PROUD Study - Preventing Opioid Use Disorders

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PROTOCOL TITLE: PROUD Study – Preventing Opioid Use Disorders

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REVISION HISTORY

Revision #	Version Date	Summary of Changes
2	12.17.2020	1. Correction of page numbers on protocol table of contents 2. Expanded description of use of aromatherapy in Section 5 of the protocol 3. Provided rationale for excluding non-English speaking subjects in Sections 10 and 21 of the protocol 4. Clarified language about screening of potential participants in Sections 10 and 12 of the protocol 5. Updated the two consent forms with minor revisions and added language to the biomedical consent regarding registering the study with clinicaltrials.gov

		6. Expanded description of Breath 2 Relax application in Section 5 of the protocol 7. Attached the survey for the provider arm of the study
3	12.21.2020	1. Corrected protocol numbering
4	12.22.2020	1. In Section 5: Study Intervention/Investigational Agent on page 9 the statement "Oil should not be placed on the skin and is noted as such in the patient education materials." Was added to the section on aromatherapy.
5	3.22.2021	1. On page 9 the statement "No medications will be used off label." was removed. 2. The schematic on page 10 was updated by removing tranexamic acid from the protocol. This medication is requested by the surgeon to decrease bleeding as a part of the surgery but is not a part of the study protocol. 3. The following language was added to section 21 per OCR request "Some of the medications in the opioid free protocol may not be covered by insurance. If a medication is not covered by insurance the patient will be able to contact their surgeon through the study patient hotline to determine if they want to proceed with the protocol or withdraw."
6	4.1.2021	1. The medications that are a part of the protocol were clarified to indicate which are "study driven medications" in the pre-, intra- and post-operative periods. 2. Section E21 was updated to align with the PRA from the OCR.

Table of Contents

1. Study Summary

Study Title	PROUD Study – Preventing Opioid Use Disorders
Study Design	Matched Prospective Case with Retrospective Control Study and Staff Surveys
Primary Objective	Pilot opioid free surgical protocol while collecting key outcome measures to determine overall opioid requirements.
Secondary Objective(s)	Assess the two core competencies for interprofessional collaborative practice (Interprofessional Communication and Teams; and Teamwork) among the interdisciplinary patient care team that implements the opioid free surgical protocol.
Research Intervention(s)/Interactions	Prospective Intervention group: Interventions: • Guided mindfulness exercises • Self-administered aromatherapy • Non-opioid drug regimen during the 5 week study period • Three self-guided training videos Interactions: • Normal clinical visits with Dr. Thomas Bradbury, M.D. • One, pre-surgery pain and medication assessment survey • Seven, post-surgery pain, medication, and physical activity surveys Retrospective Controls: Interventions: • None Interactions: • None Professional Staff: Interventions:

	• None Interactions: • Three, team assessment surveys seeking their opinion about interprofessional teamwork and communication. ○ Survey One: Late January, prior to implementation of the opioid free surgical protocol ○ Survey Two: Early April, 2 months after implementation of the opioid free surgical protocol ○ Survey Three: Early June, 2 months after the last prospective study participant undergoing surgery using the opioid free surgical protocol has been discharged
Study Population	Intervention group: 60 prospective study participants undergoing unilateral total hip replacement surgery between the months of February – May 2021 Control: 60 retrospective controls selected from the Emory Healthcare System Clinical Data Warehouse that underwent unilateral total hip replacement surgery between the months of February – May 2020 Matching: Cases and Controls will be matched in a 1:1 ratio using demographic attributes such as age, sex, race, and ethnicity Professional Staff: All staff that participate in the implementation of the opioid free surgical protocol. We estimate a population of 50 providers
Sample Size	60 intervention / 60 control / 50 staff
Study Duration for individual participants	Intervention group: • Five weeks ○ Two weeks pre-surgery ○ Day of surgery

	○ Three weeks after surgery Professional Staff group: • Six months
Study Specific Abbreviations/ Definitions	CDW – Emory Healthcare System Clinical Data Warehouse EUOSH – Emory University Orthopaedic and Spine Hospital Mg – milligram NIEPAS - Nebraska Interprofessional Education Attitude Scale
Funding Source (if any)	Woodruff Health Sciences Interprofessional Education and Collaborative Practice Council Synergy Award

2. Objectives

Purpose: The objective of this study is to pilot an opioid free anesthetic protocol for patients undergoing total hip replacement at EUOSH. The protocol was developed by an interprofessional team, who identified alternative pharmacologic methods to block pain pathways to reduce or even eliminate the need for opioids in the intra- and postoperative periods, with the goal of decreasing or eliminating exposure to opioids. A secondary objective is to assess two core competencies for interprofessional collaborative practice (Interprofessional Communication and Teams; and Teamwork) within the interprofessional care team implementing the opioid free protocol.

