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# Subanesthetic Ketamine for Postoperative Analgesia: An Evidenced-Based Project

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SUBANESTHETIC KETAMINE FOR POSTOPERATIVE ANALGESIA:

AN EVIDENCED-BASED PROJECT

by

Jeremy Alan Vance

A Capstone Project  
Submitted to the Graduate School,  
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in Partial Fulfillment of the Requirements  
for the Degree of Doctor of Nursing Practice

December 2017

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## ABSTRACT

### SUBANESTHETIC KETAMINE FOR POSTOPERATIVE ANALGESIA:

#### AN EVIDENCED-BASED PROJECT

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December 2017

Roughly 100 million surgical procedures are performed in the United States (U.S.) each year and more than 80% of these patients experience acute postoperative pain. Pain costs the U.S. an estimated \$560 to \$635 billion annually and is a significant contributor to national rates of mortality, morbidity, and disability. Despite these findings, patients continue to receive suboptimal postoperative pain relief.

The adjunct administration of subanesthetic ketamine is opioid-sparing and can improve the effectiveness of a multimodal pain management approach. This project used an exploratory descriptive design to examine how an evidence-based presentation impacted the clinical practice of certified registered nurse anesthetists (CRNAs). A questionnaire describing individual pain management practices before and after an evidence-based presentation on multimodal pain management using subanesthetic ketamine was included. Participants completed a pre-intervention questionnaire. The student registered nurse anesthetist (SRNA) then presented an evidence-based teaching intervention on subanesthetic ketamine based on a synthesis of current research. Consistent with current literature, a subanesthetic ketamine dose of 0.5 mg/kg was suggested to participants. As recommended in the literature, subanesthetic ketamine could be administered during the preoperative or intraoperative periods with effective control of pain on emergence. Two weeks later, a post-intervention questionnaire was

mailed to the SRNA using provided self-addressed envelopes. All four participants reported the evidence-based intervention influenced their consideration of subanesthetic ketamine administration. Increases in subanesthetic administration frequencies were also noted.

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## DEDICATION

I want to thank my family for supporting my endeavor to study anesthesia and advance my degree. This project is dedicated to my wife Ashley and son Jeremy. Ashley, you inspired me to begin this journey and have unconditionally supported its pursuit. I know I do not say it enough, but I appreciate you and all you have sacrificed to be by my side these last 3 years. I am proud of the mother you have become, and I love you. To my mom and dad, you believed in me my entire life, and all that I am is because of you. Thank you for instilling the value of hard work and the importance of education. I love you. To Paulie, thank you for your love and support. Your encouragement means more than you know. To the loving memory of Angela DeLaitsch.



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## LIST OF ABBREVIATIONS

<i>AACN</i>	American Association of Colleges of Nursing
<i>AHRQ</i>	Agency for Healthcare Research and Quality
<i>APS</i>	American Pain Society
<i>ASA</i>	American Society of Anesthesiologists
<i>ASRA</i>	American Society of Regional Anesthesia and Pain Medicine
<i>CBV</i>	Cerebral blood volume
<i>CDC</i>	Centers for Disease Control and Prevention
<i>CHF</i>	Congestive heart failure
<i>CINAHL</i>	Cumulative index of nursing and allied health literature
<i>CMS</i>	Centers for Medicare and Medicaid
<i>CMRO<sub>2</sub></i>	Cerebral metabolic rate
<i>COX-2</i>	Cyclooxygenase-2
<i>CRNA</i>	Certified registered nurse anesthetist
<i>DNP</i>	Doctor of Nursing Practice
<i>EBP</i>	Evidence-based practice
<i>HCAHPS</i>	Hospital consumer assessment of healthcare providers and systems
<i>HTN</i>	Hypertension
<i>ICP</i>	Intracranial pressure

<i>IRB</i>	Institutional review board
<i>IOM</i>	Institute of Medicine
<i>IOP</i>	Intraocular pressure
<i>IPPS</i>	Inpatient prospective payment systems
<i>NMDA</i>	N-methyl-D-aspartate
<i>NSAID</i>	Non-steroidal anti-inflammatory drugs
<i>PACU</i>	Post-anesthesia care unit
<i>RCT</i>	Randomized controlled trials
<i>SRNA</i>	Student registered nurse anesthetist

## CHAPTER I – INTRODUCTION

Postoperative pain is a significant concern for surgical patients in the United States (U.S.) (Ladha, Patorno, Huybrechts, Liu, Rathmell, & Bateman, 2016). Most patients undergoing a surgical procedure experience acute postoperative pain and less than half of these patients report adequate postoperative pain relief (Chou et al., 2016). Perioperative pain management is a crucial component of anesthetic care and can affect the amount of pain patients feel postoperatively. Optimal management of this pain poses unique challenges to anesthesia providers, as it requires an understanding of the pathophysiology of pain, the techniques available to decrease pain, procedure specificity, and the situational awareness to assess and direct care as needed. Inadequate treatment of this pain has major consequences to the patient, including needless suffering, delayed recovery, and extended hospital stays following surgery. It also increases the risk for developing chronic pain, leads to higher rates of complications, higher morbidity, and mortality rates, and places a financial burden on health care recipients in the U.S. (Khana et al., 2011).

### Problem Statement

Roughly 100 million surgical procedures are performed in the U.S. each year (Centers for Disease Control and Prevention [CDC], 2010). Approximately 86% of patients undergoing a surgical procedure in the U.S. experience acute postoperative pain and 75% of these patients report the severity as moderate, severe, or extreme (Apfelbaum, Chen, Mehta, & Gan, 2003; Chou et al., 2016). Pain costs the U.S. an estimated \$560 to \$635 billion dollars annually and is a significant contributor to national rates of mortality, morbidity, and disability (Institute of Medicine [IOM], 2011).

Approximately \$261 to \$300 billion per year are spent on medical care associated with pain (Gaskin & Richard, 2011). This estimate does not include indirect costs of pain, e.g., missed working days and lost wages. The Institute of Medicine (IOM) provides three estimates of indirect costs in the U.S. per year: missed working days at about \$11.6 to \$12.7 billion, missed hours of work at about \$95.2 to \$96.5 billion, and lower wages at about \$190.6 to \$226.3 billion (IOM, 2011). Inadequate treatment of postoperative pain results in higher utilization of resources and increased hospitalization and pharmaceutical costs (Strassels, Connie, & Daniel, 2002).

Poorly managed postoperative pain is associated with adverse clinical outcomes (Gan, Habib, Miller, White, & Apfelbaum, 2014). Some of these outcomes include thromboembolisms, coronary ischemia, pulmonary complications, longer hospital stays, higher readmission rates, needless suffering, increased risk of post-surgical complications, and development of chronic pain (American Society of Anesthesiologists [ASA], 2012; Apfelbaum et al., 2003). Unrelieved postoperative pain is also associated with increased morbidity and mortality rates, and increased hospital costs (Apfelbaum et al., 2003). Gan, Habib, Miller, White, and Apfelbaum (2014) examined the preoperative psychological stresses associated with surgery and found that post-surgical pain was the primary concern of 80% of patients. Of these patients, roughly 53% reported high levels of anxiety (Gan et al., 2014). Anxiety is associated with increased heart rate and blood pressure, arrhythmias, shortness of breath, and sleep problems. Anxiety can make pain worse; it enhances the pain experience and decreases a patient's coping ability (Institute for Quality and Efficiency in Health Care, 2014).



## Background and Significance

In 1996, The American Pain Society (APS) reported that pain should be addressed with the same regard as other vital signs. They emphasized the importance of routine and continual assessments with necessary interventions to treat pain (American Pain Society [APS], 2008). In 2000, The Joint Commission introduced an initiative stressing that patients have the right to appropriate assessment and management of pain, further emphasizing the importance of pain as the fifth vital sign. Over the last two decades, concerted efforts by federal and private agencies have focused on improving pain treatment and setting pain management standards (APS, 2008). Collectively, these organizations emphasized the need for change in the treatment and prevention of pain.

