This is a "preproof" accepted article for *Journal of Clinical and Translational Science*. This version may be subject to change during the production process. 10.1017/cts.2025.6

Pre-operative Anxiety and Its Impact on Surgical Outcomes: A Systematic Review and Meta-Analysis

Mohamed A. Shebl<sup>1,a</sup>, Eman Toraih<sup>2,3,\*,a</sup>, Menna Shebl<sup>4</sup>, Ahmed Mosaad Tolba<sup>5</sup>, Parisa Ahmed<sup>6</sup>, Harshdeep Singh Banga<sup>7</sup>, Mohab Orz<sup>5</sup>, Mahmoud Tammam<sup>5</sup>, Keroles Saadalla<sup>1</sup>, Mohamed Elsayed<sup>8</sup>, Mennatallah Kamal<sup>3</sup>, Mohamed Abdulla<sup>5</sup>, Ahmed Ibrahim Eldessouky<sup>3</sup>, Yousef Tarek Moustafa<sup>5</sup>, Omar Ahmed Mohamed<sup>1</sup>, Hani Aiash<sup>3,7</sup>

<sup>1</sup>Faculty of Medicine, Cairo University, Kasr Al- Ainy, Cairo, Egypt, <sup>2</sup> Department of Surgery, Tulane University School of Medicine, LA, USA, <sup>3</sup> Faculty of medicine, Suez Canal University, Ismailia, Egypt, <sup>4</sup> Faculty of medicine, modern university for technology and information, Cairo, Egypt, <sup>5</sup> Faculty of Medicine, Alexandria University, Alexandria, Egypt, <sup>6</sup> Virginia Commonwealth University, Richmond, USA, <sup>7</sup> Upstate Medical University, Syracuse, USA, <sup>8</sup> Dnipropetrovsk Medical Institute of Conventional and Alternative Medicine, Ukraine.

\*Corresponding Author: Eman Toraih, MD, PhD, MSc, DBio, Postal address: Tulane University School of Medicine, Surgery Department, 1430 Tulane Ave. (Room #8548), New Orleans, LA, 70112, USA, Tel. /Fax: (504) 722-7658 / (504)754-7949, Email: etoraih@tulane.edu, ORCID ID: 0000-0001-9267-3787

This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives licence (<a href="http://creativecommons.org/licenses/by-nc-nd/4.0/">http://creativecommons.org/licenses/by-nc-nd/4.0/</a>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is unaltered and is properly cited. The written permission of Cambridge University Press must be obtained for commercial re-use or in order to create a derivative work.

<sup>&</sup>lt;sup>a</sup>both authors contributed equally to this paper as first authors

### **Institutional Review Board Statement:**

Not applicable.

### **Informed Consent Statement:**

Not applicable.

# **Data Availability Statement:**

Data needed is available within the manuscript. Raw data will be shared upon optimum request.

Funding: None.

### **Conflict of interest:**

All authors declare no conflict of interest.

# **Ethical approval:**

Not applicable.

# **Acknowledgment:**

The authors made use of Co-pilot AI to assist with the drafting of this article. Co-pilot was accessed/obtained from Microsoft edge browser Version 129.0.2792.65 and used with modification.

#### **Authors contributions:**

Conceptualization: M.A.S., H.A.; Data curation: M.A.S., A.T., H.B,.; Formal analysis: M.A.S., E.T.; Funding acquisition: Not applicable; Investigation: M.A.S., M.S. .; Methodology: M.A.S., E.T.; Project administration: H.A., M.A.S., E.T.; Resources: M.A.S., E.T. ; Software: M.A.S., E.T..; Supervision: E.T., H.A.; Validation: M.A.S., M.S., E.T.; Visualization: M.A.S., E.T.; Writing – original draft: M.A.S., E.T.; Writing – revision, review & editing: All authors. All authors have read and agreed to the published version of the manuscript.

### **Abstract**

**Background:** Pre-operative anxiety is a common phenomenon affecting 60-80% of surgical patients, with potential implications for surgical outcomes. Despite its prevalence, there remains a lack of consensus on its precise effects and optimal management strategies.