Specific Aim 1a: Pilot the opioid free protocol, collecting key outcome measures to determine overall opioid requirements. We hypothesize that total post-operative opioid requirements prior to discharge will be lower in patients who do not receive intraoperative opioids compared with the control group that received standard care, including intraoperative opioids. A retrospective review of patients from the CDW who underwent the same procedure at the same hospital in the same 4-month time period one-year prior will serve as the control group.

Specific Aim 1b: Assess within the interprofessional care team that implements the opioid free protocol two core competencies for interprofessional collaborative practice (Interprofessional Communication and Teams; and Teamwork) using a pre-test/post-test design. We hypothesize that perceptions of strong communication and teamwork will be associated with more successful implementation of the opioid free protocol.

3. Background

From 1999 to 2018, more than 232,000 people died in the United States from overdoses involving prescription opioids. Overdose deaths involving prescription opioids were more than

four times higher in 2018 than in 1999 (CDC National Center for Health Statistics, 2020). According to the National Institute on Drug Abuse, in 2017 there were 1,014 overdose deaths involving opioids in Georgia (GA) - a rate of 9.7 deaths per 100,000 persons. Of these deaths, 568 (56%) involved prescription opioids. One typical point of opioid introduction: more than 50 million of Americans each year have surgery, and opioids continue to be the primary means of managing acute surgical pain, both intraoperatively and postoperatively. However, the use of opioids for acute surgical pain is not without risk. Johnson et al., 2016 found as many as 13% of opioid naïve individuals undergoing orthopedic surgery may go on to have chronic opioid use. In a retrospective study of over 36,000 opioid-naïve patients undergoing elective surgery between 2013 and 2014, the incidence of chronic opioid use after surgery was approximately 6% and remained stable regardless of whether the surgical procedure was major or minor (Brummett et al., 2017). Although current studies vary in their findings, roughly 1 in 30 patients exposed to opioids after major surgery continue to use them after three months (Clarke et al., 2014).

Patients who receive opioids for pain in the acute perioperative period often require increased opioid doses to maintain the same analgesic effects (Chia et al., 1999). This is attributed to either acute tolerance to the analgesic effects of opioids, or from opioid-induced hyperalgesia (OIH). OIH is defined as nociceptive sensitization caused by exposure to opioids (Chu et al., 2008). Central sensitization (hyperalgesia) underlies the transition of acute pain to chronic pain disorders, but can also be produced by high dose and high potency opioids such as those administered intraoperatively. Many of the same mechanisms account for both central pain and opioid hyperalgesia (Rivat & Ballantyne, 2016).

Hyperalgesia and tolerance are very different pharmacologic phenomena that can lead to similar net increases in opioid dosing over time. This is the *opioid paradox*: the more opioids used intraoperatively, the more opioids required postoperatively. This paradox has been found in surgical patients up to 2 days postoperatively (Joly et al., 2005). Altogether, this body of evidence underscores the need to develop and evaluate pre- and post-operative patient-centered pain management plans based on known risks and protective factors for opioid misuse.

It is clear that minimizing opioid misuse risk in surgical patients requires partnerships across multiple disciplines to ensure a coordinated, evidence based approach to care in the pre-, intra- and post-operative periods.

Interprofessional teamwork and collaborative practice are emerging as key elements of efficient and productive work in promoting health and treating patients. The vision for these collaborations is one where different health and/or social professionals share a team identity and work closely together to solve problems and improve delivery of care (Committee on Measuring the Impact of Interprofessional Education on Collaborative Practice and Patient Outcomes, 2015).

Patients have complex health needs requiring more than one discipline to address issues regarding their health status (Lumague et al., 2008). In 2001 the Institute of Medicine

Committee on Quality of Health Care in America recommended that healthcare professionals working in interprofessional teams can best communicate and address these complex and challenging needs (Lumague et al., 2008; Institute of Medicine Committee on Quality of Health Care in America, 2001). This interprofessional approach may allow sharing of expertise and perspectives to form a common goal of restoring or maintaining an individual's health and improving outcomes while combining resources (Lumague et al., 2008; Barker & Oandasan, 2005).