Critical developments in pain treatment standards further evolved in 2000 with the U.S. Congress' proclamation of the "Decade of Pain Control and Research" (Brennan, 2015, p. 212). During this time, a dissemination of science, technology, research, and evidence-based practice (EBP) began changing pain management practices (Brennan, 2015). In 2001, the Joint Commission declared pain management is the responsibility of health care providers and consequently established provider standards for assessing and managing pain. The Centers for Medicare and Medicaid (CMS) partnered with the Agency for Healthcare Research and Quality (AHRQ) in the early 2000s to develop the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) (CMS, 2016). Implemented in 2006, this survey was the first publicly reported, nationally standardized survey that measured and compared patients' perceptions of the care they received while in the hospital. For institutions receiving inpatient prospective payment systems (IPPS), a pay-for-performance culture was created

and pain management methods now had direct implications on hospital reimbursements, creating an economic motivation to improve pain management practices (CMS, 2016). Despite these efforts for the last two decades, patients continued to report moderate to severe pain after surgery (Apfelbaum et al., 2003; Gan et al., 2014).

The growing emphasis of adequate pain control and postoperative pain relief introduced the concept of multimodal analgesia in the 1990s (Kehlet & Dahl, 1993). Multimodal analgesia is the combination of two or more drug classes, or non-pharmacologic interventions, used to achieve an additive or synergistic reduction in pain through complementary mechanisms of action along multiple sites of the nociceptive pathway (Helander et al., 2017). Traditionally, the mainstay of postoperative pain relief has been opioids (Ladha et al., 2016). However, large doses of opioids have undesirable side effects such as respiratory depression, sedation, hypotension, nausea, vomiting, and constipation (Ladha et al., 2016). Large doses can also result in acute tolerance, hyperalgesia, and central sensitization (ASA, 2012). In 2012, the APS collaborated with the American Society of Anesthesiologists (ASA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) to release a guideline for perioperative pain management, strongly recommending the adoption of advanced multimodal analgesia protocols for all surgical patients (Chou et al., 2016). There are numerous treatment adjuncts available to implement a multimodal approach including gabapentinoids, acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), regional anesthesia, and ketamine. Combining two or more drug classes with different mechanisms of action, multimodal analgesia targets specific areas in multiple pain pathways, thus inhibiting patients' sensations and/or perceptions of pain (ASA, 2012; IOM, 2011).

Postoperative pain is a serious problem and concern for both anesthesia providers and patients. Despite its inception nearly 40 years ago, ketamine's resurgence as an analgesic is attributed to the low- or subanesthetic dose ranges (Ramachandran & Rewari, 2016; Yang & Moitra, 2013). The use of ketamine has been shown to decrease perioperative opioid requirements and reduce postoperative pain intensity (Hurley, Murphy, & WU, 2015). Notwithstanding this evidence, some anesthesia providers are hesitant to use this drug as a treatment for pain due to various side effects such as hallucinations, tachycardia, lacrimation, delirium, psychomimetic effects, or an increase in intracranial pressure (Yang & Moitra, 2013). Recent reports note that ketamine administered in lower doses may not produce such side effects; and, subanesthetic ketamine was associated with reduced perioperative pain scores, decreased perioperative opioid requirements, and reduced postoperative nausea and vomiting (Yang & Moitra, 2013).

Research suggests that inadequate analgesia throughout the perioperative period is associated with poor health outcomes and significantly contributes to healthcare costs in the U.S. Despite these findings, patients continue to report moderate to severe pain levels postoperatively for the last decade (Apfelbaum et al., 2003; Gan et al., 2014). Therefore, the challenge to anesthesia providers is delivering a patient specific plan of care tailored to meet the emotional, behavioral, and pharmacological needs of the individual.

#### Needs Assessment

Despite advancements in pharmacology and surgical techniques, more than 80% of patients who undergo surgical procedures experience acute postoperative pain (Gan et al., 2014). Early in a clinical rotation, I observed many postoperative patients needing

hydromorphone immediately upon arriving to post-anesthesia care unit (PACU). When I asked providers whether they considered administering subanesthetic ketamine as an analgesic adjunct, many of them admitted they had not. Over time, I assessed that patients who received intraoperative subanesthetic ketamine had smoother wake-ups and did not require an immediate dosing of analgesic upon arrival to PACU. I considered this as opportunity to change CRNAs' practice to include subanesthetic ketamine to reduce the opioid requirements of patients throughout the perioperative period.

### Clinical Question

Implementing EBP optimizes patient outcomes, lowers healthcare costs, and improves quality of care (Melnyk, Fineout-Overholt, Gallagher-Ford, & Kaplan, 2012). To identify the best evidence on subanesthetic ketamine, the EBP process began with the formulation of a clinical question. The clinical question for this project was: are CRNAs willing to change their current practice to include subanesthetic ketamine as an adjunct in the multimodal management of acute postoperative pain?

### Purpose Statement

The purpose of this project was to evaluate whether CRNAs were willing to change their practice to include subanesthetic ketamine as an adjunct in the multimodal management of acute postoperative pain. Evidence suggests that a multimodal approach that includes subanesthetic ketamine reduces total opioid consumption during the postoperative period and is an effective adjunct for postoperative analgesia (Helander et al., 2017).

## Theoretical Framework

### *Model for Evidenced-based Change in Practice*

The EBP movement represented a major paradigm shift in healthcare that is driven by research utilization and clinical expertise to inform clinical decision making and guide clinical practice (Stevens, 2013). Evaluating, integrating, and implementing EBP in the clinical setting improves patient outcomes, reduces healthcare costs, and enhances clinical judgment (Melnyk, Fineout-Overholt, Gallagher-Ford, & Kaplan, 2012). Numerous theoretical frameworks, i.e., conceptual models, were developed to organize the processes of making an evidence-based change in practice.

The EBP model by Rosswurm and Larrabee (1999) provided the theoretical framework that guided this Doctor of Nursing Practice (DNP) project. This model was designed to systematically guide practice change projects through the process of integrating evidence-based changes in practice (Melnyk & Fineout-Overholt, 2011). The model is a progression through six steps from needs assessment through sustaining a practice change. This project used steps one through five. Step six, sustaining a practice change, is discussed in the recommendation section of this paper.

Step one included identification of a problem and assessment of the need for a change in practice that improves acute pain in the postoperative period. The needs assessment was based on clinical observation regarding the use of ketamine in a multimodal pain management plan and a systematic review of the literature. Also, stakeholders were identified as CRNAs, the student registered nurse anesthetists (SRNA), and head of anesthesia at the chosen facility.

Step two involved identifying sources of evidence, planning a search, and conducting the search for the best evidence on the perioperative use of subanesthetic ketamine for acute postoperative pain. Systematic reviews on subanesthetic ketamine, clinical practice guidelines by the APS and the ASA, and single randomized controlled trials, were all considered in step two.

Step three was a critical appraisal and synthesis of the evidence on subanesthetic ketamine as an analgesic adjunct for acute postoperative pain. There was sufficient quality evidence supporting the efficacy of subanesthetic ketamine for perioperative pain management. A facility in the Southeastern U.S. was considered, as well as, the costs, time obligations, and overall feasibility of completing this DNP project in its entirety was considered.

Step four involved defining and designing the proposed practice change that included an evidenced based administration plan for subanesthetic ketamine. This plan and administration regimen was presented to the facility's CRNAs. Step five involved implementing and evaluating this project. During this time, close communication with the participating CRNAs was imperative. Obtaining verbal feedback from the CRNAs regarding implementation of the project and evaluating a need for adjustments to the implementation plan of this project was an important aspect in this step. Evaluating the processes as well as the outcomes and costs associated with this project are important for making final recommendations for adoption of the practice.

#### DNP Essentials

This project utilized the competencies as outlined in The Essentials of Doctoral Education for Advanced Nursing Practice. Fulfillment of the core essentials of the DNP

degree as defined by the American Association of Colleges of Nursing (AACN) are necessary to confer the DNP degree (Chism, 2013). This project employed a systems-based approach to conceptualize and improve practice quality within the culture and structure of the host facility (see Appendix A) (Zaccagnini & White, 2014).