**Objective:** This meta-analysis aimed to synthesize current evidence on the impact of preoperative anxiety on various surgical outcomes, including anesthetic and analgesic requirements, delirium, recovery times and pain.

**Methods:** We conducted a comprehensive literature search and meta-analysis of studies examining the relationship between pre-operative anxiety and surgical outcomes. Standardized mean differences (SMD), correlation (COR), and odds ratios (OR) with 95% confidence intervals were calculated.

**Results:** Our analysis revealed significant associations between pre-operative anxiety and increased anesthetic requirements (SMD = 0.67, 95% CI: 0.32-1.01) and analgesic requirements (SMD = 0.89, 95% CI: 0.65-1.12). Pre-operative anxiety was associated with post-operative delirium in adults (OR =1.90, 95% CI: 1.11-3.26), unlike the pediatric population. Pre-operative anxiety was associated with prolonged time to reach Modified Aldrete Score of 9 (SMD = 0.79, 95% CI: 0.50-1.07) and extubation time (SMD = 0.89, 95% CI: 0.58-1.21). Preoperative anxiety was positively correlated with propofol consumption (STAI-S COR = 0.35, 95% CI: 0.15-0.55). No significant association between preoperative anxiety and post-operative pain was found.

**Conclusions:** This meta-analysis provides evidence for the wide-ranging effects of pre-operative anxiety on surgical outcomes. The findings emphasize the need for routine preoperative anxiety screening and the development of targeted interventions. Future research should focus on long-term impacts, and the effectiveness of various anxiety management strategies.

**Keywords:** Preoperative anxiety, delirium, STAI, mYPAS, propofol.

**Abbreviations:** STAI: State-Trait Anxiety Inventory, STAI-S: STAI-state subsystem, STAI-T: STAI-trait subsystem, STAI-6: State-Trait Anxiety Inventory - six items (shortened state subsystem), BAI: Beck's Anxiety Inventory, mYPAS: modified Yale Pediatric Anxiety Scale, MAS: Modified Aldrete Score, APIAS-A: Amsterdam Preoperative Anxiety and Information Scale - Anxiety, HADS-A: Hospital Anxiety and Depression Scale - Anxiety subsystem.

#### Introduction

Surgical procedures, while often necessary for health improvement, can be a significant source of stress and anxiety for patients. Pre-operative anxiety, characterized by feelings of tension, apprehension, nervousness, and worry in the period leading up to surgery, is a common phenomenon affecting an estimated 60-80% of surgical patients <sup>1</sup>. This psychological state can have far-reaching implications, potentially influencing not only the patient's immediate well-being but also their surgical outcomes and recovery trajectory <sup>2-4</sup>.

The impact of pre-operative anxiety on surgical outcomes has been a subject of growing interest in the medical community over the past few decades. Several studies have suggested that heightened anxiety levels before surgery may be associated with a range of adverse outcomes, including increased pain perception, higher anesthetic requirements, and prolonged recovery times <sup>5</sup>. Moreover, there is emerging evidence linking pre-operative anxiety to more severe complications such as postoperative delirium and cardiac events <sup>6</sup>.

However, the relationship between pre-operative anxiety and surgical outcomes is complex and multifaceted. The manifestation and impact of anxiety may vary depending on factors such as the type of surgery, patient demographics, and the specific outcomes being measured <sup>7,8</sup>. Furthermore, the tools used to assess pre-operative anxiety are diverse, ranging from general anxiety scales to surgery-specific measures, which can lead to variability in findings across studies <sup>9</sup>.

Despite the potential significance of preoperative anxiety, there remains a lack of consensus on its precise effects and the best strategies for its management. While some healthcare systems have implemented routine preoperative anxiety screening and interventions, others have yet to incorporate such practices into standard care protocols. This variability in practice underscores the need for a comprehensive understanding of the relationship between pre-operative anxiety and surgical outcomes.

