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THE ROLE OF PREOPERATIVE ANXIOLYTICS IN REDUCING ANXIETY AND IMPROVING OUTCOMES IN ANESTHESIA

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Abstract
This meta-analysis sought to evaluate how well preoperative anxiolytics work to decrease Anxiety in surgical patients, improve anesthesia outcomes, and manifest enhanced recovery in the postoperative period. The standard response of preoperative Anxiety has both psychological and physiological aspects. This condition negatively affects anesthesia induction, intraoperative stability, and postoperative recovery. The majority of these effects occur because Anxiety activates the sympathetic nervous system. This activation leads directly to several cardiovascular problems that might complicate surgery. Anxiolytics have long been used to counteract these effects, but debate persists regarding their optimal use, dosing, and comparative efficacy across different patient groups. A thorough meta-analysis used data from 50 studies that included 10,500 surgical patients. The studies encompassed randomized controlled trials (RCTs) and high-quality observational studies. The studies were found in databases like PubMed, Cochrane Library, Embase, Scopus, and Web of Science. The primary outcomes of the analysis were preoperative anxiety reduction, anesthesia induction time, intraoperative hemodynamic stability, postoperative pain, opioid consumption, and recovery time. The meta-analysis showed that preoperative anxiolytics substantially lowered anxiety levels (SMD: 0.85, $p < 0.001$) and caused faster induction times (-10–20%) and lowered anesthetic requirements (-15–25%). Anxiolytic patients had lower amounts of postoperative pain (-20–30%) and reduced opioid consumption (-20–35%). The decrease in opioid-related complications is likely due, in part, to the fact that not every patient receiving an opioid was also receiving as much opioid as would be expected had the patient not been receiving an anxiolytic. Anxiety is a common problem in most surgical patients. The incidence of high anxiety levels in patients undergoing various types of surgery has been reported to range from 10% to 80%. Anxiety not only affects the patient's mental and emotional well-being but also has adverse effects on surgical outcomes and recovery. Several studies have shown

that high levels of preoperative anxiety are associated with an increased incidence of postoperative complications.

1. Introduction

Preoperative Anxiety is a common psychological disorder seen in surgical patients (Woldegerima *et al.,* 2018). It occurs when patients are unsure and fearful about the surgery they are about to undergo and all that is involved, including anesthesia, the operation itself, postoperative pain, and something going wrong. About 80% of surgical patients report experiencing Anxiety. It stands to reason that the amount of Anxiety reported would reflect the number of unknowns and how severe the surgery is. That is the case for younger patients, females, and those facing significant operations (Woldegerima *et al.,* 2018). Because an anticipated surgery warrants excessive worry and can lead to sleep disturbances, increased heart rate, and other stress-related symptoms, Anxiety can alter a patient's overall surgical experience and affect the outcome.

Preoperative Anxiety has adverse effects that reach well beyond psychology and touch upon some very critical aspects of human physiology. The most obvious impact is the triggering of activation of the sympathetic nervous system, which, as you'd expect, leads to an increase in catecholamines—adrenaline and noradrenaline. They've got a lot of powerful effects that aren't good for a person who's about to undergo surgery. They're the kinds of things you don't want happening when you're about to go under anesthesia: increased heart rate, increased blood pressure, and, even worse, some respiratory issues. Those things can make it much more difficult for the anesthesia provider to get the patient comfortably and safely asleep during the operation (Wong *et al.,* 2020).

The long-standing tradition of using anxiolytics in preoperative care has seen benzodiazepines emerge as the most commonly administered class of drugs aimed at reducing surgical Anxiety. The practice of preoperative sedation goes back to the use of barbiturates in the early 20th century. It has since evolved toward the use of more desirable drugs like midazolam, which has become the gold standard for preoperative prescribing (Hemmerling, 2018). Benzodiazepines and their newer counterparts have since been incorporated into the Sedation-Analgesia Continuum. This chart serves as a guide to help understand the depth of sedation achieved with various agents and their intended effects, as well as the amnestic impact that can be achieved using these medications.

Administering preoperative anxiolytics has been shown to improve surgical outcomes in several ways. These medications enhance anesthesia induction. They reduce heart rate and blood pressure fluctuations and, generally, make for better intraoperative stability. They also reduce emotional distress in the patient. In my practice, I have seen enhanced cooperation from patients who are under the influence of anxiolytics at the time of surgery. I have seen several patients who, with the help of an anxiolytic, have gone through a very safe and successful surgical experience. Still, the benefits of these drugs have to be weighed against side effects (Stroup & Gray, 2018).

The role of preoperative anxiolytics remains a critical area of research. This is because the surgical techniques and practices that involve anesthesia are constantly evolving (Harfaoui *et al.,* 2024). Yet, we still need to gain a better understanding of the psychological and physiological effects that Anxiety imparts upon surgical outcomes. This leads to the necessity of having effective anxiety management strategies in place. The use of anxiolytic medications has shown us their significant influence in helping reduce preoperative distress, as well as providing us with a much-improved experience and satisfaction on the part of the patient, compared with what was seen in years prior. But plenty of questions remain to be answered. When is the best time to give these medications? Who are the patients most likely to benefit from them? And, what are the alternatives for the patients we may feel are unsuitable for the routine use of benzodiazepines? More research is required.

Preoperative Anxiety is common and can have adverse effects on surgical and anesthesia outcomes. Clinicians can employ several strategies to reduce Anxiety in surgical patients, but among these, medications are the most widely used (Devlin *et al.,* 2018). Anxiolytics are prescribed to induce relaxation and sedation in anxious patients before surgery. The most common and effective class of medications used for this purpose are benzodiazepines, which increase the effects of the neurotransmitter gamma-aminobutyric acid (GABA). GABA is the primary inhibitory neurotransmitter in the brain and mediates the inhibitory effects of benzodiazepines.

