic.org) and on Mayo Clinic Television which participants can access while hospitalized. Brief video descriptions of each NPPC modality are imbedded in the Healing After Surgery Guide. The materials include video and print resources, with the latter being available in both electronic and paper formats. The materials offer informational, instructional, and guided experiential content for all NOHARM NPPC modalities, as appropriate. A Healing After Surgery Workbook is also available. The workbook offers patients a location to record their experiences, concerns, and successes, as well as providing motivational messages.

Patients may view the self-management educational materials during their hospital stays on Mayo Clinic television. Based on patients' NPPC modality selections, inpatient nurses will be prompted to show patients how to navigate to the materials on Mayo Television, familiarize them with the Healing After Surgery website, and provide them with print materials if desired. Nurses will also use educational materials to discuss pain management planning with patients to refine their management plans following hospital dismissal.

The materials will be available on a website, DVD, and Mayo Clinic TV. Unit nurses will be able to give patients printed PDFs, as required. Additionally, patients will receive a copy of the Healing After Surgery workbook via mail after they are enrolled onto the study. They will also have the ability to request from their portal messages that a print copy of the workbook be mailed to them.

See Section 8.1.1 NOHARM Resource List for a brief description of the NOHARM materials.

Perioperative live NPPC Support Resources

Patients have the opportunity to engage with Mayo Clinic specialists in NPPC modalities perioperatively to support their selection, troubleshooting, and use of the modalities. Patient are notified of live support resources through their patient portal upon completion of the Healing After Surgery guide. Those and are given a RACK card distributed a. he pre-operative consultation. This support is restricted to NPPC modalities and patients are clearly informed that any questions relating to

medications and other analgesic approaches should be directed to their surgical care teams. This support is set up to maximize the patient's successful self-management of the NPPC both pre and post operatively. NOHARM NPPC live support will include:

1. Toll free call for 1-on-1 discussion of individualized needs.1-833-919-1432
2. Presentations and group discussions via a virtual platform (Zoom technology).

See Appendix B NOHARM Resource List for a brief description of the NOHARM materials.

Clinical team decision support:

Patient NPPC modality selections elicited from the Healing After Surgery Guide will be converted to discrete EHR data elements that will prompt CDS after surgery. CDS tools that promote use of preference-sensitive, guideline-concordant NPPC modalities at defined touchpoints on the perioperative care trajectory will encourage clinicians, nurses, and physical/occupational therapists to discuss NPPC modalities with patients and pre-populate fields and functionalities within Epic such as the "After Visit Summary".

See Section 8.1.1 NOHARM Resource List for a brief description of the NOHARM materials.

7.1.1 NOHARM Resource List – Found in Appendix B

7.2 Handling of Study Interventions

The NOHARM intervention Healing after Surgery will be assigned to patients using an EHR Boolean logic-based algorithm that includes cluster status (intervention vs usual care control), age, surgical procedure, clinical department, and location. The algorithm is updated for each cluster that transitions from the control to the intervention state. The intervention will be delivered to patients and their care teams via the patient portal and EHR, respectively.

7.3 Concomitant Interventions

This is a pragmatic, population-based clinical trial. All eligible patients undergoing qualifying surgical procedures who receive care at the 6 participating sites will be enrolled, regardless of medications, treatment, supplements or other interventions they may be taking/receiving.

7.3.1 Allowed Interventions

The interventions in this study are a patient-facing "Healing after Surgery Guide," a clinical team-facing CDS, and a suite of vetted patient education materials to support patients use of their preferred NPPC modalities. These

interventions could prompt utilization of NPPC modalities prior to, during, and after the hospital stay.

7.3.2 Required Interventions

Among participating practices, the Healing after Surgery Guide functionality and CDS components of the intervention will be turned on according to the pre-specified randomization scheme. How or whether patients and care teams choose to interact with the various intervention components and resources will be at their discretion.

7.3.3 Prohibited Interventions

None. EHR functions cannot be fully inactivated at the patient level. However, if patients request not to receive portal messages, these will be discontinued. Patients can decide whether, how, and when to interact with the intervention components. Records of patients who have previously indicated they do not want their medical record used for research purposes will have data associated with their care redacted from final analytic datasets.

7.4 Adherence Assessment

Patients will be encouraged, but not required, to interact with the NOHARM Healing after Surgery Guide and to utilize suggested NPPC modalities.

Additionally, patients who are unable or unwilling to interact with the portal-based Healing After Surgery will not provide the NPPC selection data needed to populate and drive the EHR-based algorithms and clinical decision support tools. Therefore, these individuals will be more limitedly exposed to the intervention. They will be encouraged to use the Healing After Surgery Guide during day-of-surgery intake and post-operative care processes, but this may not occur due to many competing demands, or patient preferences.

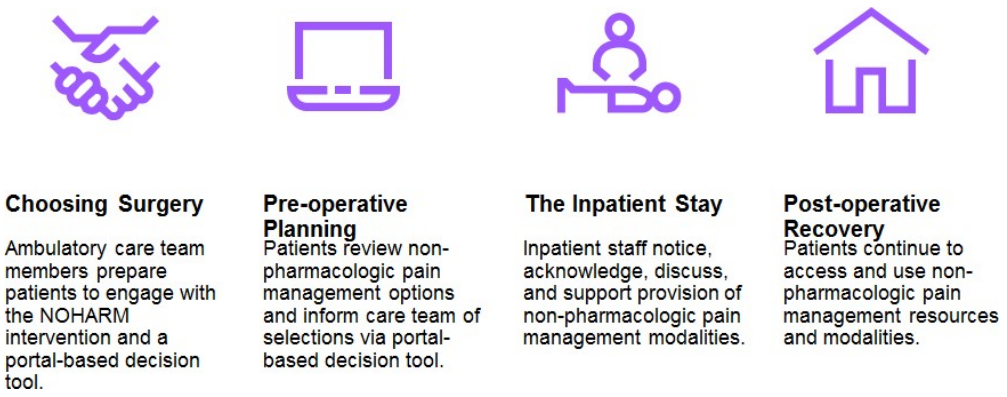
Cognitive limitations, lack of English fluency, or psychiatric illness may result in inability to use the HAS Guide or complete the electronic patient reported outcome measures (ePROMs).

Interaction with the NOHARM HAS Guide, completion of ePROMs and utilization of NPPC modalities will be assessed by time-stamped links associated with the Healing after Surgery Guide while ePROMs and NPPC modality use will be extracted from the medical record.

8 STUDY PROCEDURES

8.1 Perioperative Care Pathway/NOHARM Touchpoints

The figure below briefly summarizes the perioperative care pathway along which our bundled, EHR-based intervention will be implemented.



8.2 Description of Evaluations

8.2.1 Choosing Surgery and Pre-Operative Planning Touchpoints

Touchpoint 1- Choosing Surgery

Ambulatory care team members prepare patients to engage with the NOHARM intervention (portal-based Healing after Surgery Guide) at the time surgery is scheduled. Members of participating surgical divisions and departments will be oriented to the NOHARM trial and benefit from ongoing implementation efforts. In addition, they can contact the NOHARM team via a pager on weekdays. However, the decision to use these resources or present the NOHARM intervention to their patients was left to each team's discretion.

Touchpoint 2 – Pre-operative Planning

Patients interact with the Healing after Surgery Guide via their Epic EHR MyChart portals. The Healing After Surgery Guide will allow patients to select NPPC techniques that appeal to them and develop an individualized NPPC plan. Patients will be encouraged to familiarize themselves with and practice NPPC modalities prior to their hospital admissions. Additionally, they will be encouraged to obtain needed supplies, engage their caregivers, and even schedule appointments with NPPC practitioners prior to their hospitalizations so that their individualized pain management plans may be seamlessly transitioned from the hospital to the home or post-acute care setting.

8.2.2 Inpatient Stay Touchpoints

Touchpoint 3 – Acute Hospital Care

Nursing and physical/occupational therapy staff will offer patients the opportunity to receive preference-concordant NPPC modalities during their hospital stay. For self-administered practices, staff will validate patients' preferences and ensure the availability of needed supplies, instruction and ambient conditions (e.g. privacy).

