# The Effect of a Non-Opioid Multimodal Pain (NOMO) Protocol in Decreasing Narcotic Use after Urogynecologic Surgery

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## A. Objective

The objective of this study is to evaluate narcotic use after implementation of a Non-Opioid Multimodal Pain (NOMO) protocol in patients who are undergoing a urogynecologic procedure. NOMO protocols seek to reduce the opioid usage for patients in the postoperative period. Patients will receive multiple pain medications (usually referred to as a "pain cocktail") that work on various pain receptors throughout the body. These medications are approved for pain control; but they have few side effects and less addictive properties. The study will also evaluate secondary outcomes, including: post-operative pain rating, length of hospital stay, postoperative antiemetic use, bladder catheterization at discharge, number of post-operative phone calls, and rate of reported side effects of opioid use (nausea/constipation). Study participants will be asked to utilize the validated Brief Pain Inventory (appendix A) scale to assess post-operative pain levels. Based on inpatient post-operative opioid use and number of opioid pills prescribed at discharge, an attempt will be made to develop an algorithm for recommended opioid prescribing patterns.

### Background

Mortality from prescription opioids, heroin, and synthetic opioids (Fentanyl) has increased six-fold since 1999. In 2017, more than 47,000 individuals died from opioids, with 36% of those deaths caused by intentional/unintentional overdose from prescription opioids[1]. Although the overall prescribing rate has declined since 2012, the amount of number of morphine milligram equivalents (MME) prescribed per patient is still 3 times higher than in 1999[2]. Recent studies investigating post-operative opioid use and prescribing patterns have suggested that prescribing practices may exceed what patients need[3.]

Increasing evidence has been published in the past decade to support the use of multimodal pain regimens in colorectal, spine, bariatric, spine, and gynecology/oncology surgeries. Utilization of these pain regimens has been shown to decrease immediate post-operative opioid use[4], reduce opioid side effects (nausea/constipation), and improve post-operative pain scores. Our study aims to evaluate a Non-Opioid Multimodal Pain (NOMO) protocol in the Urogynecology population.

## B. Methods

This randomized controlled trial will take place at Prisma Health – Upstate, a single tertiary-care institution. The trial will be registered at Clinicaltrials.gov. Recruitment will occur from July 2019-May 2020. English-speaking females greater than 18 years of age, undergoing a scheduled inpatient or extended observation urogynecology procedure will be approached for inclusion in the study. Consenting patients will sign written consents at their preoperative visit as well as complete a baseline Brief Pain Inventory.

We are planning a study of a continuous response variable from independent control and experimental subjects with 1 control per experimental subject (1:1). In a previous study the response within each subject group was normally distributed with standard deviation 20 (4). If the true difference in the experimental and control means is 20, we will need to study 17 experimental subjects and 17 control subjects to be able to reject the null hypothesis that the population means of the experimental and control groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

The study aims to enroll 20 patients in each arm and accounts for a 15% dropout rate. Patients will undergo enrollment, randomization, and informed consent in the outpatient setting at a preoperative appointment. Consent will be obtained by the subject's operating surgeon in the Division of Female Pelvic Medicine and Reconstructive Surgery. A research coordinator will assist in identifying potential subjects for enrollment and data collection, consent collection/storage, marking medical records to reflect a patient's research status, and follow up phone calls as outlined below. The coordinator will also perform monthly audits to ensure consents are within policy.

Randomization will occur via a computer generated block randomization scheme in groups of 4. Allocation will not be revealed unless requested by the patient, and will only be done after consent is obtained. Surgeons will not be blinded to randomization as they will be placing the pre- and post-operative orders.

Patients in the standard postoperative pain regimen group will undergo routine induction of anesthesia prior to surgery. They will not receive a pre-operative pain cocktail. These patients will receive a postoperative regimen of scheduled acetaminophen (Tylenol) 650mg orally every 6 hours, scheduled ibuprofen (Motrin) 600mg orally every 6 hours, oxycodone 5mg every 6 hours orally PRN moderate to severe pain (pain rated as 4-7 on a scale of 1-10), IV morphine 4mg every 4 hours PRN breakthrough pain (pain rated >7 on a scale of 1-10), and diazepam (Valium) 5mg every 6 hours orally PRN rectal spasms/pressure.