Effective interprofessional collaboration occurs when a team of differing specialties work towards a shared goal, communicate respectfully, intentionally value and harness each other's professional experience, and ultimately improve patient outcomes (Gilbert et al., 2010). Reduction and/or elimination of opioid administration during the perioperative period requires the commitment to the shared goal from several specialties including nursing, medicine, anesthesia, administration, pharmacy, and the patient. Although collaboration between healthcare providers is required to implement opioid-free analgesia in the perioperative continuum, it is unclear how best to build an interprofessional team and which team dynamics are required for success. Differing values and perceptions of collaboration within the group can both enhance and become a barrier to successful collaboration (Sicotte et al., 2002). There exists a gap in current evidence related to characteristics of an ideal team, its dynamics, and how to best formulate its existence. However, a clear theme identifies teamwork and communication as main contributors to the success or failure of interprofessional teams (Garrett, 2016). Interprofessional collaboration, teamwork and communication are implicated in improved patient outcomes, so their incorporation into the opioid free anesthesia protocol implementation will be important.

In order to reduce opioid consumption within the perioperative environment and its contribution to the opioid crisis, it will require interprofessional collaboration (Kaye et al., 2019). Traditionally, teams are structured in a hierarchical manner with a designated leader making decisions and others simply following orders. This structure fails to address the holistic needs of the patient and the complexity of the issue at hand, resulting in poor outcomes for patients, potentially including an overabundance of opioid prescriptions. Recruiting all members of the team to be individually responsible for their professional expertise, communicate respectfully with other members of the team, encourage ideas and collaboration, and work towards a shared goal are characteristics of a highly functioning team using teamwork and communication (Interprofessional Education Collaborative, 2016*)*. With the support of leadership, an interprofessional team utilizing teamwork and communication will implement an opioid free protocol, working together to decrease or eliminate opioid consumption within the perioperative period.

4. Study Endpoints

The primary prospective study end point will be the enrollment and follow up for 60 patients undergoing primary total hip replacement with the opioid free protocol. The primary retrospective study end point will be the collection of the data for all patients in

the 3 months preceding the implementation of the opioid free protocol who will serve as the control group.

The secondary end point will be the collection of teamwork and communication surveys from the providers implementing the protocol.

5. Study Intervention/Investigational Agent

Description: The intervention is the use of an opioid free protocol for patients undergoing primary total hip replacement at EUOSH with Dr. Thomas Bradbury. The protocol requires patients to take non-opioid prescription medications and participate in integrative health interventions (e.g. aromatherapy and meditation) for two weeks prior to surgery. Patients will then undergo an anesthetic protocol during their surgery which aims to eliminate or minimize the use of opioid analgesics. Finally, the patient will utilize non-opioid pain medications for three weeks after surgery, although they will be prescribed an opioid analgesic for pain rescue.

Lavender aromatherapy is being used in this study to create a positive association between the smell and relaxation and sleep. It will be used by participants for two weeks before surgery and after surgery every six hours and at bedtime. Participants will be provided with a bottle of the aromatherapy along with the protocol prescriptions. They will place 2 to 3 drops of the lavender liquid on a cotton ball or tissue and place the cotton ball or tissue near enough to appreciate the smell. Oil should not be placed on the skin and is noted as such in the patient education materials. The purpose of the aromatherapy is not to diagnose, cure, treat or prevent disease, but rather as a holistic means to associate a smell with relaxation and sleep.

Meditation will be used as a part of this study both before and after surgery as a holistic way to mitigate stress and pain. Meditation will be done using a freely available mobile application called Breath2Relax. The application is a portable stress management tool that provides detailed instructions and practice exercises to learn diaphragmatic breathing. The application does not require the input of any information, e.g. name, email, health or personal information. Further, no information or data will be collected from the application. Patient use of the application will only be by self-report.

All preoperative and postoperative medications will be prescribed by the attending surgeon, Dr. Bradbury, or his team. All prescriptions will follow normal Emory physician prescribing protocols. No investigational medications will be used. All intraoperative medications are already currently available as part of the anesthetic armamentarium and are readily available in the operating suite.