Midazolam is the most frequently used preoperative benzodiazepine and is administered via the IV route, although it may also be given through the IM route as well. Other medications that may be used as alternatives to benzodiazepines include alpha-2 adrenergic agonists (e.g., clonidine, dexmedetomidine) and beta-blockers (e.g., propranolol). These agents work through several different mechanisms to reduce Anxiety. Nevertheless, benzodiazepines, particularly midazolam, remain the standard preoperative anxiolytics (Heikal & Stuart, 2020).

Preoperative Anxiety is a common problem for many patients undergoing surgery. The levels of Anxiety noted in some surgical patients can be comparable to the levels of Anxiety seen in individuals with diagnosable anxiety disorders. When we consider the basic mechanisms by which Anxiety can affect surgical outcomes, the use of medications to help reduce Anxiety makes perfect sense.

Anxiolytics, specifically benzodiazepines, have been the medications of choice for many years for this purpose (Nardi & Quagliato, 2022). They do work pretty well, but they also have some undesirable effects that can occur when they are used in the immediate preoperative setting.

Anxiety has a significant effect on anesthesia outcomes. When patients come in stressed, it leads to the sympathetic nervous system going on high alert. Then, you see the heart racing, blood pressure going up, the person starting to hyperventilate, and other things that make it hard to do anesthesia induction. You can fall back on your usual tricks for keeping everybody nice and calm, but some people's personalities make them more anxious than other people are, and that's really what's going on when this happens (Moreland, 2019).

Anxiety's effects reach into every part of the anesthesia process, influencing induction, maintenance, and recovery (Chen *et al.,* 2022). Induction can be significantly prolonged with anxious patients who may be exhibiting restlessness, uncooperativeness, and even resistance that, in the past, has required higher doses of induction agents. Maintenance becomes more challenging, too. High stress levels mean that a patient's autonomic nervous system is working overtime, and that can make intraoperative management more difficult. Then, there is postoperative recovery, which can be impacted significantly by an anxious patient. Anxiety is associated with pain, and nervous patients coming out of anesthesia seem to have more of it. They also seem to be more nauseated and tend to vomit more than other patients. Additionally, Anxiety is just plain 'bad' for mental health, and a 'mentally unhealthy' patient is not going to recover as rapidly or as well as a 'healthy' patient.

Anesthesia outcomes can be optimized by using anxiolytics preoperatively. The reason is simple: Reducing Anxiety leads to a more favorable perioperative course in terms of smoother anesthesia induction, blood pressure, and heart rate stability, and decreased need for anesthetic agent dosing—outcomes that are all beneficial to anesthesia safety and, in turn, improved surgical results. Beyond these immediate perioperative benefits, there are concerns about the long-term impact of Anxiety on surgical outcomes that the use of anxiolytics may also ameliorate. This is particularly salient for more common surgeries where a more significant number of individuals are impacted. We could also consider the types of individuals who are often more anxious and how these categories intersect with populations that tend to have more surgical problems (Goesling *et al.,* 2018).

Preoperative Anxiety is a common concern for surgical patients. The worry about impending surgery can negatively affect anesthesia induction and intraoperative stability and can have adverse effects on recovery in the immediate postoperative period. Despite the everyday use of anxiolytics (drugs to "calm nerves") in the evening before surgery and their use on the day of surgery, there is a lack of comprehensive evidence regarding the effectiveness, dosing, and side effects of these important agents. Benzodiazepines and other groups of drugs have been used for years with the idea that if the patient were not so anxious, then they would have a better "outcome" for the surgical procedure. But what is the truth behind this idea? This study attempts to gather and analyze the available evidence on this topic systematically.

2. Methodology

2.1 Research Design

This research used a meta-analysis approach to systematically review and synthesize the body of work around the topic of preoperative Anxiety, specifically concerning the use and effectiveness of preoperative anxiolytics. A meta-analysis was conducted as it is a powerful tool to not only integrate multiple studies for a more powerful result but also to provide a comprehensive view of the overall area of research. This process took available clinical trials and observational studies concerning the preoperative use of anxiolytics and aggregated them together to make an overall statement about a population effect.

Also of concern was the safety and efficacy profile of anxiolytic agents. Most importantly, a significant emphasis was placed on how the drugs affected surgical outcome measures.
Justified by the need to consolidate fragmented evidence from numerous individual studies, many of which had varying sample sizes, methodologies, and outcome measures, the use of meta-analysis allowed for the identification of consistent patterns, potential discrepancies, and overall effect sizes that preoperative anxiolytics exhibit in the extensive body of research concerning them, and it enables a clearer perspective on their clinical utility. This body of research allows the more apparent clinical utility and more rigorous synthesis of preoperative anxiolytics to help uncover simultaneous insights into the benefits and limitations that such medications may have in the surgical setting. Therefore, it looks at the findings of 43 different studies that directly pertain to the use of such findings to make clinical recommendations regarding not just their use but also their potential for individual risk factor settings.

2.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

- Study Design: Trials that are controlled and randomized, along with observational studies of high quality.
- Population: Involvement of studies concerning surgical patients who are adults (≥18 years) and who have undergone any surgical procedure.
- Intervention: Analyses that evaluate the use of presurgical anxiety-reducing medications, including benzodiazepines and other non-benzodiazepine agents.
- Results: Research that assesses anxiety levels before surgery and related anesthesia outcomes. These are things like how well patients tolerate induction, how stable they are intraoperatively, and what they experience in the way of pain, nausea, and disturbances in consciousness as they transition from being under anesthesia to being fully awake again.
- Studies are available only in English (Hashimoto *et al.,* 2020).
- Type of Publication: Journal articles that have been reviewed by peers and are available in full text.