### Review of Literature

A literature search was conducted in July of 2017 using Ovid (MEDLINE), Pubmed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Scopus to identify, appraise, and synthesize current evidence on the use of ketamine in acute perioperative pain management (see Figure 1). Studies meeting inclusion and exclusion criteria were identified by title and abstract. Inclusion criteria included: systematic reviews, randomized controlled trials (RCTs), and studies published in English between 2002 and 2017. Exclusion criteria included: animal or laboratory studies and non-English studies. The following search terms were used in various orders and combinations: *ketamine, postoperative, pain, analgesia, multimodal, low-dose, and subanesthetic*. The initial literature search identified 312 studies. Of these, 259 studies were duplicates and excluded. A total of 53 articles resulted from this search. An additional 36 articles were excluded according to defined criteria and 17 articles remained. After full text screening data extraction, five studies were appropriate for use in this DNP project (see Appendix B).

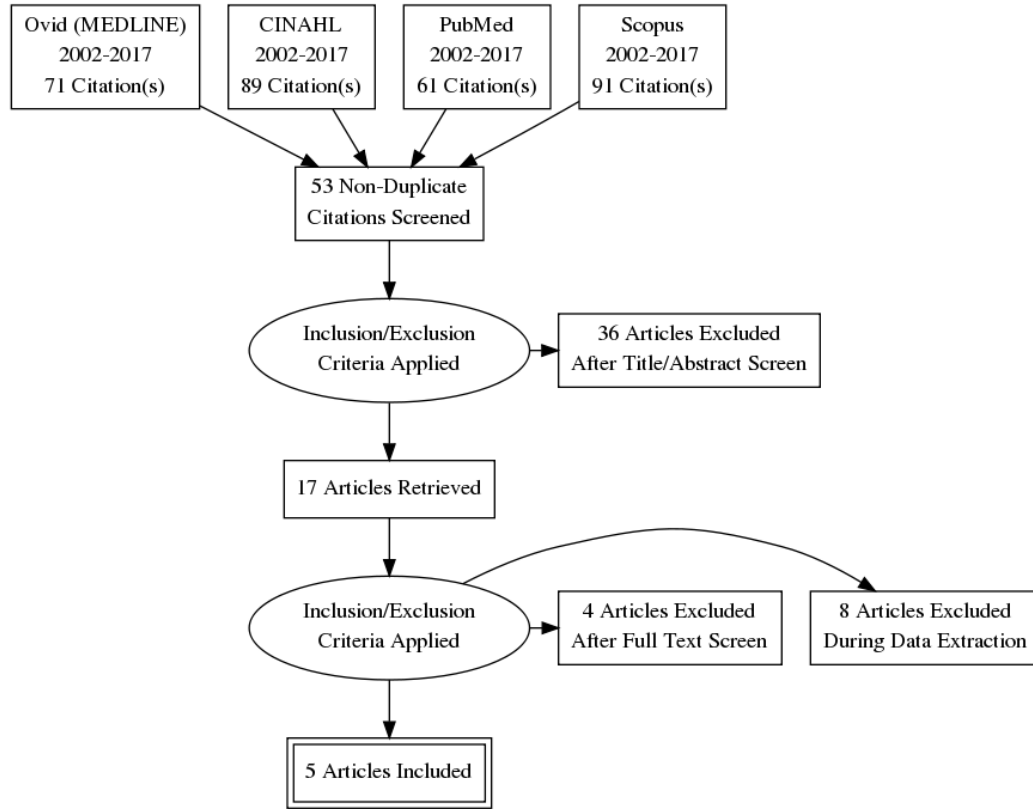


Figure 1. Review of Literature PRISMA Flow Diagram.

Note: Flow diagram for article selection. Adapted from Moher, D., Liberati A., Tetzlaff J., & Altman, D. (2009). "The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement." *PLoS Med* 6(7): e1000097. doi:10.1371/journal.pmed1000097

Ketamine has unique anesthetic properties that make it adaptable to various clinical situations. It is often described as unique because no other single drug has the combined hypnotic, analgesic, and amnesic effects that ketamine distinctly shows (Gao, Rejaei, & Liu, 2016). Ketamine is traditionally used as a general anesthetic, especially in high risk patients with shock or cardiovascular instability, hypovolemia, trauma, severe anemia, and bronchospasm (Nagelhout & Plaus, 2013). It is also used in obstetrics for induction of high risk patients such as those with fetal distress and acute hemorrhage, and



ketamine is used to supplement regional techniques during delivery and the postpartum period (Nagelhout & Plaus, 2013). Renewed clinical interest in ketamine has recently led to its use in the treatment of depression, suicidal ideations, complex regional pain syndromes, cancer pain, alcohol addiction, heroin addiction, asthma exacerbations, wheezing, and pain during Propofol injection, (Gao, Rejaei, & Liu, 2016).

Ketamine is a phencyclidine derivative that predominately effects N-methyl-D-aspartate (NMDA) receptors via noncompetitive antagonism (Yang & Moitra, 2013). It is primarily supplied as a racemic mixture of the R(-) and S(+) isomer forms (Patel, Patel, & Roth, 2011). The S(+) isomer has 4 times the affinity to bind with NMDA receptors, two times the analgesic potency, and fewer psychomimetic effects with its administration, than the R(-) isomer. Ketamine is water and lipid soluble and rapidly crosses the blood brain barrier. Hepatic cytochrome P450 enzymes CYP3A4 and CYP2B6 metabolize ketamine into norketamine that is excreted in urine and bile (Patel, Patel, & Roth, 2011).

Ketamine has the unique characteristic of creating dissociation between the thalamocortical and limbic systems; in fact, the term referred to as dissociative anesthesia was coined specifically for ketamine (Nagelhout & Plaus, 2013). Unlike other general anesthetics, the pharmacokinetic and pharmacodynamic properties of ketamine make it an ideal drug for the unstable and high risk patient. It increases cerebral metabolic rate (CMRO<sub>2</sub>), intracranial pressure (ICP), and cerebral blood volume (CBV). The cardiovascular effects of ketamine occur via sympathetic mediated stimulation and inhibition of catecholamine reuptake, producing an increased blood pressure, heart rate, and cardiac output. Ketamine is a potent bronchodilator and enhances thoracic

compliance. Patients maintain airway reflexes, functional residual capacity, minute ventilation, and tidal volume. Ketamine causes nystagmus, increased intraocular pressure (IOP), increased oral and respiratory secretions, and increased muscle tone (Kurdi, Theerth, & Deva, 2014; Nagelhout & Plaus, 2013).

Ketamine administration should be carefully considered in patients who are comorbid with increased ICP, hypertension (HTN), congestive heart failure (CHF), psychiatric disorders, increased IOP, or angina (Kurdi, Theerth, & Deva, 2014).

However, the pharmacological effects of ketamine are dose dependent. At lower subanesthetic doses, ketamine is primarily an analgesic. In the subanesthetic dose range, there is no respiratory depression and rarely are there psychological and major sympathomimetic effects that are observed at general anesthetic dose ranges (Kurdi, Theerth, & Deva, 2014; Nagelhout & Plaus, 2013).

Ketamine's analgesic properties are attributable to NMDA receptor antagonism (White, 2013). Blocking nociceptive and inflammatory mediators of pain at the NMDA receptor decreases a patient's pain perception. Evidence supports the analgesic properties of ketamine; however, many studies cite the heterogeneity of studies and differences in dose ranges for low dose ketamine (White, 2013).

Numerous studies investigate ketamine administration as an analgesic adjunct during the perioperative period. A systematic review by Laskowski, Stirling, McKay, and Lim (2011) focused on randomized clinical trials (RCTs) and identified 70 studies involving 4,701 patients that used ketamine for perioperative pain control (Laskowski, Stirling, McKay, & Lim, 2011). The study limited ketamine administration without the use of regional anesthesia and found that ketamine administration had an opioid sparing

effect. This means that there was a decrease in total opioid consumption and a prolonged time to first analgesic administration postoperatively, that was significant for thoracic, abdominal, and orthopedic procedures (Laskowski et al., 2011).

Jouguelet-Lacoste, La Colla, Schilling, and Chelly (2015) examined the use of infusion or single, subanesthetic ketamine bolus for postoperative pain control. A systematic review of clinical trials and meta-analyses between 1966 and 2013 identified 5 meta-analyses and 39 clinical trials that met inclusion criteria. Of the 39 clinical trials on subanesthetic ketamine administration, 26 were conducted using a single bolus followed by continuous infusion, 11 using only single boluses, and 2 using continuous infusions. Out of the 2,482 patients in the 39 clinical trials, 1,403 received ketamine. The distribution of studies according to surgery type were: 7 spine surgeries; 1 cardiac surgery; 22 bowel surgeries; 6 arthroplasties; 1 each of ear, nose, and throat surgeries; and 2 studies that combined surgeries (Jouguelet-Lacoste et al., 2015).

