11-28-2023

# Advantages of Intravenous Administration of Remimazolam Over Midazolam in Inflammatory Bowel Disease Patients Undergoing Endoscopic Procedures: An Educational Module

Alexis Perez
*Florida International University*, apere616@fiu.edu

Jorge Valdes
*Florida International University*, jvalde@fiu.edu

Jillian Gil

# Advantages Of Intravenous Administration of Remimazolam Over Midazolam In Inflammatory Bowel Disease Patients Undergoing Endoscopic Procedures: An Educational Module

A DNP Project Presented to the Faculty of the
Nicole Wertheim College of Nursing and Health Sciences

Florida International University

In partial fulfillment of the requirements
For the Degree of Doctor of Nursing Practice

By

Alexis Perez, MSN, RN, CCRN

Supervised By

Jorge Valdés, DNP, CRNA, APRN, FAANA
Jillian Gil, DNP, CRNA, APRN

Approval Acknowledged _____, DNA Program Chair

DocuSigned by:
Ann Miller
A986D8685093471...

Date: 11/28/2023

Approval Acknowledged: _____, DNP Program Director

DocuSigned by:
27267E9FF76F400...

Date: 11/28/2023

## Abstract

*Background:* Inflammatory bowel disease (IBD) patients experience more pain and discomfort during colonoscopy due to the nature of the disease. They are often young, highly anxious before the procedure, and have undergone many previous colonoscopies, which are known risk factors for intolerance to the procedure. Currently, the sedative drugs used with these procedures are primarily propofol and midazolam. Midazolam possesses a prolonged half-life, necessitating a lengthier recovery period from anesthesia for patients. In this patient population, the utilization of a new drug called remimazolam as an alternative can lead to improved outcomes.

*Methods:* A thorough search of research was performed utilizing PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Google Scholar to distinguish research studies published within the past ten years that have assessed the efficacy of remimazolam to midazolam and/or another anesthetic agent in similar populations. Using the literature review, an educational module was presented to educate providers on the use of remimazolam.

*Results:* The educational module resulted in a boost in providers' knowledge and attitudes concerning remimazolam, leading to its increased utilization for IBD patients undergoing endoscopic procedures.



*Keywords:* remimazolam, midazolam, colonoscopy, endoscopy, endoscopic procedures, procedural sedation, inflammatory bowel disease, randomized controlled trial, RCT

**TABLE OF CONTENTS**

# Introduction

## Problem Identification

Endoscopic procedures like colonoscopies are widely used in clinical practice. These non-surgical procedures require a flexible tube to be inserted via the anus to examine a patient's gastrointestinal tract. Patients with IBD, including Crohn's Disease (CD) and Ulcerative Colitis (UC), require these endoscopic procedures for diagnosis, disease assessment, and dysplasia surveillance.[1] It is common for patients to experience distress such as anxiety, fear, and cramps.[2] Severe complications like airway obstruction, aspiration, and bleeding can also be possible.[2]

Common techniques for sedation during these procedures include moderate sedation and monitored anesthesia care (MAC).[1] Usually, administering sedatives and analgesics during endoscopic procedures can reduce anxiety and pain in patients. The appropriate sedation can also shorten the duration of the procedure by reducing its difficulty.[2] Currently, the sedative drugs used with these procedures are primarily propofol and midazolam.

Sedation and analgesia are areas of significance for patients with IBD. The presence of IBD has been recognized as a factor associated with higher sedation and analgesia needs.[1] Furthermore, patients with IBD reported lower satisfaction with sedation during endoscopic procedures and increased procedural pain compared with patients without CD or UC.[1] This project aims to educate anesthesia providers on the use of remimazolam (compared to midazolam) for IBD patients to improve outcomes.

## Background

Endoscopic procedures play an essential role in the diagnosis and management of IBD.[3] For patients with CD or UC, colonoscopy is often recommended for evaluation before changes in medical management to check for post-operative disease recurrence and to observe for the

presence of abnormal cells, as these patients are at increased colorectal cancer risk.[1] In comparison, non-IBD patients are primarily recommended to have a colonoscopy for colorectal cancer screening, hemoccult positive stool, iron deficiency anemia, hematochezia, or other lower gastrointestinal symptoms.[1] Therefore, patients with IBD will likely be subject to a relatively higher number of colonoscopies throughout their lifetimes.[1]

Due to the clinical manifestations of the disease, IBD patients tend to experience more pain and discomfort than most patients undergoing colonoscopy for other indications.[3] Moreover, IBD patients are young, with high levels of preprocedural anxiety, and have already undergone many previous colonoscopies: these characteristics are known risk factors for intolerance to colonoscopy.[3]

Midazolam, a benzodiazepine in clinical use for over 40 years, is the most used benzodiazepine in the perioperative period. It increases the affinity of GABA to its binding site on the $GABA_A$ receptor.[4] The elimination half-life of midazolam is 1–4 hours and is metabolized by the liver via cytochrome P450 enzymes to active and inactive metabolites.[4] Due to the long duration of action, patients require more time to recover from anesthesia. Midazolam should be avoided in patients with hepatic or renal impairment.

**Scope of the Problem**

Approximately 1.6M Americans are affected by IBD, with 785,000 patients with CD and 910,000 with UC.[5] Patients with IBD are reluctant to undergo endoscopic procedures due to difficulties with bowel cleansing, anxiousness, the expectation of pain, and embarrassment.[6] Sedation during colonoscopy can reduce pain, anxiety, and embarrassment and likely ensures a higher success rate and examination quality.[6]

## Consequences of the Problem

Not addressing this problem has many consequences for the patient and the healthcare system. Weber et al. stated in their study that patients with IBD have increased sedation requirements. Patients reported lower satisfaction with sedation and increased procedural pain during colonoscopies.[1] Patients also reported lower endoscopy tolerability than other modes of testing for disease monitoring and diagnostics.[1] Furthermore, Steenholdt et al[6] reported that many patients opt out of colonoscopies due to the unpleasantness related to this procedure. The use of midazolam for this patient population is often required to meet their sedation needs. However, midazolam has a prolonged duration, increasing the time necessary for patients to recover. Increased recovery times disrupt the efficiency of patient flow from the procedural room to PACU and discharge. When patients are held longer than necessary, they consume valuable resources and contribute to costly patient backlogs.[7] In addition, the PACU becomes crowded compromising patient safety and quality of care. Failure to address this issue will result in continued reported patient dissatisfaction with sedation/analgesia, increased PACU times, and increased healthcare costs.

## Knowledge Gaps

Multiple studies have shown that remimazolam is a safe and effective sedative for patients undergoing endoscopic procedures.[8] Rex et al. evaluated the use of remimazolam in high-risk ASA patients undergoing colonoscopy, showing a safety profile comparable to low-risk ASA patients.[9] While the efficacy of an intervention is reliable, effectiveness is influenced by institutional compliance. A reason for the uncommonness of remimazolam as an option can also be due to the provider's lack of knowledge of the treatment.

## Proposal Solution

The Food and Drug Administration (FDA) approved Byfavo (remimazolam), by Acacia Pharma, in July 2020 for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less due to its favorable results in clinical trials.[10] Remimazolam is a new benzodiazepine that exerts its effect by binding to $GABA_A$ receptors in the brain like its parent compound, midazolam. This new drug combines remifentanil and midazolam with a carboxylic ester linkage.[8] Due to the addition of a carboxylic ester linkage, tissue esterases rapidly metabolize remimazolam. It has a half-life of 37-57 minutes, thus a fast onset and short recovery time.[8,10] Since remimazolam does not depend on the kidneys or liver for elimination, it is appropriate for patients with renal or hepatic impairment.[8]

Remimazolam's advantages over midazolam are due to its fast onset and quick recovery. This reduces the risk of prolonged sedation after the procedure and decreases the patient's post-anesthesia care unit (PACU) time.[8,10] Studies have found that when remimazolam is used in endoscopic sedation, it achieves the same level of sedation as propofol. It is associated with a lower incidence of hypotension and hypoxemia and a faster awakening time.[1,10]

# Methodology of Literature Review

## Eligibility Criteria

During the screening process, peer-reviewed articles were selected based on inclusion and exclusion criteria. Inclusion criteria included RCTs published within the last ten years in English, studies comparing the effects of remimazolam to midazolam and another anesthetic agent in patients undergoing endoscopic procedures. Exclusion criteria included studies with patients under 18 years of age, a small sample size, and offering only published abstracts. Florida

International University's (FIU) library service was used to access the research studies through medical journal databases.

### Information Sources

The search was conducted using three primary databases: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Google Scholar.

### Search Strategy

The search utilized keywords and phrases like remimazolam, midazolam, colonoscopy, endoscopy, endoscopic procedures, procedural sedation, inflammatory bowel disease, randomized controlled trial, and RCT. The Boolean modifiers AND and OR were also used to broaden the search. The initial search identified 161 articles. Once enough articles were produced, given the keywords provided, screening methods and inclusion/exclusion criteria were used to sort through irrelevant data. RCTs published within the last ten years in English comparing the effects of remimazolam to midazolam and/or another anesthetic agent in patients undergoing endoscopic procedures were included. Studies with patients under 18 years of age, a small sample size, and offering only published abstracts were excluded. Following these inclusion and exclusion criteria, nine articles remained and were analyzed.

## Results of Literature Review

### Study Characteristics

The literature review collected necessary data from RCTs, either comparing the effectiveness of remimazolam to midazolam and/or another anesthetic agent in similar populations. The data was reviewed to establish a correlation. This method compares the effectiveness of two medications, remimazolam, and midazolam, to a placebo or another anesthetic agent.

**Results of Individual Studies**

The articles analyzed in this literature review evaluated the safety and efficacy of remimazolam to midazolam (or another anesthetic agent) in improving outcomes in patients undergoing endoscopic procedures.

Chen and colleagues[11] compared remimazolam versus propofol in patients undergoing colonoscopy. The study was a multicentered, blinded RCT, considered level-I evidence.[11] Chen and associates enrolled 384 eligible patients about to undergo a colonoscopy and randomized them into a remimazolam (n=194)and propofol group (n=90).[11] In accordance with the center's standard protocol, all patients underwent bowel preparation within 24 hours before administration.[11] Intravenous (IV) Fentanyl was administered to patients before the assigned trial sedative medication at 1mcg/kg.[11] Shortly after, the remimazolam group received an initial IV dose of 5mg, and the propofol group received an initial IV dose of 1.5mg/kg.[11] Once adequate sedation was achieved through a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score $\leq$3), the colonoscopy was started.[11] If patients did not achieve adequate sedation after the initial dose of remimazolam or propofol, they were given a maximum of 5 doses of remimazolam (2.5 mg) or propofol (0.5 mg/kg) at least 15 minutes apart.[11] If the 5 doses (in either group) were insufficient to obtain/maintain adequate sedation, the patient was designated a treatment failure, and the rescue sedative medication was administered.[11] The procedure was successful if the colonoscopy was completed without administering a rescue sedative or more than 5 top-ups of remimazolam or propofol.[11] The primary outcome was the procedure success rate, with the remimazolam group having a 96% success rate and the propofol group having a 100% success rate.[11] Although the propofol group had a greater success rate, the confidence interval for the lower limit was greater than the non-inferiority margin of -8.00%,

meaning remimazolam's effectiveness was not inferior propofol.[11] The remimazolam group had an increased induction time but demonstrated decreased hypotension and respiratory depression compared to the propofol group.[11] Time to fully alert or time to discharge were unchanged.[11] Adverse effects were decreased in the remimazolam group compared to the propofol group, especially, administration site pain, increased bilirubin, decreased respiratory rate, and decreased $SpO_2$.[11] As a result, remimazolam is non-inferior in sedation efficacy while safer than propofol in patients undergoing colonoscopy.[11]

Chen and associates[12] compared remimazolam versus propofol in patients undergoing endoscopy. The study was a multicentered, single-blinded RCT, and is considered level-I evidence.[12] Chen and colleagues enrolled 378 eligible patients who were about to undergo endoscopy and randomized them into a remimazolam (n=189) and propofol group (n=189).[12] All patients received 10g of lidocaine viscous oral liquid and fentanyl 0.5 mcg/kg before the assigned sedative medication on the day of the procedure.[12] The remimazolam group received an initial IV dose of 5mg, and the propofol group received an initial IV dose of 1.5mg/kg.[12] The endoscopy was started after adequate sedation was achieved through a Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score ≤3). If patients did not achieve adequate sedation after the initial dose of remimazolam or propofol, they were given a maximum of 5 doses of remimazolam (2.5 mg) or propofol (0.5 mg/kg) at least 15 minutes apart.[12] If the 5 doses (in either group) were insufficient to obtain/maintain adequate sedation, the patient was designated a treatment failure, and the rescue sedative medication was administered.[12] The procedure was a success if the endoscopy was completed without administering a rescue sedative or more than 5 top-ups of remimazolam or propofol.[12] The primary endpoint was the procedure success rate, with the remimazolam group having a 97.34% success rate and the propofol group

having a 100% success rate.[12] The remimazolam group had an increased induction time but demonstrated decreased hypotension and respiratory depression compared to the propofol group.[12] Time to fully alert was also decreased for the remimazolam group.[12] Adverse effects were decreased in the remimazolam group (n=94) compared to the propofol group (n=220), especially urinary tract infection, hyperuricemia, elevated unbound bilirubin, elevated bilirubin, and pain at the injection site.[12] As a result, remimazolam is non-inferior in sedation efficacy while safer than propofol in patients undergoing endoscopy.[12]

Rex et al.[13] conducted a prospective, randomized, double-blind, and multicenter study comparing remimazolam to placebo and midazolam in patients undergoing colonoscopy. The study included 461 participants who were randomized into three groups: remimazolam (n=298), placebo (n=60), and open-label midazolam (n=103).[13] All patients received up to 1L of 0.9% sodium chloride IV before the procedure and fentanyl before the assigned sedative medication.[13] The first 80% of the study received an initial fentanyl dose of 75mcg, and the last 20% received an initial fentanyl dose of 25mcg.[13] The Data Safety Monitoring Board made this change due to the number of patients in the placebo and/or remimazolam groups that had reached a MOAA/S score of 0.[13] The remimazolam group received an initial IV dose of 5mg, and the placebo group received an equal volume of placebo over 1 minute.[13] The colonoscopy was started once a MOAA/S score of 3 was achieved.[13] To maintain sedation (MOAA/S score of 4), remimazolam 2.5mg and a placebo of an equal volume could be administered to their respective groups in a 15-minute window (up to 5 doses).[13] If the 5 doses were insufficient to obtain adequate sedation, the patient was designated a treatment failure.[13] The midazolam group received an initial IV dose of 1.75mg and 1mg top-up doses (up to 3) for patients aged under 60 years in a 12-minute window.[13] Patients over 60 years of age received an initial IV dose of 1mg and 0.5mg top-up

doses (up to 3) in a 12-minute window.[13] If more than 3 doses were required for adequate sedation, the patient was designated a treatment failure.[13] After treatment was designated a failure (in any group), midazolam was the only medication used for rescue with dosing up to the endoscopist's discretion.[13] Procedure success was determined by completion of the colonoscopy, no more than 5 top-ups for the remimazolam and placebo group, and/or no more than 3 top-ups for the midazolam group.[13] The primary outcome was the procedure success rate, with the remimazolam group having a 91.3% success rate, the placebo group having a 1.7% success rate, and the midazolam group having a 25.2% success rate.[13] Patients in the remimazolam group received less fentanyl, had faster recovery of neuropsychiatric function, were ready for discharge earlier, and felt back to normal sooner compared to patients in the placebo and midazolam groups.[13] Hypotension was decreased with remimazolam.[13] Hypoxia happened with remimazolam or midazolam in 1% of patients.[13] Remimazolam is safe and effective for administration in patients undergoing colonoscopy.[13]