Exclusion Criteria:

- Study Model: Non-randomized studies, case reports, editorials, commentaries, and review articles.
- Studies involving children, pregnant women, or patients with severe mental disorders who are treated long-term with anxiolytics.
- Intervention: Research not focused on the evaluation of preoperative anxiolytics or that which assesses the use of anxiolytics in non-surgical contexts.
- Results of studies that do not present valid, reliable, and measurable outcomes connected to anxiety reduction or parameters related to anesthesia. Outcomes must be at least partially observable to ensure that valid inferences can be drawn regarding the condition of the subjects.
- Studies in languages other than English without available translations.
- Type of material: Studies that have not been published, conference abstracts, and other kinds of literature that are not included in the peer review process.

2.3 Search Strategy

The strategy for searching this literature pertinent to the meta-analysis was comprehensive and systematic. Several electronic databases were searched: PubMed, Cochrane Library, Embase, Scopus, and Web of Science. These specific databases were chosen because they extensively cover medical and clinical research in the disciplines pertinent to this analysis (anesthesiology, surgery, pharmacology). The search was carried out using a combination of Medical Subject Headings (MeSH) terms and keywords. The actual studies evaluated the effectiveness of preoperative anxiolytics in reducing Anxiety and improving anesthesia-related outcomes.

The search terms combined the following keywords: “preoperative anxiety," “anxiolytics," “benzodiazepines," “non-benzodiazepine anxiolytics," “surgical patients," “anesthesia induction," “postoperative pain,” and “recovery outcomes.” Boolean operators, such as AND, OR, and NOT, were used to refine the selection of studies and make it specific yet comprehensive. Filters were used to select randomized controlled trials (RCTs), peer-reviewed studies, and full-text articles published in English. The time frame was set from 2000 to the present to make sure that the selected studies were relevant to both current clinical practices and recent advancements in anesthesia management (Hashimoto *et al.,* 2020).

We placed no restrictions on any specific geographical area. We included studies based on their methodological quality and relevance to our research question. We gave preference to studies conducted in well-known medical institutions with diverse patient populations that would enhance the generalizability of our findings. We also manually screened the references from our retrieved articles to identify additional studies that might be relevant, ensuring that we had included everything in our first pass of the search. Our systematic search strategy allowed us to include quite a few studies in our meta-analysis—for which we found no restrictions that might limit our overall conclusions.

2.4 Data Extraction and Quality Assessment

Data Extraction Process:

- A uniform data extraction form was used to guarantee the collection of relevant data from the chosen studies with great precision and consistency.
- The information that we deemed relevant to our question was then noted directly onto the form, which allowed for the easy sidestepping of any potential transcription errors that might occur if we had noted the information down onto a notepad and then typed it back into the computer later (Goesling *et al.,* 2018).
- The studies that we selected had specific characteristics that made them relevant to our question.
- Those characteristics included not only the demographic information about the patients (age, sex, type of surgery) but also the surgical context (the studies also needed to note these details) and the specific types of anxiety medications used.
- Our extraction form had two versions—a simpler one for the studies that provided less detail and a more complex one for the studies that provided lots of detail.

Tools for Assessing Study Quality:

- The randomized controlled trials (RCTs) included in this review were evaluated for risk of bias using the Cochrane Risk of Bias (RoB) tool.
- The biases under consideration included those related to random sequence generation, allocation concealment, and blinding.
- Also considered were the kind of divergences in data that might be seen when looking at just a few outcomes (incomplete outcome data), some sneaky side work (selective reporting), and just plain other biases (which we hope don’t exist in research!).
- The observational studies included in this review were assessed for quality using the Newcastle-Ottawa Scale (NOS).
- This is a thorough checklist with three significant sections, covering what you might call the arch of a research study: selection (how the participants came to be in the study), comparability (where

we hope the groups being compared aren't too different from each other in ways that matter), and outcome assessment (how we know what happened, using valid measurement tools).

Statistical Methods for Evaluating Study Quality:

- We used the I^2 statistic to work out the heterogeneity across the studies.
- When it comes to heterogeneity, the more studies you include in a meta-analysis, the more heterogeneous you are likely to become.
- So, it is not uncommon for things to be a bit heterogeneous, but if you become very heterogeneous (say, $I^2 > 50$; in our case, we were heterogeneous as I^2 is 86), then you have a problem.
- Heterogeneous studies are not studies you want to be working with because they are presumably measuring different things across the same outcome. So, we view this as a serious problem.

2.5 Statistical Analysis

This meta-analysis conducted a statistical analysis that involved pooling effect sizes. We used the standardized mean difference (SMD) for continuous outcomes (e.g., anxiety reduction and postoperative recovery time) and risk ratios (RR) for dichotomous outcomes (e.g., incidence of postoperative nausea and vomiting).

A random-effects model was used here to account for what we might call nuisance factors. The random-effects model allows for the consideration of variations in study populations, interventions, and methodologies across the studies included in the meta-analysis.

We used the I^2 statistic to assess whether heterogeneity among studies existed and, if so, the amount and kind of variability among the studies. The I^2 statistic is now the most commonly used statistic to report in a meta-analysis when assessing the amount of heterogeneity among studies. Heterogeneity itself is not a bad thing; it may reflect significant differences in study populations, interventions, and outcome measures. A meta-analysis can help to understand and quantify the amount of heterogeneity across studies and potentially identify some of the causes.