To address this gap in knowledge, we conducted a systematic review and meta-analysis of the available literature on pre-operative anxiety and its association with various surgical outcomes. Our study aimed to synthesize current evidence on the impact of pre-operative anxiety on

anesthetic and analgesic requirements, the relationship between pre-operative anxiety and postoperative delirium, the effectiveness of different anxiety scales in predicting surgical outcomes, and the influence of pre-operative anxiety on recovery times.

By consolidating and analyzing data from multiple studies, we sought to provide a more comprehensive understanding of how pre-operative anxiety influences surgical outcomes. This knowledge is crucial for informing evidence-based practices in pre-operative care, potentially leading to improved patient experiences, optimized resource utilization, and enhanced surgical outcomes.

### **Methods**

This systematic review and meta-analysis were performed and reported following the Cochrane Collaboration Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement guidelines.

## Search strategy

We conducted a comprehensive literature search in PubMed, Scopus and Web of Science from inception to 30th March 2024. The search strategy employed key terms such as "preoperative anxiety" and "delirium" to identify relevant studies. The complete search strategy is provided in Supplementary Information Methods S3. After removing duplicates, two authors (A.T. and P.A) independently screened titles and abstracts and assessed full-text articles for inclusion based on predefined criteria. Discrepancies were resolved through discussion with the senior author. Additionally, we reviewed reference lists of included studies to identify any further eligible articles.

### Eligibility criteria

Studies were included if they met the following criteria: (1) published in English; (2) reported data on effect of preoperative anxiety on perioperative outcomes; and (3) employed observational study designs including cross-sectional, case-control, and cohort studies (both prospective and retrospective). We excluded editorials, letters to the editor, commentaries, reviews, systematic reviews, meta-analysis, case reports, case series, and animal studies.

#### Data extraction

Two authors independently extracted data from the included studies using a standardized form. Extracted information included the first author's surname, publication year, study design, sample characteristics (age, gender, race) and baseline comorbidities. Outcomes of interest included the effect of anxiety on anesthetic and analgesic drug requirements, delirium incidence, recovery times and postoperative pain.

### Quality Assessment

For included observational studies, the Newcastle–Ottawa scale (NOS) was used to assess the quality of each study included  $^{10}$ . This scale evaluates studies based on selection, comparability, and outcome/exposure, with a maximum score of 9 points. Studies were categorized as low risk of bias (score  $\geq$ 7), intermediate risk (score 4-6), or high risk (score <4).

# Statistical analysis

Continuous variables were reported as mean  $\pm$  standard deviation (SD), and binary variables were reported as totals and percentages. For meta-analysis, we used a Mantel-Haenszel random-effects model for binary outcomes, calculating odds ratio (OR) and 95% confidence interval (CI), while mean differences (MD) were computed for continuous variables. The standardized mean difference (SMD) was employed to measure the effect size across studies that reported different surgeries or measuring systems. The DerSimonian and Laird (DL) method estimated between-study variance ( $\tau^2$ ). For correlation analyses, we calculated correlation coefficients (COR) with 95% confidence intervals. A two-tailed p-value of < 0.05 was considered statistically significant.

Heterogeneity was assessed using Cochrane's Q test and I<sup>2</sup> statistics, with  $p \le 0.05$  indicating statistical significance. The consistency of the studies was determined based on I<sup>2</sup> values of 0%,  $\le 25\%$ ,  $\le 50\%$ , and > 50%, indicating no observed, low, moderate, and substantial heterogeneity, respectively. Subgroup analyses were conducted to examine the effects of preoperative anxiety in different populations (pediatric vs. adult) and for different outcomes (e.g., post-operative pain at various time points). We performed sensitivity analysis by leave-one-out analysis according to specified criteria in the supplementary file. All analyses were conducted using Revman version

5.4 and R version 4.4.1 with "*meta*" and "*dmetar*" for all calculations and graphics <sup>11–13</sup>.For correlation analyses, we used the "metacor" function from the "meta" package in R to perform meta-analysis of correlation coefficients.

#### **Results**

# Characteristics of eligible studies

Our initial search yielded 5064 articles (Figure 1). After removing duplicates and screening titles and abstracts, we retrieved 191 articles for full-text review. Ultimately, 24 articles <sup>14–37</sup> met the inclusion criteria and were included in the analysis. The studies included 3,388 patients. Table 1 provides a detailed summary of the baseline characteristics of the included studies.