If patients are not experiencing adequate pain relief, they will be prompted by nurses to try alternative NPPC modalities in order to raise awareness of potential opioid harms and enhance clinician support for patients' preferred NPPC use. Additionally, NPPC nurse and physician specialists will be "on call" to assist unit nurses, therapists, and members of the surgical care team in how to optimize the safety and effectiveness of NPPC modalities for specific patients.

Touchpoint 4 – Hospital Discharge

During the discharge process, patients will be asked to revise their NPPC plan, as needed, based on their preferences and responses to specific NPPC modalities, and provided with support and resources. Discharge planning will facilitate continuation of patients' NPPC use in their post-acute care settings (e.g. home, rehabilitation facility, etc.). Patients will be given prescriptions to receive local NPPC, if available and/or appropriate.

Patients' discharge summaries will be auto-populated with selection-concordant NPPC instructions and resources to find local NPPC providers.

8.2.3 Post-Hospital Discharge Recovery Touchpoints

Touchpoint 5 – Remote Healing After Surgery Guide Use and Postoperative Follow-up

Patients will be encouraged to use the Healing After Surgery and follow their individualized pain management plans during their post-surgical recovery.

Opioid refill requests during the 3-month postoperative interval will trigger messaging via the patient's portal with information regarding how to access resources to support their NPPC use. Patients will be encouraged to utilize the live support resources, particularly the 1-on-1 calls in order to select and adapt use of modalities for optimal benefit.

9 SAFETY ASSESSMENTS

This is a minimal risk study. Participants are considered "enrolled" as soon as they meet study inclusion criteria. Participants will be automatically assigned to receive study interventions and/or measurements.

9.1 Specification of Safety Parameters

There are no pre-specified safety parameters, as they are not applicable to the intervention being studied. This study engages patients in strategies for post-surgery pain management that conform to guideline-based care, all of which have far lower risk profiles (almost zero risk) and greater benefit-to-risk ratio compared to usual post-surgical pain management that involves opioid medications. Patients whose pain cannot be sufficiently managed with non-pharmacological pain management strategies will be supported by their surgical team (with assistance from pain management clinicians, as needed) using conventional pain management approaches.

9.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

Our interventions are informational and logistical and designed to enhance safe, patient-centered approaches to patient care. If they were to prompt, for instance, less opioid use, in theory, that could lead to worse function or increased pain. That is why we chose the co-primary outcome measures of pain interference and physical function. Whether it is accurate to associate that "risk" to our intervention itself, versus the treatments prompted by our intervention is a topic of debate. Nevertheless, this is a minimal risk study. If we conservatively assume that downstream prescribing practices are attributable to our interventions, usual care (using opioid medications as a first line approach to pain management in the acute and post-acute recovery periods following a surgical procedure) introduces greater risk of dependency, addiction, and overdose, than those posed by the intervention we are providing in the NOHARM trial which is guideline concordant.

9.3 Adverse Events and Serious Adverse Events

Adverse Event (AE): Any untoward or unfavorable medical occurrence resulting unambiguously from the misuse or overuse of non-pharmacological pain management strategies facilitated by the intervention. All untoward or unfavorable medical occurrences will be first assumed to be associated with the patient's surgery. Untoward or unfavorable medical occurrences will be deemed an adverse event only if they can be clearly associated with use of non-pharmacological pain management strategies recommended and/or facilitated by the intervention and could not, under any circumstances, have otherwise happened.

Serious Adverse Event (SAE): Any adverse event unambiguously associated with the intervention that:

- Results in death

- Is life threatening, or places the participant at immediate risk of death from the event as it occurred.
- Requires or prolongs hospitalization.
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- It is another condition which investigators judge to represent significant hazards

There are no laboratory or other clinical values which may be used to assess safety concerns related to the intervention. Patient reported pain, requests for assistance with pain management, and other health outcomes, while measurable, are associated with the patient's surgical procedure and will be gather as part of the ultimate outcome data. If patients were to experience a paradoxical response to a modality –massage, for example – those effects would likely be transient, and they would have access to all the usual care resources of Mayo Clinic as any other patient should those symptoms persist.

Adverse events that may be anticipated in the study involve any patient misuse or overuse of non-pharmacological pain management strategies. Patients who elect to incorporate non-pharmacological pain management strategies in their recovery from surgery will be instructed in the use of those strategies, including whether (and when) the use of those strategies is appropriate in their situation.

Because non-pharmacological pain management modalities recommended by the intervention are guideline concordant approaches to pain management under normal circumstances, they will be monitored by the patient's surgical team as a part of usual post-acute care. Therefore, we will not actively review for potential events with scheduled promptings, apart from those that we will collect via the EHR for Data and Safety Monitoring Board and trial outcome reporting.

Unprompted adverse events are possible but not expected. Surgical teams will inform the study team if they are made aware of any untoward medical occurrence that could reasonably be attributed to a patient's misuse or overuse of non-pharmacological pain strategies as a direct result of the facilitation provided by the NOHARM intervention. Such events are highly unlikely, and the risks of such events leading to unfavorable outcomes are almost non-existent. The risks of participant cooperation in the NOHARM intervention are far less than the risks of usual care which often involve opioid medications alone in the acute and post-acute recovery periods.

9.3.1 Reporting Procedures

An AE or SAE will be suspected if a member of the patient's surgical team or any member of the study team who interfaces with the patient for any reasons suspects that a patient is experiencing a medical issue that is unambiguously related to the patient's interaction with the NOHARM intervention.

The principal investigator, relevant study team members, and any relevant members of the surgical team will adjudicate the relevance of the patient's experience to the NOHARM intervention (versus an anticipated result of the patient's surgical procedure).

If a patient's experience or outcome is determined to be an AE or SAE by protocol definition, then that patient's experience will be documented and reported per institutional procedures. The surgical team and/or members of the study team with expertise in post-surgical pain management will follow up with that patient to ensure that appropriate steps are taken to mitigate any negative outcomes and ensure that the patient is properly informed and educated about safe use of non-pharmacological pain management strategies for the remainder of their surgical recovery.

Severity of the Event

All AEs will be assessed by a qualified medical professional using a protocol defined grading system.

Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities.

Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

Relationship to the Study Intervention

Because this is a minimal risk study and the intervention may be construed as less risky than usual care, it would be inappropriate to regard the study intervention as suspect, by default, for all medical occurrences in the perioperative period. For this reason, the principal investigator, clinical experts on the study team, and the patient's surgical team will adjudicate the relevance of patient events outcomes in a binary fashion:

- Not related to the NOHARM intervention. This will be the presumption, unless proven otherwise. Patients may be expected to have many challenges to overcome following a surgical procedure. These challenges are unrelated to the intervention.
- Related to the NOHARM intervention. The study team will evaluate all occurrences suspected of being associated unambiguously with the NOHARM intervention and adjudicate their relevance. We do not expect any AEs or SAEs to result from the NOHARM intervention.

9.3.2 Follow-up for Adverse Events

Patient events suspected of being AEs or SAEs will be addressed immediately by the Principal Investigator, relevant experts on the study team, and/or the patient's surgical team. Upon determination that an event is indeed an AE or SAE, appropriate actions will be taken, including contacting the patient and providing instructions.

All events suspected of being AE will be documented, and documentation for recorded events subsequently determined to be an AE or SAE will be updated. All AEs and SAEs will be followed to adequate resolution.

The study coordinator will record all events reportable by the definitions above occurring any time following patient enrollment and limited to the last data collection point in the study. All events are expected to occur in the acute or early post-acute periods of recovery.

For safety monitoring, Data and Safety Monitoring Board reporting, and trial outcomes reporting, participants were monitored via the EHR for adverse events potentially related to use of NOHARM modalities. These included electrode burns, myalgias or muscle strain, and falls.

Because the intervention could inadvertently lead to opioid underdosing among patients with cancer-related or other severe chronic pain, we also monitored episodes of severe pain meeting criteria for failure to rescue, defined as three consecutive numerical pain ratings of at least 7 on a 0–10 scale during intervention and usual care periods.

9.4 Safety Monitoring

The Data and Safety Monitoring Board and/or Safety Officer appointed by the NIA will monitor the conduct of the study.

10 INTERVENTION DISCONTINUATION

This study is a pragmatic clinical trial, and as such, patients will not be individually consented. However, voluntariness is preserved as patients and surgical teams are encouraged, but not required, to engage with any component of the intervention. Additionally, as a pragmatic clinical trial, "the intervention" will be systematically implemented at the surgical practice level, per the stepped-wedge schedule, as an element of usual care.