In a prospective, double-blind, randomized, multicenter study by Rex et al.[9], the aim was to determine the safety and efficacy of remimazolam in ASA III/IV patients undergoing colonoscopy. The study included 77 participants who were randomized into three groups: remimazolam (n=31), placebo (n=16), and midazolam (n=30).[9] All groups were given 50mcg of fentanyl, unless contraindicated, before the study medication.[9] The remimazolam and placebo group received an initial dose between 2.5 to 5mg.[9] The midazolam group received an initial dose of 1mg.[9] The colonoscopy was started once a MOAA/S score of ≤3 was achieved. To maintain sedation, 4 top-up doses of remimazolam 1.25–2.5 mg or placebo and up to 2 top-up doses of midazolam 0.5 mg were allowed.[9] Treatment would be designated a failure if sedation was insufficient to start the procedure and all top-up doses were given for each study group.[9] A

successful procedure was measured by completion of the colonoscopy, no rescue sedative medication, no necessity for more than 5 doses of remimazolam/placebo, and no more than 3 doses of midazolam.[9] The primary outcome was the procedure success rate, with the remimazolam group having a 87.1% success rate, placebo group having a 0% success rate, and the midazolam group having a 13.3% success rate.[9] In conclusion, remimazolam can be used safely and effectively in high-risk ASA patients and maintains its advantages relative to midazolam in high-risk patients.[9]

Borkett et al.[14] conducted a randomized, double-blind study comparing remimazolam to midazolam in an upper endoscopy. This is level 1 evidence. The study included 100 participants who were randomized into four groups: three remimazolam groups (n=25 per group) and a midazolam group (n=25).[14] Each remimazolam group was assigned a dose of 0.10, 0.15, or 0.20 mg/kg; the midazolam group dose was 0.075 mg/kg.[14] The assigned treatment for each group was a single IV dose, so a rescue sedative (midazolam 1-2mg) was allowed if sedation was not adequate.[14] The endoscopy was started once a MOAA/S score of ≤3 was achieved. Procedure success was assessed by a MOAA/S ≤4 for 3 consecutive measurements, completion of the endoscopy, no rescue sedative, and no manual or mechanical ventilation.[14] The primary endpoint was the procedure success rate, with the remimazolam group having 32%, 56%, and 64% in the 0.10, 0.15, and 0.20 mg/kg groups and the midazolam group having a 44%% success rate.[14] Blood pressure and heart rate were stable in the remimazolam treatment groups, with one case of hypotension occurring in the midazolam treatment group.[14] Respiratory depression (8 breaths per minute) was seen in the remimazolam 0.15 mg/kg treatment group, but no action was taken.[14] The midazolam group also had respiratory depression after receiving propofol for inadequate

sedation. In the remimazolam 0.10 mg/kg group, 3 patients received supplemental oxygen for a transient decrease in SpO2 and 1 in the remimazolam 0.20 mg/kg group.[14]
Based on the findings from this study, remimazolam could induce rapid sedation with a quick recovery in patients undergoing an upper endoscopy.[14]

Liu et al.[15] conducted a prospective, randomized, single-blind study in 260 elderly patients to compare the efficacy and safety between remimazolam and etomidate-propofol. Of the 260 participants, 129 were allocated to the remimazolam group and 131 to the etomidate-propofol group.[15] All patients received up to 500mL of 0.9% sodium chloride IV before the procedure and fentanyl 0.5mcg/kg before the assigned sedative medication.[15] After, remimazolam 0.15mg/kg or 0.1mL/kg of etomidate-propofol was administered to their respective groups.[15] The colonoscopy was started once a MOAA/S score of ≤3 was achieved. If sedation was inadequate, up to 5 top-up doses could be administered at a dose 0.075 mg/kg for remimazolam and 0.05 mL/kg for etomidate-propofol with a 15-minute period.[15] Midazolam was administered as rescue sedative medication.[15] Procedure success was defined by completion of the procedure, no requirement for rescue sedative, and no more than 5 top-ups.[15] The primary endpoint was the success rate, with the remimazolam group having a 96.52% success rate and the etomidate-propofol group having a 100% success rate.[15] Four patients in the remimazolam group required rescue midazolam.[15] Secondary outcomes like time to fully alert, readiness for discharge, and hospital discharge were significantly higher in the etomidate-propofol group.[15] The onset time of the etomidate-propofol group was significantly lower.[15] Completion of the study concluded that remimazolam is non-inferior with a high safety profile, making it more suitable for elderly outpatients undergoing colonoscopy.[15]

In a prospective, randomized, single-blind study by Guo et al.[16] the sedative effects of remimazolam were compared to propofol in patients undergoing endoscopy. The study included 77 patients divided into two groups: remimazolam (n=39) and propofol (n=38).[16] Alfentanil 5mcg/kg was administered before the assigned trial sedative medication.[16] After, remimazolam 0.15 mg/kg or propofol 1.5 mg/kg was administered.[16] The endoscopy began when a MOAA/S score ≤ 1 (loss of consciousness) was achieved.[16] If MOAA/S scores increased above 1, up to 5 top-up doses administered as IV boluses (RT 0.05 mg/kg or propofol 0.5 mg/kg) were allowed.[16] Inadequate sedation after the 5 top-up doses results in a treatment failure and necessitates the administration of the sedative rescue medication (propofol).[16] The primary outcomes were the success rate of sedation, the time to loss of consciousness, and the recovery time between the remimazolam and propofol groups.[16] The success rate of sedation in both groups was 100%.[16] The time to loss of consciousness in the remimazolam group was longer than in the propofol group.[16] Respiratory depression in the remimazolam group was less frequent than in the propofol group.[16] The two groups had no significant difference in the recovery time.[16] In conclusion, remimazolam is safe and efficacious for use in upper endoscopy in elderly patients. The incidence of adverse events like respiratory depression are decreased.[16]

Pambianco et al.[17] conducted a randomized, double-blind study comparing remimazolam to midazolam in patients undergoing colonoscopy. The study included 162 participants (ages 18-70) divided into three remimazolam groups and one midazolam group.[17] Each remimazolam group received an initial dose of 8, 7, or 5mg, while the midazolam group received 2.5mg.[17] All participants were given 100mcg of fentanyl before starting the procedure.[17] The colonoscopy was started once a MOAA/S score of ≤3 was achieved. If sedation was not adequate, six top-up doses of 3, 2, or 3mg for the remimazolam groups, respectively, or 1.0 mg of midazolam, were

allowed.[17] Procedure success was defined as MOAA/S ≤ 4 on 3 consecutive measurements, completion of colonoscopy, no alternative sedative, and no manual or mechanical ventilation.[17] The primary outcome was the procedure success rate with remimazolam having 92.5%, 95%, and 97.5% in the 8, 7, and 5mg groups and the midazolam group having a 75%% success rate.[17] Pambianco et al showed that a single dose of remimazolam and top-up doses could provide a higher success of sedation compared to midazolam.[17]

Pastis et al.[18] conducted a prospective, double-blind, randomized, multicenter study comparing the safety and efficacy of remimazolam to midazolam and placebo in patients undergoing bronchoscopy. The study included 446 patients that were divided into three groups: remimazolam (n=310), midazolam (n=73), and placebo (n=63).[18] Fentanyl was administered to patients before the assigned trial sedative medication at 25-75mcg.[18] The remimazolam group received an initial IV dose of 5mg, and the placebo group received an equal volume of placebo over 1 minute.[18] In the midazolam group, 1 to 1.75 mg was administered. The first 20% of the study received an initial fentanyl dose of 75mcg and the last 20% received an initial fentanyl dose of 50mcg.[18] The Data Safety Monitoring Board made this change due to the number of patients in the placebo and/or remimazolam groups that had reached a MOAA/S score of 0.[18] Bronchoscopy was started when adequate sedation (MOAA/S score, 3) was achieved. If sedation was inadequate, up to 5 top-up doses could be administered at a dose 2.5 mg for remimazolam and a placebo of an equal volume.[18] Midazolam was allotted 3 top-up doses at 1mg for healthy adults less than 60 and 0.5mg for adults greater than 60.[18] Top-up doses of fentanyl 25 mcg every 5-10 minutes were allowed in all three arms to achieve adequate analgesia (up to a maximum of 200 mcg).[18] Midazolam was the sedative rescue medication. The primary outcome was the success rate, with the remimazolam group having an 80.6% success rate, the placebo

group having a 4.8% success rate, and the midazolam group having a 32.9% success rate.[18] Other outcomes measured in the study included the time to start the procedure, time to peak sedation, discharge time, time to fully alert, recovery times, and procedural recall.[18] Remimazolam demonstrated faster start times and shorter recovery times.[18]

**Conclusion**

Sedation and analgesia are critical aspects for patients with IBD, as their condition is associated with increased needs in these areas. Additionally, patients with IBD have reported lower satisfaction with sedation during endoscopic procedures and higher procedural pain when compared to patients without Crohn's disease or ulcerative colitis. Remimazolam is a new benzodiazepine known for its fast onset and quick recovery and can be used to improve patient outcomes. fast onset and quick recovery.

Current evidence-based research focusing on the use of remimazolam over midazolam (or another anesthetic agent) was reviewed. The goal of the review was to establish evidence on the efficacy of remimazolam. The information in the nine studies will create the foundation of the quality improvement (QI) project, which centers on educating anesthesia providers on the use of remimazolam for IBD patients undergoing endoscopic procedures. By utilizing the most recent evidence-based research, the QI project is anticipated to improve anesthesia providers' knowledge and attitudes toward using remimazolam.

## Purpose and PICO Question

### Purpose

The purpose of this project is to educate anesthesia providers on the use of remimazolam versus midazolam for IBD patients undergoing endoscopic procedures to improve outcomes.

### PICO Clinical Question

In adult patients with inflammatory bowel disease undergoing endoscopic procedures, how does using remimazolam compared to midazolam improve patient outcomes and recovery time?

Population (P): Adult patients with inflammatory bowel disease undergoing an endoscopic procedure

Intervention (I): Use of remimazolam

Comparison (C): Midazolam

Outcomes (O): Improve patient outcomes and recovery time

### Primary DNP Project Goal

## Goals and Outcomes

SMART is an acronym that stands for specific, measurable, achievable, relevant, and time-based.[19] The objective of using this tool is to serve as a guide for setting and achieving goals.[19]

### Specific

Anesthesia providers will receive an evidence-based educational module underlining the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures.

**Measurable**

The success of the educational intervention will be assessed through the analysis of a survey administered to the participants as a pre and post-test. Outcomes will be evaluated by appraising the changes in the anesthesia providers' knowledge and attitudes toward remimazolam, current standard treatments (midazolam), and the advantages of remimazolam usage in IBD patients. Qualtrics software will be utilized to generate the surveys and analyze the records.

**Achievable**

With the assistance of DNP Preceptor Jillian Gil, DNP, CRNA, ARNP, and DNP Advisor Jorge Valdes, DNP, CRNA, APRN, FAANA, an online educational module will be created that focuses on the administration of remimazolam as an alternative to midazolam, in IBD patients to improve patient outcomes and recovery times.

**Realistic**

Anesthesia providers will be educated on remimazolam via an online educational module. The online module will be available for anesthesia providers to access at their earliest convenience.

**Time-Based**

The "Advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures" educational module will be finalized and presented to anesthesia providers within six months. The educational module will be available for a set period to allow enough time for providers to build competency. After the predetermined period, the module will close, and the results will be analyzed.

## Program Structure/SWOT Analysis

To create an educational module on the advantages of remimazolam over midazolam in IBD patients, a collaborative effort is required from anesthesia providers and educators. A thorough analysis will assess the current practices for this patient population and procedure(s). The idea is to identify any areas or factors that may impact the success of this module. Utilizing the SWOT analysis technique, an evaluation of the project's strengths, weaknesses, opportunities, and threats will be completed.

This program will determine the providers' knowledge and understanding of the current clinical practice and the use of remimazolam as an alternative to midazolam. The understanding of all these areas will be evaluated through an initial questionnaire. An educational course will then be electronically distributed focusing on remimazolam as an alternative to midazolam and its efficacy and benefits. Following the educational intervention, the participants will receive a questionnaire to assess the changes in their knowledge and attitudes toward remimazolam.

### Strengths

Remimazolam has a faster onset and quick recovery. This reduces the risk of prolonged sedation after the procedure and decreases the patient's post-anesthesia care unit (PACU) time when compared to midazolam.[8,10] Studies have found when remimazolam is used in endoscopic sedation, it achieves the same level of sedation as propofol. It is associated with a lower incidence of hypotension and hypoxemia and a faster awakening time.[1,10]

### Weaknesses

Midazolam is a common benzodiazepine used in clinical practice.[20] It is used for its amnestic properties, as well as to relieve anxiety and fear preoperatively.[20] That being said, midazolam has a long-acting metabolite, which leads to prolonged sedation and even respiratory

depression.[20] RCTs have identified that patients recovered faster from remimazolam than midazolam in procedural sedation.[11-18]

**Opportunities**

Remimazolam is a new benzodiazepine that exerts its effect by binding to $GABA_A$ receptors in the brain like its parent compound, midazolam. This new drug combines the properties of remifentanil and midazolam with a carboxylic ester linkage.[8] Due to adding a carboxylic ester group, remimazolam is rapidly metabolized by tissue esterases. It has a half-life of 37-57 minutes, thus a fast onset and short recovery time.[8,10] Since remimazolam does not depend on the kidneys or liver for elimination, it is appropriate for patients with renal or hepatic impairment.[8]

Remimazolam has advantages over midazolam due to its fast onset and quick recovery. This reduces the risk of prolonged sedation after the procedure and decreases the patient's post-anesthesia care unit (PACU) time.[8,10] Studies have found that when remimazolam is used in endoscopic sedation, it achieves the same level of sedation as propofol. It is associated with a lower incidence of hypotension and hypoxemia and a faster awakening time.[1,10]

**Threats**

Resistance or an unwillingness to adapt to a new way of doing things can be a common theme when proposing a change in practices.[21] Anesthesia providers may already follow a protocol for IBD patients and/or endoscopic procedures or base their methods on what has worked for them in the past. Other providers place trust in traditional or unproven processes that are not centered around evidence-based practice and can harm clinical practice.[21] Additionally, the financial aspect of acquiring a new drug like remimazolam may also threaten the success of this project.

## Organizational Factors

Implementation of the "Advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures" learning module will be achieved through a collaborative approach. The educational module will be developed under the guidance of a DNP advisor and clinical mentors' guidance. Once approved, the educational module will be disseminated among anesthesia providers, and their learning will be assessed via pre and post-tests. Findings will be compared to determine the effectiveness of the quality improvement project.

## Theoretical Framework

The healthcare environment is constantly evolving with the invention of new technology and medications. As a result, organizations must be adaptable to change to succeed. Change theories are essential because they can provide a framework for organizations to modify their strategies, processes, and structures.[22] Lewin's theory of planned change (TPC) consists of three stages: unfreezing, moving, and refreezing.[22] In the unfreezing phase, new and current information provided in the educational module will help providers let go of old thinking patterns.[22] Information about the use of remimazolam as a new short-acting benzodiazepine will be provided to ensure practitioners are aware of this option. In the moving phase, the organization will make remimazolam available as an alternative to midazolam while still providing education and addressing any concerns.[22] In the refreezing phase, the implemented change (remimazolam) becomes the new standard or protocol.[22]

## Methodology of Quality Improvement

### Setting and Participants

The setting for this DNP project is the largest private, independent, not-for-profit teaching hospital located in Miami Beach, Florida.[23] Anesthesia services are provided by anesthesiologists and certified registered nurse anesthetists (CRNAs) in areas like the main operating room, cardiac catheterization laboratories, the GI suite, obstetrics, and more.