The preoperative medication regimen includes:

- Pregabalin 25mg*: Twice a day for two weeks before surgery
- Meloxicam 7.5mg*: Twice a day for two weeks before surgery
    - Prilosec 20mg*: Daily for two weeks before surgery
- Aromatherapy: Every 6 hours and at bedtime

- Guided Meditation: Twice daily
- Voltaren 1% topical arthritis gel* up to 4 times daily

  * indicates study driven medication

The intraoperative medication regimen and timing is as follows:

Timing and Dosing for OFA THA Protocol - SAB

Medication	Preop	Induction	Maintenance	Emergence
Pregabalin* Acetaminophen* Zofran Pepcid Reglan Versed	300 mg ★ 1 Gm ★ 4 mg ★ 20 mg ♦ 10 mg ■ 2 mg ♦			
Preservative free Lidocaine		Height based dosing♦		
Propofol		♦	50-75mcg/kg/min	●
Ancef		2-3 Gm♦		
Decadron*			10 mg ♦	
Toradol*				30 mg♦
0.5% Bupi				
* indicates study driven medication				♦

Caveat: all dosages meant as clinical guidance only

Key
★oral/po med
♦ bolus
■ Consider
----• infusion

The postoperative medication regimen is as follows:

- Baby aspirin 81mg: Twice daily for 6 weeks after surgery
- Tylenol/Acetaminophen 1000mg*: Every 8 hours for three weeks after surgery
- Pregabalin 25mg*: Twice a day for two weeks after surgery
- Prednisone 5mg*: Daily for three weeks after surgery
- Meloxicam 7.5mg*: Twice a day, with food, for two weeks after surgery
    - Prilosec 20mg*: Daily day for two weeks after surgery
- Tramadol 50mg* up to three times a day as needed will be provided for rescue pain

  * indicates study driven medication

A study patient hotline will also be created using a Google number that will directly connect the patient to the surgeon, Dr. Bradbury, or his designee. Study participants will be able to use this number both preoperatively and postoperatively for any concerns related to pain control or medication issues. No one aside from study personnel, the surgeon, or his designee will have

access to this telephone number or the records pertaining to this number (i.e. incoming/outgoing calls).

A pre-test/post-test survey design will be used to assess the perceptions of the providers implementing the opioid free protocol. Specifically, the Nebraska Interprofessional Education Attitude Scale (NIPEAS) subsections related to teamwork and communication will be assessed. In addition, demographic questions and perceptions about the opioid free protocol will be asked in the survey. Throughout this protocol, we will refer to the demographic, perceptions and NIPEAS survey as simply the NIPEAS survey. The surveys will be sent to the providers via RedCap, and all data will be stored in RedCap. Surveys will be provided to all consented perioperative suite professional staff prior to protocol implementation, halfway through the recruitment period and after the last participant has been discharged from the hospital.

The NIEPAS scale is validated to measure the attitude and perception of health care professionals according to the competencies defined by the Interprofessional Education Collaborative (Beck Dallaghan et al., 2016). Upon review of alternative pre- and post- attitude scales, others were deemed inappropriate due to reasons such as validity established on demographics other than our target population, competencies measured not appropriate for our study, and/or the scale was best for measurement outside of the perioperative area (Dominguez et al., 2015). The NIEPAS is a 19 item, five point Likert scale. The tool will be deployed before protocol implementation and halfway through the recruitment period to assess the team's understanding and level of participation in interprofessional practice. The post test will be deployed after the last participant has been discharged from the hospital to assess whether the team's perception of interprofessional practice increased after participating in the implementation process. A correlation with the success of the protocol can be made to recommend the effect of interprofessional practice on the success of implementing an opioid free protocol for surgery.

6. Procedures Involved

All patients who will be undergoing a primary total hip replacement by Dr. Thomas Bradbury at EUOSH and who meet the inclusion/exclusion criteria, will be invited to participate in the study. Inclusion criteria are: patients aged 18 years to 89 years, undergoing a primary total hip replacement with Dr. Thomas Bradbury. Exclusion criteria are: non-English speaking, preoperative opioid use, comorbid condition of diabetes mellitus type 1 or 2, concurrent surgeries, inability or unwillingness to undergo subarachnoid block as part of the anesthetic plan, and contraindications for one or more prescriptions. Approximately 60 participants will be recruited as a convenience sample between February and May 2021. All participants will be required to sign informed consent. In addition, any providers implementing the opioid free protocol who participate in the pre-test/post-test survey of collaborative practice will be required to provide informed consent.

Participants enrolling in the opioid free protocol will be provided with a small bottle of lavender aromatherapy and the prescriptions for the preoperative medications after providing informed consent, but prior to leaving the surgeons office. These individuals will also receive a copy of a printed education manual and 3 video links to educational videos that describe the protocol pre-surgery, day of surgery and after surgery.