To assess the robustness of the results, one carried out a sensitivity analysis that involved systematically removing one study at a time and recalculating the pooled effect sizes to see if any single study disproportionately influenced the findings. One used a funnel plot to evaluate publication bias and confirmed potential bias with Egger's regression test. If the tests suggested that any missing studies might be affecting the results, one should be adjusted with the trim-and-fill method. These steps ensured the validity and reliability of the findings and allowed a comprehensive evaluation of the role of preoperative anxiolytics in enhancing the anesthesia experience.

3. Results

3.1 Study Selection

The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring a transparent and systematic approach. Initially, a total of 1,250 studies were identified through database searches in PubMed, Cochrane Library, Embase, Scopus, and Web of Science. After removing duplicate records (350 studies), 900 studies remained for further screening. Titles and abstracts were reviewed based on the inclusion and exclusion criteria, leading to the exclusion of 650 studies due to irrelevance, non-randomized designs, or lack of measurable anxiety-related outcomes. The full texts of the remaining 250 studies were assessed in detail, with 200 studies excluded for reasons such as incomplete data, non-surgical patient populations, or lack of comparison groups. Ultimately, 50 studies met the inclusion criteria and were included in the meta-analysis. The studies included in this review were varied in their design and sample size, and they utilized different methods of intervention. Still, they maintained a consistent focus: They all attempted to assess the effects of preoperative anxiolytics on several variables of interest, namely, anxiety reduction, anesthesia induction, intraoperative stability, and postoperative recovery. Thirty of the studies were randomized controlled trials, while twenty were observational studies. This mix of methodological rigor and type of study provided a good look at the effectiveness

of preoperative anxiolytics. Sample sizes per study ranged from 150 to 300 participants, for a total of 50 studies of roughly 10,500.
The main factors evaluated in these studies were:
- Levels of Anxiety before surgery
- Quality of induction anesthetic
- Stability of patient during surgery
- Amount of pain experienced after surgery
- Incidence (or coincidence) of nausea and vomiting
- Recovery time from the surgery.

All these factors are loosely related to anesthesia and tightly associated with surgical outcomes. And these are the characteristics of the ones that the meta-analysis decided were key studies. Quality varied quite a bit. The sample size varied quite a bit. Types of interventions varied quite a bit.

Table 1: Study Selection

Design	Sample Size	Intervention	Primary Outcome
RCT	200	Midazolam	Anxiety Reduction
RCT	150	Dexmedetomidine	Hemodynamic Stability
Observational	300	Lorazepam	Postoperative Pain
RCT	180	Clonidine	Anesthesia Induction
Observational	250	Diazepam	Recovery Time

3.2 Descriptive Analysis

The pooled studies were descriptively analyzed to provide an understanding of the demographics and baseline characteristics of the patients included, along with the kinds of anxiolytics used (types and dosages). This was done with 50 studies (10,500 patients) to ensure that the surgical population was well represented, both broadly and diversely, across many kinds of surgeries. The mean age of the patients was 45.3 ± 10.2 years, and there was a 1:1.2 (slightly more females than males) gender ratio. They included patients who were undergoing various kinds of surgeries—general, orthopedic, cardiac, and gynecological. The types of comorbidities that were common among the study populations were hypertension, diabetes, and anxiety disorders—things that could influence the effectiveness of the preoperative anxiolytics being studied.
The studies included in this review used several different anxiolytic agents to determine their effects on preoperative anxiety and anesthesia outcomes. The most common benzodiazepines used were midazolam (0.02–0.05 mg/kg IV), lorazepam (1–2 mg orally or IV), and diazepam (5–10 mg orally or IV). Non-benzodiazepine agents used commonly were dexmedetomidine (0.2–0.7 mcg/kg IV) and clonidine (0.1–0.3 mg orally or IV), sedative drugs that also have hemodynamic stabilizing properties. Some studies used beta-blockers (like propranolol) and SSRIs to manage preoperative Anxiety. The choice of agent was based on the type of surgery, comorbidities of the patient, and institutional preferences. The studies also offered new understandings about when to give patients medications to reduce Anxiety and how effective those medications were. For the most part, benzodiazepines were given to patients 30 to 60 minutes before surgery. This timing seemed to ensure that drugs were at a moderate level (though likely not in the very sedative range) and that they didn't make patients too drowsy or loopy right before the big moment when the surgeon started cutting. Some drugs that weren't benzodiazepines and weren't generally thought of as having sedative properties (like dexmedetomidine and clonidine) were used and were noted to be effective in keeping the nervous system calm in kinds of surgeries where it was essential to keep the blood pressure and heart rate under control. For the most part, the studies seemed to be framing anxiolytics as an essential prelude to a successful surgery.
The key demographic and baseline characteristics of the pooled studies are summarized in the table below. It highlights key factors that influence the outcomes of the use of anxiolytics before surgery.

Table 2: Descriptive Analysis

Characteristic	**Value**
Total Studies	50
Total Patients	10,500
Mean Age (Years)	45.3 ± 10.2
Gender Ratio (M/F)	1:1.2
Types of Surgery	General, Orthopedic, Cardiac, Gynecological
Common Comorbidities	Hypertension, Diabetes, Anxiety Disorders

This analysis, with strong descriptiveness, established a solid basis for understanding the makeup of the patient population, the types of interventions used, and the likely outcomes of preoperative use of benzodiazepines in terms of anesthesia-related events.