Primary participants include anesthesia providers employed at the aforementioned hospital. Approval through the Institutional Review Boards (IRB) was requested for this project. Email addresses for CRNAs and anesthesiologists will be collected and used to send links to the pretest, the educational module, and the post-test questionnaire. Participation in the quality improvement project is anonymous and voluntary. Participants can drop out at any time, for any reason.

### Intervention and Procedures

The educational intervention is designed to increase anesthesia providers' knowledge about the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures. An email invite to the intervention will be sent to the anesthesia staff. An online pre-test survey will be administered to participants to assess their existing knowledge and perceptions of remimazolam and current standard treatments. Following this pre-test, participants will view an educational module. A voiceover PowerPoint will be used to present the educational module. After the educational module, participants will fill out a post-test survey to assess any accomplished learning. The author will address any questions or concerns via email and phone number.

## Protection of Human Subjects

No individual identifiers will be collected or stored from the anesthesia providers participating in this project, nor will medical records be accessed. All participants will remain anonymous for the entirety of the quality improvement project to protect the rights and confidentiality of those involved. Data collected will be kept in a secure, password-protected computer.

## Data Collection

Participant demographics and data from the pre and post-test will be collected using Qualtrics. Participants will have the option of providing demographic information like race, ethnicity, gender, and the highest level of education before completing the pre-test. The pre-test will include 10 questions to establish knowledge of remimazolam, current standard treatments (midazolam), and the advantages of remimazolam usage in IBD patients. The post-test survey will contain the same 10 questions to determine the extent of learning that occurred and if a practice change is feasible. Both pre and post-test survey questions will be structured as multiple-choice or true/false.

## Data Management and Analysis

The co-investigator of this project will disseminate the survey via email to the participants. The participants will have two weeks to do the surveys and review the educational module. All responses will be transferred from Qualtrics to Excel software to compare pre- and post-test responses. By doing so, it can be determined if learning occurred after the introduction of the educational module.

## Discussion of Results

At the end of the data collection, results will be analyzed. Conclusions can be drawn from the comparisons made between the pre-test questionnaires and the post-test questionnaires. The comparisons will show if significant learning has occurred and if providers are more likely to consider using remimazolam for IBD patients undergoing endoscopic procedures.

# Quality Improvement Project Results

## Demographics

A total of 38 invitations were distributed via email to Miami Beach Anesthesiology Associates (MBAA) providers. Three participants consented to participate and completed the educational module, including the pre- and post-test. The demographics of those who participated are as follows: male (n = 1, 33.3%), female (n = 2, 66.6%), age in years 25-35 (n = 2, 66.6%), age 36-45 (n =1, 33.3%), age 46-55 (n =0, 0%), Hispanic (n = 2, 66.6%), Caucasian (n = 1, 33.3%), African American (n =0, 0%), and other (n = 0, 0%). All participants were certified registered nurse anesthetists (n = 3, 100%), with a Doctorate's degree (n = 3, 100%), and 1-2 years experience (n = 1, 33.3%), 2-5 years experience (n = 1, 33.3%), or 5-10 years experience (n = 1, 33.3%) as an anesthesia provider.

The demographics of the participants surveyed are represented below in table 1.

**Table 1.** ***Participant Demographics***

| **Demographics** | **N (%)** |
|---|---|
| Total Participants | 3 (100%) |
| **Gender** | |
| Male | 1 (33.3%) |
| Female | 2 (66.6%) |
| Non-binary/third gender | 0 (0%) |
| Prefer not to say | 0 (0%) |
| **Age** | |
| 25 - 35 yr | 2 (66.3%) |
| 36 - 45 yr | 1 (33.3%) |
| 46 - 55 yr | 0 (0%) |
| 56 - 65 yr | 0 (0%) |
| > 65 yr | 0 (0%) |
| **Ethnicity** | |
| Hispanic | 2 (66.6%) |
| Caucasian | 1 (33.3%) |
| African American | 0 (0%) |
| Asian/Pacific-Islander | 0 (0%) |
| Other | 0 (0%) |
| **Position/Title** | |
| CRNA | 3 (100%) |
| MD Anesthesia | 0 (0%) |
| Other Anesthesia | 0 (0%) |
| **Education** | |
| Masters | 0 (0%) |
| Doctorate | 3 (100%) |
| MD | 0 (0%) |
| Other | 0 (0%) |
| **Years of Practice** | |
| 1 – 2 yr | 1 (33.3%) |
| 2 – 5 yr | 1 (33.3%) |
| 5 – 10 yr | 1 (33.3%) |
| > 10 yr | 0 (0%) |

**Pre-test knowledge of the advantages of Remimazolam**

The pre-test consisted of 10 questions that assessed providers' knowledge of remimazolam. All participants were able to identify the drug class and receptor that remimazolam acts on (n=3, 100%). More than half of the participants (n=2, 66.6%) could identify that remimazolam is contraindicated in patients with a history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40. Less than half of the participants (n=1, 33.3%) could identify how remimazolam is metabolized and its half-life, common adverse reactions, fluid compatibility, the standard dose of remimazolam in healthy patients, and the standard dose of remimazolam in ASA III/ASA IV patients. None of the participants could correctly identify how many hours remimazolam could be stored in the vial after reconstituting.

The pre-test questions concerning provider attitude elicited varied responses. Regarding their likelihood of using remimazolam, "extremely unlikely" received two responses (n=2, 66.6%) and "somewhat likely" received one response (n=1, 33.3%). Regarding their likelihood to recommend remimazolam, one participant each selected "extremely unlikely", "somewhat likely", and "extremely likely" (n=1, 33.3%).

**Post-test knowledge of the advantages of Remimazolam**

After the voiceover PowerPoint educational module, participants completed a post-intervention questionnaire, which included the same questions as the pre-test. The results, shown in Table 2, indicated a significant increase in knowledge following the educational module. Nearly every question showed a rise in the number of correct answers selected in the post-test compared to the pre-test, providing evidence of the increased knowledge gained. The most significant increase was noted on the question asking how many hours remimazolam can be stored in the vial after it is reconstituted; this question saw an increase of 100% in participants

(n=3) who answered correctly. The other four questions which asked about how remimazolam is metabolized and its half-life, fluid compatibility, the standard dose of remimazolam in healthy patients, and the standard dose of remimazolam in ASA III/ASA IV patients, saw a 66.6% increase in participants (n=2) identifying these answers correctly.

There was no change in the results of two questions in the pre and post-test. The question regarding remimazolam's drug class and receptor had 3 correct responses both before and after the educational module. In addition, the question addressing remimazolam's contraindication in patients with a history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40 had 2 correct responses both before and after the educational module.

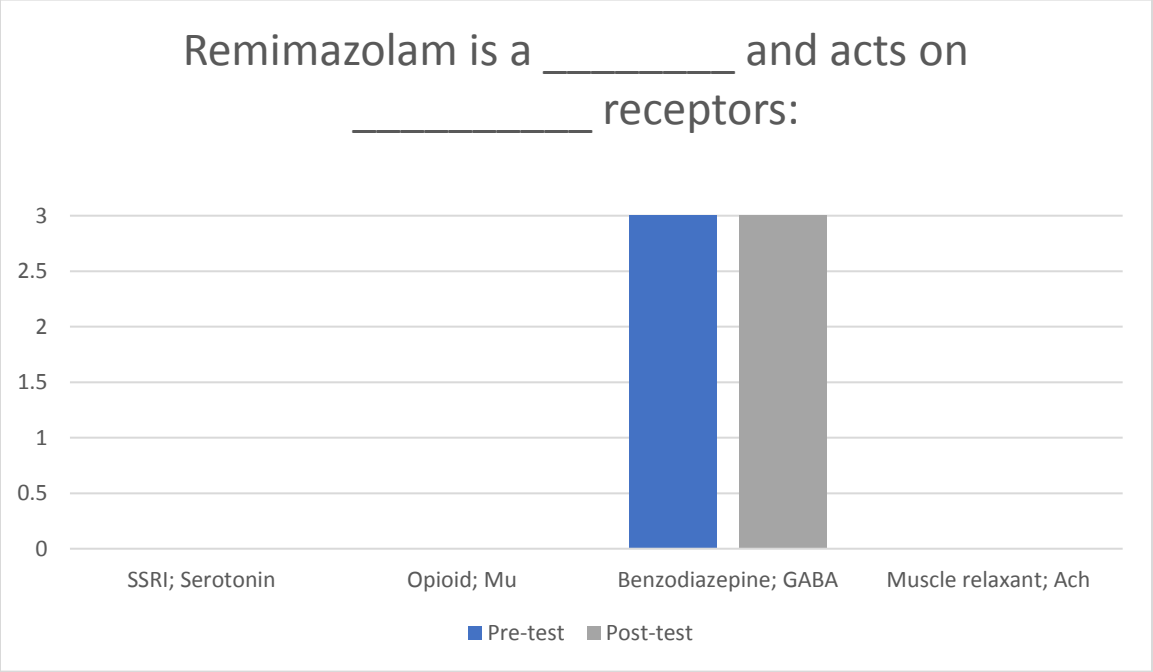
The questions concerning providers' attitudes toward remimazolam had significant increases in positive responses following the educational module. A positive response was counted if participants selected "somewhat likely" or "extremely likely". Regarding the question about the likelihood of using remimazolam, all three participants responded with "extremely unlikely", representing a 66.6% increase (two additional participants answered correctly) compared to the pre-test. This indicates a higher likelihood of providers using remimazolam. Furthermore, all three participants responded with "extremely unlikely" about their likelihood to recommend remimazolam. An increase of 33.4% (one additional participant answered correctly) was observed. This indicates a higher likelihood of recommending remimazolam for use in IBD patients undergoing endoscopic procedures.

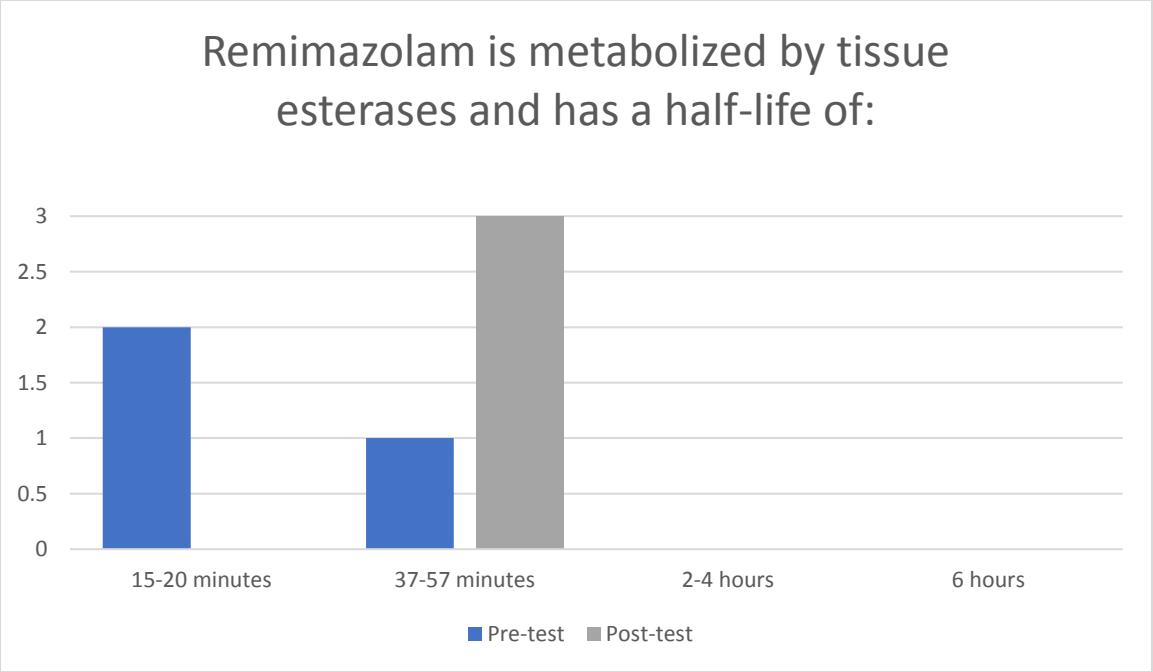
**Table 2.** ***Difference in Pre- and Post-Test Responses***

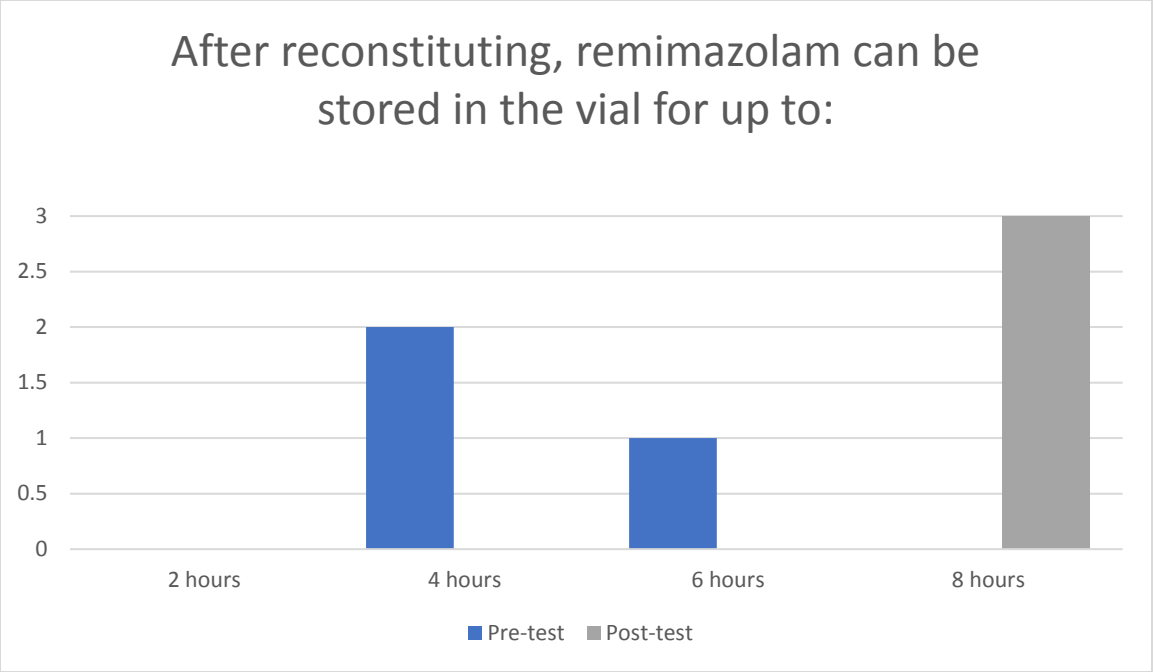
| CORRECT RESPONSES | PRE-TEST (N=3) | POST-TEST (N=3) | DIFFERENCE (%) |
|---|---|---|---|
| *REMIMAZOLAM IS A _____ AND ACTS ON _____ RECEPTORS:* | 3 | 3 | *0* |
| *REMIMAZOLAM IS METABOLIZED BY TISSUE ESTERASES AND HAS A HALF-LIFE OF:* | 1 | 3 | 66.6 |
| *AFTER RECONSTITUTING, REMIMAZOLAM CAN BE STORED IN THE VIAL FOR UP TO:* | 0 | 3 | 100 |
| *ALTHOUGH DECREASED WHEN COMPARED TO MIDAZOLAM, COMMON ADVERSE DRUG REACTIONS OF REMIMAZOLAM INCLUDE:* | 1 | 2 | 33.3 |
| *REMIMAZOLAM IS CONTRAINDICATED IN PATIENTS WITH A HISTORY OF SEVERE HYPERSENSITIVITY REACTION TO DEXTRAN 40 OR PRODUCTS CONTAINING DEXTRAN 40.* | *2* | 2 | 0 |
| *REMIMAZOLAM IS COMPATIBLE WITH ALL OF THE FOLLOWING FLUIDS EXCEPT:* | 1 | 3 | 66.6 |
| *FOR HEALTHY ADULT PATIENTS, THE STANDARD INDUCTION DOSE OF REMIMAZOLAM IS A SINGLE INTRAVENOUS BOLUS OF _____MG OVER 1 MINUTE AND A MAINTENANCE DOSE OF ____MG OVER 15 SECONDS.* | 1 | 3 | 66.6 |
| *FOR ASA III AND IV ADULT PATIENTS, THE STANDARD INDUCTION DOSE OF REMIMAZOLAM IS A SINGLE INTRAVENOUS BOLUS OF _____MG OVER 1 MINUTE AND A MAINTENANCE DOSE OF ____MG OVER 15 SECONDS.* | 1 | 3 | 66.6 |
| *HOW LIKELY ARE YOU TO USE INTRAVENOUS REMIMAZOLAM?* | 1 | 3 | 66.6 |
| *HOW LIKELY ARE YOU TO RECOMMEND INTRAVENOUS REMIMAZOLAM FOR USE IN IBD PATIENTS UNDERGOING ENDOSCOPIC PROCEDURES?* | 2 | 3 | 33.4 |