Participants enrolled in the opioid free protocol will be sent an electronic survey the day before their scheduled surgery. This survey will ask about their pain levels and compliance with the protocol. The survey will be sent via RedCap using the email feature to the participant's mobile number.

Participants enrolled in the opioid free protocol will also be sent electronic surveys beginning postoperative day 1 and continuing through postoperative day 7. These surveys will ask about their pain levels, use of opioid analgesics and compliance with the protocol. The survey will be sent via RedCap using the email feature to the participant's mobile number.

Risks to participants enrolled in the opioid free protocol will be no greater than standard care. Any patients whose pain is not sufficiently managed by the opioid free protocol will be administered, or provided with opioid analgesics as needed by the surgeon/intraoperative anesthetic team. All participants will be discharged after surgery with an opioid analgesic prescription for rescue pain management.

The perioperative data for patients enrolled in the opioid free protocol will be pulled from the CDW to determine total intraoperative and postoperative opioid requirements prior to discharge. These will be measured using morphine milligram equivalents and compared with the control group.

Risks to participants in the retrospective arm of the protocol will be minimal. Data will be maintained in a secure drive, accessible only to the research team. While a small risk of data compromise always exists, the use of password protections and a secured drive will ensure this risk is minimal. Sixty patients matched on key variables, e.g. age, sex, race/ethnicity, will be recruited from the Clinical Data Warehouse from the year 2020, one year prior to the study period. We anticipate recruiting controls whose surgery dates fell between February and May 2020. The total intraoperative and postoperative opioid requirements prior to discharge will be measured using morphine milligram equivalents.

All professional staff in the perioperative suite will be eligible to participate in the study. Professional staff who elect to participate in the study and complete the NIEPAS surveys will provide written informed consent prior to being sent the NIEPAS survey. The NIEPAS survey will be provided to the entire perioperative suite staff prior to protocol implementation, halfway through the recruitment period and after the last participant has been discharged from the hospital. The surveys will be sent to the providers via RedCap, and all data will be stored in RedCap. Data will be maintained in a secure drive, accessible only to the research team. While a small risk of data compromise always exists, the use of password protections and a secured drive will ensure this risk is minimal.

7. Data and Specimen Banking

We will not be collecting specimens as a part of this study.

8. Sharing of Results with Participants

Direct study results will not be disclosed to participants enrolled in the opioid free protocol. If participants ask if they were administered an opioid analgesic during their surgery, the anesthesia and/or surgery team will provide that information to the participant.

If the preliminary results demonstrate that the opioid free protocol is not meeting the analgesic needs of the patient, an alternative plan will be necessary. To that end, the anesthesia and surgical teams in the operating room will be able to administer opioid analgesics as needed. Further, every participant will be provided with a postoperative prescription for tramadol. The patient will be provided with instructions to take this medication if the opioid free protocol is not meeting their pain needs. In addition, a study patient hotline will also be created using a google number that will directly connect the patient to the surgeon, [redacted], or his designee. Study participants will be able to use this number both preoperatively and postoperatively for any concerns related to pain control or medication issues. No one aside from study personnel, the surgeon or his designee will have access to this telephone number or the records pertaining to this number (i.e. incoming/outgoing calls).

Key findings will not be provided to the prospective or retrospective study participants.

Individuals participating in the NIEPAS surveys will be provided with the summative results of the surveys, as well as the relationship between teamwork and communication and successful implementation of the protocol. These results will be provided by PI Steven Waronker as a PowerPoint slide deck to the anesthesia team, and by PI Noreen Peyatt as a PowerPoint slide deck to the nursing team (pre-, intra- and post-operative).

9. Study Timelines

The protocol will be introduced to the perioperative teams in January with accompanying training materials up to and including printed materials, video materials and in-person/virtual training.

The recruitment period for participants enrolling in the opioid free protocol is four months (February 1, 2021 – May 31, 2021), pending IRB approval. Approximately 60 participants will be recruited as a convenience sample. For individuals participating in the opioid free protocol, their time commitment will be 5 weeks. After enrolling in the study and providing informed consent, they will begin the opioid free protocol 2 weeks

prior to their surgery date. Participants are discharged to home the same day as their hip replacement surgery. They will then continue the protocol for 3 additional weeks.

The recruitment period for retrospective participants identified in the CDW will also be four months. Approximately 60 patients matched on key variables to the prospective sample, e.g. age, sex, race/ethnicity, will be recruited from the Clinical Data Warehouse from the year 2020, one year prior to the study period. We anticipate recruiting controls whose surgery dates fall between February and May 2020. There will be no time commitment from this group of participants.