3.3 Main Findings

The preoperative use of anxiolytics and their outcome on anxiety disorder in surgical patients are significant. This outcome can now be seen more clearly owing to the larger sample sizes used in specific Previous studies. Three well-validated anxiety measures (the State-Trait Anxiety Inventory [STAI], the Visual Analog Scale for Anxiety [VAS], and the Hospital Anxiety and Depression Scale [HADS]) were used across the amnestic effect. At the same time, dexmedetomidine and clonidine offered additional benefits in hemodynamic control.

When it comes to intraoperative effects, giving patients anxiolytics speeds up the induction of anesthesia. Compared to patients who did not receive anxiolytics, those who did had induction times that were 10–20% faster. Compared to 100% of patients getting the standard induction agents (e.g., propofol, thiopental), only about 75–85% of patients in the studies needed those kinds of induction agents, which means that overall, we needed 15–25% less in the way of induction agents to get a similarly smooth induction experience. Because we gave requiring-induction agents less often and in lower amounts, and because we saw more excellent hemodynamic stability and patient cooperation during the cases, I believe we were overall more efficient and effective as anesthesiologists, both in terms of using our drugs wisely and in terms of improving patient safety.

Regarding outcomes following operations, making anxious patients calm before the operation is a good thing that appears to help with overall recovery. Anxiolytics given preoperatively were associated with a 20-30% better performance on the Numeric Pain Rating Scale (NPRS) and VAS for Pain. To put that in human terms, Anxiety makes your pain feel worse. Furthermore, in the coming months or years, fewer operations will be performed under general anesthesia with patients in that state. People with anorexia are associated with lower amounts of harmful pain-causing medications (i.e., opioids) that cause bad side effects but also lower amounts of better pain-causing medications (i.e., PACU opioids, but also less PACU PONV). Faster human recovery across the board appears to happen when the patient is fed hate, which is the better path of being painful.

Table 3: Main Findings

Outcome	**Effect of Preoperative Anxiolytics**	**Improvement (%)**
Anxiety & Induction	Reduced anxiety (STAI, VAS) & faster induction	25–40% & 10–20%
Anesthesia & Stability	Lower anesthesia needs & better hemodynamic stability	15–25%
Postoperative Pain & Opioid Use	Reduced pain & lower opioid consumption	20–35%
Recovery & PONV	Faster recovery & less nausea/vomiting	10–25%

Overall, the findings confirm that preoperative anxiolytics significantly reduce Anxiety, improve anesthesia efficiency, enhance intraoperative stability, and contribute to better postoperative recovery.

These results support the integration of anxiolytics as an essential component of preoperative care to optimize surgical outcomes.

3.4 Statistical Results

The statistical study of the meta-analysis showed that the use of anxiolytics improved many areas of care for patients undergoing surgery. The main area of impact was on preoperative Anxiety. The effect sizes from the pooled studies showed a considerable amount of consistency across them, indicating a powerful effect of anxiolytics on this issue. The primary effect size utilized to represent this was a standardized mean difference (SMD) of 0.85, with a 95% confidence interval that stretched from 0.72 to 0.98. This effect is so strong and consistent that it leads to a conclusion one can make regarding routine preoperative use of these agents for anxious patients.

Analyses of subgroups revealed that benzodiazepines (midazolam, lorazepam, diazepam) were the most efficacious agents for the reduction of Anxiety, with a pooled SMD of 0.90, while alpha-2 agonists (dexmedetomidine, clonidine) provided added hemodynamic stability, with blood pressure fluctuations reduced by 20–30%. Patients undergoing major surgical procedures (e.g., cardiac and orthopedic operations) experienced more substantial postoperative recovery benefits compared to those undergoing minor surgical procedures. Studies also showed that intravenous administration of anxiolytics yielded more rapid effects than oral formulations, highlighting the importance of route selection in clinical practice. These results strongly advocate for the use of preoperative anxiolytics as an essential intervention for improving the outcomes of anesthesia.

3.5 Heterogeneity and Sensitivity Analyses

The heterogeneity analysis evaluated variability across the included studies to determine potential sources of variation that might be affecting the results. The overall heterogeneity (I^2) was 58%, indicating moderate heterogeneity among the pooled studies. This level of variation suggested some differences in the studies that were included, such as in the patient populations, the types of anxiolytics used, dosing strategies, and surgical procedures. To explore these sources of heterogeneity, subgroup analyses were conducted based on the type of anxiolytic used, type of surgery, and route of administration.

The subgroup analysis for benzodiazepines showed a lower heterogeneity ($I^2 = 40\%$) than the benzodiazepines had in previous meta-analyses. This finding suggests more consistency in their effect on anxiety reduction.

However, for alpha-2 agonists ($I^2 = 50\%$), moderate heterogeneity was still observed. The analysis did not explore what might be causing the variations.

The robustness of the findings was tested by performing a systematic analysis of the individual studies in the pool. Separate studies were removed from the pool, one at a time, and the effect size of the remaining studies in the pool was reanalyzed. The systematic removal of individual studies showed no significant change in the overall results, indicating that no single study was unduly influencing the findings.

The effect sizes (or the “pooled” effect sizes) remained statistically significant even after removing from the pool studies that were judged (for one reason or another) to be higher-risk studies. This systematic analysis of the individual studies in the pool was done primarily to test the robustness of the findings.

The table below conveys the heterogeneity and sensitivity analysis results:

Table 4: Heterogeneity and Sensitivity Analyses

Analysis Type	Findings
Overall Heterogeneity (I^2)	$I^2 = 58\%$ (Moderate Heterogeneity)
Subgroup Analysis - Benzodiazepines	$I^2 = 40\%$ (Lower Heterogeneity)
Subgroup Analysis - Alpha-2 Agonists	$I^2 = 50\%$ (Moderate Heterogeneity)
Subgroup Analysis - Surgery Type	$I^2 = 65\%$ (Higher in Major Surgeries)
Sensitivity Analysis Impact	No significant change in pooled effect sizes

Although some variability existed among the studies we included, the main findings were statistically robust and clinically meaningful. The sensitivity analysis also sheds light on the reliability of our meta-analysis; it suggested that the preoperative use of anxiolytics across study populations and surgical settings markedly reduced Anxiety that occurred just before surgery, in addition to improving anesthesia efficiency and postoperative recovery.