All five meta-analyses identified by Jouguelet-Lacoste, et al. concluded that subanesthetic ketamine used as an analgesic adjunct decreased pain scores of and opioid consumption by surgical patients (Jouguelet-Lacoste et al., 2015). Three of these studies reported a mean reduction of morphine consumption of 32% to 50% and a reduction of postoperative rescue analgesics of 30% to 50%. Four out of 5 meta-analyses found that pain scores 24 hours postoperatively were significantly reduced in 87.5% of patients who received intravenous (iv) ketamine (Jouguelet-Lacoste et al., 2015). To assess subanesthetic ketamine, study heterogeneity was noted; however, these studies were included in this project based on their primary outcomes, i.e, postoperative opioid consumption and/or 24-hour postoperative pain scores (Jouguelet-Lacoste et al., 2015).

Six studies, representing 456 patients, 252 of whom received ketamine, assessed the use of subanesthetic ketamine as an intraoperative bolus (Jouguelet-Lacoste et al., 2015). Four out of 6 studies reported an opioid sparing effect and 2 of the 6 studies reported significant reduction in postoperative pain scores. Subanesthetic ketamine administration reduced opioid consumption by an average of 39.25% at 24 hours postoperatively. This study defined subanesthetic ketamine as less than 1.2-mg/kg as an infusion and no more than 1-mg/kg when administered as a bolus. The findings indicate that a subanesthetic ketamine infusion at a rate of <1.2-mg/kg/h during the intraoperative period decreased opioid consumption by 40% and lowered pain scores. There were no reported complications of subanesthetic ketamine at 48 hours after surgery; however, optimal dose or treatment regimen was not ascertained (Jouguelet-Lacoste et al., 2015).

Kaur, Saroa, and Aggarwal in 2015 identified 80 patients undergoing an open cholecystectomy and found subanesthetic ketamine was an effective analgesic up to 6 hours postoperatively (Kaur, Saroa, & Aggarwal, 2015). These patients received a pre-incisional 0.2-mg/kg bolus of ketamine followed by a 0.1-mg/kg/h infusion that ran intraoperatively to the end of the procedure. Pain scores and opioid consumption were significantly reduced in the first 6 hours postoperatively. None of the patients experienced ketamine associated side effects such as hallucinations, prolonged sedation, or marked dissociation on emergence (Kaur, Saroa, & Aggarwal, 2015).

Ketamine has a wide margin of safety at subanesthetic and general anesthetic dose ranges; and, 4 out of 5 of the meta-analyses identified by Jouguelet-Lacoste et al., concluded subanesthetic ketamine was safe when administered as an analgesic adjunct and did not increase the incidence of adverse effects (Jouguelet-Lacoste et al., 2015).

Subanesthetic ketamine use had no impact on sedation scores and was found to decrease the incidence of postoperative nausea and vomiting. The one study that did report negative effects did not deem the effects a safety issue, rather the effects noted in the study were psychomimetic in nature, short term, and stopped with the administration of a benzodiazepine (Jouguelet-Lacoste et al., 2015).

Five studies assessed the administration of a single subanesthetic ketamine bolus or repeated boluses intraoperatively (Jouguelet-Lacoste et al., 2015). Subanesthetic ketamine was not associated with any serious side effects or any increase in serious side effects. Eleven of the studies reported no difference in subanesthetic ketamine versus placebo administration with regards to side effects, i.e., postoperative nausea and vomiting, sedation, and psychomimetic effects. No indications of liver toxicity were observed in any of the 39 clinical trials included in this review (Jouguelet-Lacoste et al., 2015).

A systematic review by Bell, Dahl, Moore and Kalso (2006) identified 37 randomized controlled clinical trials and 53 other studies with treatment regimens exploring the use of intravenous ketamine for perioperative pain control. A total of 2,137 patients were studied, of which 1,210 received ketamine. Postoperative opioid consumption was reduced 24 hours postoperatively with pre-incisional ketamine administration in 76% of the treatment groups (Bell, Dahl, Moore and Kalso, 2006). This study reviewed the optimal analgesic doses of ketamine and divided its findings into 4 groups: 1 group with an estimated dose of 10-mg, 1 group with an estimated dose of 30-mg, 1 group with an estimated dose of approximately 65-mg, and a final group with an estimated dose of approximately 250-270-mg. The evidence revealed that there was no

significant difference in morphine-sparing effects when the ketamine dose was increased above a dose of approximately 30mg (Bell et al., 2006).

The adverse effects of ketamine reported by Bell et al. (2006) were found to be equal in the placebo treated groups. Twenty-one of the 37 trials found no psychomimetic effects such as hallucinations, bad dreams, or dysphoria, in the groups receiving intravenous ketamine for perioperative pain. Psychomimetic effects were reported in four trials and in one placebo group; however, the study determined these occurrences did not impair patient safety. Four of the trials reported increased sedation scores, specifically during the first fifteen minutes postoperatively after extubation. Diplopia was reported as an adverse effect in three of the trials (Bell et al., 2006).

#### Summary

Postoperative pain is undertreated in most surgical patients in the U.S. and has been so for over a decade (Chou et al., 2016). Unrelieved postoperative pain puts patients at risks, and, these risks have immediate and potentially chronic consequences. This project was guided by Rosswurm and Larrabee (1999) EBP model. A clinical need was identified and a comprehensive literature review appraisal identified the best evidence supporting the use of subanesthetic ketamine in a multimodal pain management regimen. Evidence supports the analgesic properties of subanesthetic ketamine administration and its efficacy in treating acute perioperative pain. When added as an adjunct to multimodal pain management regimens, subanesthetic ketamine reduced postoperative pain scores and opioid requirements postoperatively.

## CHAPTER II – METHODOLOGY

Effective postoperative pain management improves clinical and economic outcomes (Apfelbaum et al., 2003; Gan et al., 2014). Despite evidence on the benefits of a multimodal perioperative analgesic regimen, a multimodal approach is often underused in clinical practice (Benhamou et al., 2008). This project used an exploratory descriptive design to examine how an evidence-based presentation impacted the clinical practice of CRNAs.

### Ethical Considerations

A letter of support from the host facility and an approval from the Institutional Review Board (IRB) at The University of Southern Mississippi (USM) was obtained (Protocol number 17091103) (see Appendix C and D). The questionnaires contained the following statements: “[p]articipation in this project is voluntary and not required. Completion of this survey implies your consent to participate. You may choose to withdraw from this project at any time” (see Appendix E and F). No personally identifiable data was collected.

### Participants

A convenience sample of CRNAs practicing at a facility located in the Southeastern U.S. was recruited. Recruitment involved the SRNA approaching each of the CRNAs and briefly discussing the project, its purpose and goals, and time requirements. Four out of the 5 (80%) CRNAs approached agreed to participate. The fifth CRNA indicated that she was not a full-time employee and declined to participate in the project.

## Design

This project included a questionnaire describing individual pain management practices before and after an evidence-based presentation on multimodal pain management using subanesthetic ketamine. At the start of the project, participants were provided with a packet containing a pre-intervention questionnaire with an envelope and a post-intervention questionnaire with self-addressed stamped envelope. Each packet had identically numbered pre- and post-intervention questionnaires that were unique to that packet. Using this numbering system preserved anonymity and provided a means of evaluating changes in individual participants.

The SRNA presented an evidence-based teaching intervention on subanesthetic ketamine, based on a synthesis of current research. This presentation provided key points on: multimodal pain management, the pharmacokinetics and pharmacodynamics of subanesthetic ketamine, the role of subanesthetic ketamine in a multimodal pain management regimen, and the clinical applications of subanesthetic ketamine. Consistent with current literature, a subanesthetic ketamine dose of 0.5-mg/kg was suggested to participants. As recommended in the literature, subanesthetic ketamine could be administered during the preoperative or intraoperative periods with effective control of pain on emergence.