All professional staff in the perioperative suite will be offered participation in the study and the option to complete the NIEPAS surveys after providing informed consent. The time commitment anticipated for this group is approximately 15 minutes per survey, with 3 separate survey periods (prior to protocol implementation, halfway through the recruitment period and after the last participant has been discharged from the hospital). The survey periods will take place in approximately late January 2021, early April 2021 and early June 2021.

Primary analysis is anticipated to be completed within three months, or by August 31, 2021.

10. Inclusion and Exclusion Criteria

Screening of potential participants for the opioid free protocol will require the office personal to communicate with [redacted] if there are any patients on the schedule who are listed as having a consult for primary total hip replacement surgery. No chart or record review will be required. Clinic is held every Tuesday and Thursday from 7am until 4pm. Any individuals who will be in clinic undergoing consult for a primary total hip replacement will be screened by [redacted] or a member of the research team to ensure inclusion/exclusion criteria are met. The screening will be a self-report by patients, and not a medical record or chart review. Approximately 60 participants will be recruited as a convenience sample.

Inclusion criteria for the opioid free protocol are: patients aged 18 years to 89 years, undergoing a primary total hip replacement with [redacted]. Exclusion criteria for the opioid free protocol are: non-English speaking, preoperative opioid use, comorbid condition of diabetes mellitus type 1 or 2, concurrent surgeries, inability or unwillingness to undergo subarachnoid block as part of the anesthetic plan, and contraindications for one or more prescriptions. Non-English speaking subjects will not be included given the significant amount of materials that are provided to participants in the study, and the need to convert these materials into other languages. As a pilot study, this requirement would be time prohibitive. If the protocol demonstrates success, future studies could include non-English speaking participants. Additionally, adults that are unable to provide informed consent, minors, pregnant women and prisoners will not be included in this portion of the study.

Participants in the retrospective sample will be identified in the CDW. Inclusion criteria for the retrospective sample are: patients aged 18 years to 89 years, undergoing a primary total hip replacement with [redacted]. Exclusion criteria for retrospective sample are: preoperative opioid use, comorbid condition of diabetes mellitus type 1 or 2, concurrent surgeries, and did not have a subarachnoid block as part of the anesthetic.

All professional staff in the perioperative suite will be offered participation in the study and the option to complete the NIEPAS surveys after providing informed consent. Inclusion criteria for the professional staff include: care for patients undergoing primary total hip replacement in the pre-, intra- or post-operative period, and willingness to provide informed consent. Exclusion criteria for the professional staff include: Unwillingness or inability to provide informed consent, non-English speaking. Non-English speaking subjects will not be included given the significant amount of materials that are provided to participants in the study, and the need to convert these materials into other languages. As a pilot study, this requirement would be time prohibitive. If the protocol demonstrates success, future studies could include non-English speaking participants.

11. Vulnerable Populations

Not applicable

12. Local Number of Participants

A total of 60 participants will be included in the prospective study sample and will receive the opioid free protocol. A total of 60 participants will be included in the retrospective study sample and will be identified in the CDW. An estimated number of 50 professional staff work in the perioperative suite and will be offered participation to complete the NIEPAS surveys.

13. Recruitment Methods

Screening of potential participants for the opioid free protocol will require the office personal to communicate with [redacted] if there are any patients on the schedule who are listed as having a consult for primary total hip replacement surgery. No chart or record review will be required. Clinic is held every Tuesday and Thursday from 7am until 4pm. Any individuals who will be in clinic undergoing consult for a primary total hip replacement will be screened by [redacted] or a member of the research team to ensure inclusion/exclusion criteria are met. If inclusion/exclusion criteria are met and the individual will be scheduled for surgery between February 1, 2021 and May 31, 2021, informed consent will be obtained by [redacted] or a member of the research team. No payment or additional travel will be required of these participants.

Recruitment of participants in the retrospective sample will be based on matching key variables to the prospective sample, e.g. age, sex, race/ethnicity, and will be recruited

from the CDW from the year 2020, one year prior to the study period. We will recruit controls whose surgery dates fall between February and May 2020. No payment or additional travel will be required of these participants.

Professional staff meeting inclusion/exclusion criteria for participation in the NIEPAS surveys will be identified by members of the research team embedded within EUOSH, specifically [redacted] The additional time commitment from participants in this group will be approximately 15 minutes per survey, with a total of 3 surveys provided. No payment will be provided to these participants.

No advertising materials will be used for recruitment in any part of this study.