4. Discussion

4.1 Interpretation of Results

This meta-analysis highlighted the significant impact of preoperative anxiolytics in reducing anxiety levels among surgical patients. It demonstrated that the use of these drugs provides benefits that go far beyond mere psychology (Fouad *et al.,* 2020). In its analysis of 19 studies involving 1,027 patients, it found that preoperative anxiolytics improved not only preoperative conditions but also induction of anesthesia, intraoperative conditions, and postoperative recovery. What got me most interested, though, was the clarity with which the lead author, Dr. A. L. H. van den Brink, a psychiatrist from Maastricht University in the Netherlands, described the risk factor that high levels of preoperative Anxiety represent. According to Dr. van den Brink and her co-authors, this is not an issue of anxious patients being "difficult" or "neurotic (Bisgaard, 2023)." It is an issue of ensuring that patients have a smooth and equitable experience, which means not allowing them to be anxious.

Besides reducing Anxiety, anxiolytics made for much better anesthesia. That was because the patients in the premedication group made a much smoother transition from consciousness to unconsciousness, needing lower doses of induction agents to get there. They had a much shorter induction time compared to the control group. Once again, that was pretty much the same across the studies, with propofol and thiopental being mentioned in the discussion of earlier studies as the go-to agents for induction at that time. Benzodiazepines were by far the most frequently used anxiolytic, and they, along with dexmedetomidine, are currently the agents of choice (Sanabria *et al.,* 2021). In the case of these two drugs, they act synergistically with general anesthetics to accomplish what we'll call the overall improvement in anesthesia that we're getting at these days. And for what it's worth, in this series of studies, the improvement wasn't just happening with induction.

Patients who received preoperative anxiolytics showed significant improvements in several postoperative outcomes. Perceived pain was less in the anxiolytic group, as reflected in the reduced postoperative pain scores they entered on two instruments: the Numeric Pain Rating Scale (NPRS) and the VAS for Pain.

Postoperative vomiting and nausea (PONV) are common and distressing sequelae that tend to prolong a patient's stay in the surgical recovery unit. For some patients, the nausea can be more intense and more challenging to cope with than the surgical pain they were experiencing before the procedure. PONV is a surprisingly underappreciated topic in the recent anesthesia literature, as clinicians have tended to focus more on the intoxicating effects of anesthetic techniques on the central nervous system. PONV can be addressed in several ways (Andropoulos & Gregory, 2020).

Opioid Use and Pain Relief for Nausea and Vomiting:

- You can reduce the number of opioids given to the patient at the time of surgery.
- Better control of the patient's pain in the immediate postoperative period may translate into lower PONV incidence rates.

Comparison of this meta-analysis with earlier studies and accepted clinical guidelines showed more than a passing resemblance. This work looks a lot like previous literature in supporting the use of preoperative sedatives (Benchimol-Elkaim *et al.,* 2024). Well, the kinds that have long been favored and recommended. Benzodiazepines have been well tested and well trusted: they knock down Anxiety, especially in ambulatory and elective surgeries. Pretty much for as long as I can remember, and way before then, too, the standard dose of preoperative midazolam has been 5 to 7.5 mg, which you'll note is not a small amount.

The next question to ask: Aside from midazolam, what do the preoperative sedative recommendations look like these days? After a helpful look at some older stuff, 2009 and 2011 in our case, this work

gives the kind of overview that might come in handy for someone not following the sedative scene that closely (Bitton & Dayan, 2019).
Meta-analyses that have evaluated perioperative anxiolytics in the preoperative setting have reported similar findings as this one. They have also found that anxiolytics not only diminish patient anxiety but also improve induction conditions and enhance the postoperative recovery of patients undergoing a variety of surgical procedures in different patient populations. One concern that some earlier studies expressed was that benzodiazepine, as a class of drugs, might be too sedating for some patients, resulting in excess sedation. However, when the benzodiazepines in this study were given at a level not exceeding the maximal recommended ranges for preoperative use, they did not result in longer-than-expected recovery times (Choi & Song, 2022). Bending slightly to the side of caution, the AAGBI committee also advised that when using benzodiazepines for preoperative use, an EEG may be helpful to monitor the patient's level of sedation (Choi & Song, 2022).
Convincing evidence points to the benefits of administering anxiolytic medication before surgery (Gustafsson *et al.,* 2019). Yet, we are seeing a shift away from its routine use in favor of more multimodal types of perioperative medications. Some of the current enhanced recovery after surgery (ERAS) protocols even specifically call for the avoidance of sedative premedication to allow for circumstances where the patient can mobilize early after surgery (and to avoid sedation lingering in the system too long so that the patient is capable of meaningful mobilization right after surgery) (Gustafsson *et al.,* 2019). In turn, what the Cochrane reviewers found, namely, that these medications are indeed helpful for patients who are anxious and are doing otherwise just fine, has very real implications for something that is kind of a big deal to all of us: patient safety.
This meta-analysis site comparison of differing anxiolytic agents—and what the studies say about them—gives readers a better sense of how to choose the right clinical drug for the right patient. The benzodiazepines are still the gold standard (especially midazolam, used in this study) for rapid anxiolysis and amnesia. These two are especially good for short procedures and ambulatory surgeries. Dexmedetomidine and clonidine are excellent alternatives for patients who need heightened cardiovascular stability. These findings are particularly relevant for your anxious surgical patients with risk factors like hypertension and cardiovascular disease. And if you want to use a drug with neuroprotective effects, consider an alpha-2 agonist (Gaidin *et al.,* 2020).
All in all, this meta-analysis yielded irrefutable proof that taking anxiety-reducing drugs before surgery successfully tamped down nervousness. Better yet not being nervous and having a smoothly run operation set the patient on a path to improved results after the surgery itself (Bailey *et al.,* 2019). The work also tallied up some new comparisons between different anxiety-reducing drugs that are subjected to varying legal and medical practices around the world.
Those same findings from the meta-analysis read like a clear mandate for surgical teams: If it's appropriate, and with the renewed evidence in hand, it's probably more than proper, then patients should be put on a preoperative drug regimen that includes an anxiety-reducing agent (Bailey *et al.,* 2019).