# **Quality assessment**

Individual appraisal of included studies is reported in Supplementary Table S4. 7 of studies were given a score of 4 to 6. Furthermore, 17 studies had scores of  $\geq$  7 and were deemed as high quality studies.

#### **Anesthesia-related outcomes**

Our pooled analysis demonstrated a significant increase in anesthetic drug requirements among individuals with per-operative anxiety (SMD = 0.67, 95%CI: 0.32-1.01) with moderate heterogeneity ( $I^2 = 63\%$ ) (**Figure 2A**). Similarly, we observed a significant increase in analgesic drug requirements among individuals with pre-operative anxiety (SMD = 1.02, 95%CI: 0.29-1.76), with significant heterogeneity ( $I^2=89\%$ ) (**Figure 2B**).

# **Post-operative delirium**

Our pooled analysis of studies classifying individuals dichotomously revealed increased odds of delirium occurrence among those classified as anxious pre-operatively (OR=1.89, 95%CI: 1.00-3.55) with significant heterogeneity ( $I^2$ =80%) (**Figures 3**). Subgroup analysis showed varying results across different populations. In the pediatric population, our analysis revealed a non-significant association between anxiety status and emergence delirium incidence (OR = 1.42, 95% CI: 0.22-9.09). Conversely, in the adult population, we found a significant increase in the odds of

post-operative delirium among individuals with pre-operative anxiety (OR = 2.03, 95% CI: 1.49-2.76).

# **Anxiety Scales**

Our pooled analysis of anxiety scales revealed varying associations between anxiety scores and odds of delirium across different measures (**Table 2**). The Modified Yale Preoperative Anxiety Scale (mYPAS) showed a significant positive association (OR = 1.23, 95% CI: 1.16-1.30). However, other scales demonstrated non-significant associations: State-Trait Anxiety Inventory - State (STAI-S) (OR = 0.98, 95% CI: 0.89-1.08), State-Trait Anxiety Inventory - Trait (STAI-T) (OR = 1.01, 95% CI: 0.93-1.11), Amsterdam Preoperative Anxiety and Information Scale - Anxiety (APAIS-A) (OR = 0.97, 95% CI: 0.88-1.07), Hospital anxiety and depression scale - Anxiety (HADS-A) (OR = 1.10 95% CI: 1.01-1.21) and State-Trait Anxiety Inventory-6 (STAI-6) (OR = 1.18, 95% CI: 0.89-1.56). Thus, most scales showed non-significant associations, except for mYPAS and HADS-A, which demonstrated a significant positive association with delirium odds.

# **Recovery times**

We found a significant increase in the time to reach a MAS score of 9 among individuals with preoperative anxiety (MD=1.83 minutes, 95%CI:1.21-2.46) (**Figure 4A**). Our analysis demonstrated a significant increase in extubation time among individuals with pre-operative anxiety (MD=2.50 minutes, 95%CI:-0.93-5.93). This analysis showed significant heterogeneity (I<sup>2</sup>=95%) (**Figure 4B**).

# **Propofol consumption**

Our pooled analysis demonstrated a significant correlation between STAI-S score and propofol consumption (COR=0.35, 95%CI: 0.15-0.55) with significant heterogeneity ( $I^2 = 88\%$ ) (**Figure 5A**). Similarly, we observed a significant correlation between STAI-T score and propofol (COR = 0.43, 95%CI: 0.18-0.68), with significant heterogeneity ( $I^2=89\%$ ) (**Figure 5B**).

### Pain

Our pooled analysis demonstrated a non-significant increase in post-operative pain 1h among individuals with per-operative anxiety (SMD = 0.63, 95%CI: 0-1.26). This analysis showed moderate heterogeneity ( $I^2 = 86\%$ ) (**Figure 6A**). Similarly, we observed non-significant increase in post-operative pain 2h among individuals with pre-operative anxiety (SMD = 0.36, 95%CI: -0.38-1.10), with significant heterogeneity ( $I^2 = 85\%$ ) (**Figure 6B**). Our analysis revealed non-significant

increase in post-operative pain 24h among individuals with pre-operative anxiety (SMD = 0.36, 95%CI: -0.38-1.10), with significant heterogeneity ( $I^2$ =90%) (**Figure 6C**).