At the end of the presentation, the participants' email addresses were collected for a post-intervention reminder message that was sent one week. The email, which was not associated with the uniquely numbered pre- and post-intervention questionnaires, reminded participants to complete and mail the post-intervention questionnaire. Two weeks after the education intervention, each CRNA completed the post-intervention



questionnaire and mailed it to the SRNA in the self-addressed stamped envelope provided.

### Data Collection

The data collection instrument for this DNP project consisted of two seven-item Likert type questionnaires (see Appendix E and F). The pre-intervention questionnaire assessed each CRNA's pre-intervention approach to managing perioperative pain, their use of analgesic adjuncts, and their use of subanesthetic ketamine in multimodal analgesia. Participants completed the pre-intervention questionnaire, sealed it in the provided blank envelope, and handed the envelope to the SRNA. The post-intervention questionnaire was designed to assess changes in ketamine use by participating CRNAs. Each questionnaire took less than 5 minutes to complete. The SRNA developed the questionnaire. Face validity was achieved through the presentation of the questionnaire to subject matter experts.

Data collected during this project was secured in a locked file cabinet that only the SRNA could access. Electronic data was secured on the SRNA's password protected laptop to which only the SRNA had access. Six months after the completion of degree requirements have been verified, written data will be shredded. Electronic data will be permanently deleted.

### Data Analysis

Data collected for this project measured individual practice patterns pre- and post-intervention. Demographic data limited to gender, age, and number of years in practice, was collected. Frequency counts were used to describe the participants. Upon completion of the project, results were drafted in a final paper for the DNP project.

Findings were disseminated to the group of participating CRNAs as well as other interested persons at the host organization at which time the project was openly discussed.

### Summary

An exploratory descriptive design was used to examine how an evidenced-based presentation impacted the clinical practice of CRNAs. CRNAs were recruited and data was collected using pre- and post-intervention questionnaires. The evidenced-based presentation was based on a synthesis of current research and served as the intervention for this project. After collection of the post-intervention questionnaires, data was analyzed and the results computed.

### CHAPTER III – RESULTS

A total of four CRNAs completed the pre- and post-intervention questionnaires and engaged in the evidence-based teaching intervention. Two of the 4 were female (50%) and 2 of the 4 were male (50%) (see Figure 2). The four CRNAs amassed 62 years of anesthesia experience between them, ranging 6 to 31 years of anesthesia experience (see Figure 3).

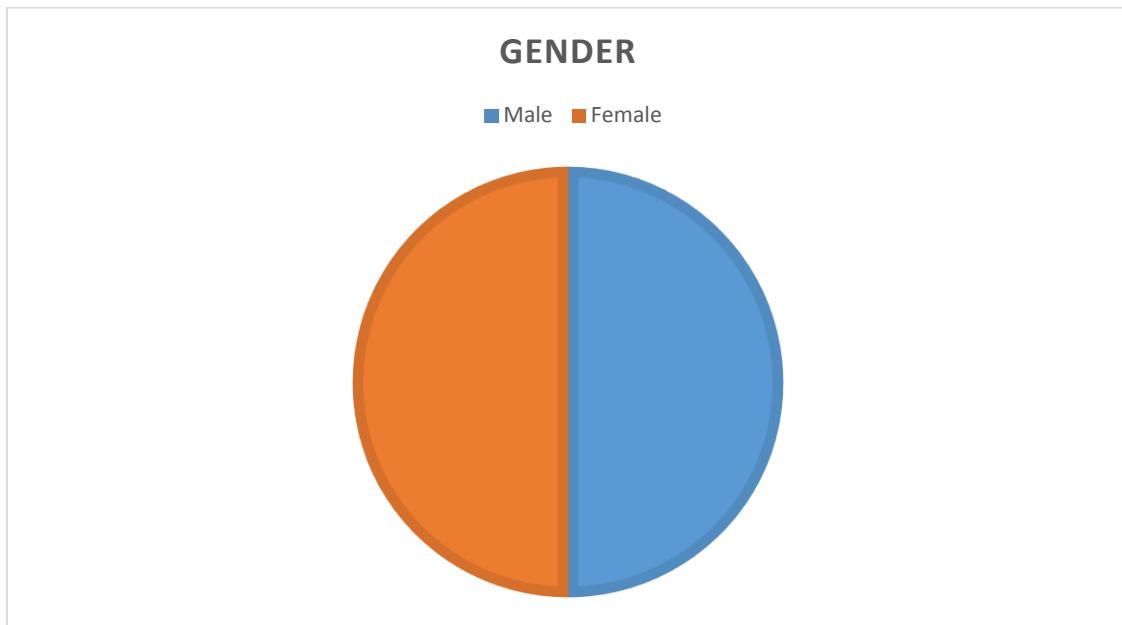


Figure 2. Demographic Data.

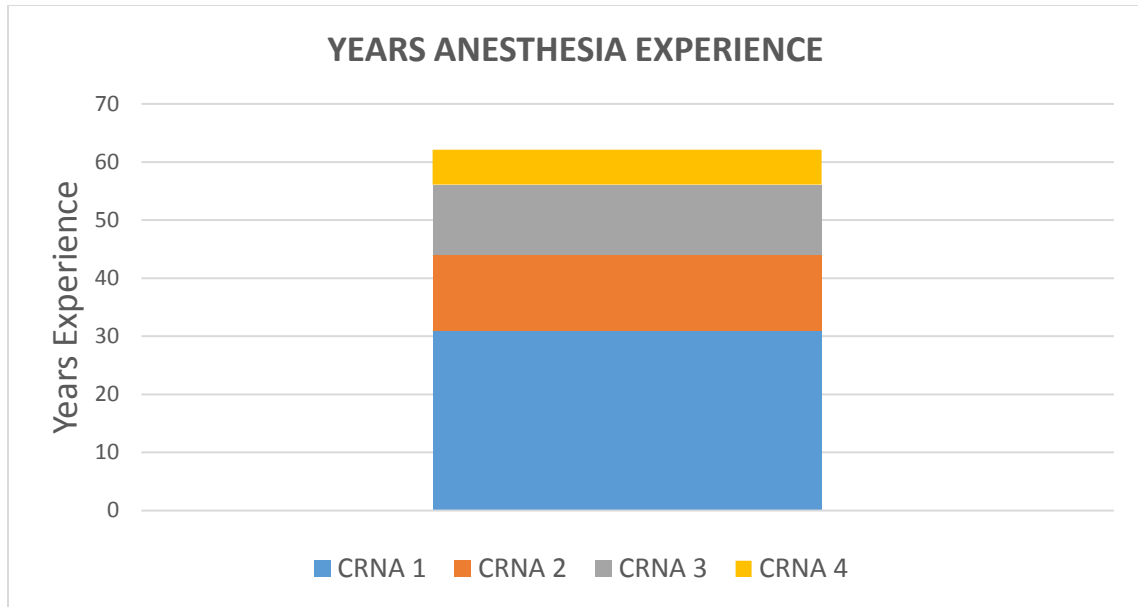


Figure 3. Years of Anesthesia Experience

When asked if a unimodal or multimodal pain management approach described their typical practice, 3 out of 4 (75%) use a multimodal approach and 1 out of 4 (25%) use a unimodal approach (see Figure 4). When asked to rank analgesic adjuncts from most to least likely to use, 3 out of 4 (75%) of respondents ranked cyclooxygenase-2 (COX-2) selective nonsteroidal anti-inflammatory drugs (NSAIDs) as their number one or top analgesic adjunct choice. Three out of 4 (75%) of respondents ranked ketamine as their second go to analgesic adjunct. Calcium channel  $\alpha$ -2- $\delta$  antagonists, acetaminophen, and nonselective NSAIDs, had the third, fourth, and fifth ranking (see Figure 5).