Therefore, discontinuation of the study, whether for an individual participant or for all participants at once is defined as the cessation of study measurements prespecified by the study timeline. The discontinuation of the study intervention components, if merited, will be at the discretion of the surgical specialties in conjunction with the DSMB; discontinuation is not anticipated.

Removal individual patients from the trial will be functionally achieved in the following situations:

- The patient actively requests to have their records withdrawn from the NOHARM study dataset.
- Patients previously indicating their unwillingness to have medical record data used for research purposes will have their records redacted from final study datasets prior to analysis.

Cessation of study measurement will happen for the entire trial in the event that:

- Institutional needs / priorities preclude our ability to conduct study procedures (e.g. in the case of institutional response to COVID-19).
- The study funder requests that study activities cease.

In the event that an individual patient withdraws from the study or the entire study ceases, patients will still be monitored by their surgical team per usual care practices for the duration of their post-acute recovery period. Cessation of study procedures will not impact patients' access to standard supportive care following surgery.

11 STATISTICAL CONSIDERATIONS

11.1 General Design Issues

This study will address the primary objective using a cluster randomized stepped wedge design. Surgical practices, or clusters, will be randomized in 5 sequences to receive the NOHARM intervention; outcomes of patients treated by these practices (also referred to as departments and divisions) will be compared by intervention status of the practice. The primary statistical hypothesis is that pain interference and physical function measures will be lower and higher, respectively, in the patients treated during intervention periods, when compared with those treated during control (non-intervention) periods in those same practices.

The cluster randomized stepped-wedge design will allow us to stagger the NOHARM implementation while increasing statistical power. The alternative to staggering the implementation would be to implement at all sites at the same time, which is impractical from a resource and implementation perspective. The stepped-wedge design allows each site to serve as its own control, reducing the bias due to imbalanced risk factors across clusters. Contamination does pose some threat to the internal validity of stepped wedge designs when, as here, the intervention rolls out sequentially in adjacent clusters. The 22 NOHARM clusters will minimize potential contamination by capitalizing on geographical separations in the built environments used to deliver perioperative care including different buildings in some cases, as well as subspecialty-designated inpatient wards, office suites, etc.

In cases where post-operative care for two or more clusters was delivered on the same hospital unit, only the largest cluster by historical patient volume was retained. This approach ensured that unit nurses would not simultaneously care for patients in clusters assigned to both control and intervention periods.

The primary hypothesis was that the NOHARM intervention would reduce patient-reported pain interference and improve physical function following index surgical procedures, relative to usual care. Co-primary outcomes, pain interference and physical function during the 3 months following index surgery, were assessed using PROMIS CATs.

The secondary hypothesis was that the NOHARM intervention would reduce total opioid exposure during the 3 months following index surgery, without adversely affecting anxiety (assessed using PROMIS CAT) or health care utilization, defined as counts of emergency department visits, hospitalizations, and intensive care unit admissions.

Sample Size and Randomization

Using pain data for 6,261 patients with these procedures at six sites, we estimated the intra-cluster correlation coefficient (ICC) for the pain score to be modest ρ = 0.037. To assess minimal detectable effects, we simulated a large number of randomizations and estimated the detectable effect for each. Specifically, for P = 1….,5000 permutations, the 22 clusters were randomly assigned to 5 waves. For each permutation, the closed form solution of Harrison et al (2019) was used to

estimate SE(Q) (derived from the formula of Hussey, Hughes (2008)) for true effect Q. We used the values $\sigma^2 = 1$ and $\tau^2 = 0.488$ for the within and between variance components so that detectable effects would be in SDs, and assumed ICC would be 0.037. Over the 5,000 permutations, the detectable effect ranged between 0.048SD and 0.055SD.

11.1.1 Treatment Assignment Procedures

In order to balance cluster characteristics, we applied a constrained randomization procedure. Constrained randomization allows us to balance a larger number of cluster characteristics than is possible through stratification. Here the key cluster characteristics to be balanced were: site (6 locations), volume (estimated using 2018 data), procedures (3 groups), and number of practices (1-4). Given only 22 sites, it would not be practical to stratify or apply minimization, while constrained randomization allows us to select an allocation of sites to waves from among a set of allocations that has better balance on these factors.

Specifically, we generated 100,000 allocations of the 22 clusters to 5 waves. For each allocation, we then calculated a balance metric B as follows. For each characteristic c listed above, let $X(c)_i$ be the value of c for each cluster i=1,...,22. For categorical factors X is an indicator, for volume and number of teams X is a number, rescaled to range from 0-1. Let w=0,...,5 be the baseline (w=0) and 5 intervention waves; and for a given allocation, let S_i = the first wave at which cluster i is allocated to intervention. Then we calculate for each allocation the balance metric

$$BB = \sum_{ww=0,\ldots,5} \left(\left| \frac{1}{\#\{S_{ii} = ww\}} \sum_{cc} XX(cc)_{ii}(SS_{ii} = ww) - \frac{1}{\#\{SS_{ii} > ww\}} \sum_{cc} XX(cc)_{ii}(SS_{ii} > ww) \right| \right)$$

After generating 100,000 allocations, we constrained selection to those with values of B in the lowest decile; we then selected one allocation randomly from those 10,000 'acceptable' allocations. This process resulted in a full allocation of all 22 sites to waves 1-5 prior to initial intervention.

11.2 Interim analysis and Stopping Rules

This is a minimal risk study for which there is no planned interim analysis. Interim analysis may be conducted at the request of the DSMB or if necessitated by unforeseen changes in the study plan (e.g. loss of a study site). Similarly, there are no pre-specified stopping rules as the probability and magnitude of adverse experiences are not greater than those ordinarily encountered in daily life.

11.3 Outcomes

Outcomes will be collected via the Epic EHR. PROMs will be collected using interfaces available to patients in their MyChart patient portals and the Welcome tablet functionality at point of care as available. Because outcomes will be either PROMs or data entered by providers during routine care delivery, requirements for

adjudication will be minimal. Health care utilization is an exception in that criteria for hospitalizations vary based on designations of observational status. The NOHARM Data Management working group will identify hospitalizations that may require adjudication, including emergency department stays that exceed 24 hours. A committee blinded to a patient's affiliation with an activated or control cluster will determine whether to designate such instances as hospitalizations.

The cadence and mode of PROM data collection are outlined below. PROMs comprise the NOHARM trial's co-primary and many of its secondary outcomes. PROMs will additionally be collected for use in describing the study population and for analytic adjustments.

11.3.1 Primary outcome

Physical function and pain interference, as measured with the Patient Reported Outcome Measurement System (PROMIS) computer adaptive tests (CATs) are the co-primary outcomes. The CATs in the Mayo Clinic Epic EHR have been parameterized with stopping rules based on number of items administered rather than a standard error of measurement-defined threshold. IRT-based instruments have generally better discrimination across the entire trait range than legacy PROMs,[19,20] and CAT administration enhances measurement efficiency and precision.[21,22] The PROMIS item banks have been validated in the target populations.[23-25] The PROMIS physical function and pain interference CATs will be assigned via an automated Epic function at precisely months 1, 2, and 3 following each patient's index surgery. Patients will receive an automated reminder message via their patient portals prompting them to complete the PROMs.

Because post-operative visit requirements and sequences vary across surgical practices, administration of the PROMIS CATs will not be linked to a specific visit, but rather assigned automatically after 1, 2, and 3 months have elapsed since the index surgery. If this data coincides with a clinic visit, then patients will be encouraged to complete the PROMIS CATs via the Epic Welcome interface using a tablet in the waiting room prior to their clinic visit.

Because some participants may lack patient portal accounts, potentially more common in certain sociodemographic subgroups, we will use mailed PROMIS 6-item short forms to assess the co-primary outcomes in these individuals. In addition, because some participants with portal accounts are infrequent users, PROMIS 6-item short forms will be mailed to those who did not complete the month 1 PROMIS CATs.

PROM data collected via printed short forms will only be included in sensitivity analyses because their inclusion was not part of our initial design as documented in our published protocol manuscript, as well as the trial description in clinicaltrials.gov. Additionally, the short forms differ

from the CATs in administration mode, item content, and standard error of measurement. The sensitivity analyses will allow for the assessment of response bias.