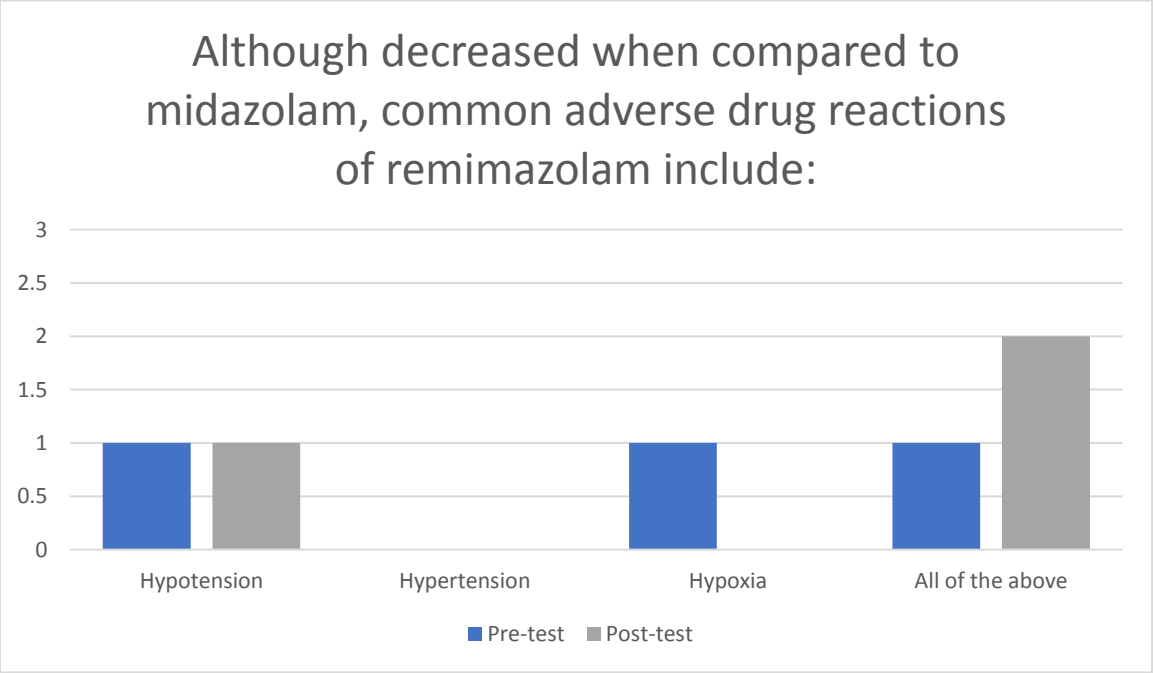
**Summary of Data**

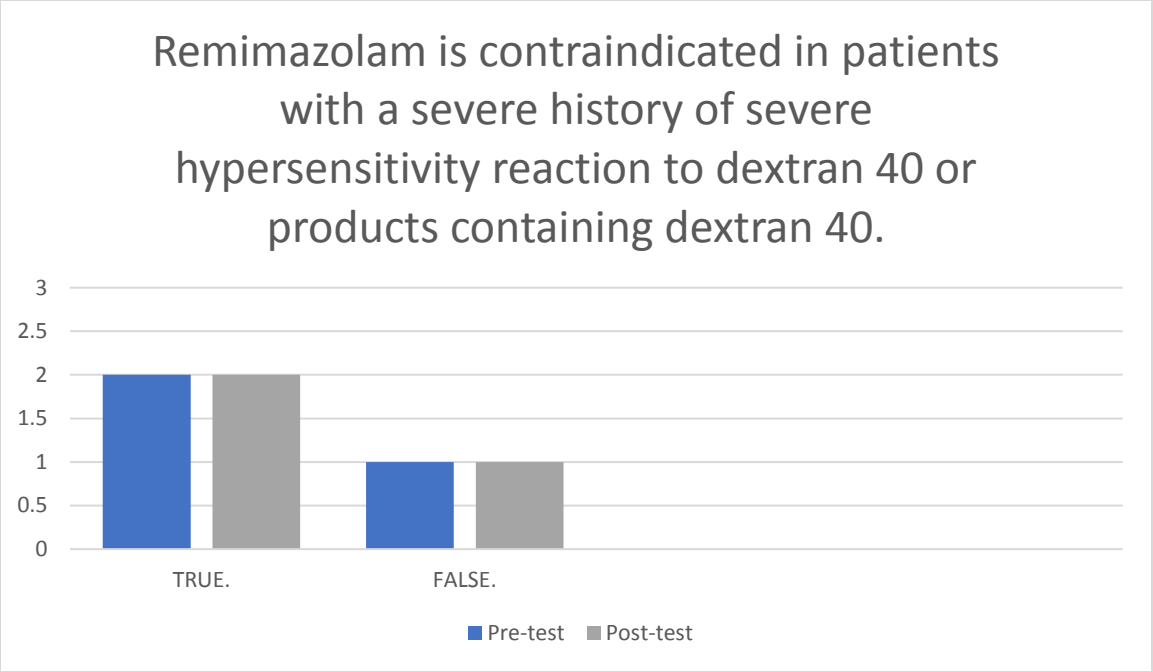
Overall, the outcome of the educational intervention verified an increase in knowledge between the pre-test and post-tests and an increase in the likelihood of participants using or recommending Remimazolam. The graphs below show the change between the pre-and post-test answers for each question.

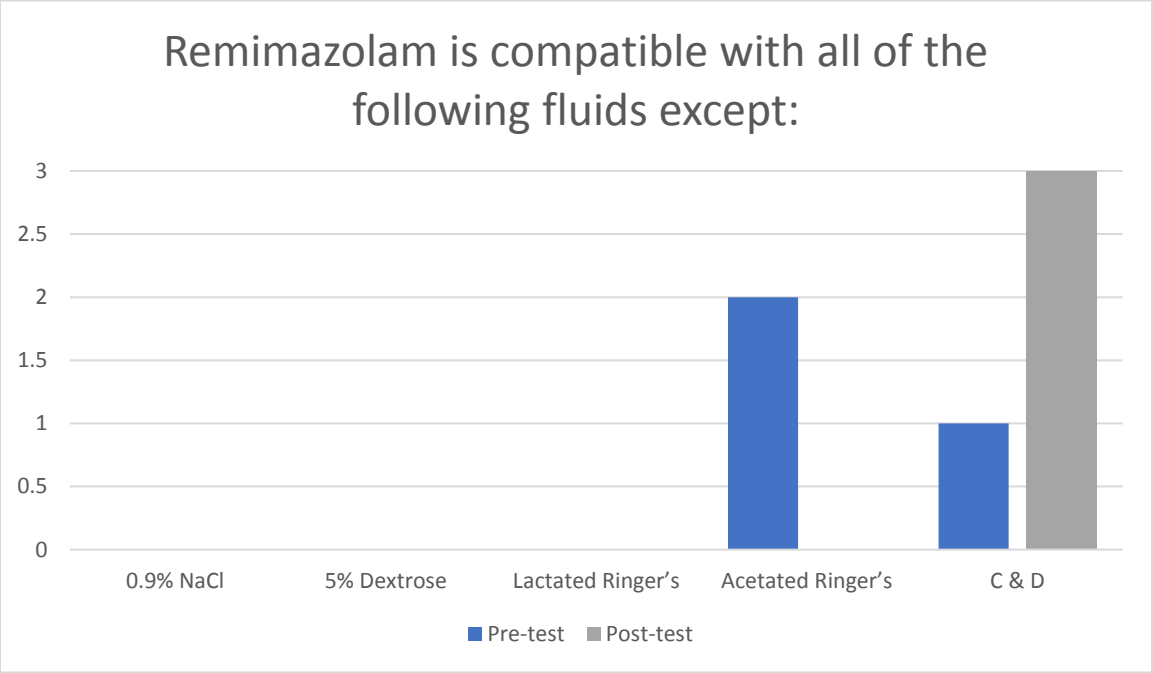

Remimazolam is a _____ and acts on _____ receptors:
3
2.5
2
1.5
1
0.5
0
SSRI; Serotonin
Opioid; Mu
Benzodiazepine; GABA
Muscle relaxant; Ach
Pre-test
Post-test

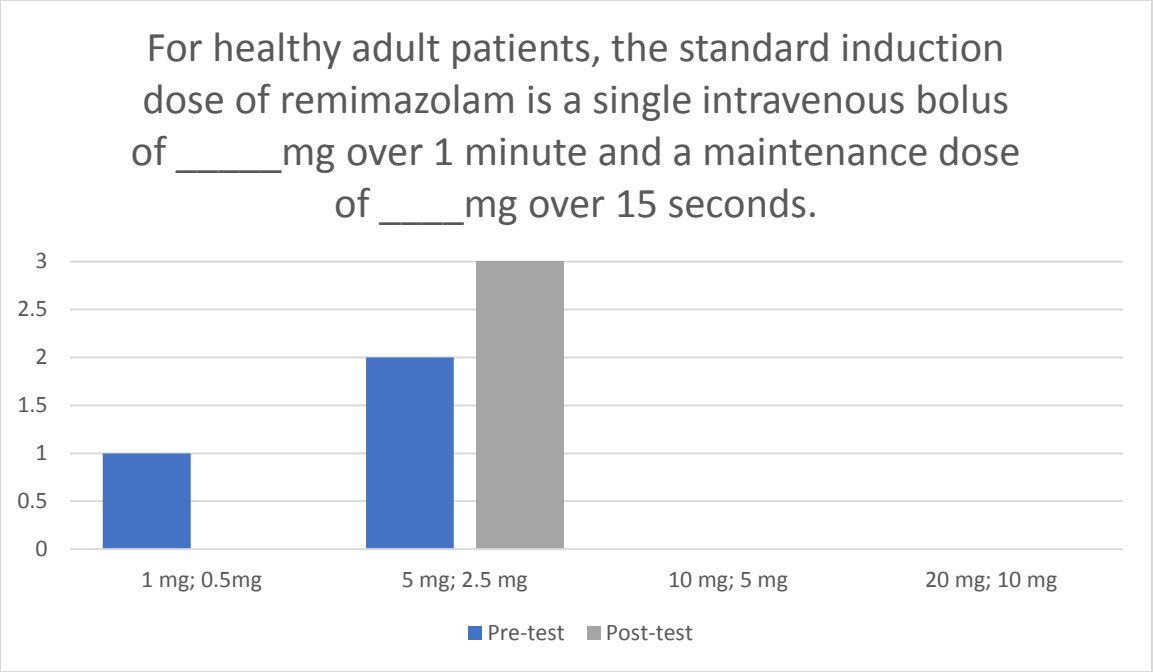

Remimazolam is metabolized by tissue esterases and has a half-life of:
3
2.5
2
1.5
1
0.5
0
15-20 minutes
37-57 minutes
2-4 hours
6 hours
Pre-test
Post-test

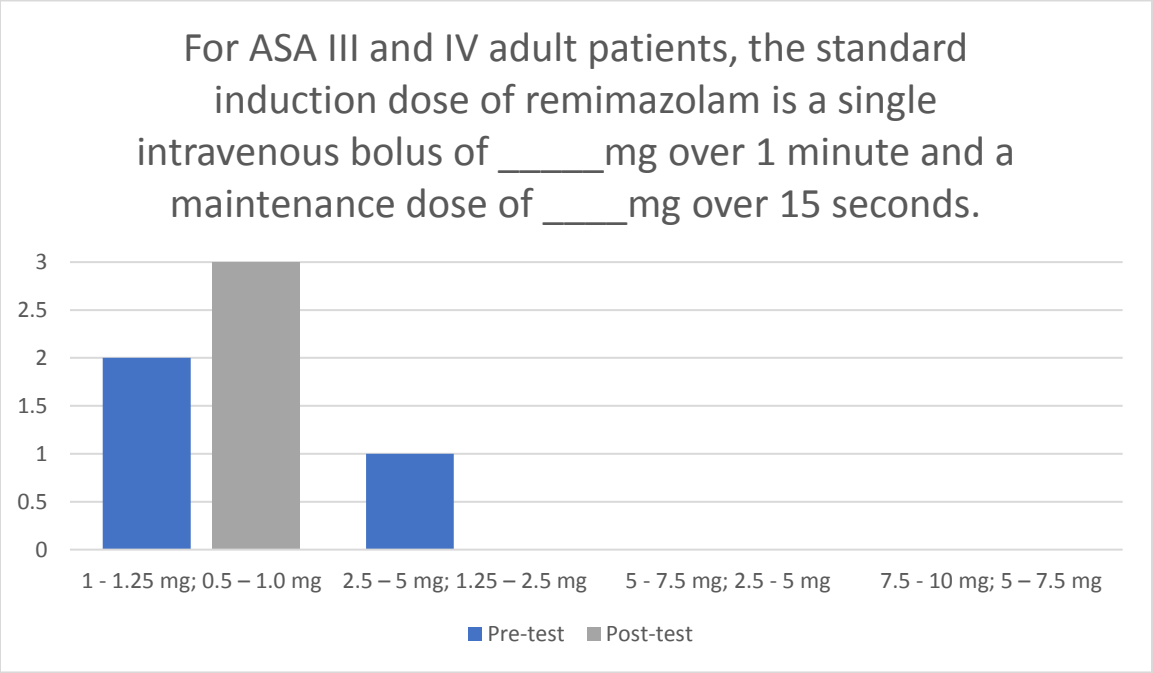

After reconstituting, remimazolam can be stored in the vial for up to:
3
2.5
2
1.5
1
0.5
0
2 hours
4 hours
6 hours
8 hours
Pre-test
Post-test