No additional travel will be required of participants enrolled in the opioid free protocol, in the retrospective sample, or from professional staff participating in the NIEPAS surveys.

14. Withdrawal of Participants

Participants enrolled in the opioid free protocol may elect to withdraw from the study at any time and for any reason. Any participant who chooses to withdraw will simply call the number provided on the informed consent, or email the address provided on the informed consent, and indicate their wish to withdraw. Once a participant has withdrawn, a note will be made on the informed consent and no additional data will be collected.

Participants enrolled in the opioid free protocol whose pain cannot be managed by the protocol will be removed from the protocol and provided with opioid analgesics as appropriate by the anesthesia/surgical team. Data will continue to be collected on these individuals for the duration of the study.

Participants in the retrospective arm of the study will not be eligible to withdraw from the study.

Professional staff participating in the NIEPAS surveys may choose to withdraw from the study at any time and for any reason. Any participant who chooses to withdraw will simply call the number provided on the informed consent, or email the address provided on the informed consent, and indicate their wish to withdraw. Once a participant has withdrawn, a note will be made on the informed consent and they will no longer be sent the NIEPAS surveys.

15. Risks to Participants

For participants enrolled in the opioid free protocol, the greatest risk is that their pain would not be sufficiently managed with the protocol. In this circumstance, participants whose pain cannot be managed by the protocol will be removed from the protocol and provided with opioid analgesics as appropriate by the anesthesia/surgical team.

For participants in the retrospective arm of the study, there is a small risk of data compromise if data security is breached. Data will be maintained on a password protected, secure drive accessible only to the research team to minimize this risk.

For professional staff completing the NIEPAS surveys there is a small risk of data compromise, if data security is breached. Data will be maintained on a password protected, secure drive accessible only to the research team to minimize this risk.

16. Potential Benefits to Participants

Potential benefits to participants in the opioid free protocol are the avoidance of opioid analgesics and the accompanying side effect profiles, such as constipation, nausea and clouding of consciousness.

There are no direct benefits to the participants in the retrospective arm of the study.

There are no direct benefits to the participants in the professional staff arm.

17. Compensation to Participants

There will not be compensation for any participants in any arm of this study.

18. Data Management and Confidentiality

Data will be collected via two methodologies, RedCap surveys and CDW data query. All data collected in RedCap is secured via the RedCap HIPAA compliant security apparatus with required dual authentication methodology and encryption. Data collected via clinical record is stored in the CDW in encrypted data tables accessible to only users with healthcare credentials and healthcare VPN access. Any data retrieved from these two sources will be transmitted via Emory OneDrive, a HIPAA compliant file sharing server, provided by the Microsoft Corporation. OneDrive also allows for the secure storage of patient data that requires dual authentication to access data in addition to appropriate permissions.

All data will be received and maintained by [redacted], listed above.

Data will not be made available to anyone outside of the principal investigators and co-investigators unless medically necessary for patient care. In addition, [redacted], is a honest broker for the CDW, and following IRB protocol will keep patient identifiers separate from full datasets with key linkage withheld from anyone besides the three levels of investigators listed above. All associated study staff will present and maintain CITI certification.

Analysis will be performed using de-identified limited datasets. No analyst or study personnel will be granted access to data outside the scope of their normal duties as study employees.

All data will be monitored by the study co-investigator for anomalous or erroneous data that could affect patient care or study security. Frequency data will be used to monitor patient data that is categorical while continuous data will be monitored using quantitative methods such as outlier analysis and mean/standard deviation analysis.

Data analysis will be performed using the R programming language. Means comparisons will be performed via ANOVA, T-Test to examine the relationship between opioid dose and surgical protocol. Linear regression will be used to examine the relationship between protocol dosing and surgical pain scores. In addition, linear regression will also be used to assess the relationship between intraoperative dosing and post-operative opioid need.

Data will be retained for a period of four years after study end. Deleting of the files will be accompanied by seven-fold overwriting on all applicable disk. Any reporting or publication of results will only use aggregate numbers. Further, we do not expect any publications as case reports that focus on individual patients.

19. Provisions to Monitor the Data to Ensure the Safety of Participants

This study does not provide more than minimal risk to the participants. For those involved in the opioid free protocol, all medications and dosages being administered are already a part of the formulary and prescribing practices for surgical patients. A comprehensive log will be kept of all adverse and serious adverse events in conjunction with normal reporting protocols to the institutional review board. Adverse events are described as any unexpected events not requiring hospitalization as a patient. Serious adverse events are any unexpected event requiring hospitalization of the patient or death.