For participants who submitted more than one short form within a given assessment period, the response with a timestamp closest to the target time point was used.

11.3.2 Secondary outcomes

Secondary outcome measures will include opioid consumption, NPPC use, health care utilization and anxiety. Anxiety will be measured in a manner similar to physical function and pain interference with a PROMIS CAT administered via the Epic MyChart portal or the Welcome tablet interface prior to a clinic visit that coincides with the 3-month post-surgical time point.

Opioid consumption will be collected using three methods. First, opioid administration per hospital day, will be extracted from the medication administration log in the EHR. Opioid data extraction will be performed for the hospitalization of index surgery as well as any subsequent hospitalizations during the 3 months following the index surgery. As in previous work, [26-28] parenteral, transdermal, and oral opioid consumption will be expressed as morphine milligram equivalents (MMEs). Oral and transdermal opioids prescribed by a Mayo Clinic provider at the time of hospital discharge and during the interval between hospital discharge and the 3 month post-surgical assessment point will be extracted from the EHR and converted to MMEs. Last, because outpatient prescriptions do not accurately capture opioid consumption, patients will be queried at the 3 month post-operative time point regarding their opioid use using a subscale from a validated opioid consumption questionnaire.[28]

NPPC use will be collected using two methods. First, the frequency with which patients use specific NPPCs during their hospital stays will be extracted from Epic flowsheets. Nurses, as well as occupational and physical therapists will record delivery of NPPC modalities, as well as education delivered regarding NPPC modalities in Epic flowsheets. This information will be electronically extracted and expressed as count data. Second, patients' use of NPPC modalities will be assessed using self-report. At the 1-, 2- and 3-month assessment points patients will be queried regarding which of the NOHARM NPPC modalities they have used since hospital discharge. They will be presented with a list of the NOHARM modalities and asked to indicate those that they have used. Epic cascading logic will then present a second item for each modality that a patient has used which will ask them "How many times per week, on average, do you use *modality*?" Healthcare utilization for NOHARM will consider hospitalizations, ED visits, and ICU admissions. EHR entries and administrative billing data will be aggregated to construct a comprehensive

data set of all clinical encounters. Data collected for hospitalizations will include procedures and admission and discharge diagnoses. For ED encounters, we will capture diagnoses and procedures. Clinic visits will be captured using billing data which will include CPT codes, ICD-10 codes, location, and clinician NPI numbers.

11.4 Data Analyses

Because surgeries are randomized in clusters, all statistical methods will account for potential correlation of measures within clusters. Such methods include cluster adjusted standard errors for t-tests and χ^2-tests, and mixed effects models. Factors assessed for balance and potential inclusion in pre-specified analyses are those listed in Section 13.1.1 and all baseline measures listed in 13.1.2. We will impute baseline characteristics, as needed, using multiple imputation when included in models.

The co-primary and secondary outcomes will be compared between intervention and usual care periods using mixed effects generalized linear models to account for correlation of outcomes within surgery, patient, and cluster, as appropriate for each model. Each model will include an indicator for intervention (vs control) period; random effects for surgery nested within patient and cluster; cluster level factors that were used to constrain randomization; calendar time; baseline PROMIS CAT T score; surgery type; and any patient factors that were imbalanced across groups. The model details for each outcome are as follows:

1. PROMIS CATs (physical function (1°), pain interference (1°), and anxiety (2°)). These are continuous measures, collected at four time points, baseline (covariate), as well as 1, 2, and 3 months post-operative (dependent variables). To assess the impact of the intervention on these we will estimate three separate models. If Yijt is the measure at time t =1,2 of the ith patient treated by the jth cluster, then we will estimate

$$YY_{iiii2} = \beta\beta_0 + \beta\beta_{II}II_{iiii} + \beta\beta_{BB}YY_{iiii0} + \beta\beta_{TT}TT + \mathbf{BB}_{XX}\,\boldsymbol{XX}_{iiii} + \mathbf{BB}_{ZZ}\boldsymbol{ZZ}_{ii} + uu_{ii} + ee_{iiii} \quad (1)$$

where I_{ij} indicates the intervention status, T is calendar time, $u_j \sim N(0,\tau^2)$ is a cluster level random effect, $\boldsymbol{X_{ij}}$ is a vector of patient characteristics, including surgery type, $\boldsymbol{Z_j}$ is a vector of cluster characteristics used for randomization, and e_{ij} is a residual error. By testing $\beta_I = 0$ we can assess whether the intervention is associated with changes in the corresponding measure. We will replicate these models in sensitivity analyses that will include PROMIS CAT and short form data. Due to differences in mode and measurement properties only CAT data will be included in the primary analyses.

2. NPPC use. This is collected as a binary value for each of 13 modalities, collected at 1, 2, and 3 months post-operative. We will sum these to create a score, and use a model similar to (1) but without a baseline value Y_{ij0}:

$$YY_{iiii} = \beta\beta_0 + \beta\beta_{II}II_{iiii} + \beta\beta_{TT}TT + \mathbf{BB}_{XX}\,\boldsymbol{XX}_{iiii} + \mathbf{BB}_{ZZ}\boldsymbol{ZZ}_{ii} + uu_{ii} + ee_{iiii} \quad (2)$$

Again, by testing $\beta_1 = 0$ we can assess whether the intervention is associated with changes in the corresponding measure.

3. Opioid use. We restricted opioid analyses to each participant's first qualifying NOHARM surgery to avoid bias from correlated observations and potential contamination across procedures. Given that participants with advanced cancer or severe chronic pain may have very high opioid consumption, extreme outliers (above the 99th percentile) will be trimmed as needed to support model stability. Opioid use will be measured using 4 outcomes.

   a. Hospital-based opioid administration will be quantified as morphine milligram equivalents (MMEs) per day of hospitalization. This continuous outcome will be modeled as a function of postoperative day (DD_{iiii}) and other covariates:

$$YY_{iiii} = \beta\beta_0 + \beta\beta_{II}II_{iiii} + \beta\beta_{DD}DD_{iiii} + \beta\beta_{TT}TT + \mathbf{BB}_{XX}\,\boldsymbol{XX}_{iiii} + \mathbf{BB}_{ZZ}\boldsymbol{ZZ}_{ii} + uu_{ii} + ee_{iiii} \quad (3)$$

   Postoperative day (DD_{iiii}) will be modeled first as a continuous variable and then as a categorical variable. Days occurring during the index hospitalization will be modeled separately from those during subsequent hospitalizations, as the latter may occur on medical units without NOHARM intervention components. Results will be reported as odds ratios (ORs) for binary outcomes and rate ratios (RRs) for opioid exposure, derived from generalized linear models with a log link and offset for exposure time.

   b. Discharge and post-discharge prescriptions, daily morphine milligram equivalents (MMEs). For this outcome, we will use a model analogous to (3), where D_{ij} is replaced by number of days post discharge.

   c. Number of post-discharge prescriptions. These are counts for the 3-month period following surgery. The impact of the intervention will be assessed using a model similar to (2) but with a Poisson link function:

$$\begin{aligned} llll\big(EE(YY_{iiii})\big) &\sim \beta\beta_0 + \beta\beta_{II}II_{iiii} + \beta\beta_{TT}TT + \mathbf{BB}_{XX}\,\boldsymbol{XX}_{iiii} + \mathbf{BB}_{ZZ}\boldsymbol{ZZ}_{ii} + uu_{ii} + ee_{iiii} \quad (4)\\ YY_{iiii} &\sim PPPPPPPPPPPPll(\mu\mu) \end{aligned}$$

   We will assess the distribution first using an empty model, and potentially adopt a zero inflated Poisson, negative binomial, or zero inflated negative binomial according to the corresponding AIC values.

d. Daily use of opioids; this is binary outcome collected once, at 3 months post-surgery. To assess the impact of the intervention we will use a model similar to (4) but with a logit link:

$$llPPllPPll\blacklozenge YY_{iiii}\blacklozenge \sim \beta\beta_0 + \beta\beta_{II}II_{iiii} + \beta\beta_{TT}TT + \mathbf{BB}_{XX}\,\mathbf{XX}_{iiii} + \mathbf{BB}_{ZZ}\mathbf{ZZ}_{ii} + uu_{ii} + ee_{iiii} \quad (5)$$

For a-d we can again test $\beta_I = 0$ we can assess whether the intervention is associated with changes in the corresponding measure.