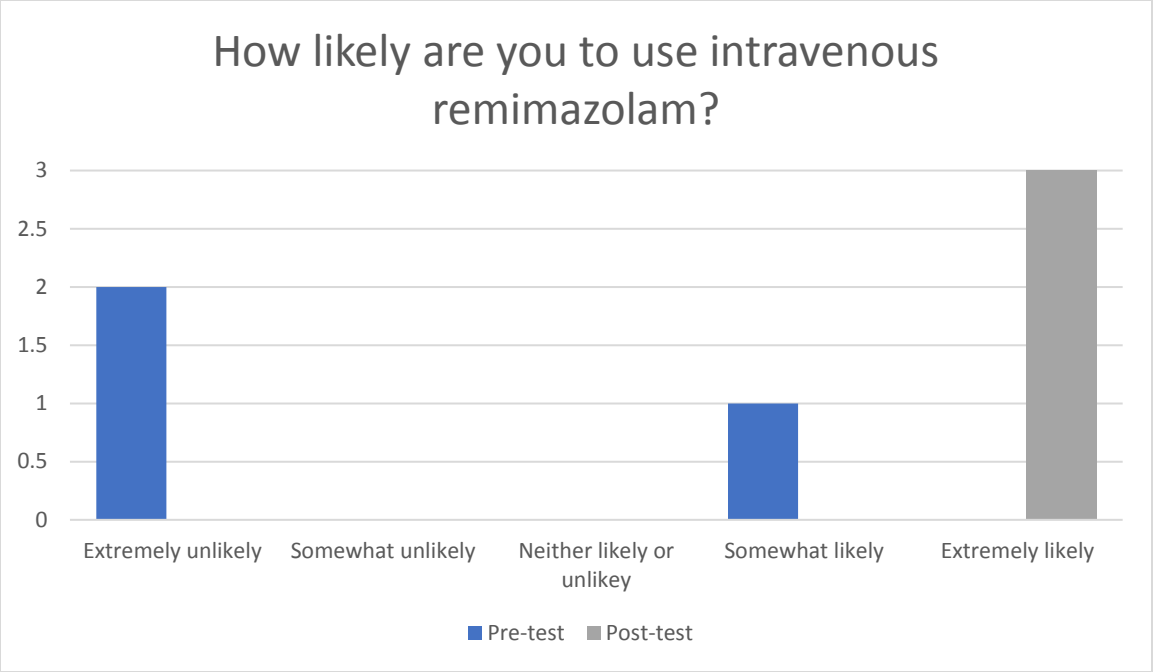

Although decreased when compared to midazolam, common adverse drug reactions of remimazolam include:
3
2.5
2
1.5
1
0.5
0
Hypotension
Hypertension
Hypoxia
All of the above
Pre-test
Post-test

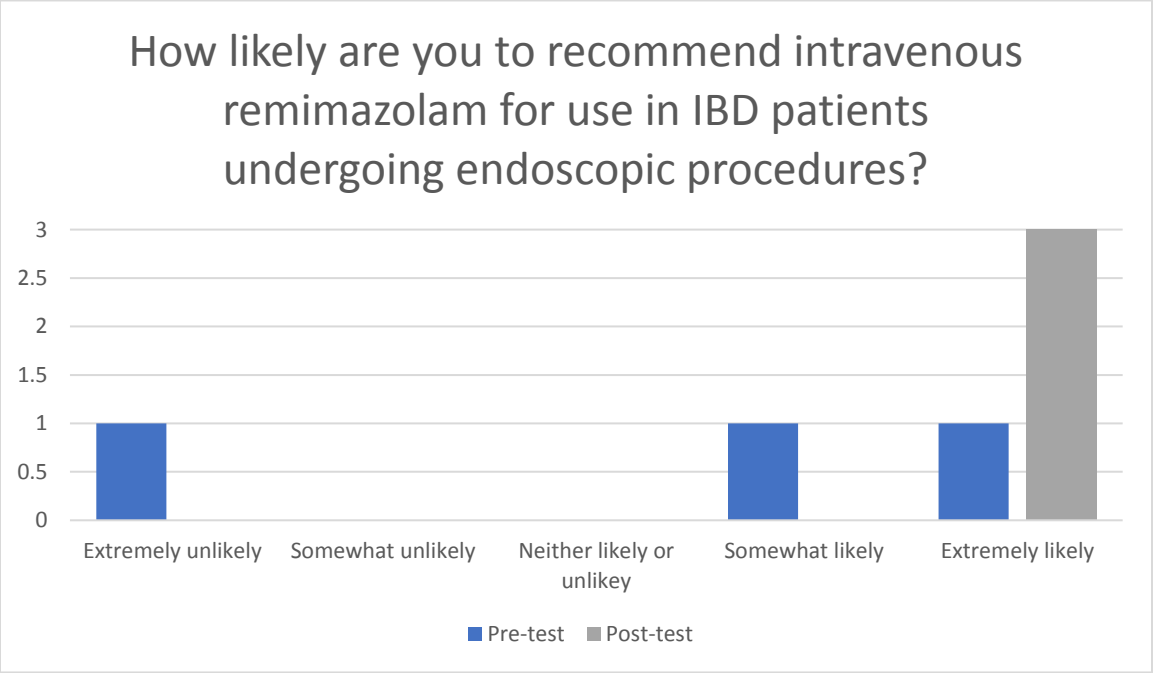

Remimazolam is contraindicated in patients with a severe history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40.
3
2.5
2
1.5
1
0.5
0
TRUE.
FALSE.
Pre-test
Post-test


Remimazolam is compatible with all of the following fluids except:
3
2.5
2
1.5
1
0.5
0
0.9% NaCl
5% Dextrose
Lactated Ringer's
Acetated Ringer's
C & D
Pre-test
Post-test


For healthy adult patients, the standard induction dose of remimazolam is a single intravenous bolus of _____mg over 1 minute and a maintenance dose of ____mg over 15 seconds.
3
2.5
2
1.5
1
0.5
0
1 mg; 0.5mg
5 mg; 2.5 mg
10 mg; 5 mg
20 mg; 10 mg
Pre-test
Post-test


For ASA III and IV adult patients, the standard induction dose of remimazolam is a single intravenous bolus of _____mg over 1 minute and a maintenance dose of ____mg over 15 seconds.
3
2.5
2
1.5
1
0.5
0
1 - 1.25 mg; 0.5 – 1.0 mg
2.5 – 5 mg; 1.25 – 2.5 mg
5 - 7.5 mg; 2.5 - 5 mg
7.5 - 10 mg; 5 – 7.5 mg
Pre-test
Post-test


How likely are you to use intravenous remimazolam?
3
2.5
2
1.5
1
0.5
0
Extremely unlikely
Somewhat unlikely
Neither likely or unlikey
Somewhat likely
Extremely likely
Pre-test
Post-test


How likely are you to recommend intravenous remimazolam for use in IBD patients undergoing endoscopic procedures?
3
2.5
2
1.5
1
0.5
0
Extremely unlikely
Somewhat unlikely
Neither likely or unlikey
Somewhat likely
Extremely likely
Pre-test
Post-test

## Limitations

Several limitations were noted in this quality improvement project. The first limitation was the small sample size. The survey was distributed to 38 email addresses; however, only 3 people chose to participate in the survey. To gain a more accurate picture of providers' preexisting knowledge of the use of Remimazolam in IBD patients undergoing endoscopic procedures, a larger, more diverse sample would be optimal. A larger sample size would also serve to solidify the findings of this survey and demonstrate the effectiveness of the educational intervention.

The limited time frame of this survey may have contributed to the small sample size, as participants were only given two weeks to respond to the email survey link. A more extended period could have allowed participants more time to respond to their invitations. Another limitation of this project is that the survey was exclusively distributed to participants at a single facility. To achieve a more accurate representation of anesthesia providers' knowledge and practices, it would be beneficial to distribute the survey to providers at multiple facilities or locations, avoiding the influence of one facility's culture or standard practices.

## Future Implications for Advanced Nursing Practice

The results of this project may be useful in establishing approaches accessible to participants, which will enhance knowledge and possibly alter providers' practices to improve patient outcomes. The data collected demonstrates that the educational intervention was successful in improving anesthesia provider knowledge on the use of remimazolam. Additionally, the conclusions drawn from this project show that providers have an increased likelihood of using remimazolam in IBD patients undergoing endoscopic procedures after viewing the educational intervention. The findings of this project can be applied to a larger

audience of anesthesia providers. As more research is performed on the efficacy of remimazolam in the IBD population, it will only serve to strengthen the evidence in the educational module and encourage providers to utilize this lower-risk, effective treatment.

## Conclusion

Educational interventions, such as this quality improvement project, have the potential to enhance provider knowledge and attitudes, consequently promoting greater utilization of remimazolam over midazolam in IBD patients undergoing endoscopic procedures. Ultimately, this shift in practice can contribute to improved patient outcomes.

## References


1. Weber AT, Ather N, Tran V, Sauk J, Ha C. Higher sedation requirements among inflammatory bowel disease patients undergoing colonoscopy for disease activity assessment or dysplasia surveillance. *Crohn's & Colitis 360.* 2019;1(1). https://doi.org/10.1093/crocol/otz006

2. Zhu X, Wang H, Yuan S, et al. Efficacy and safety of remimazolam in endoscopic sedation-a systematic review and meta-analysis. *Front Med*. 2021;8:655042. doi:10.3389/fmed.2021.655042

3. Bezzio C, Schettino M, Manes, G, et al. Tolerability of Bowel Preparation and Colonoscopy in IBD Patients: Results From a Prospective, Single-Center, Case–Control Study, *Crohn's & Colitis 360*, 2020; 2(4)Volume 2, Issue 4. https://doi.org/10.1093/crocol/otaa077

4. Flood P, Rathmell JP, Urman RD. *Stoelting's Pharmacology and physiology in anesthetic practice.* 6th edition. Wolters Kluwer Health; 2021.

5. Flynn S, Eisenstein S. Inflammatory Bowel Disease Presentation and Diagnosis. *Surg Clin North Am*. 2019;99(6):1051-1062. doi:10.1016/j.suc.2019.08.001

6. Steenholdt C, Jensen JT, Brynskov J, et al. Patient Satisfaction of Propofol Versus Midazolam and Fentanyl Sedation During Colonoscopy in Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol*. 2022;20(3):559-568.e5. doi:10.1016/j.cgh.2020.10.037.

7. Gabriel RA, Waterman RS, Kim, JMS, Ohno-Machado, Lucila. A predictive model for extended postanesthesia care unit length of stay in outpatient surgeries. *Anesth & Analg*. 2017;124(5). doi: 10.1213/ANE.0000000000001827.

8. Ul-Haque I, Shaikh TG, Ahmed SH, et al. Efficacy of remimazolam for procedural sedation in american society of anesthesiologists (ASA) I to IV patients undergoing colonoscopy: a systematic review and meta-analysis. *Cureus*. 2022;9(3):e22881. doi:10.7759/cureus.22881.

9. Rex DK, Bhandari R, Lorch DG, Meyers M, Schippers F, Bernstein D. Safety and efficacy of remimazolam in high risk colonoscopy: A randomized trial. *Dig Liver Dis*. 2021;53(1):94-101. doi:10.1016/j.dld.2020.10.039

10. Pharmacology and mechanism of action. Byfavo. Accessed June 25, 2022. https://byfavo.azurewebsites.net/pharmacology/

11. Chen S, Wang J, Xu X, et al. The efficacy and safety of remimazolam tosylate versus propofol in patients undergoing colonoscopy: a multicentered, randomized, positive-controlled, phase III clinical trial. *Am J Transl Res*. 2020;12(8):4594-4603. Published

2020 Aug 15.

12. Chen SH, Yuan TM, Zhang J, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. *J Gastroenterol Hepatol*. 2021;36(2):474-481. doi:10.1111/jgh.15188

13. Rex DK, Bhandari R, Desta T, et al. A phase III study evaluating the efficacy and safety of remimazolam (CNS 7056) compared with placebo and midazolam in patients undergoing colonoscopy. *Gastrointest Endosc*. 2018;88(3):427-437.e6. doi:10.1016/j.gie.2018.04.2351

14. Borkett KM, Riff DS, Schwartz HI, et al. A Phase IIa, randomized, double-blind study of remimazolam (CNS 7056) versus midazolam for sedation in upper gastrointestinal endoscopy. *Anesth Analg*. 2015;120(4):771-780. doi:10.1213/ANE.0000000000000548

15. Liu X, Ding B, Shi F, et al. The Efficacy and Safety of Remimazolam Tosilate versus Etomidate-Propofol in Elderly Outpatients Undergoing Colonoscopy: A Prospective, Randomized, Single-Blind, Non-Inferiority Trial. *Drug Des Devel Ther*. 2021;15:4675-4685. Published 2021 Nov 16. doi:10.297/DDDT.S339535

16. Guo J, Qian Y, Zhang X, Han S, Shi Q, Xu J. Remimazolam tosilate compared with propofol for gastrointestinal endoscopy in elderly patients: a prospective, randomized and controlled study. *BMC Anesthesiol*. 2022;22(1):180. Published 2022 Jun 10. doi:10.1186/s12871-022-01713-6

17. Pambianco DJ, Borkett KM, Riff DS, et al. A phase IIb study comparing the safety and efficacy of remimazolam and midazolam in patients undergoing colonoscopy. *Gastrointest Endosc*. 2016;83(5):984-992. doi:10.1016/j.gie.2015.08.062

18. Pastis NJ, Yarmus LB, Schippers F, et al. Safety and Efficacy of Remimazolam Compared With Placebo and Midazolam for Moderate Sedation During Bronchoscopy. *Chest*. 2019;155(1):137-146. doi:10.1016/j.chest.2018.09.015

19. Tips for Writing SMART Objectives. SAMHSA Native Connections. https://www.samhsa.gov/sites/default/files/nc-smart-goals-fact-sheet.pdf. Accessed November 10, 2021.

20. Wang F, Zhou Q, Shen M, et al. Efficacy and safety of remimazolam in procedural sedation and analgesia: A protocol for systematic review and meta analysis. *Medicine (Baltimore)*. 2020;99(27):e20765. doi:10.1097/MD.0000000000020765

21. Spath PL, Kelly DL. *Applying quality Management in Healthcare: A Systems Approach*. 4th ed. Chicago, IL: Health Administration Press; 2017.

22. Hussain ST, Lei S, Akram T, Haider MJ, Hussain SH, Ali M. Kurt Lewin's change model: A critical review of the role of leadership and employee involvement in organizational change. *J of Innov & Knowledge*. 2018/09/01/ 2018;3(3):123-127. doi:https://doi.org/10.1016/j.jik.2016.07.002

23. About Mount Sinai Medical Center. Mount Sinai Medical Center. https://www.msmc.com/about-msmc/our-story/.Published 2022. Accessed January 11, 2023.

## Appendix A: IRB Exemption

FIU Research & Economic Development
FLORIDA INTERNATIONAL UNIVERSITY

# MEMORANDUM

**To**: Dr. Jorge Valdes

**CC:** Alexis Perez

**From:** Carrie Bassols, BA, IRB Coordinator CeB

**Date:** March 7, 2023

**Proposal Title:** "Advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures: an educational module"

---

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

| | | | |
|---|---|---|---|
| **IRB Protocol Exemption #:** | IRB-23-0100 | **IRB Exemption Date:** | 03/07/23 |
| **TOPAZ Reference #:** | 112738 | | |

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
1) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

***Special Conditions:*** N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

## Appendix B: QI Project Consent

**CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT**

"Advantages of intravenous administration of remimazolam over midazolam in inflammatory bowel disease patients undergoing endoscopic procedures: an educational module"

**SUMMARY INFORMATION**

Things you should know about this study:

- **Purpose:** Educational module to improve participants knowledge on the use of remimazolam for inflammatory bowel disease (IBD) patients undergoing endoscopic procedures in order to improve outcomes.
- **Procedures**: If the participant chooses to participate, they will be asked to complete a pretest, watch a voice PowerPoint, and then a post test
- **Duration:** This will take about a total of 20 minutes.
- **Risks**: There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.
- **Benefits:** The main benefit to you from this research is increase the participants knowledge on the advantages of remimazolam for IBD patients undergoing endoscopic procedures.
- **Alternatives:** There are no known alternatives available to the participant other than not taking part in this quality improvement project.
- **Participation:** Taking part in this quality improvement project is voluntary.