Patients randomized to the NOMO treatment arm will receive a pre-operative pain cocktail in the pre-operative holding area prior to induction of anesthesia. This cocktail will include Celebrex PO 400mg, Lyrica PO 75mg, and Tylenol PO 1000mg. These patients will receive intra-operative ketamine bolus of 0.5mg/kg over a ten minute period. Anesthesia teams will manage the administration of these medications per their standard protocols that are already in place. These patients will receive a postoperative regimen of scheduled Lyrica 75mg orally every 12 hours, Celebrex 200mg orally every 12 hours, and acetaminophen (Tylenol) 650mg orally every 6 hours. As needed medications will be based on routine nursing assessment and evaluations. Patients reporting pain of 1-3 will receive no medications as this will be acceptable for postoperative period. Patients reporting pain of 4-7 will receive Toradol 15mg IV; pain of greater than 7 will warrant one time narcotic administration, starting with oxycodone 5mg by mouth.

NOMO patients will not be prescribed opioids during their hospital-stay unless they report a pain score of > 7 (on a scale of 1-10) as ascertained by nursing during routine vital examination. They will not be prescribed opioids at discharge unless they require more than 5 doses of opioids during their hospital stay. Patients who require an opioid prescription at discharge will be prescribed a 3-day opioid pain medication based on their opioid inpatient requirement. Their prescription will then be converted in morphine milligram equivalents for data analysis.

Based on inpatient opioid requirement and number of pills at discharge, an attempt will be made to develop an algorithm for recommended opioid prescribing patterns. A Brief Pain Inventory will be completed by all participants on the morning of POD#1 (>/= 12 hours after completion of surgery) and again on POD#7. Patients will be contacted by phone to obtain the postoperative day 7 pain scores. The research coordinator will contact patients to collect data regarding day 7 pain scores 7-9 days after surgery. The range allows extra time should day 7 fall on a weekend or holiday.

**Comparison Groups**

The study compares the NOMO protocol to current post-operative routine care in patients undergoing a scheduled extended stay observation or inpatient urogynecologic procedure. Regimens are described as above.

**C. Outcomes**

Primary outcome: Use of opioids during hospital stay as measured in morphine milligram equivalents,

Secondary outcomes: post-operative pain scores on Days 1, and 7 as measured by the Brief Pain Inventory Survey, length of hospital stay, prescription refills, and number of pills left in a prescription at the two week post-operative follow-up appointment. Postoperative antiemetic use, bladder catheterization at discharge, readmission rates within 30 days, number of post-operative phone calls, and rate of reported side effects of opioid use (nausea/constipation).

**D. Inclusion Criteria**

The study population includes English-speaking females greater than 18 years old scheduled for a urogynecologic procedure at GHS requiring inpatient stay or extended observation.

**E. Exclusion Criteria**

Exclusion criteria includes: Patients under 18 years of age, non-English speaking patients, unscheduled urogynecologic surgeries, patients expected to undergo a simple reconstructive surgery with same-day discharge, patients with a history of chronic pain, patients with chronic Lyrica or Celebrex use, psychiatric disorder, narcotic dependence or narcotic prescription in the past six weeks, patients with current liver disease, kidney disease (defined as GFR <60), malignancy, or patients with a sulfa allergy.

**F. Data Collection**

Demographic data, medical and surgical history, and degree of prolapse will be abstracted from the medical chart. Data will be collected from chart review of primary and secondary end points (opioid use, length of hospital stay, prescription refills, and number of pills left in a prescription at the two week post-operative follow-up appointment, antiemetic use, bladder catheterization, rate of readmission, number of phone calls, and rate of reported side effects. Post-operative pain will be evaluated with the validated Brief Pain Inventory Survey.

**Analytic Plan**

Patients will be randomized to either the standard routine care arm or the NOMO arm via a block randomization scheme in blocks of 4; data will be stored on Redcap. Subjects within these two arms will then be stratified by surgery type (laparoscopic surgery, total vaginal surgery, or abdominal surgery) based on surgery selected by the patient and surgeon through a shared decision making process. Data analyzed with an intention-to-treat analysis using an Obstetrics and Gynecology departmental statistician. The statistician will be blinded to treatment arms.

**G. Risks**

Potential risks include: Loss of confidentiality

**H. Benefits**

Potential benefits include: Decreased opioid use in the NOMO arm, reduced cost to the health system and patient, improved quality of care and overall patient satisfaction.

**I. Procedures to Maintain Confidentiality**

All research and hospital staff involved in this study will be trained in patient confidentiality via Learning Hub assigned HIPPA module. Individual chart review will be accessed through a password-protected Epic log-on on Prisma Health – Upstate computers. Once data has been entered into an electronic excel spreadsheet, patient information will be de-identified using a computer-generated number. Data will be maintained on password-protected electronic files, accessed through password-protected computers.

## J. References


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3. Hussein A, et al. Opioid use following gynecologic and pelvic reconstructive surgery. *International Urogynecology Journal.* 2017: pp1-5
4. Reagan, KM, et al. Decreasing postoperative narcotics in reconstructive pelvic surgery: A randomized controlled trial. *AJOG*. 2017; 217 (3): 325