4. Healthcare utilization

   a. Hospitalizations
   b. Emergency department visits
   c. Intensive care unit admissions

All three of these are count outcomes, and so we will assess the impact of the intervention using a model similar to (4) above. As with (4), we will compare model specifications using an empty model first to determine the best count family (Poisson, negative binomial, zero inflated or not) using AIC, then apply that in the final model.

11.5 Subgroup analyses

11.5.1 Clinical and Demographic subgroups

Subgroup analyses will be performed for a) separate procedures b) separate age groups c) separate genders and d) separate racial/ethnic groups. Patients will be stratified using each classifier and the primary analyses replicated in each subgroup.

11.5.2 Patients at risk of unplanned prolonged opioid use (UPOU).

Hypothesis: Patients at moderate to high risk for UPOU, defined by score on the pain catastrophizing scale, pre-operative opioid use, and/or chronic pain will use NPPC modalities significantly less frequently than patients who are at low risk of UPOU.

Self-reported use of NPPC, expressed as a binary (Yes/No) response and assessed at 3 month post-surgical time point, will be compared between patient subgroups stratified by UPOU risk.

11.5.3 Patients who are rural.

Hypothesis. Patients who are rurally situated, as defined by US Census Bureau criteria, will use NPPC modalities significantly less frequently than patients who are situated in urbanized areas and urban clusters.

Self-reported use of NPPC, expressed as a binary (Yes/No) response and assessed at 3-month post-surgical time point, will be compared across patient subgroups defined by US Census Bureau urban/rural criteria.

11.6 Supplementary Analyses

11.6.1 Moderators

In supplementary analyses we will assess whether procedure, age, sex, or race/ethnicity moderate the intervention effect. The models (1)-(5) used in the primary analysis will be expanded to include indictors for one of these subgroup classifiers, as well as the interaction with intervention status. By testing whether the interaction effect differs from zero, we can assess whether these factors moderate the intervention.

11.6.2 Mediators

In related supplementary analyses, we will test whether interim patient measures mediate the effect of the intervention on the separate outcomes. We will adapt models (1)-(5) to path analysis, a type of structural equation model, which will allow us to specify an indirect effect (of the intervention through the potential mediator) and test whether it is non-zero.

12 DATA COLLECTION AND QUALITY ASSURANCE

12.1 Data Collection Forms

All data points for the NOHARM study will be extracted from the electronic health record. In addition to demographic, diagnostic, and procedural clinical variables, this includes patient reported outcomes and medication information that are captured electronically from patients as part of routine (i.e. usual) perioperative care at Mayo Clinic, and/or the NOHARM trial.

12.1.1 Sociodemographic, Clinical, Surgical, and Hospital stay variables.

- Sociodemographic
  - Age
  - Sex
  - Race/ethnicity
  - Insurance status
  - Educational level
  - Employment status
  - Marital status
  - Zip code of residence (for classification as rural or non-rural residence)
- Surgical characteristics
  - Surgical Procedure
  - Length of surgery
  - Same day surgery
  - Open (vs laparoscopic) surgery
  - Hip/knee arthroplasty or gastrointestinal surgery, given their association with intense post-operative pain
- Comorbidities
  - Elixhauser comorbidity index
  - Cancer present on problem list 6 months prior to index surgery
- Hospitalization characteristics
  - Length of stay
  - Site
  - Disposition

12.1.2 Treatment and trial outcome variables

The following items will be captured in addition to clinical and demographic variables:

- Patient Reported Medical Information System (PROMIS) computer adaptive test (CAT)
  - Pain interference @ baseline and 1, 2 and 3-months post-surgery
  - Physical functioning @ baseline and 1, 2 and 3-months post-surgery
  - Anxiety @ baseline 3 months post-surgery
  - Numerical rating scale pain scores reported q shift during hospitalization.
- Pain catastrophizing scale
- TAPS prescription medication use item.
- PHQ-4 (four item patient health questionnaire for anxiety (GAD 2) and depression (PHQ 2))
- Opioid prescribing survey
- History of opioids prescribed during 3 months prior to the index surgery.
- Hospital-based administration of opioids during hospitalization for the index surgery
- "Discharge" opioid prescriptions, which may be prescribed prior to the surgical procedure or prior to the discharge date depending on perioperative workflows.
- Opioids administered during emergency department visits and hospitalizations occurring after discharge from the index surgery hospitalization.
- Outpatient opioid prescriptions up to 3 months following the index surgery ("refills")

Data will be extracted and curated by study team members, including data managers, analysts, and/or statisticians. All data will exist prior to the time of access, and no further patient contact is needed for the above data points.

Once extracted from the EHR, data will be maintained on secure, encrypted, password protected research servers at Mayo Clinic. Access to data files will be restricted to individuals listed in the protocol approved by the Mayo Clinic IRB.

12.2 Data Management

Individual sites in the NOHARM project (specifically MC Rochester, MC Arizona, MC Jacksonville, MC La Crosse, MC Mankato, and MC Eau Claire) will not be required to conduct any site- or study-specific, manual data collection. All study sites use a unified electronic medical record (Epic) and programmatic data extraction can be conducted by study team personnel at the coordinating center

(MC Rochester).

The coordinating center (MC Rochester) will extract data from the electronic medical record as needed to assess the fidelity of routine data collection activities, evaluate the completeness of data collection, and conduct comprehensive data pulls for the final analysis.

Data collection forms are not applicable to our study design as all data will be recorded as part of usual care and electronically retrieved from the medical record by study staff.

12.3 Quality Assurance

12.3.1 Training

Data will be extracted, compiled and analyzed by personnel on the study team who have expertise in data management, informatics and statistical methods.

12.3.2 Quality Control Committee

Data will be electronically extracted from the EHR and validated against the clinical record. Chart-audit will occur at 3-month intervals, on 2-5%, depending on capacity, of patients for each of the most recently activated clusters. These audits are intended to ensure that data extraction procedures are functioning as expected for each cluster.

12.3.3 Metrics

The study team will validate electronic data pulls against the EHR as needed.

12.3.4 Protocol Deviations

Protocol deviations will be reported promptly to the Mayo Clinic IRB upon the study team being made aware of the deviations. The main opportunity for protocol deviations is the misrouting of patients to wrong study arm (intervention or control). Care will be taken to make sure the EHR assignment algorithms are functioning properly. Protocol modifications will be made as new tranches are brought into the intervention arm of the study.

The following are examples of potential protocol deviations which will be carefully avoided, but reported if they occur:

1. Implementing the intervention without practice approvals.

As indicated in the protocol and elsewhere, we will be engaging with practice leadership in advance of implementing the NOHARM intervention. Failure to duly engage practice leadership and obtain documented approval prior to implementing the intervention in specific surgical practices would violate expectations set in the protocol.

2. Incorrect routing of patients to intervention/control arms.

Patient assignment to either the treatment or control arm of the study within the EHR will be done via pre-specified algorithms. Rigorous testing and validation will be done to ensure the algorithms are functioning as expected. Should the algorithms fail to properly assign patients to the treatment or control arm of the study, appropriate action will be taken to refine the algorithms to prevent further mis-assignment and the affected patients will be accounted for, as appropriate, in the study analyses.

3. Failure to monitor trial for data quality and patient safety.

Per the protocol, we will monitor study implementation—particularly within the surgical practices in which the NOHARM intervention has been implemented—to ensure that the intervention is functioning as designed/intended and that critical data points are being captured. Further, the protocol assumes that data essential for monitoring patient safety and ensuring data quality will be extracted as needed and made available to the data safety and monitoring board for review.

4. Study staff not included in IRB documentation.

All personnel on the study who will be involved with the conduct of the research must be included in IRB documentation per Mayo Clinic policy. This excludes members who are involved with NOHARM as Standard of Care. Failure to disclose personnel actively involved in the study conduct will constitute a protocol deviation.

5. Failure to apprise the IRB of updated patient contact materials or study procedures.

It is possible that some of the patient contact materials, including elements of the decision aid, after visit summaries, and resource materials provided to patients will be updated with alternate and/or additional information throughout the course of the study. Failure to apprise the IRB of these modifications and/or to document these updates as potentially important covariates in analysis will be considered a deviation from protocol.