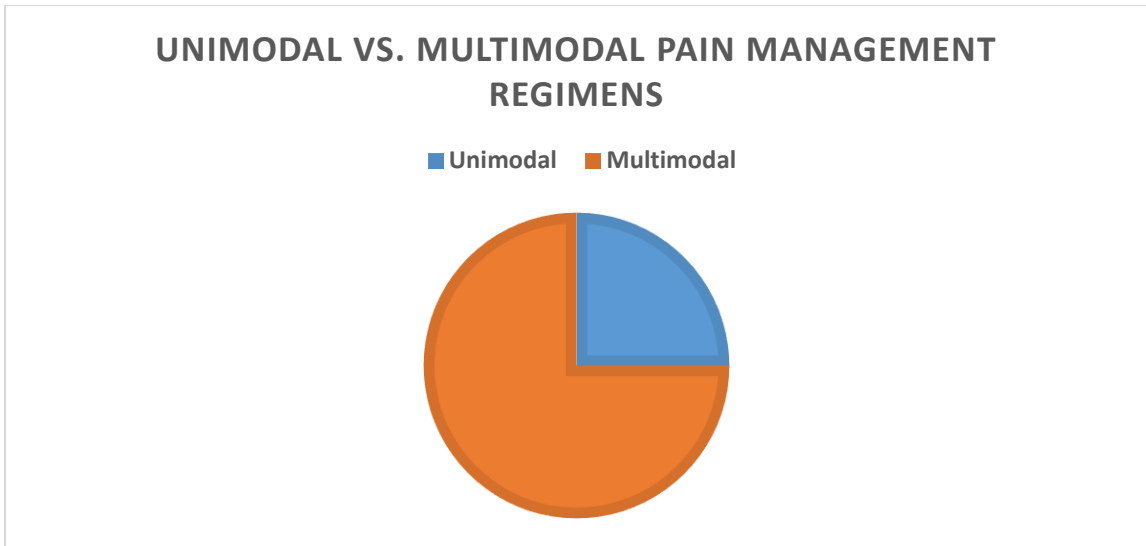


Figure 4. Unimodal vs Multimodal Pain Management Regimens.

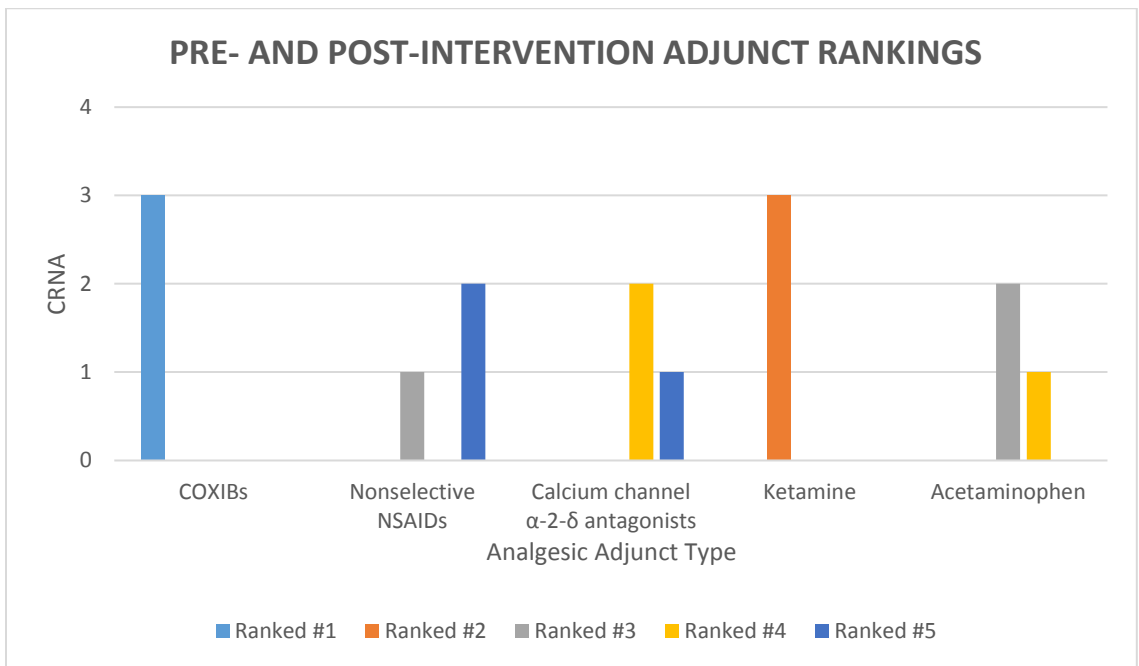
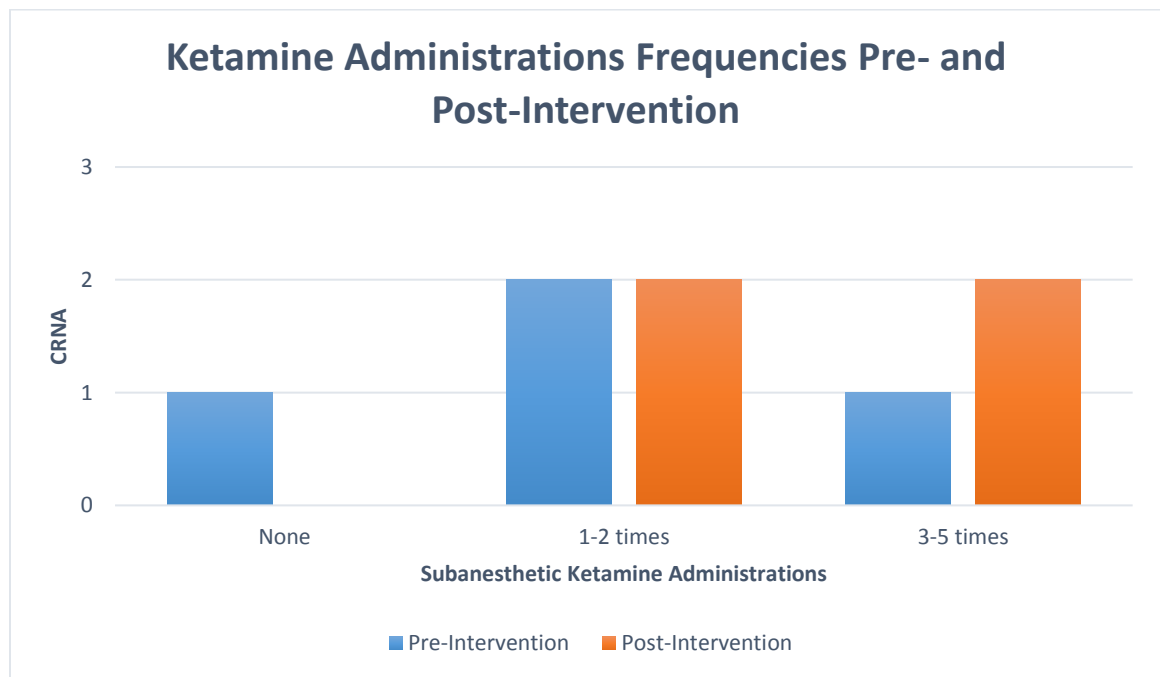


Figure 5. Pre- and Post-Intervention Adjunct Rankings. Adjunct rankings remained unchanged pre- and post-intervention.

When asked how many times participants administered subanesthetic ketamine in the previous two weeks, 2 out of 4 (50%) of participants administered subanesthetic ketamine approximately 1 to 2 times, 1 out of 4 (25%) participants administered subanesthetic ketamine 3 to 5 times, and 1 out of 4 (25%) did not administer subanesthetic ketamine. Four out of 4 (100%) of the participants completed the pre- and post-intervention questionnaires. Of the participants, 4 out of 4 (100%) stated that the evidenced-based intervention influenced their decision to consider the administration of subanesthetic ketamine as an adjunct for perioperative pain control. In the post-intervention questionnaire, four participants stated he or she used subanesthetic ketamine for pain. Most participants increased their use of subanesthetic ketamine over the two-week period (see Figure 6).



*Figure 6.* The Number of Post-Intervention Ketamine Administrations.

Note: Number of times subanesthetic ketamine was administered over a two-week period, post-intervention.

## Summary

This project examined CRNA practice regimens for managing postoperative pain. The adjunct use of subanesthetic ketamine in a multimodal pain management plan pre- and post-intervention was obtained and described in this section. Discussion of the results including implications and limitations are discussed in the following chapter.