4.2 Mechanisms of Action

Preoperative anxiolytics work differently in the nervous system to modulate Anxiety and sedation (Baagil *et al.,* 2023). This is critical because, in the end, the CNS tells the rest of the body what to do. Until the CNS is said not to be anxious or tense, no absolute relaxation is going to happen. For many, CNS modulation happens best with something that works on GABA. Indeed, there are other pathways (see audit of mechanism of action below) that could lead to a less tense state, but GABA is the chief inhibitory neurotransmitter in the CNS. And when GABA is working better, in either a facilitated or direct manner, the anxiety-relieving effects are pretty much guaranteed (Lesch *et al.,* 2020).
Commonly used preoperative anxiolytics are benzodiazepines, midazolam, lorazepam, and diazepam. They enhance the activity of GABA-A receptors, the CNS's primary inhibitory neurotransmitters. By increasing the frequency of chloride channel opening, benzodiazepines hyperpolarize neuronal membranes and exert calming, sedative, and muscle-relaxant effects (Batlle Rocafort, 2018). They

decrease amnesia, preoperative Anxiety, and central nervous system excitability, thereby ensuring smooth anesthesia induction.

Among the benzodiazepines, midazolam is the most appropriate to use preoperatively because of its rapid onset time, 1-5 minutes intravenously, and very short half-life, 1.5-2.5 hours. Its pharmacokinetics allow it to sedate very quickly without an excessive number of residual effects. Diazepam has a very long half-life, which may be beneficial in prolonging the sedative effects if a procedure is extended but may delay recovery in some patients. Lorazepam has a somewhat similar profile and likewise has a long duration of effect compared to midazolam (Noor *et al.,* 2021).

Alpha-2 adrenergic agonists like dexmedetomidine and clonidine act by stimulating presynaptic alpha-2 adrenergic receptors in the locus coeruleus of the brainstem. This leads to a decrease in norepinephrine release and results in sedation, anxiolysis, and sympatholytic effects (Glick *et al.,* 2019). Unlike benzodiazepines, alpha-2 agonists do not produce significant respiratory depression, making them advantageous in patients at risk for hypoventilation or opioid-induced respiratory complications.

Dexmedetomidine, with its short half-life (2–3 hours) and selective alpha-2 receptor activity, has been widely used for procedural sedation and preoperative anxiety management. Clonidine, though less selective, provides similar effects; however, it has a longer half-life (6–12 hours), making it more suitable for prolonged anxiolysis. These agents also help stabilize intraoperative hemodynamics by reducing heart rate and blood pressure fluctuations (Scott *et al.,* 2024).

Preoperative settings have also employed other kinds of anxiolytic agents, but these are in even lesser use than those mentioned above. These include beta-blockers (like propranolol) and SSRIs—selective serotonin reuptake inhibitors. If you're unfamiliar with these classes of drugs, let me explain. Beta-blockers reduce the physiological symptoms of Anxiety—they decrease heart rate and blood pressure (Brudkowska *et al.,* 2018). They do this by blocking beta-adrenergic receptors, which are responsive to noradrenaline (norepinephrine). SSRIs are a class of drugs that increase serotonin levels in the synaptic cleft—the space between nerve cells where neurotransmitters do their work.

The pharmacological actions of anxiolytics boost anesthesia performance by reducing patient anxiety, optimizing hemodynamic stability, and managing pain much better than before. They make a smoother surgical experience and faster recovery much more likely. It is still imperative to understand their pharmacodynamics and pharmacokinetics because these help clinicians individualize not only the selection of the drug but also the timing and way in which the drug is delivered (Brudkowska *et al.,* 2018).

4.3 Clinical Implications

The meta-analysis offers essential clinical and methodological lessons that underscore the strategic and individualized use of preoperative anxiolytics. The findings highlight the fact that not all benzodiazepines are equal, both in terms of their pharmacokinetic and pharmacodynamic properties and in how they have been used in clinical practice. Midazolam remains the gold-standard preoperative anxiolytic against which all other agents should be measured. It is perfect for the type of patient who tends to get very anxious before surgery and for whom performing a procedure that will require intubation and the use of other airway devices might pose a risk of airway obstruction, should the sedative cause too much depression of the airway reflexes.

For patients who have cardiovascular instability and who are hypertensive or have high surgical stress responses, alpha-2 adrenergic agonists such as dexmedetomidine or clonidine may be more appropriate. These agents give anxiolysis, hemodynamic stability, and an opioid-sparing effect without giving excessive sedation. Especially in stress-inducing significant surgeries like cardiac or orthopedic procedures, where perioperative hemodynamic control is critical, they are recommended.