# **Sensitivity analysis:**

Leave-one-out analysis was performed using the criteria explained in the supplementary Figures 5.

#### **Discussion**

Our meta-analysis provides compelling evidence for the significant impact of pre-operative anxiety on various surgical outcomes. These findings underscore the critical importance of recognizing and addressing anxiety in surgical patients, as it demonstrably influences anesthetic requirements, post-operative delirium risk, and recovery times. The observed increase in anesthetic and analgesic drug requirements among anxious patients aligns with previous research suggesting that anxiety can alter pain perception and drug metabolism <sup>38–41</sup>.

The increased need for anesthesia and the consumption of propofol observed in our metaanalysis are critical findings that warrant further discussion. Sensitivity analyses by removing the
only study with minor procedure (Sahin et al. 2023) further increased the magnitude of association.
Increased dosages of anesthetics and analgesics, such as propofol, can lead to several specific
adverse effects. For instance, higher doses of propofol can increase the risk of hypotension,
respiratory depression, and prolonged recovery times due to its sedative properties <sup>42–47</sup>.
Additionally, frequent administration of higher doses can increase the likelihood of developing
propofol infusion syndrome, a rare but potentially fatal condition characterized by metabolic
acidosis, rhabdomyolysis, and cardiovascular collapse<sup>48–51</sup>.

From an economic perspective, the increased consumption of anesthetics also has significant implications for healthcare costs. The precise cost implications can vary widely depending on the healthcare setting and country. However, rough estimates suggest that increased drug usage could result in substantial additional costs for hospitals. For instance, studies indicate that higher anesthesia requirements can lead to increased expenditure on drug procurement, extended operating room times, and longer hospital stays due to slower recovery<sup>52,53</sup>. Specifically, propofol, while cost-effective per dose, can accumulate to significant costs when used in higher quantities over multiple surgeries <sup>54–56</sup>.

Our analysis of post-operative delirium reveals a nuanced relationship with pre-operative anxiety. The significant association found in the overall population, particularly in adults, corroborates earlier studies linking psychological distress to post-surgical cognitive complications <sup>57,58</sup>. The analysis revealed that association between preoperative anxiety and delirium in pediatrics was statistically insignificant. This is closely associated with the high heterogeneity in the result. However, sensitivity analysis removing the only study with minor surgery (Jooma et al.2020) didn't change the non-significance of the association another explanation could be the small sample size and relatively low number of studies in this group. The non-significant finding in the pediatric population is intriguing and merits further investigation. Potential explanations may lie in children's neuroplasticity or differences in anxiety manifestation, which could act as mediating factors<sup>59</sup>. The varying associations between different anxiety scales and delirium risk highlight the importance of tool selection in pre-operative assessments. The significant association found with the Modified Yale Preoperative Anxiety Scale (mYPAS) suggests its potential utility for delirium risk stratification. Conversely, the non-significant findings with other scales underscore the complexity of anxiety measurement and emphasize the need for further validation of these tools in surgical contexts.

Our study highlights a significant association between preoperative anxiety and both extubation time and the time to reach a Modified Aldrete Score (MAS) of 9. These findings are consistent with previous research, which has demonstrated that higher levels of preoperative anxiety can negatively impact various aspects of postoperative recovery.

The correlation between preoperative anxiety and prolonged extubation time suggests that anxious patients may experience delayed recovery from anesthesia. This delay could be attributed to the physiological effects of anxiety, such as increased sympathetic nervous system activity, which may interfere with the smooth transition from anesthesia to wakefulness<sup>60</sup>.

The Modified Aldrete Score is a widely used tool to assess recovery from anesthesia, with a score of 9 indicating readiness for discharge from the post-anesthesia care unit. Our results indicate that patients with higher preoperative anxiety take longer to achieve this score, suggesting a slower overall recovery process. This finding aligns with the study by Turksal et al. (2017), which found a

significant correlation between preoperative anxiety and delayed recovery times, including the time to reach a MAS of  $9^{60}$ .