## CHAPTER IV - Discussion

### Implications for Clinical Practice

Well-managed postoperative pain is important to anesthesia providers because it improves patient outcomes (Gan et al., 2014). Integrating an opioid-reduced multimodal pain management plan that includes subanesthetic ketamine has implications on several fronts (see Appendix F). Opioid related mortalities continue to rise in the U.S. and surgical patients receiving opioids are more likely to become opioid dependent and long-term users (Brummett et al., 2017; Rudd, 2016). Multimodal pain management plans that effectively treat postoperative pain reduces patient opioid consumption, improves patient satisfaction, enhances patient recovery, reduces hospital stay, and decreases the likelihood of acute pain transitioning to chronic pain (Gan et al., 2014). Second, improving the management of pain reduces healthcare cost in the U.S (Meissner et al., 2015). An efficient opioid-reduced anesthetic that incorporates multimodal pain management strategies is also cost-effective and would reduce pain related healthcare costs (Meissner et al., 2015). Lastly, opioid-related side effects and adverse events would decrease through opioid-reduced multimodal management of postoperative pain (Helander et al., 2017).

### Limitations

There were several limitations in this project. First, this project used a self-selected group that collected self-reported data, thus introducing bias into the results. Second, although a subanesthetic dose of 0.5-mg/kg was suggested, it is not known for certain that this dosage was used. Third, the total number of patients eligible to receive subanesthetic ketamine during the two-week period is unknown. As a result, it is



impossible to know what percent of eligible patients received the intervention. Fourth, data on the effect of subanesthetic ketamine on patient pain postoperatively was not assessed because the project was not able to follow patients through their first 24-hours postoperatively to determine the impact on eventual opioid use. Finally, 2 weeks may be too short to assess sustainability of a practice change. The long-term benefit of non-opioid anesthesia for patients could not be assessed within the timeframe of this project. Thus, the efficiency and effectiveness of subanesthetic ketamine as part of a multimodal pain management regimen could not be established.

Other circumstances limited the findings of this project. A small sample size produced non-generalizable results with no reliability, minimal internal validity, and no external validity. This project also had an insufficient time frame. Patients with contraindications to ketamine administration may have limited the number of times participants could safely utilize the medication in such a short time period which could have effected results.

#### Recommendations for Future Study

Based on evidence cited in this project, the use of subanesthetic ketamine for postoperative analgesia can be anticipated to improve patient outcomes when part of a multimodal pain management plan. Future studies should examine barriers to subanesthetic ketamine administration. For example, some CRNAs cite the cost of a multi-dose vial and the necessity of wasting doses as barriers for adoption. Therefore, it would be important to understand what the impact of prefilled syringes would be on the decision to include ketamine in a multimodal pain management plan. A study looking at ketamine usage before and after pharmacy provides single dose syringes would provide

data for this potential barrier. Future studies should examine the opioid-sparing effects of subanesthetic ketamine by measuring the amounts opioids patients receive postoperatively using morphine equivalents. What procedure and patient specific attributes increase postoperative opioid consumption despite subanesthetic ketamine administration?

Future studies should monitor patient outcomes over time. The sixth and final step of the EBP model by Rosswurm and Larrabee involves integrating and maintaining a change in practice that includes subanesthetic ketamine as an adjunct in the multimodal management of acute postoperative pain (Rosswurm & Larrabee, 1999). To sustain a change in practice patient outcomes must be periodically monitored

### Conclusion

This project described pain management practices before and after an evidence-based presentation on multimodal pain management using subanesthetic ketamine. Unmentioned until now, and relevant to this project, is the opioid crisis. Opioid addiction and abuse is a public health problem that is now an epidemic of opioid overdoses and opioid related deaths (Rudd, 2016). The problem is so widespread that many surgical patients are concerned with taking opioids preoperatively and post-discharge (Apfelbaum, Chen, Mehta, and Gan, 2003). If given a choice, roughly 72% of surgical patients prefer a non-narcotic analgesic after surgery (Apfelbaum, Chen, Mehta, and Gan, 2003). Their reasoning was because non-narcotic medication are less addictive (49%) and have fewer side effects (18%) (Apfelbaum, Chen, Mehta, and Gan, 2003). Over 500,000 Americans have died from drug overdose from 2000 to 2015 and 91 people die

the same fate every day (Rudd, 2016). Exploring opioid sparing multimodal approaches that utilize subanesthetic ketamine has national implications to public health.

Postoperative pain management is a challenging and pivotal component of anesthesia. Despite their efficacy and place in anesthesia, opioids as mainstay analgesics have failed to provide patients with optimal postoperative pain control for more than a decade. Unimodal opioid use increases postoperative risk for opioid related adverse events and can increase patient risk for becoming opioid dependent and long-term users (Brummett et al., 2017).

## APPENDIX A – DNP Essentials

Table A1.

*The AACN Essentials of Doctoral Education for Advanced Nursing Practice*

<b>Essential</b>	<b>How the Essential was Achieved</b>
<p>I. Scientific Underpinnings for Practice</p>	<p>This project described the pathophysiological effects of acute pain, explained the pharmacology of multimodal analgesia, and discussed the pharmacokinetics and pharmacodynamics of ketamine. Considering this information, strategies to translate research to practice were developed.</p>
<p>II. Organizational and Systems Leadership for Quality Improvement and Systems Thinking</p>	<p>This project evaluated pain management regimens of CRNAs in a facility in the Southeastern U.S. Strategies for effective perioperative pain management using subanesthetic ketamine as an adjunct in the multimodal management of acute postoperative pain were presented to improve quality of care.</p>
<p>III. Clinical Scholarship and Analytical Methods for Evidence-Based Practice</p>	<p>This project appraised and disseminated the most current evidence on subanesthetic ketamine administration for acute</p>

postoperative pain. This evidence was presented to CRNAs and a evidence-based change in practice that included subanesthetic ketamine was proposed.

V. Health Care Policy for  
Advocacy in Health Care

This project advocated for surgical patients by proposing an evidenced-based change in practice to improve the quality of pain management in this population and influence institutional leadership to support implementation of this evidenced-based practice change. This project proposed an evidence-based practice change utilizing subanesthetic ketamine to improve the treatment of pain through the postoperative period.

VII. Clinical Prevention and  
Population Health for  
Improving the Nation's  
Health

To avert the opioid crisis in the U.S., this project asserted that effective pain management during the postoperative period decreases the risk for acute pain transitioning to chronic pain and the prolonged need and/or dependency on opioid.

VIII. Advanced Nursing  
Practice

This project proposed a practice change that includes the use of subanesthetic ketamine as an adjunct in the multimodal management of acute postoperative pain.

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Note: Chism, L. (2013). The doctor of nursing practice: A guidebook for role development and professional issues (2nd ed.). Burlington, MA: Jones & Bartlett Learning.

APPENDIX B – Review of Literature

Table A2. Literature Matrix

Author, Year, Title	Level/ Grade	Purpose	Design	Sample/ Data Collection	Outcome, Recommendations
Gao, M., Rejaei, D., & Liu, H. (2016). Ketamine use in current clinical practice.	I	Pharmacokinetics and pharmacodynamics of ketamine; clinical application of ketamine including risks and benefits	Meta-analysis	Systematic review of literature	Analgesic/Low dose range 0.25-1 mg/kg; evidence supports the use of ketamine for acute pain management in postoperative period. Preoperative dose of 0.1mg/kg showed opioid sparing effect. For postoperative pain, low-dose reduced opioid requirements in first 24 hours postoperatively and reduced postoperative nausea and vomiting.
Jouguelet-Lacoste, J., La Colla, L., Schilling, D., & Chelly, J. E. (2015). The Use of Intravenous Infusion or Single Dose of Low-Dose Ketamine for Postoperative Analgesia: A Review of the Current Literature.	I	Evaluate the efficacy of low-dose ketamine in managing postoperative pain	Systematic Review	Review of literature including all randomized controlled trials, meta-analysis, and systematic reviews	39 clinical trials assessed infusion and bolus of low dose ketamine. Low dose defined as < 1.2 mg/kg. Mean reduction in opioid use in 40% of patients. Low-dose ketamine also result in lower pain scores and no major complications were found up to 48 hours postoperatively.
Kaur, S., Saroa, R., &	II	Evaluate the effect of low-dose bolus	Double blind	80 patients undergoing	Treatment group received preoperative

