INTRODUCTION:

The opioid epidemic has raised awareness of the risks and benefits of utilizing these addictive narcotics for the treatment of pain. Many patients are first exposed to opioids and other addictive, controlled substances such as benzodiazepines in the perioperative setting. Six percent of opioid naïve patients continue to request opioids beyond 90 days following surgery, despite CDC guidelines for safe opioid prescribing, which recommend their discontinuation. It is unclear whether intraoperative opioid use is truly of benefit for reducing postoperative pain, or whether its increased use can lead to increased harm, including respiratory depression (as indicated by oxygen desaturation), delayed arousal, tolerance, and addiction. The post-anesthesia care unit (PACU) includes highly trained staff to monitor patients for complications related to anesthesia and surgery. Common indications for prolonged PACU stay include inadequately controlled pain and oxygen desaturation related to respiratory depression, nausea, vomiting, and surgical complications. Because the PACU can be costly, prior studies have attempted to optimize PACU resource utilization and case sequencing using predictive modeling for PACU length of stay (LOS); of the risk factors included in modeling, the best predictors of increased PACU LOS included morbid obesity, hypertension, surgical specialty, primary anesthesia type, and scheduled case duration. Though previous studies have used intraoperative opioid administration as a categorical variable (yes/no) to predict increased PACU LOS, studies have not evaluated total intraoperative opioid dosing in predictive modeling.

Prior studies indicate that opioids can lead to adverse events that are associated with PACU LOS (Fig 1). In one study, intraoperative infusion of the short-acting opioid remifentanil increased early postoperative opioid requirements, suggesting the development of acute opioid tolerance. In another study of 155 postoperative patients, 52% experienced episodes with oxygen desaturation, and 47% experienced moderate-severe pain (preoperative opioid use was a significant risk factor for moderate-severe pain in the PACU). Thus, it is suggested that minimizing perioperative opioid use, potentially through the application of perioperative opioid-sparing techniques (regional anesthesia, acetaminophen, non-steroidal anti-inflammatory medication) may decrease both the incidence of respiratory events as well as increase analgesia for opioid tolerant patients. This is further highlighted by a study of premature infants, in which opioid-sparing techniques have been demonstrated to reduce the incidence of postoperative apnea. Additionally, opioids can induce nausea, which can also prolong PACU LOS. Not only are respiratory depression, nausea, and increased opioid tolerance important healthcare quality outcome measures, so is PACU length of stay, which leads to increased direct costs related to intense PACU monitoring. Increased PACU LOS also indirectly leads to increased operating room costs and surgical delays since a full PACU prevents transfers from the operating room (high utilization cost) until a space becomes available.

Current practice regarding intraoperative opioid administration is open to interpretation by the anesthetist and based on a combination of hemodynamic measures and provider intuition. Intraoperative opioid administration is therefore subject to provider bias, habit, and preference. It is therefore critical for perioperative caregivers including anesthesiologists, nurse anesthetists, and
anesthesia assistants to acquire knowledge of the risks and benefits of intraoperative opioid administration to better inform practice. The current proposal addresses this knowledge gap by investigating the short- and long-term sequelae of dose-related intraoperative opioid administration. We hypothesize that in our adult population at Emory, the increased use of intraoperative opioids and other sedating medications leads to increased length of PACU stay, related to both desaturation and inadequately controlled pain. Should we find an association between increased opioid use and increased PACU LOS, we can propose opioid-sparing techniques to reduce intraoperative opioid use and mitigate risks associated with opioids (respiratory depression, nausea, tolerance, addiction) and costs associated with increased PACU LOS.

**SPECIFIC AIMS:**

**Aim 1. Assess the association between intraoperative opioid administration and PACU length of stay (primary outcome).** *Hypothesis:* Increased intraoperative opioid administration is associated with increased need for PACU recovery time in a dose-dependent manner. *Approach:* We will utilize existing electronic medical records to analyze the association between intraoperative opioid administration and time spent in PACU. Charts will be reviewed for indications for prolonged PACU stay, including oxygen desaturation, oxygen requirement, nausea, and poorly controlled pain. Covariates including the use of other sedating agents such as preoperative benzodiazepines (midazolam), gabapentin, age, gender, and length of surgery will also be analyzed.

**Aim 2. Identify risk factors for increased intraoperative opioid use (secondary outcome).** *Hypothesis:* Based on existing literature, we hypothesize that patients using opioids preoperatively require higher intraoperative dosages of opioids. *Approach:* We will utilize existing electronic medical records to analyze the association between preoperative opioid requirements and intraoperative opioid requirements. The use of intraoperative opioid sparing techniques including intravenous acetaminophen or regional anesthesia will also be analyzed for ability to decrease intraoperative opioid use in similar patients.

**Aim 3. Determine the effects of intraoperative opioid administration on short- and long-term pain control (exploratory outcome).** *Hypothesis:* Higher doses of intraoperative opioids lead to acute tolerance, and place patients at risk for chronic opioid use. *Approach:* Utilizing existing electronic medical records, we will analyze the association between intraoperative opioid administration, PACU opioid administration, and PACU pain scores as a surrogate marker of acute opioid tolerance and amount of opioid prescribed to the patient within 90 days postoperatively to assess long-term opioid requirements.

**METHODS:**

**Inclusion criteria** for this study will include patients undergoing surgical procedures under general anesthesia at Emory University Hospital and Emory University Hospital Midtown from 1/1/2014 through 12/31/2018. Men, women, and minorities will be included (Age 18-100). No children will be included.
Exclusion criteria include:

1) Patients undergoing endoscopic procedures (i.e. colonoscopies, ERCP, EGD)
2) Patients who are transferred directly between an ICU and the OR
3) Patients who are intubated prior to transfer to the operating room.
4) Patients with multiple surgical procedures during their admission.
5) Patients who receive monitored anesthesia care (MAC) without general anesthesia.

Using data recorded in the Emory Healthcare Clinical Data Warehouse, records will be identified that meet the above criteria. We will collect data including patient demographics (Patient name, medical record number, surgical case number, age, ASA-PS score, surgery type, outpatient medications prescribed), information related to the surgical procedure (surgeon of record, anesthesia personnel, surgery times (start and stop), anesthesia times (start, stop, extubation, and PACU transfer time), PACU times (ready for discharge and actual discharge), concomitant regional pain procedures performed (e.g. TAP blocks, epidural blocks, surgical injection of local anesthetic), and medications administered intraoperatively and in the PACU. Charts will be independently reviewed by two investigators (C.B. and M.N.) credentialed as students at Emory, using Dr. Woodbury as a resource, given her sub-specialization in pain medicine, for identification of different types of opioids and opioid-sparing analgesics. Dr. Woodbury will also guide the two students in opioid dose conversions.

Data will be stored in Emory Box and will be encrypted per Emory University and Emory Healthcare Guidelines.

We will use a combination of techniques for data analysis including algorithms for associative rule mining, linear or logistical regression and chi-square analysis where appropriate, and survival analysis. Data analysis will be performed by data analysts currently contracted by Dr. Lynde as part of a team to improve perioperative care and resource utilization. Dr. Lynde will perform guidance for interpretation of results and plans for resource optimization at the conclusion of the study.

IMPACT:

Should this study identify an association between perioperative opioid administration and PACU length of stay (Aim 1), then processes would be developed to modify risk factors associated with opioid administration as identified in Aim 2, to reduce PACU length of stay and potentially reduce the development of opioid tolerance and/or addiction (Aim 3).
**REFERENCES:**