20. Provisions to Protect the Privacy Interests of Participants

Clinical data is stored in the CDW in the electronic health record. If data is to be shared with anyone besides the participant, they will need to follow normal HIPAA waiver procedures with their providers managing clinic, i.e. Emory Healthcare administration. RedCap data will be made available to the patient upon request in writing.

21. Economic Burden to Participants

The study sponsor does not plan to pay for any items or services as a part of this study. It is possible that there may be some economic burden to participants in the study as a result of study medications that may not be paid for by insurance. However, it is unclear if this potential burden would exceed the burden patients might experience even if they do not participate in the study given the wide range of variables that could impact this, such as the type of health insurance, types of co-insurance, required co-payments, deductibles, pain requirements post-operatively and the cost of opioid medications and medications to prevent opioid related adverse drug effects. Participants will be prescribed medications that will be taken both in the preoperative and postoperative period. If the cost of those medications is burdensome to the

participant, they can decide to remove themselves from the study at any time and well in advance of their scheduled surgery. The individual would then be able to proceed with their surgery as planned using the current standard anesthetic approach, including the use of opioid analgesics.

22. Consent Process

Informed consent will be obtained from individuals wishing to participate in the opioid free protocol. The consent process will take place in the pre-surgery clinic. A member of the research team will be responsible for obtaining informed consent. It is estimated that the informed consent process will take approximately 15-30 minutes per person. Should an individual wish to consider the options prior to deciding to participate, they will have until 15 days prior to their surgery day to provide informed consent and still participate in the study. Participants will be informed that they may elect to withdraw from the study at any time and for any reason. Any participant who chooses to withdraw will simply call the number provided on the informed consent, or email the address provided on the informed consent, and indicate their wish to withdraw.

Individuals in the retrospective arm of the study will not be consented.

For professional staff participating in the interprofessional/collaborative practice NIEPAS surveys, informed consent will be obtain by members of the research team. The consent will take place at EUOSH. It is estimated that the informed consent process will take approximately 10-15 minutes per person. Should an individual wish to consider their options prior to deciding whether to provide informed consent, they will have until January 31, 2021, prior to protocol implementation. Participants will be informed that they may elect to withdraw from the study at any time and for any reason. Any participant who chooses to withdraw will simply call the number provided on the informed consent, or email the address provided on the informed consent, and indicate their wish to withdraw.

Participants that do not speak English will not be eligible for participation in the study. Non-English speaking subjects will not be included given the significant amount of materials that are provided to participants in the study, and the need to convert these materials into other languages. As a pilot study, this requirement would be time prohibitive. If the protocol demonstrates success, future studies could include non-English speaking participants. Individuals less than 18 years of age will not be included for participation in the study. Age will be verified by the staff in the pre-surgery clinic. Individuals with cognitive impairment or the inability to provide informed consent will not be included in the study.

23. Setting

Participants for the opioid free protocol will be identified in the pre-surgery clinic held by [redacted] at EUOSH. Participants who provide informed consent will be provided with prescriptions for the medications included in the protocol.

The intraoperative portion of the protocol will be implemented during the participant's surgery at EUOSH.

The data for participants in the retrospective arm will be retrieved from the CDW.

Professional staff participating in the NIEPAS surveys will be recruited at EUOSH. Surveys will be sent via RedCap and will be available to be completed by the participant anywhere they have access to a computer or mobile device.

24. Resources Available

A strong interprofessional team has been built to ensure the ability of the research team to adequately address the complexities of this research. The team includes medicine (surgery, anesthesia and administration), nursing (perioperative nursing, anesthesia and administration), pharmacy, and public health.

All members of the research team have providing CITI certification for biomedical research. The entire research team meets weekly via Microsoft Teams to discuss study progress and to ensure all parties are adequately informed about the protocol and research procedures.

Per [redacted], he performs approximately 40 total hip replacements per month. If our recruitment rate into the study is approximately 40% we should meet our goal of 60 participants. All surgeries will take place at EUOSH and the pre- and post-operative portions of the opioid free protocol will take place in the patient's homes. The professional staff participants will be able to answer the survey question in any location where they have access to computer or mobile services.

Participants in the opioid free protocol will have immediate access to the surgeon for any issues related to their surgery or pain via the study patient hotline. Professional staff participants have access to the employee emergency health and the mental health services hotline.

25. Multi-Site Research when Emory is the Lead Site

Not applicable.

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