<p>Aggarwal, S. (2015). Effect of intraoperative infusion of low-dose ketamine on management of postoperative analgesia.</p>		<p>followed by intraoperative infusion on postoperative pain.</p>	<p>randomized controlled trial</p>	<p>open cholecystectomy</p>	<p>bolus of 0.2 mg/kg and pre-incision infusion of 0.1 mg/kg/h up to the end of surgery where it was discontinued. Effective analgesia for first six hours postoperatively.</p>
<p>Laskowski, K., Stirling, A., McKay, W. P., &amp; Lim, H. J. (2011). A systematic review of intravenous ketamine for postoperative analgesia.</p>	<p>I Evaluate the efficacy of ketamine as adjunct in multimodal pain management plan.</p>	<p>Systematic Review</p>	<p>Review of literature from 1966 to 2010 that included all randomized controlled trials, double-blind, and placebo-controlled, that utilized ketamine to decrease postoperative pain</p>	<p>Ketamine effective adjunct in reducing postoperative pain. 47 studies identified, reduction in total opioid consumption and an increase in time to first analgesic were observed in all studies (P&lt;0.001). Greatest efficacy by surgical site identified as: thoracic, upper abdominal, major orthopedic procedures. When ketamine efficacious for pain, patients experienced less postoperative nausea and vomiting.</p>	



## APPENDIX C – IRB Approval Letter



**INSTITUTIONAL REVIEW BOARD**  
118 College Drive #5147 | Hattiesburg, MS 39406-0001  
Phone: 601.266.5997 | Fax: 601.266.4377 | [www.usm.edu/research/institutional.review.board](http://www.usm.edu/research/institutional.review.board)

### NOTICE OF COMMITTEE ACTION

The project has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services (45 CFR Part 46), and university guidelines to ensure adherence to the following criteria:

- The risks to subjects are minimized.
- The risks to subjects are reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered regarding risks to subjects must be reported immediately, but not later than 10 days following the event. This should be reported to the IRB Office via the "Adverse Effect Report Form".
- If approved, the maximum period of approval is limited to twelve months.  
Projects that exceed this period must submit an application for renewal or continuation.

PROTOCOL NUMBER: 17091103  
PROJECT TITLE: Subanesthetic Ketamine for Postoperative Analgesia: An Evidence-Based Project  
PROJECT TYPE: New Project  
RESEARCHER(S): Jeremy Alan Vance  
COLLEGE/DIVISION: College of Nursing  
DEPARTMENT: Advanced Practice  
FUNDING AGENCY/SPONSOR: N/A  
IRB COMMITTEE ACTION: Exempt Review Approval  
PERIOD OF APPROVAL: 09/13/2017 to 09/12/2018  
**Lawrence A. Hosman, Ph.D.**  
**Institutional Review Board**

APPENDIX D – Letter of Approval

August 23, 2017

[REDACTED]  
[REDACTED]

RE: Jeremy Vance Request for Letter of Support

I am the [REDACTED] and a practicing Certified Registered Nurse Anesthetist. I am pleased to offer this letter of support for SRNA doctoral candidate Jeremy Vance and his DNP project [REDACTED]

I understand Jeremy Vance is a doctoral candidate in the nurse anesthesia program at The University of Southern Mississippi who is planning to graduate in December of 2017. This letter of support will be included in the University of Southern Mississippi IRB application. I understand that open participation will be presented to anesthesia providers practicing at this facility. There is no compensation for their participation.

I understand the project will take place over a two period. The project is set to begin [REDACTED] or after USM IRB approval is received. [REDACTED] Marjorie Geisz-Everson is chair of the project and her contact information is:  
[REDACTED]

I understand that participation is anonymous and voluntary. Participants may withdraw at any time.

I am looking forward to hearing the results of his research and its impact on clinical practice.

Sincerely,  
[REDACTED]

[REDACTED]

## APPENDIX E – Pre-Intervention Questionnaire

### Data Collection Instrument: Pre-Intervention Questionnaire

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This questionnaire is intended to assess your current practice and typical approach to managing pain during the perioperative period. Please complete each of the following questions. When you are finished, place the questionnaire in the provided self-addressed envelope and mail to the principal investigator.

Participation in this project is voluntary and not required. Completion of this survey implies your consent to participate. You may choose to withdraw from this project at any time. Thank you for your participation in this project.

---

1. Gender:
  - a. Male
  - b. Female
2. Age: \_\_\_\_\_years
3. Years practice anesthesia: \_\_\_\_\_years
4. Do you typically use a unimodal or multimodal pain management regimen?
  - a. Unimodal
  - b. Multimodal
  - c. Don't know
  - d. Comments:  
\_\_\_\_\_
5. If you do use a multimodal regimen, rank the following adjuncts by how frequently you administer the drugs for their analgesic properties (rank from most frequent #1 to least frequent #)
  - a. \_\_\_ Cyclooxygenase-2(COX-2) selective nonsteroidal anti-inflammatory drugs (NSAIDs)(COXIBs)
  - b. \_\_\_ Nonselective NSAIDs
  - c. \_\_\_ Calcium channel  $\alpha$ -2- $\delta$  antagonists (gabapentin, pregabalin)
  - d. \_\_\_ Ketamine
  - e. \_\_\_ Acetaminophen
6. Over the last two weeks, how many times have you administered subanesthetic ketamine for pain?
  - a. 1-2 times
  - b. 3-5 times
  - c. None, I did not administer subanesthetic ketamine
  - d. Don't know
7. Based on the evidence provided during this evidenced-based project, are you more likely to consider subanesthetic ketamine as an adjunct for perioperative pain control?
  - a. Yes
  - b. No

## APPENDIX F – Post-Intervention Questionnaire

### Data Collection Instrument: Post-Intervention Questionnaire

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This questionnaire is intended to assess your current practice and typical approach to managing pain during the perioperative period. Please complete each of the following questions. When you are finished, place the questionnaire in the provided self-addressed envelope and mail to the principal investigator.

Participation in this project is voluntary and not required. Completion of this survey implies your consent to participate. You may choose to withdraw from this project at any time. Thank you for your participation in this project.

---

1. Gender:
  - a. Male
  - b. Female
2. Age: \_\_\_\_\_years
3. Years practice anesthesia: \_\_\_\_\_years
4. Do you typically use a unimodal or multimodal pain management regimen?
  - a. Unimodal
  - b. Multimodal
  - c. Don't know
  - d. Comments:  
\_\_\_\_\_
5. If you do use a multimodal regimen, rank the following adjuncts by how frequently you administer the drugs for their analgesic properties (rank from most frequent #1 to least frequent #)
  - a. \_\_\_ Cyclooxygenase-2(COX-2) selective nonsteroidal anti-inflammatory drugs (NSAIDs)(COXIBs)
  - b. \_\_\_ Nonselective NSAIDs
  - c. \_\_\_ Calcium channel  $\alpha$ -2- $\delta$  antagonists (gabapentin, pregabalin)
  - d. \_\_\_ Ketamine
  - e. \_\_\_ Acetaminophen
6. Over the last two weeks, how many times have you administered subanesthetic ketamine for pain?
  - a. 1-2 times
  - b. 3-5 times
  - c. None, I did not administer subanesthetic ketamine
  - d. Don't know

APPENDIX G – Logic Model

Table A3. *Logic Model*

Resources	Activities	Outputs	Short & Long Term Outcomes	Impact
<ul style="list-style-type: none"> <li>• CRNA</li> <li>• Researcher</li> <li>• Time</li> </ul>	<ul style="list-style-type: none"> <li>• Conduct a comprehensive and systematic review of the literature</li> <li>• Present findings to CRNA</li> <li>• Discuss current pain management plan with CRNA</li> </ul>	<ul style="list-style-type: none"> <li>• Summary of major findings to propose practice change</li> <li>• Conduct an evidenced-based practice change proposal</li> </ul>	<ul style="list-style-type: none"> <li>• Short term (1-3 years) improved management of postoperative pain</li> <li>• Long term (4-6 years) facility guideline on the use of multimodal pain management strategies that includes subanesthetic ketamine</li> </ul>	<ul style="list-style-type: none"> <li>• Multi-modal a standard of care</li> <li>• Reduction in facility costs</li> <li>• Improved patient outcomes</li> </ul>

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