12.3.5 Monitoring

The study will be monitored by the DSMB in a manner and frequency prescribed by NIA/NIH.

13 PARTICIPANT RIGHTS AND CONFIDENTIALITY

13.1 Institutional Review Board (IRB) Review

This protocol and any subsequent modifications will be reviewed and approved by the Mayo Clinic IRB.

13.2 Informed Consent Forms & Authorization Considerations

A waiver of informed consent is being requested for this study, which presents no more than minimal risk of harm to subjects. Because this is a population-based, EHR-embedded study, it is not practical to conduct the research without the waiver of consent. We do not feel the waiver of informed consent will adversely affect the rights or welfare of the subjects.

In lieu of consent, we have sought out and confirmed Mayo Clinic Practice leadership support for the trial. In the 3-6 months prior to each wave of trial implementation, we will confirm each individual practices' willingness to participate in the trial. Because some practices will not be randomized until 2023, securing their endorsement now, did not make sense.

See Section 15 – Ethical Considerations for more information.

13.3 Participant Confidentiality

Information about study subjects will be kept confidential.

Only NOHARM study team members (study investigators, project coordinators, research assistants, data managers, biostatisticians, etc.) who are IRB-approved study staff will have access to individually identifiable private information collected for study purposes, except as necessary for monitoring, audits and/or inspections by the IRB, the NIA, and/or government regulatory agencies.

Data that are transferred outside of the Mayo Clinic firewall will be de-identified, stripped of personal health information, and encrypted.

13.4 Study Discontinuation

The study may be discontinued at any time by the principal investigators, the IRB, the NIA, the DSMB, or other government agencies as part of their duties to ensure that research participants are protected.

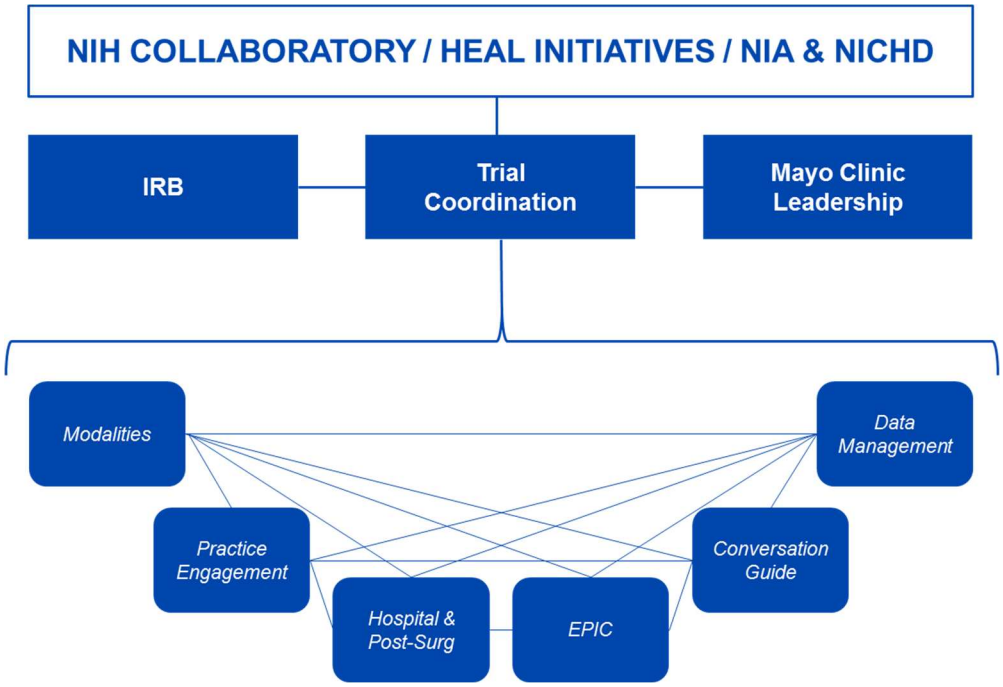
14 ETHICAL CONSIDERATIONS

This is a population-based study, where all eligible patients undergoing qualifying surgeries at participating Mayo Clinic locations will be "enrolled." Neither current regulations, nor the peer-reviewed literature explicitly defines when a formal patient consent process is required for pragmatic clinical trials, particularly when testing the implementation of proven-effective interventions at scale. This type of research, sometimes referred to as "standard of care" research, in which the primary research objective is to implement and evaluate a strategy that better satisfies the existing clinical standard of care, has been debated in recent high-profile cases.[70-72] Opinions from ethicists vary but all emphasize the vital importance of IRB engagement and assiduous efforts to foster disclosure and transparency across all relevant stakeholders.[73-75] We believe, and in consultation with our local Research Ethics Consult Service have confirmed, that this study meets the criteria for being standard of care research in which the marginal incremental risks of the proposed interventions do not foreseeably introduce even incremental net risk to individuals in the participating practices being studied. The Mayo Clinic IRB has been an active partner in developing the NOHARM application and its involvement will continue. Preliminary discussions with the Mayo Clinic IRB executive committee in January 2020 concluded this study is minimal risk and that waiver of consent was warranted so long as practice endorsement was secured.

IRB members and the Mayo Clinic Family Advisory Council contributed to the current NOHARM "Transparency Promotion and Patient Preference Protection Plan." The Transparency Promotion and Patient Preference Protection Plan is a multi-pronged approach that was in place prior to planning and design of the NOHARM trial, but that has further matured as a consequence of these efforts. The Mayo Clinic Enterprise, in an effort to proactively anticipate ethics, human subject protections, and institutional oversight concerns related to the conduct of quality improvement, pragmatic, and "standard of care" trials convened a group of key stakeholders. These stakeholders include members of the Mayo Clinic IRB, Mayo Clinic Patient and Family Advisory Council, representatives from Enterprise Research Administration, and clinicians representing surgical specialties, pain management, pharmacy, rehabilitation medicine, and general internal medicine. This stakeholder group is entrusted to provide impartial oversight of trial activities that may challenge the goal of complete pan-stakeholder transparency and prioritization of patient preference.

15 COMMITTEES

The following schematic illustrates the Mayo Clinic research team workgroup structure.



15.1 Project Workgroups/Responsibilities

The NOHARM PIs established six workgroups to develop the intervention, engage practice partners, create training material and implement with the surgical practices identified for the trial. Team members meet face-to-face and virtually on weekly/bi-weekly basis and report to the trial coordination team. Meeting notes and progress reports are maintained on a project folder share for team members' reference.

- Trial Coordination
  - Interfaces with the Duke Center, NIH, NIA, and Mayo Clinic IRB, practice leaders and committees.
  - Manages the budget, provides oversight and guidance to the project team.
  - Development and maintenance of study materials including the Manual of Procedures and study forms
  - AE and SAE monitoring and reporting
  - Quality control procedures
  - Distribution of all changes, updates and policies of reports and documents to all participating study sites, NIA and to the DSMB as necessary.

- Modalities
  - Identify scalable NPPC approaches that can be broadly delivered at high fidelity throughout the Enterprise.
  - Develop supportive education material, develop staff training materials, and ensure distribution at target sites.
  - Collaborate with Healing after Surgery Guide and Epic team to develop system content.
- Practice Engagement
  - Characterize peri-operative workflows in the target specialties.
  - Develop and deliver training material.
  - Identify and engage key stakeholders and practice champions.
  - Provide support during implementation
  - Conduct site visits to ensure adherence to the protocol and procedures.
  - Communicates with study sites, responding to and documenting ad hoc communications.
- Hospital / Post-Surgical
  - Develop NPPC discharge plan integration and opioid taper counseling.
  - Determine Patient reported outcome assessment and response strategy.
- Epic
  - Define the EHR technical requirements. The EHR components include orders, documentation, best practice alerts, patient questionnaires and reports.
  - Identify and engage technical resources to configure, validate and advance changes through the EHR environments.
  - Obtain approval for the EHR changes from the appropriate committees.
  - Document all components of the EHR build and identify/implement changes required for each tranche implementation.
- Healing after Surgery Guide
  - Conduct interviews, focus groups, and shadowing to gain insights into the user experience from both the healthcare staff and patient perspective to inform the design of the Healing after Surgery guide.
  - Develop and refine the Healing after Surgery guide, collaborating with Mayo Clinic's Office of Patient Education, Integrative Medicine & Health and Department of Physical Medicine and Rehabilitation to define patient educational content.
  - Coordinates the GC build with the Epic MyChart and patient portal teams.