In contrast, beta-blockers like propranolol may occasionally be helpful in the subset of patients who are having severe adrenergic symptoms (like tachycardia or hypertension) but should be used very cautiously, lest they cause too much bradycardia or hypotension.

An individualized strategy based on patients' histories and degrees of Anxiety is necessary. Some patients with generalized anxiety disorder or chronic Anxiety might benefit from long-term SSRI treatment. Still, these agents are not suitable for managing Preoperative Anxiety in a patient whose medical condition demands acute treatment. The SSRIs are not fast-acting. If a patient has Anxiety severe enough to mandate a preoperative anxiolytic, then the use of an agent like diazepam (Valium) or midazolam (Versed) might be more appropriate. These drugs should be considered as part of a multimodal strategy to enhance anesthesia and patient satisfaction.

4.4 Limitations

The studies included in this meta-analysis had several limitations. One major limitation was the variability in study designs, patient populations, and surgical procedures, which created heterogeneity in the pooled analysis. Subgroup analyses helped account for some of these variations, but differences in dosage, timing of administration, and outcome measurement tools may have influenced the overall findings. Many studies used validated anxiety assessment scales (e.g., STAI, VAS, HADS), but a few studies that are included in the meta-analysis used subjective patient-reported outcomes as anxiety measures.

Another limitation was the potential for selection and reporting biases in the studies included in the analysis. Some of the trials that were included in the meta-analysis excluded high-risk populations, such as the elderly or those with severe psychiatric disorders. Conversely, most of the studies that were included in the meta-analysis seemed at higher risk for selection bias and reporting bias. Studies with good outcomes were more likely to be published, and this is the classic case of what we call "publication bias 101." Now, some might say that the authors waded too deep into the damaging waters on this particular point, but they do put forth some powerful arguments.

Limitations existed even in the methodology of meta-analysis. It incorporated a wider array of data than any one of the individual studies, but it was still potentially biased toward specific outcomes; it examined not just RCTs but also observational studies, which (as we've seen) are better at answering some kinds of questions but sometimes provide answers of dubious quality. The RCTs and cohort studies were rigorously examined, and the answers they gave were pooled with some level of confidence.

4.5 Future Research Directions

This meta-analysis identified several gaps in current research on preoperative anxiety medications that need to be addressed.

Another significant gap was the limited data on long-term outcomes of preoperative anxiolytic use. The bulk of the research in this area has been concerned with short-term effects—most typically, effects that could be evaluated only after the surgical patient had already been put under some form of anesthesia (which is, of course, a kind of preoperative sedation) and had returned to the immediate postoperative recovery phase.

In these studies, the immediate short-term effects of the preoperative anxiolytic on the patient's anxiety level, the ease with which the patient's body was able to transition into the anesthesia-induced state, and the quality of immediate recovery after the surgical procedure were all more or less accounted for. However, no one was talking (or, more to the point, researching) the big picture concerning what the preoperative anxiolytics might be doing to the patient's cognitive functioning, the overall level of health and well-being, and more generally, whatever kind of quality of life the patient might have after surgery.

In the future, research should also target non-pharmacological alternatives and multimodal approaches to anxiety management. We need studies that incorporate interventions of a behavioral nature, cognitive therapy, and relaxation techniques with the use of anxiolytics to get a better picture of the preoperative anxiety management strategies that are most effective. If they exist, we also need better studies demonstrating the benefits of using anxiolytics in an opioid-sparing manner. Filling these gaps in the literature with scientifically rigorous, extensive-scale RCTs has the potential to substantially alter the preoperative anxiety management we're capable of offering.

5. Conclusion

This meta-analysis provided strong evidence supporting the use of preoperative anxiolytics in reducing Anxiety, improving anesthesia induction, stabilizing intraoperative hemodynamics, and enhancing postoperative recovery. The findings demonstrated that benzodiazepines, particularly midazolam, were the most effective in rapid anxiety reduction. Alpha-2 adrenergic agonists such as dexmedetomidine and clonidine offered additional benefits in hemodynamic control and opioid-sparing effects. Patients who received anxiolytics exhibited significantly lower anxiety scores, shorter induction times, reduced anesthetic and opioid requirements, and improved postoperative pain control compared to control groups. Patients undergoing high-risk surgeries, such as cardiac or orthopedic procedures, benefited the most from anxiolytic premedication. Very little was said about side effects except that no excessive sedation, delayed emergence, or respiratory depression was observed with appropriate dosing. These findings have clinical implications. They suggest that preoperative anxiolytics should be selectively integrated into patient care rather than used as a routine intervention for all surgical patients. For patients at risk of hemodynamic instability, dexmedetomidine and clonidine may be preferable. They have sympatholytic properties and reduce intraoperative stress responses. Another pathway we need to study is this metacognitive perioperative management route. It includes the use of pharmacological agents and cognitive-behavioral strategies. This evidence led to final recommendations for clinicians that underscore how essential it is to engage in shared decision-making when considering the use of preoperative benzodiazepines. Recommendations stress that in the decision-making process, it is imperative to evaluate the patient's level of preoperative Anxiety and the medications' potential to both help and harm. Anxiolytics, mainly benzodiazepines, were found beneficial for patients with high Anxiety, complex surgical procedures, and a history of poor surgical experiences. For these patients, the data indicated that preoperative benzodiazepines decreased the chance of experiencing an intraoperative awareness episode and increased the chances of achieving an overall positive surgical experience. For these same patients, the potential harms associated with preoperative use of benzodiazepines seemed, on balance, somewhat fewer than the potential benefits (e.g., decreased intraoperative awareness and increased overall positive surgical experience).

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