Please carefully read the entire document before agreeing to participate.

**NUMBER OF STUDY PARTICIPANTS**

If the participant decides to be in this study, they will be one of 10-15 people in this research study.

**PURPOSE OF THE PROJECT**

The participant is being asked to be in a quality improvement project. The goal of this project is to increase providers' knowledge on the use of remimazolam over midazolam for IBD patients undergoing endoscopic procedures in order to improve outcomes. If you decide to participate, you will be 1 of 15 participants.

**DURATION OF THE PROJECT**

Your participation will require about 20 minutes of your time. (5 Minutes Pre-test, 10 minute PowerPoint Module, and 5 minute Post-test

**PROCEDURES**

If the participant agrees to be in the project, PI will ask you to do the following things:
1. Complete an online 10 question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided
2. Review the educational PowerPoint Module lasting 10 minutes via Qualtrics, an Online survey product for which the URL link is provided.
3. Complete the online 10 question post-test survey via Qualtrics, an Online survey product for which the URL link is provided.

**RISKS AND/OR DISCOMFORTS**

The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

**BENEFITS**

The following benefits may be associated with participation in this project: An increase in your knowledge on the use of remimazolam over midazolam for IBD patients undergoing endoscopic procedures in order to improve outcomes. The overall objective of the program is to increase the providers' knowledge based on the current literature.

**ALTERNATIVES**

There are no known alternatives available to the participant other than not taking part in this project. However, if the participant would like to receive the educational material, it will be provided to them at no cost.

## CONFIDENTIALITY

The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, PI might publish, it will not include any information that will make it possible to identify the participant. Records will be stored securely, and only the project team will have access to the records.

**PARTICIPATION:** Taking part in this quality improvement project is voluntary.

## COMPENSATION & COSTS

There is no cost or payment to the participant for receiving the health education and/or for participating in this project.

## RIGHT TO DECLINE OR WITHDRAW

Participation in this project is voluntary. The participant is free to participate in the project or withdraw the consent at any time during the project. The participant's withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove the participant without their consent at such time that they feel it is in their best interest.

## RESEARCHER CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Alexis Perez at 786-291-3310 or apere616@fiu.edu and Dr. Jorge Valdes at 305-302-8348 or jvalde@fiu.edu.

## IRB CONTACT INFORMATION

If the participant would like to talk with someone about their rights pertaining to being a subject in this project or about ethical issues with this project, the participant may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

## PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

## Appendix C: Recruitment Letter

FIU Department of Nurse Anesthesiology

Nicole Wertheim College of Nursing & Health Sciences

**Advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures: an educational module**

Dear Miami Beach Anesthesiology Associates (MBAA) Perioperative Providers:

My name is Alexis Perez, and I am a student in the Anesthesiology Nursing Program Department of Nurse Anesthesiology at Florida International University. I am writing to invite you to participate in my quality improvement project. The goal of this project is to increase healthcare providers' awareness of the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures. You are eligible to participate in this project because you are a part of the anesthesia department for MBAA at Mount Sinai Medical Center.

If you decide to participate in this project, you will be asked to complete and sign a consent form for participation. Next, you will complete a pre-test questionnaire, which is expected to take approximately 5 minutes. You will then be asked to view an approximately 10 minutes long educational presentation online. After going through the educational module, you will be asked to complete the post-test questionnaire, which will take approximately 5 minutes. No compensation will be provided.

Remember, this is completely voluntary. You can choose to be in the study or not. If you'd like to participate or have any questions about the study, please email at apere616@fiu.edu or contact me at 786-291-3310.

Thank you very much.

Sincerely,

Alexis Perez, BSN, RN, CCRN
786-291-3310
Apere616@fiu.edu

## Appendix D: Letter of Support


**Miami Beach Anesthesiology Associates, Inc.**

*Mount Sinai Medical Center • Division of Anesthesia*

S. Howard Wittels MD
Chairman

Hector Davila MSS, MD
Executive Director

Guillermo Garcia MD
Vice Chairman

Sebastian Baquero MD

Christopher Bauer MD
Obstetrics Chief

Vicente Behrens MD

Mario Consuegra MD

Jayanand D'Mello MD
Research Coordinator

Laura Foster MD

Pablo Fumero MD

Pedro Garcia MD
Residency Program
Assist. Director

Howard Goldman MD

Alejandro Guzman MD

Rick Hasty MD

Flor Marin MD

Mark Nakajima MD

Gerald Rosen MD
Residency Program
Director

Jason Wigley MD

Alexander Volsky MD

J.P. Mato DNP, CRNA
CRNA Director & SRNA
Coordinator

Paula Schultz DNP, CRNA
OB-Chief CRNA


February 2, 2023

Jorge Valdes, DNP, CRNA, APRN, FAANA
Clinical Associate Professor
Department of Nurse Anesthesiology
Florida International University

Dr. Valdes,

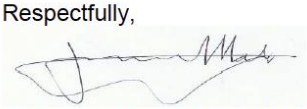
Thank you for inviting Miami Beach Anesthesiology Associates to participate in the Doctor of Nursing Practice (DNP) project conducted by Alexis Perez entitled "Advantages of intravenous administration of remimazolam over midazolam in inflammatory bowel disease (IBD) patients undergoing endoscopic procedures: an educational module" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthesiology at Florida International University. I have granted the student permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best patient outcomes by selecting interventions supported by the evidence. This proposed quality improvement project seeks to utilize the latest literature to increase provider's awareness on the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures.

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password-encrypted digital cloud, and only be accessible to the investigators of this study: Alexis Perez and Dr. Valdes.

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Alexis Perez will behave professionally, follow standards of care, and not impede hospital performance. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

Respectfully,




Jampierre (J.P.) Mato, DNP, CRNA, APRN
Executive CRNA Director
SRNA Coordinator/Supervisor
*Electronic Mail: Jampierre@bellsouth.net*
*Mobile Phone: 954-668-6080*

4300 Alton Road, Suite 2454, Miami Beach, FL 33140
Office (305) 674-2742 • Facsimile (305) 674-9723

## Appendix E: QI Project Survey

**Pretest and Posttest Questionnaire:**

**Advantages of intravenous administration of remimazolam over midazolam in inflammatory bowel disease (IBD) patients undergoing endoscopic procedures: an educational module**

**INTRODUCTION**

The primary aim of this QI project is to increase providers awareness of the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format and are meant to measure knowledge on the advantages of intravenous administration of remimazolam over midazolam in IBD patients undergoing endoscopic procedures.

**PERSONAL INFORMATION**

1. **Gender:** Male Female Other_____ Prefer not to answer
2. **Ages:** 25-35 36-45 46-55 56-65 >65
3. **Ethnicity:** Hispanic Caucasian African American Asian Other_____
4. **Position/Title:** CRNA Anesthesiologist Resident Anesthesiologist Assistant
5. **Level of Education:** Bachelors Masters DNP PhD

6. How many years have you been a perioperative provider?

1-2 years 2-5 years 5-10 years Over 10

**QUESTIONNAIRE**

1. **Remimazolam is a _____ and acts on _____ receptors:**
    a. SSRI; Serotonin
    b. Opioid; Mu
    c. Benzodiazepine; $GABA_A$
    d. Muscle relaxant; Ach
2. **Remimazolam is metabolized by tissue esterases and has a half-life of:**
    a. 15-20 minutes
    b. 37-57 minutes
    c. 2-4 hours
    d. 6 hours
3. **After reconstituting, remimazolam can be stored in the vial for up to:**
    a. 2 hours
    b. 4 hours
    c. 6 hours
    d. 8 hours
4. **Although decreased when compared to midazolam, common adverse drug reactions of remimazolam include:**
    a. Hypotension
    b. Hypertension
    c. Hypoxia
    d. All of the above

5. **Remimazolam is contraindicated in patients with a severe history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40.**
    a. True
    b. False
6. **Remimazolam is compatible with all of the following fluids except:**
    a. 0.9% NaCl
    b. 5% Dextrose
    c. Lactated Ringer's
    d. Acetated Ringer's
    e. C & D
7. **For healthy adult patients, the standard induction dose of remimazolam is a single intravenous bolus of _____mg over 1 minute and a maintenance dose of ____mg over 15 seconds.**
    a. 1 mg; 0.5mg
    b. 5 mg; 2.5 mg
    c. 10 mg; 5 mg
    d. 20 mg; 10 mg
8. **For ASA III and IV adult patients, the standard induction dose of remimazolam is a single intravenous bolus of _____mg over 1 minute and a maintenance dose of ____mg over 15 seconds.**
    a. 1 - 1.25 mg; 0.5 – 1.0 mg
    b. 2.5 – 5 mg; 1.25 – 2.5 mg
    c. 5 - 7.5 mg; 2.5 - 5 mg

d. 7.5 - 10 mg; 5 – 7.5 mg

**9. How likely are you to use intravenous remimazolam?**

a. Extremely unlikely

b. Somewhat unlikely

c. Neither likely nor unlikely

d. Somewhat likely

e. Extremely likely

**10. How likely are you to recommend intravenous remimazolam for use in IBD patients undergoing endoscopic procedures?**

a. Extremely unlikely

b. Somewhat unlikely

c. Neither likely nor unlikely

d. Somewhat likely

e. Extremely likely

## Appendix F: Table with Overview of Literature Review Results

| Author(s) | Purpose | Methodology/ Research Design | Intervention(s) / Measures | Sampling/Setting | Primary Results | Relevant Conclusions |
|---|---|---|---|---|---|---|
| **Borkett et al., 2015** | The purpose of this study was to explore the safety and efficacy of remimazolam (different single doses) in patients undergoing upper endoscopy. | Randomized controlled trial | The enrolled subjects were randomly assigned to four groups: three remimazolam groups (n=25 per group) and a midazolam group (n=25). Modified Observer's Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | 100; United States/ multicenter<br><br>Upper gastrointestinal endoscopy<br><br>Age 18–65 (46M/54F)<br><br>ASA I, II | This exploratory dose-finding study showed that a single administration of remimazolam (0.10–0.20 mg/kg) was capable of inducing rapid sedation with a quick recovery profile in patients undergoing a diagnostic upper gastrointestinal endoscopy. The safety profile was favorable and appeared to be similar to that of midazolam, warranting further development of this short-acting compound. | While the results of this study are very encouraging, further work needs to be done to establish remimazolam's efficacy and safety profile including a multiple dose setting, and its ability to induce and maintain appropriate levels of sedation for both short procedures such as this, as well as longer procedures such as colonoscopy. |
| **Chen et al., 2020** | This study aimed to evaluate the efficacy and safety of remimazolam versus propofol in patients | Randomized controlled trial | Included 384 patients were divided into a remimazolam (n=194) and propofol group (n=90).<br><br>Modified Observer's | 384; China/multicenter<br><br>Colonoscopy<br><br>Age18–65 (161M/223F)<br><br>ASA I, II | The sedative efficacy of remimazolam tosylate was non-inferior to propofol in patients undergoing colonoscopy; (2) re-mimazolam | Remimazolam is non-inferior in sedative efficacy and more tolerable than propofol in patients undergoing colonoscopy, which could |

| | | | | | | |
|---|---|---|---|---|---|---|
| | undergoing colonoscopy. | | Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | | presented a relatively longer induction time of sedation, and similar recovery time compared to propofol; (3) remimazolam presented higher safety profile compared to propofol. | be a relatively ideal sedative agent for colonoscopy. |
| **Chen et al., 2021** | This study aimed to compare the efficacy and safety of Remimazolam with propofol in patients undergoing upper gastrointestinal endoscopy. | Randomized controlled trial | 378 eligible patients who were divided into a remimazolam (n=189) and propofol group (n=189).<br><br>Modified Observer's Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | 378; China/multicenter<br><br>Upper gastrointestinal endoscopy<br><br>Age 18–60 (148M/230F)<br><br>ASA III, IV | The success rate of sedation in the remimazolam group was non-inferior to that in the propofol group (97.34% vs 100.00%; difference in rate 2.66%, 95% CI 4.96 to0.36, meeting criteria for non-inferiority). Patients in the Remimazolam group had longer time to adequate sedation (P < 0.0001) but shorter time to fully alert (P < 0.0001) than that in the propofol group. The incidences of hypotension (13.04% vs 42.86%, P < 0.0001), | Remimazolam is a safe and effective sedative for the patients undergoing upper GI endoscopy. It allows a rapid recovery from sedation and has the lower potential to cause cardiovascular and respiratory depression compared with propofol. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | treatment-related hypotension (0.54% vs 5.82%, P < 0.0001), and respiratory depression (1.09% vs 6.88%, P = 0.0064) were significantly lower in the remimazolam group. AEs were reported in 74 (39.15%) patients in the remimazolam group and 114 (60.32%) patients in the propofol group, with significant difference (P < 0.0001). | |
| **Guo et al., 2022** | The purpose of this study is to compare the sedative effect of remimazolam and propofol for gastrointestinal endoscopy in elderly patients. | Randomized controlled trial | The study included 77 patients divided into two groups: remimazolam (n=39) and propofol (n=38). | 77; China/<br><br>Gastrointestinal endoscopy<br><br>Age ≥65 years (47M/30F) | Remimazolam had a slower onset of sedation in elderly individuals, but the incidence of related side effects was lower, especially the incidence of hemodynamic events and respiratory depression. There was no significant difference in the recovery time between the two groups. In addition, the number of supplemental doses after successful induction may have increased. | Remimazolam can be safely and effectively used for gastrointestinal endoscopy sedation in elderly patients, and the incidence of sedation-related adverse reactions, especially hemodynamic events and respiratory depression, is lower. When remimazolam is used, the number of supplemental doses after |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | | successful induction may increase slightly. |
| **Liu et al., 2021** | In this study, the authors compared the efficacy and safety between remima-zolam and etomidate-propofol in elderly outpatients undergoing colonoscopy. | Randomized controlled trial | Of the 260 participants, 129 were allocated to the remimazolam group and 131 to the etomidate-propofol group | 260; China/single center<br><br>Colonoscopy | The procedure success rate was 96.52% in the remimazolam group and 100% in the etomidate-propofol (EP) group. The difference in procedure success rate between the remimazolam and EP groups was −3.48% (95% confidence interval: −6.81%, −0.15%). Four patients in the remimazolam group required rescue midazolam. Compared with patients in the remimazolam group, the onset time of the EP group was significantly lower ($p < 0.05$), whereas time to fully alert ($p = 0.001$), ready for discharge ($p = 0.001$), and hospital discharge ($p = 0.002$) were all significantly higher in the EP group. However, there were no significant differences in procedure time ($p = 0.846$) or cecal intubation time (p = | Remimazolam may have non-inferior efficacy and a higher safety profile than etomidate-propofol in elderly outpatients undergoing colonoscopy, which suggests that Remimazolam may be more suitable for elderly outpatients undergoing colonoscopy. |