- Data Management
  - Identify clusters based on surgical procedures and sites.
  - Develop the randomization scheme and procedures.
  - Develop data flow and data management procedures including data entry, error identification and correction.
  - Perform programmatic extraction and curation to support trial analyses as described in section 13.
  - Maintain data security and integrity in concordance with section 13.1 of the IRB protocol.
- Mayo Clinic Leadership

  While the NOHARM intervention is designed to seamlessly integrate into clinical practice and hospital workflows, meaningful stakeholder engagement and collaboration is critical to successful implementation. The project team seeks endorsement from Mayo Clinic leaders and practice partners through the established committee structure including:
  - Mayo Clinic Clinical Practice Committee
  - Opioid Stewardship Program
  - Mayo Clinic Nursing Practice Council
  - EHR/RMC Oversight Committee
  - Surgical and Procedural Committee
  - Surgical Specialty Councils

16 PUBLICATION OF RESEARCH FINDINGS

The trial will be registered on ClinicalTrials.gov and the NOHARM investigative team will follow the requirements outlined in the NIH Policy on Dissemination of NIH-Funded Clinical Trial Information. Mayo Clinic has an established internal policy in place to ensure that clinical trials registration and reporting results occur in compliance with the policy requirements.

Mayo Clinic strongly supports investigators to present at relevant regional, national, and international meetings. Opportunities such as these are both opportunities to share knowledge and also cultivate new ideas among colleagues. Given our expertise, diverse collaborators, and distinct focus in the project, we foresee a number of manuscript and presentation opportunities. We will publish rigorous visible results in quality journals.

Mayo Clinic's office of Scientific Publications also supports investigators in developing journal articles, chapters, and complete books for academic publication. Additionally, the Mayo Clinic College of Medicine supports the development of educational content throughout its five schools, ensuring that new, groundbreaking ideas are quickly spread to learners at nearly every level of medical education. Importantly, new education spreads beyond our own doors in numerous ways. Especially important is the Mayo School of Continuous Professional Development, accredited by the ACCME.

17 REFERENCES

1. Control CfD. *Changes in Opioid Prescribing Practices.* Atlanta, GA: National Center for Health Statistics;2018.
2. Hooten WM, Brummett CM, Sullivan MD, et al. A Conceptual Framework for Understanding Unintended Prolonged Opioid Use. *Mayo Clin Proc.* 2017;92(12):1822-1830.
3. Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ.* 2014;348:g1251.
4. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg.* 2017;152(6):e170504.
5. Goesling J, Moser SE, Zaidi B, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. *Pain.* 2016;157(6):1259-1265.
6. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med.* 2012;172(5):425-430.
7. Johnson SP, Chung KC, Zhong L, et al. Risk of Prolonged Opioid Use Among Opioid-Naive Patients Following Common Hand Surgery Procedures. *J Hand Surg Am.* 2016;41(10):947-957 e943.
8. Holman JE, Stoddard GJ, Higgins TF. Rates of prescription opiate use before and after injury in patients with orthopaedic trauma and the risk factors for prolonged opiate use. *J Bone Joint Surg Am.* 2013;95(12):1075-1080.
9. Rosenbloom BN, McCartney CJL, Canzian S, Kreder HJ, Katz J. Predictors of Prescription Opioid Use 4 Months After Traumatic Musculoskeletal Injury and Corrective Surgery: A Prospective Study. *J Pain.* 2017;18(8):956-963.
10. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period. *JAMA Intern Med.* 2016;176(9):1286-1293.
11. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain.* 2016;17(2):131-157.
12. Wardhan R, Chelly J. Recent advances in acute pain management: understanding the mechanisms of acute pain, the prescription of opioids, and the role of multimodal pain therapy. *F1000Res.* 2017;6:2065.
13. American Society of Anesthesiologists Task Force on Acute Pain M. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology.* 2012;116(2):248-273.
14. Tick H, Nielsen A, Pelletier KR, et al. Evidence-Based Nonpharmacologic Strategies for Comprehensive Pain Care: The Consortium Pain Task Force White Paper. *Explore (NY).* 2018;14(3):177-211.
15. Chaudhry B, Wang J, Wu S, et al. Systematic review: impact of health information technology on quality, efficiency, and costs of medical care. *Ann Intern Med.* 2006;144(10):742-752.

16. Keasberry J, Scott IA, Sullivan C, Staib A, Ashby R. Going digital: a narrative overview of the clinical and organisational impacts of eHealth technologies in hospital practice. *Aust Health Rev.* 2017;41(6):646-664.
17. Leppin AL, Fernandez C, Tilburt JC. Missed Opportunities: A Mixed-Methods Analysis of CAM Discussions and Practices in the Management of Pain in Oncology. *J Pain Symptom Manage.* 2016;52(5):719-726.
18. Soos SA, Jeszenoi N, Darvas K, Harsanyi L. [Attitudes, knowledge and use of complementary and alternative medicine among perioperative healthcare professionals]. *Orv Hetil.* 2017;158(10):368-375.
19. Fries JF, Krishnan E, Rose M, Lingala B, Bruce B. Improved responsiveness and reduced sample size requirements of PROMIS physical function scales with item response theory. *Arthritis Res Ther.* 2011;13(5):R147.
20. Fries J, Rose M, Krishnan E. The PROMIS of better outcome assessment: responsiveness, floor and ceiling effects, and Internet administration. *J Rheumatol.* 2011;38(8):1759-1764.
21. Rose M, Bjorner JB, Gandek B, Bruce B, Fries JF, Ware JE, Jr. The PROMIS Physical Function item bank was calibrated to a standardized metric and shown to improve measurement efficiency. *J Clin Epidemiol.* 2014;67(5):516-526.
22. Choi SW, Reise SP, Pilkonis PA, Hays RD, Cella D. Efficiency of static and computer adaptive short forms compared to full-length measures of depressive symptoms. *Qual Life Res.* 2010;19(1):125-136.
23. Pilkonis PA, Yu L, Dodds NE, Johnston KL, Maihoefer CC, Lawrence SM. Validation of the depression item bank from the Patient-Reported Outcomes Measurement Information System (PROMIS) in a three-month observational study. *J Psychiatr Res.* 2014;56:112-119.
24. Amtmann D, Kim J, Chung H, et al. Comparing CESD-10, PHQ-9, and PROMIS depression instruments in individuals with multiple sclerosis. *Rehabil Psychol.* 2014;59(2):220-229.
25. Junghaenel DU, Schneider S, Stone AA, Christodoulou C, Broderick JE. Ecological validity and clinical utility of Patient-Reported Outcomes Measurement Information System (PROMIS(R)) instruments for detecting premenstrual symptoms of depression, anger, and fatigue. *J Psychosom Res.* 2014;76(4):300-306.
26. Thiels CA, Anderson SS, Ubl DS, et al. Wide Variation and Overprescription of Opioids After Elective Surgery. *Ann Surg.* 2017;266(4):564-573.
27. Thiels CA, Ubl DS, Yost KJ, et al. Results of a Prospective, Multicenter Initiative Aimed at Developing Opioid-prescribing Guidelines After Surgery. *Ann Surg.* 2018;268(3):457-468.
28. CC W, M H, Trousdale ER, et al. Developing and implementing a novel institutional guideline strategy reduced postoperative opioid prescribing after TKA and THA. *Clin Orthop Rel Res.* 2019;Jan 477(1):104-113.

18 DESCRIPTION OF SUPPLEMENTS/APPENDICES

18.1 Appendix A: Clinician Participants

Description of the status of clinicians in the NOHARM pragmatic trial.

18.2 Appendix B: Resource List

A brief handout provided to patients before discharge that points them to resources to help them further pursue information on non-pharmacological pain management strategies.