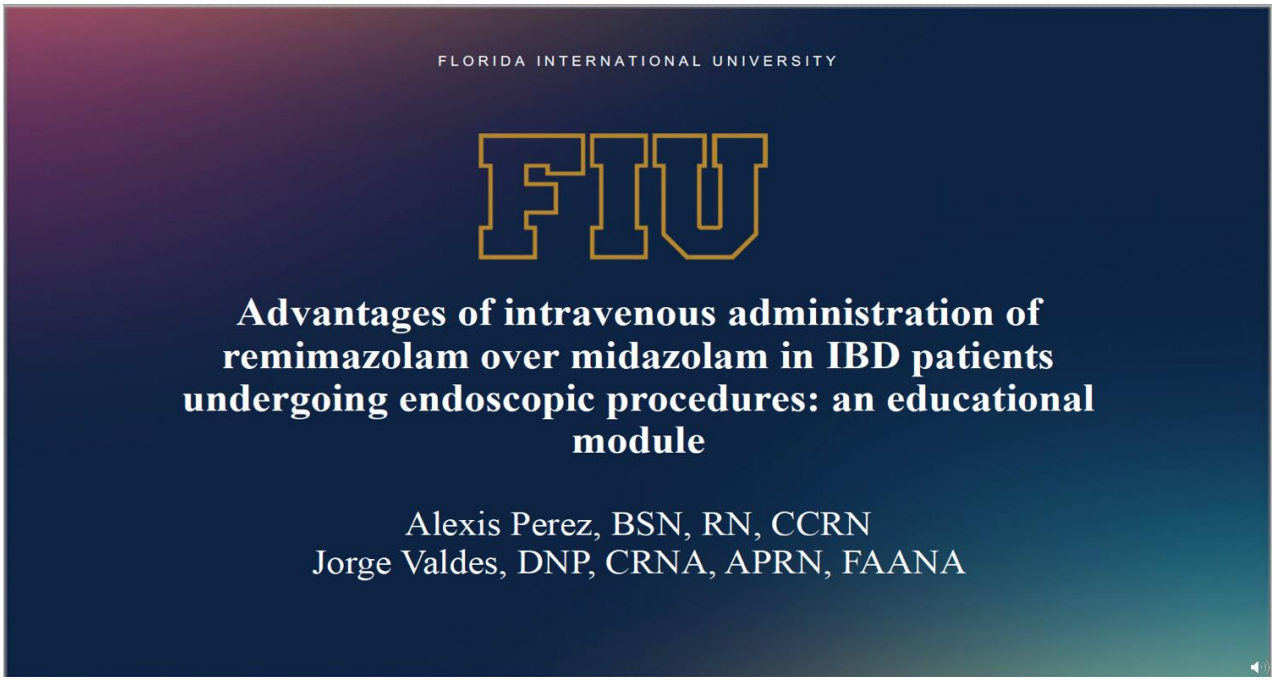
| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | 0.320) between the two groups. | |
| **Pambianco et al., 2016** | The aim was to compare the safety and efficacy profile of remimazolam and to refine suitable doses for subsequent studies. | Randomized controlled trial | The study included 162 participants and divided them into three remimazolam groups and one midazolam group.<br><br>Modified Observer's Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | 162; United States/ multicenter<br><br>Colonoscopy<br><br>Ages 18–70 (72M/88F)<br><br>ASA I-III | This study showed that 100 μg of fentanyl, followed immediately by a single dose of remimazolam or midazolam administered as a short IV infusion over 1 minute, followed by top-up doses as necessary, provided adequate sedation with a very high success rate (>92%) for all of the remimazolam groups, compared with 75% for midazolam. | The high success rates and good safety profile of remimazolam observed in this study warrants further investigation and confirmation in phase III trials. |
| **Pastis et al., 2019** | This study was undertaken to evaluate the safety and effectiveness of remimazolam for moderate sedation during flexible | Randomized controlled trial | The study included 446 patients that were divided into three groups: remimazolam (n=310), midazolam (n=73), and placebo (n=63).<br><br>Modified Observer's Alertness/Sedati | 439; United States/ multicenter<br><br>Bronchoscopy<br><br>Age 22–95 (206M/233F)<br><br>ASA I-III | The success rates were 80.6% in the remimazolam arm, 4.8% in the placebo arm ($P < .0001$), and 32.9% in the midazolam arm. Bronchoscopy was started sooner in the remimazolam arm (mean, 6.4 ± 5.82 min) compared with placebo (17.2 ± 4.15 min; $P < .0001$) and | Remimazolam administered under the supervision of a pulmonologist was effective and safe for moderate sedation during flexible bronchoscopy. In an exploratory analysis, it |

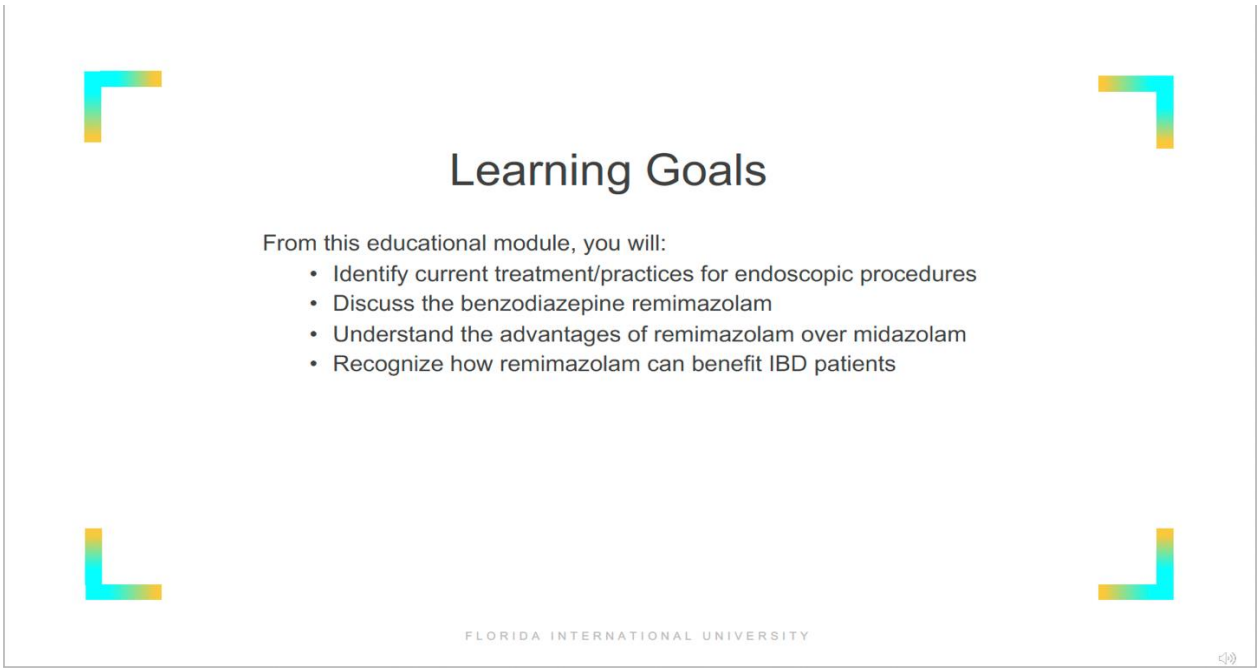
| | | | | | | |
|---|---|---|---|---|---|---|
| | bronchoscopy. | | on Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | | midazolam (16.3 ± 8.60 min). Time to full alertness after the end of bronchoscopy was significantly shorter in patients treated with remimazolam (median, 6.0 min; 95% CI, 5.2-7.1) compared with those treated with placebo (13.6 min; 95% CI, 8.1-24.0; *P* = .0001) and midazolam (12.0 min; 95% CI, 5.0-15.0). Remimazolam registered superior restoration of neuropsychiatric function compared with placebo and midazolam. Safety was comparable among all three arms, and 5.6% of the patients in the remimazolam group had serious treatment-emergent adverse events as compared with 6.8% in the placebo group. | demonstrated a shorter onset of action and faster neuropsychiatric recovery than midazolam. |
| **Rex et al., 2018** | This study aimed to evaluate the efficacy and safety of remimazolam versus midazolam | Randomized controlled trial | The study included 461 participants who were randomized into three groups: remimazolam (n=298), placebo (n=60), | 461; United States/ multicenter<br><br>Colonoscopy<br><br>Age 19–92 (226M/232F) | The procedure success rate was 91.3% for the remimazolam group, 1.70% for the placebo group, and 25.2% for the midazolam group. | Remimazolam can be administered safely under the supervision of endoscopists for outpatient colonoscopy, |

| | | | | | | |
|---|---|---|---|---|---|---|
| | in patients undergoing colonoscopy. | | open-label midazolam (n=103).<br><br>Modified Observer's Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated.<br><br>Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | ASA I-III | | and it allows faster recovery of neuropsychiatric function compared with placebo (midazolam rescue) and midazolam. |
| **Rex et al., 2021** | This study aimed to evaluate the efficacy and safety of remimazolam versus midazolam in high risk patients undergoing colonoscopy. | Randomized controlled trial | The study included 77 participants who were randomized into three groups: remimazolam (n=31), placebo (n=16), and midazolam (n=30).<br><br>Modified Observer's Alertness/Sedation Scale (MOAA/S) scores were used to measure the level of alertness in subjects who were sedated. | 77; United States/ multicenter<br><br>Colonoscopy<br><br>Ages 42–84 (43M/34F)<br><br>ASA III, IV | Incidence and frequency of treatment emergent adverse events (TEAEs) were comparable in all three treatment arms, and independent of ASA status. One TEAE leading to discontinuation and one serious TEAE were reported; both in the open label midazolam arm. The efficacy endpoint was achieved for remimazolam, placebo, and midazolam in 87.1%, 0%, and | Remimazolam is safe and efficient in procedural sedation of high risk ASA patients undergoing colonoscopy, showing a safety profile comparable to that in low risk ASA. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | Initiated sedation: MOAA/ S ≤3; Maintained sedation: MOAA/S≤4 | | 13.3% of patients ( $p < 0.00001$ for remimazolam versus placebo and versus midazolam, respectively). | |

## Appendix G: QI Educational Module



# Background

Endoscopic procedures play an essential role in the diagnosis and management of IBD (Crohn's and Ulcerative Colitis).[1]

For patients with Crohn's Disease (CD) or Ulcerative Colitis (UC), colonoscopy is often recommended for evaluation before changes in medical management to check for post-operative disease recurrence and to observe for the presence of abnormal cells, as these patients are at increased colorectal cancer risk.[2]

Patients with IBD will likely be subject to a relatively higher number of colonoscopies throughout their lifetimes.[2]

Due to the clinical manifestations of the disease, IBD patients tend to experience more pain and discomfort than most patients undergoing colonoscopy for other indications.[1]

The presence of IBD has been identified as a patient variable associated with higher sedation and analgesia requirements during colonoscopy.

FLORIDA INTERNATIONAL UNIVERSITY

# Scope of the Problem

- Approximately 1.6 million Americans are affected by IBD, with 785,000 patients with Crohn's Disease and 910,000 with Ulcerative Colitis.[3]
- Patients with IBD are reluctant to undergo endoscopic procedures due to difficulties with bowel cleansing, anxiousness, the expectation of pain, and embarrassment.[4]
- Sedation during colonoscopy can reduce pain, anxiety, and embarrassment and likely ensures a higher success rate and examination quality.[4]

## Current Practice

Commonly used techniques for sedation during these procedures include moderate sedation and monitored anesthesia care (MAC).[2]

The sedative drugs used with these procedures are primarily propofol and midazolam.[2]

## Midazolam

- In clinical use for over 40 years and is the most used benzodiazepine in the perioperative period
- It increases the affinity of GABA to its binding site on the $GABA_A$ receptor[5]
- Elimination half-life is 1–4 hours[5]
- Metabolized by the liver via cytochrome P450 enzymes to active and inactive metabolites[5]

## Remimazolam

- In July 2020, the Food and Drug Administration (FDA) approved remimazolam for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less due to its favorable results in clinical trials[6]
- A new benzodiazepine that exerts its effect by binding to $GABA_A$ receptors in the brain[6]
- Combination of remifentanil and midazolam[6]
- Rapidly metabolized by tissue esterases so half-life is 37-57 minutes, thus a fast onset and short recovery time[6]

## Remimazolam cont.

- Each vial contains 20mg lyophilized powder for reconstitution with 8.2mL sterile 0.9% Sodium Chloride Injection[6]
- Incompatible with Lactated Ringer's and Acetated Ringer's[6]
- The reconstituted product will deliver a final concentration of 2.5 mg/mL[6]
- Can be stored in the vial for up to 8 hours under controlled room temperature at 20°C to 25°C (68°F to 77°F).[6] Protect vials from light.

## Remimazolam recommended dosage for procedural sedation[6]

| For Adult Patients | For ASA III-IV Adult Patients |
|---|---|
| **Induction** | |
| Administer 5 mg intravenously over a 1-minute time period. | Administer 2.5 mg to 5 mg intravenously over 1 minute based on the general condition of the patient. |
| **Maintenance (as needed)**<br>At least 2 minutes must elapse prior to administration of any supplemental dose and assessment of level of sedation | |
| Administer 2.5 mg intravenously over 15 seconds. | Administer 1.25 mg to 2.5 mg intravenously over 15 seconds. |

## Remimazolam Vs Midazolam

- Remimazolam can be used safely and effectively in high-risk ASA patients and maintains its advantages relative to midazolam in high-risk patients[8]
- Remimazolam was capable of inducing rapid sedation with a quick recovery in patients undergoing an upper endoscopy and/or colonoscopy[9]
- Remimazolam demonstrated faster start times and shorter recovery times[10]
- The incidence of adverse events like respiratory depression are decreased[11]

# Take home points

Remimazolam is a benzodiazepine and binds to $GABA_A$ receptors in the brain[6]

Indicated for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less[6]

Remimazolam is a safe and effective sedative for patients undergoing endoscopic procedures[7]

Remimazolam resulted in a higher rate of procedure success, lesser administration of rescue medication, shorter time to recovery, and better cognitive recovery than the use of midazolam during procedural sedation[8-10]

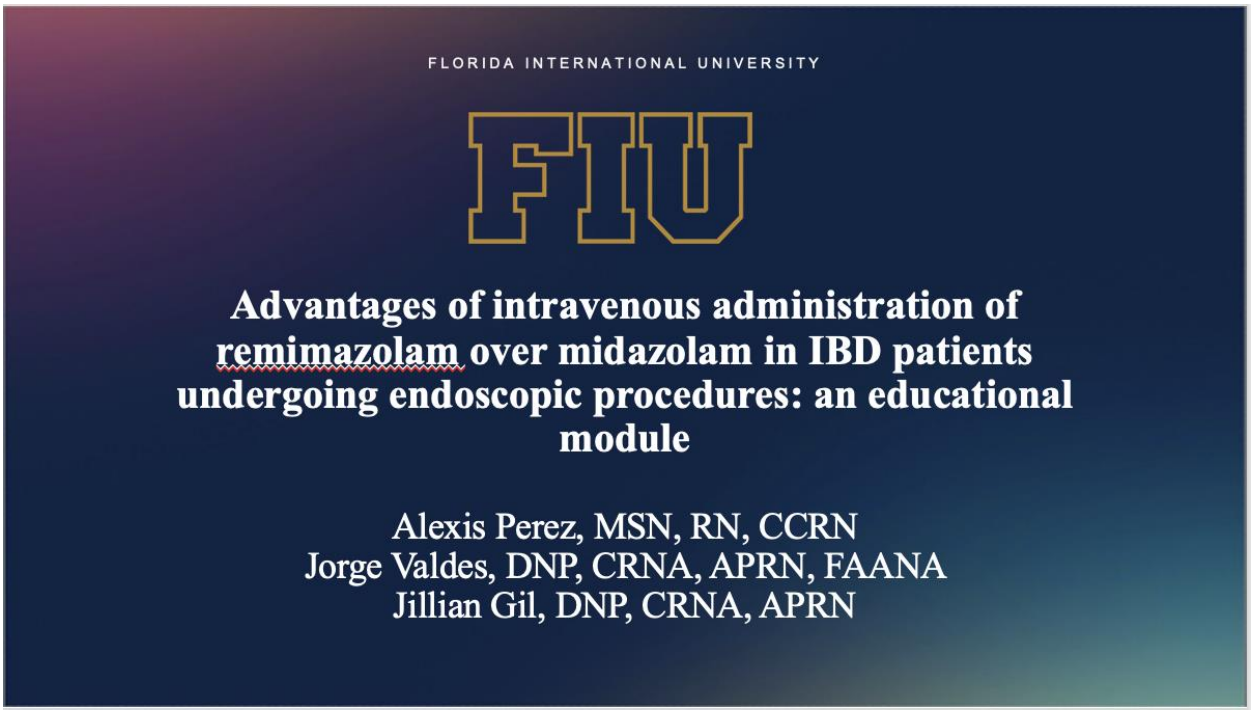
Several original studies have shown that remimazolam facilitates faster onset and recovery, has higher sedative efficacy than midazolam, and is associated with lower incidence of hypotension and hypoxemia[8,12]

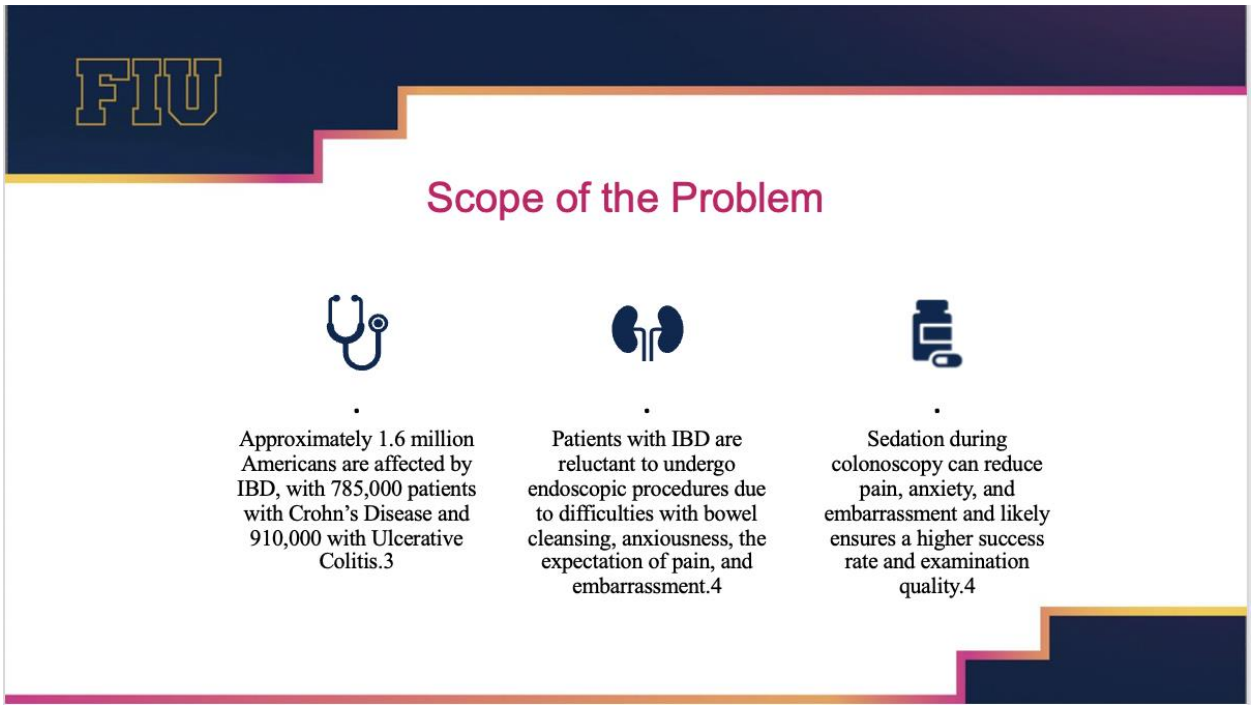
FLORIDA INTERNATIONAL UNIVERSITY

# References


1. Bezzio C, Schettino M, Manes, G, et al. Tolerability of Bowel Preparation and Colonoscopy in IBD Patients: Results From a Prospective, Single-Center, Case–Control Study, *Crohn's & Colitis 360*, 2020; 2(4)Volume 2, Issue 4. https://doi.org/10.1093/crocol/otaa077
2. Weber AT, Ather N, Tran V, Sauk J, Ha C. Higher sedation requirements among inflammatory bowel disease patients undergoing colonoscopy for disease activity assessment or dysplasia surveillance. *Crohn's & Colitis 360. 2019;1(1).* https://doi.org/10.1093/crocol/otz006
3. Flynn S, Eisenstein S. Inflammatory Bowel Disease Presentation and Diagnosis. *Surg Clin North Am*. 2019;99(6):1051-1062. doi:10.1016/j.suc.2019.08.001
4. Steenholdt C, Jensen JT, Brynskov J, et al. Patient Satisfaction of Propofol Versus Midazolam and Fentanyl Sedation During Colonoscopy in Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol*. 2022;20(3):559-568.e5. doi:10.1016/j.cgh.2020.10.037.
5. Flood P, Rathmell JP, Urman RD. *Stoelting's Pharmacology and physiology in anesthetic practice.* 6th edition. Wolters Kluwer Health; 2021.
6. Pharmacology and mechanism of action. Byfavo. Accessed June 25, 2022. https://byfavo.azurewebsites.net/pharmacology/
7. Ul-Haque I, Shaikh TG, Ahmed SH, et al. Efficacy of remimazolam for procedural sedation in american society of anesthesiologists (ASA) I to IV patients undergoing colonoscopy: a systematic review and meta-analysis. *Cureus*. 2022;9(3):e22881. doi:10.7759/cureus.22881.
8. Rex DK, Bhandari R, Lorch DG, Meyers M, Schippers F, Bernstein D. Safety and efficacy of remimazolam in high risk colonoscopy: A randomized trial. *Dig Liver Dis*. 2021;53(1):94-101. doi:10.1016/j.dld.2020.10.039
9. Borkett KM, Riff DS, Schwartz HI, et al. A Phase IIa, randomized, double-blind study of remimazolam (CNS 7056) versus midazolam for sedation in upper gastrointestinal endoscopy. *Anesth Analg*. 2015;120(4):771-780. doi:10.1213/ANE.0000000000000548
10. Pastis NJ, Yarmus LB, Schippers F, et al. Safety and Efficacy of Remimazolam Compared With Placebo and Midazolam for Moderate Sedation During Bronchoscopy. *Chest*. 2019;155(1):137-146. doi:10.1016/j.chest.2018.09.015
11. Guo J, Qian Y, Zhang X, Han S, Shi Q, Xu J. Remimazolam tosilate compared with propofol for gastrointestinal endoscopy in elderly patients: a prospective, randomized and controlled study. *BMC Anesthesiol*. 2022;22(1):180. Published 2022 Jun 10. doi:10.1186/s12871-022-01713-6
12. Chen SH, Yuan TM, Zhang J, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. *J Gastroenterol Hepatol*. 2021;36(2):474-481. doi:10.1111/jgh.15188

## Appendix H: DNP Dissemination PowerPoint



## Background

- Endoscopic procedures play an essential role in the diagnosis and management of IBD (Crohn's and Ulcerative Colitis).[1] .
- For patients with Crohn's Disease (CD) or Ulcerative Colitis (UC), colonoscopy is often recommended for evaluation before changes in medical management to check for post-operative disease recurrence and to observe for the presence of abnormal cells, as these patients are at increased colorectal cancer risk.[2]
- Patients with IBD will likely be subject to a relatively higher number of colonoscopies throughout their lifetimes.[2]
- Due to the clinical manifestations of the disease, IBD patients tend to experience more pain and discomfort than most patients undergoing colonoscopy for other indications.[1]
- The presence of IBD has been identified as a patient variable associated with higher sedation and analgesia requirements during colonoscopy.

## DNP Project Purpose

- The purpose of this project is to educate anesthesia providers on the use of remimazolam versus midazolam in IBD patients undergoing endoscopic procedures to improve outcomes.

## PICO Clinical Question

**In adult patients with inflammatory bowel disease undergoing endoscopic procedures, how does using remimazolam compared to midazolam improve patient outcomes and recovery time?**

## Quality Improvement Methods

IRB APPROVAL REQUESTED AND GRANTED FROM FIU AND HOSPITAL

ANONYMOUS LINK SENT TO PROVIDERS VIA EMAIL WITH LINK TO QUALTRICS CONTAINING PRE AND POST QUESTIONNAIRES AND THE EDUCATIONAL MODULE.

A VOICEOVER POWERPOINT WAS USED TO PRESENT THE EDUCATIONAL MODULE.

DATA GENERATED VIA QUALTRICS QUESTIONNAIRES WERE EXPORTED INTO EXCEL SPREADSHEET FOR COMPARISON BETWEEN THE PRE AND POST-TESTS.

| Ethnicity | |
|---|---|
| Hispanic | 2 (66.6%) |
| Caucasian | 1 (33.3%) |
| African American | 0 (0%) |
| Asian/Pacific-Islander | 0 (0%) |
| Other | 0 (0%) |
| **Position/Title** | |
| CRNA | 3 (100%) |
| MD Anesthesia | 0 (0%) |
| Other Anesthesia | 0 (0%) |
| **Education** | |
| Masters | 0 (0%) |
| Doctorate | 3 (100%) |
| MD | 0 (0%) |
| Other | 0 (0%) |
| **Years of Practice** | |
| 1 – 2 yr | 1 (33.3%) |
| 2 – 5 yr | 1 (33.3%) |
| 5 – 10 yr | 1 (33.3%) |
| > 10 yr | 0 (0%) |

## Quality Improvement Results

- The audience size was 38
- 3 responsive participants
  - 3 completed pre-test
  - 3 completed post-test

## *Difference in Pre- and Post-Test Responses*

| CORRECT RESPONSES | PRE-TEST (N=3) | POST-TEST (N=3) |
|---|---|---|
| *REMIMAZOLAM IS A _____ AND ACTS ON _____ RECEPTORS:* | 3 | 3 |
| *REMIMAZOLAM IS METABOLIZED BY TISSUE ESTERASES AND HAS A HALF-LIFE OF:* | 1 | 3 |
| *AFTER RECONSTITUTING, REMIMAZOLAM CAN BE STORED IN THE VIAL FOR UP TO:* | 0 | 3 |
| *ALTHOUGH DECREASED WHEN COMPARED TO MIDAZOLAM, COMMON ADVERSE DRUG REACTIONS OF REMIMAZOLAM INCLUDE:* | 1 | 2 |
| *REMIMAZOLAM IS CONTRAINDICATED IN PATIENTS WITH A HISTORY OF SEVERE HYPERSENSITIVITY REACTION TO DEXTRAN 40 OR PRODUCTS CONTAINING DEXTRAN 40.* | 2 | 2 |
| *REMIMAZOLAM IS COMPATIBLE WITH ALL OF THE FOLLOWING FLUIDS EXCEPT:* | 1 | 3 |
| *FOR HEALTHY ADULT PATIENTS, THE STANDARD INDUCTION DOSE OF REMIMAZOLAM IS A SINGLE INTRAVENOUS BOLUS OF _____MG OVER 1 MINUTE AND A MAINTENANCE DOSE OF ____MG OVER 15 SECONDS.* | 1 | 3 |
| *FOR ASA III AND IV ADULT PATIENTS, THE STANDARD INDUCTION DOSE OF REMIMAZOLAM IS A SINGLE INTRAVENOUS BOLUS OF _____MG OVER 1 MINUTE AND A MAINTENANCE DOSE OF ____MG OVER 15 SECONDS.* | 1 | 3 |
| *HOW LIKELY ARE YOU TO USE INTRAVENOUS REMIMAZOLAM?* | 1 | 3 |
| *HOW LIKELY ARE YOU TO RECOMMEND INTRAVENOUS REMIMAZOLAM FOR USE IN IBD PATIENTS UNDERGOING ENDOSCOPIC PROCEDURES?* | 2 | 3 |

## Discussion

- **Limitations**:
  - -Small sample size
  - -Limited time frame
  - -Conducted in one facility
- **Further Implications:**
  - -Increased knowledge
  - -Improved standard of practice
  - -Improved patient outcomes

## Conclusions

- In conclusion, this quality improvement project was designed to increase the anesthesia provider's knowledge of the use of remimazolam in IBD patients undergoing endoscopic procedures.
- The comprehensive understanding gained in this educational module promotes awareness about the effectiveness of using remimazolam to improve outcomes in IBD patients.
- In addition, this educational module positively influenced the attitudes and perceptions regarding remimazolam.

# Thank You

- DNP Advisor:
  - Jorge Valdes, DNP, CRNA, APRN, FAANA
- DNP Clinical Mentor:
  - Jillian Gil, DNP, CRNA, APRN
- Participants in the project

# References


1. Bezzio C, Schettino M, Manes, G, et al. Tolerability of Bowel Preparation and Colonoscopy in IBD Patients: Results From a Prospective, Single-Center, Case–Control Study, *Crohn's & Colitis 360*, 2020; 2(4)Volume 2, Issue 4. https://doi.org/10.1093/crocol/otaa077
2. Weber AT, Ather N, Tran V, Sauk J, Ha C. Higher sedation requirements among inflammatory bowel disease patients undergoing colonoscopy for disease activity assessment or dysplasia surveillance. *Crohn's & Colitis 360. 2019;1(1).* https://doi.org/10.1093/crocol/otz006
3. Flynn S, Eisenstein S. Inflammatory Bowel Disease Presentation and Diagnosis. *Surg Clin North Am*. 2019;99(6):1051-1062. doi:10.1016/j.suc.2019.08.001
4. Steenholdt C, Jensen JT, Brynskov J, et al. Patient Satisfaction of Propofol Versus Midazolam and Fentanyl Sedation During Colonoscopy in Inflammatory Bowel Disease. *Clin Gastroenterol Hepatol*. 2022;20(3):559-568.e5. doi:10.1016/j.cgh.2020.10.037.
5. Flood P, Rathmell JP, Urman RD. *Stoelting's Pharmacology and physiology in anesthetic practice.* 6th edition. Wolters Kluwer Health; 2021.
6. Pharmacology and mechanism of action. Byfavo. Accessed June 25, 2022. https://byfavo.azurewebsites.net/pharmacology/
7. Ul-Haque I, Shaikh TG, Ahmed SH, et al. Efficacy of remimazolam for procedural sedation in american society of anesthesiologists (ASA) I to IV patients undergoing colonoscopy: a systematic review and meta-analysis. *Cureus*. 2022;9(3):e22881. doi:10.7759/cureus.22881.
8. Rex DK, Bhandari R, Lorch DG, Meyers M, Schippers F, Bernstein D. Safety and efficacy of remimazolam in high risk colonoscopy: A randomized trial. *Dig Liver Dis*. 2021;53(1):94-101. doi:10.1016/j.dld.2020.10.039
9. Borkett KM, Riff DS, Schwartz HI, et al. A Phase IIa, randomized, double-blind study of remimazolam (CNS 7056) versus midazolam for sedation in upper gastrointestinal endoscopy. *Anesth Analg*. 2015;120(4):771-780. doi:10.1213/ANE.0000000000000548
10. Pastis NJ, Yarmus LB, Schippers F, et al. Safety and Efficacy of Remimazolam Compared With Placebo and Midazolam for Moderate Sedation During Bronchoscopy. *Chest*. 2019;155(1):137-146. doi:10.1016/j.chest.2018.09.015
11. Guo J, Qian Y, Zhang X, Han S, Shi Q, Xu J. Remimazolam tosilate compared with propofol for gastrointestinal endoscopy in elderly patients: a prospective, randomized and controlled study. *BMC Anesthesiol*. 2022;22(1):180. Published 2022 Jun 10. doi:10.1186/s12871-022-01713-6
12. Chen SH, Yuan TM, Zhang J, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. *J Gastroenterol Hepatol*. 2021;36(2):474-481. doi:10.1111/jgh.15188