Appendix A: Clinician Participants

Clinician Participants

The clinical practices of care teams involved in the care of surgery patients targeted by the NOHARM intervention—including surgeons, nurses, physical therapists, pain management specialists—will be impacted by the bundled NOHARM intervention. In the course of providing care to surgical patients in active intervention clusters, clinicians will be alerted to non-pharmacological pain management strategies (via CDS tools embedded in the EHR) for which patients have expressed preference. Within their routine workflows (i.e. interface with patients), clinicians will be prompted to engage patients about their preferred post-acute pain management strategies.

Because of this practice impact, clinicians will be considered "participants" in the NOHARM pragmatic trial (in the same way as they have been construed in the pilot application IRB# 20-001864). This determination has been affirmed by the Mayo Clinic IRB executive committee (January 2020 meeting).

Accrual

Based on data from 2018 on the 22 surgery types targeted by the NOHARM trial (minus neuro / spine surgery which is the focus of the NOHARM pilot trial – IRB# *20-001864)* we estimate there to be approximately 225 surgeons in the enterprise who are routinely performing NOHARM qualifying surgeries. We will inflate this number to 300 to account for physicians performing one of the target surgery types less frequently. To this figure, we will add 0.5 residents / and 0.5 physician assistants per surgeon (+300). Assuming a median hospital stay of 3 days (9 nursing shift changes), we will add 9 nurses X 300 surgeons (+2700). Finally, assuming 0.5 physical therapist per surgeon and 0.2 integrative medicine specialist per surgeon, we will add 210 clinicians. This brings our total estimated clinician accrual to 3510 participants.

Consent and Data Collection

1. Given the ubiquity of the intervention and the volume of clinicians touched by the trial it will not be practicable to obtain individual consent for participation.
2. Clinician "consent" will be granted in the form of "whole practice consent" granted by individual surgical practice leadership within the institution as a pre-requisite for implementation in specific surgical practices.
3. It would be impracticable to formally track clinicians as we are not documenting individual consent nor collecting data from clinicians. Although we could potentially identify the number of clinicians who log into Epic to provide care for discreet surgery patients, this approach would be imprecise.
4. No clinician variables—including clinician ordering or prescribing behaviors—are being assessed. All study outcomes are patient outcomes, as the intervention is intended to guide the patient's surgical recovery experience.

Risks and Benefits

The risks to clinicians involved in the NOHARM trial are minimal. Clinicians are already motivated to employ clinical guidelines for non-pharmacological pain management, and the NOHARM study may enhance their personal success in that effort. Clinicians may find, perhaps

at first, that the EHR-based prompts interfere with the rhythms of their workflow, but great effort has been invested to ensure that the EHR-embedded clinical decision support tools integrate seamlessly into existing workflows. Further, the Mayo Clinic Clinical Practice Committee has endorsed the intervention as an appropriate element for institutional improvement in the management of post-surgical pain. Ongoing care will be taken to minimize the workflow burden while making the EHR prompts an effective tool in promoting institutional adherence to clinical guidelines. Clinicians will always be able to make professional judgments about the appropriateness of engaging patients in specific conversations about pain management throughout the patients' post-surgical recovery. Clinicians may freely disregard EHR-prompts as they deem appropriate in their professional judgment. Clinicians will be amply supported by the study team by way of education and through access to study team members with expertise in non-pharmacological pain management modalities and in the management of complex pain management cases.

Appendix B: Resource List

Patient Support

- Zoom group support calls will help patients by answering questions about the patients' selected modalities. Answers will be provided by NOHARM trial staff. Resources include:
  - Zoom Group Call Instructions
  - Welcome Instructions
  - Zoom Group Call Talking Points
- Toll-free number (1-833-919-1432) will help support patients by answering questions about the patients' selected modalities and the NOHARM trial staff will provide answers
- Healing After Surgery Website (www.healingaftersurgery.mayoclinic.org was developed to support patients who are portal users
- Healing After Surgery Workbook was developed to support patients, who may not be portal users, may not have access to a computer or to the internet or may not be comfortable with technology
  - Workbook Cover Letter
- Transcutaneous Electrical Nerve Stimulation (TENS) Patient Education Video is a 5-minute patient education instructional video
- 13 Modality videos. Each video provides a brief modality overview
- Modality Flyers Each flyer provides a brief overview of each modality and resource list
- Rack Card - Healing After Surgery Managing Pain is a quick reference guide (rack card) about NOHARM and the NOHARM resources
- Healing after Surgery DVD includes all patient education video content used in the NOHARM intervention. The DVD mirrors what is on MCTV.
- Mayo TV NOHARM Resource List provides the NOHARM patient education resources available on Mayo Clinic Television (MCTV)
- NOHARM TENS units: the NOHARM trial will purchase TENS units for the surgical clusters
- Portal messages
  - Pre-op sending/assignment of Healing after surgery guide: message sent when the patient is assigned the Healing after surgery guide
  - Pre-op Healing after surgery guide non-response reminder message: if the patient hasn't completed the Healing after surgery guide, this reminder is sent.
  - Pre-op post-Healing After Surgery Guide follow-up message/Thank you (4 confidence): 4 messages based on the patient's response to the confidence questions.
  - Post-Op Discharge ("Welcome Home") Message: reminds patients of NOHARM resources after they are discharged from the hospital.
  - 1, 2 and 3 month post-op questionnaire reminder (send 4 days after initial questionnaire was sent): Standard Epic reminder message
  - PROMIS CATs Questionnaire Follow-up Message: 3 versions depending on the patient's PROMIS CAT scores; reminds patient of NOHARM resources and if their pain and or physical function is severe, then suggest actions the patient should take

Epic Components (Standard of Care)

- Healing after Surgery Guide is an Epic questionnaire with additional HTML to help patients understand what to expect when recovering from surgery, learn about pain management techniques and to make a plan to manage pain after surgery. There is a Desktop version and mobile version

- Pre-op questionnaires: Pre-surgery questionnaires are existing PROMIS CAT questionnaires: Pain Interference, Physical Function, Anxiety questionnaires
- 1, 2 and 3 month post-op questionnaires: (Identify intervention patients that need help/struggling; collect data)
- Physical function, Pain Interference, and NPPC usage -and at 3 months a Opioid Usage questionnaire (content complete) along with the PROMIS Anxiety are also given
- After Visit summary (AVS) (search the folder for AVS to find all files)
    - Patient facing: Provides patients with information specific to their selected modalities.
    - Discharge to facility AVS: A significant number of NOHARM participants will be dismissed to post-acute care (PAC) facilities, e.g., skilled nursing facilities. For those patients, the AVS content will be directed to clinicians at PAC facilities

Mayo Clinic Care team Support

- Pager (3-5519): NOHARM staff will provide Epic and workflow support
- Department of Nursing Healing after Surgery (NOHARM) Intranet page provides a NOHARM overview as well as available NOHARM resources
- Provider NOHARM Overview and Talking Points (elevator speech) reminds the care team of NOHARM
- MyLearning classes: provide a NOHARM overview, set expectations and teach the NOHARM workflow for each role
    - NOHARM: Introduction and Overview (COURSE 502E00NOHM0001)
    - NOHARM: Provider Training(COURSE 502E00NOHM0004)
    - NOHARM Inpatient Nursing Training (COURSE 502E00NOHM005)
    - NOHARM: Outpatient Nursing Training(COURSE 502E00NOHM0002)
    - NOHARM: Physical Therapy Training (COURSE 502E00NOHM0003)
    - NOHARM: Pre/post-op and PACU Nursing Training (COURSE 502E00NOHM0006)

Epic Components (Standard of Care, support for clinical team)

- NOHARM Just in Time Training: role based training that is linked in the Epic NOHARM banner
    - Inpatient nursing
    - PACU
    - PT
    - Surgeons APP resident
- RN Education points helps RNs provide NOHARM education to patients
- RN Task/Brain/worklist: NOHARM tasks the RN has to complete
- NOHARM Banner: the NOHARM banner is pink to help with awareness
- RN Orders (search folder for Orders for all the files)
- Best Practice Alerts: alert Mayo Clinic care teams about key steps to take for NOHARM. Triggered off of certain Epic event
    - PT/OT BPA
    - Pain > 1 BPA
    - Opioid Rx BPA

Trial Coordination

- NOHARM Data and Safety Monitoring Board (DSMB) Charter
- NOHARM Data and Safety Monitoring Plan (DSMP)
- Letters of Support

1544