The implications of these findings are substantial. Delayed extubation and prolonged recovery times can increase the risk of postoperative complications, extend hospital stays, and elevate healthcare costs. Therefore, it is crucial to identify and manage preoperative anxiety effectively. Interventions such as preoperative counseling, anxiolytic medications, and relaxation techniques could be beneficial in mitigating the adverse effects of anxiety on postoperative recovery.

The findings of this study indicate that preoperative anxiety does not have a significant association with postoperative pain. This result contrasts with several previous studies that have suggested a link between preoperative anxiety and increased postoperative pain levels <sup>6,61</sup>. However, after conducting sensitivity analysis by removing the only study with minor procedure (Sahin et al.2023) caused the association of pain 1h post-operatively and preoperative anxiety to be significant.

One possible explanation for this discrepancy could be the differences in the methodologies used across studies. For instance, variations in the scales used to measure anxiety and pain, the timing of these measurements, and the types of surgeries performed might contribute to differing outcomes. In our study, multiple scales were used for anxiety assessment which might yield different results<sup>6</sup>.

Another factor to consider is the role of perioperative care and pain management protocols. Advances in anesthesia and analgesia techniques, as well as enhanced recovery protocols, may mitigate the impact of preoperative anxiety on postoperative pain. Our study population received standardized pain management, which could have minimized the variability in pain outcomes related to anxiety levels<sup>61</sup>.

The implications of our findings are significant for clinical practice. They suggest that while managing preoperative anxiety is important for overall patient well-being, it may not necessarily translate to reduced postoperative pain. Therefore, healthcare providers should continue to focus on comprehensive pain management strategies that address multiple aspects of patient care.

A comprehensive meta-analysis of perioperative anxiolytic medications highlights the efficacy and safety profiles of various drugs. **Benzodiazepines**, such as alprazolam, diazepam, lorazepam, midazolam, and triazolam, are frequently used due to their rapid onset and short duration of action.

However, The association between postoperative delirium and benzodiazepine is a contentious topic, as study results vary, indicating a lack of consensus <sup>62–64</sup>. **Melatonin** has emerged as a promising alternative, demonstrating significant reductions in preoperative anxiety without substantial adverse effects<sup>65</sup>.

The choice of anxiolytic medication is influenced by the type of anesthesia planned<sup>66</sup>, as certain medications may interact with anesthetic agents. However, effective communication between the patient, surgeon, and anesthesiologist is crucial to ensure the safest and most effective anxiolytic regimen is chosen.

Future research should aim to further elucidate the relationship between preoperative anxiety and postoperative outcomes by exploring different patient populations, surgical procedures, and anxiety and pain assessment tools. Longitudinal studies that track patients over extended periods could provide deeper insights into how preoperative anxiety might affect long-term recovery and pain management.

### Limitations

Several limitations of our study should be acknowledged. The significant heterogeneity observed in some analyses suggests considerable variability across studies, which could be attributed to differences in patient populations, surgical procedures, or anxiety assessment methods. Additionally, the observational nature of the included studies limits our ability to establish causality.

One of the primary limitations of this study is the confounding effect of the type of surgery on the observed differences in postoperative delirium between pediatric and adult patients. The data for pediatric surgeries being derived from dental procedures introduces a significant confounding effect, as the effect of patient age is intertwined with the nature of minor versus major surgeries. However, we conducted sensitivity analysis as discussed earlier with change in results explained. Another limitation is the high heterogeneity in pediatric subgroup analysis. Although jooma et al. 2020 was excluded for using a minor procedure, this didn't change the insignificance of association between pediatric population anxiety and risk of postoperative delirium. This insignificance might be due to the small sample size. More studies need to be conducted on the pediatric population to explore the effect of anxiety on delirium.

#### Conclusion

In conclusion, our meta-analysis provides robust evidence for the wide-ranging effects of preoperative anxiety on surgical outcomes. These findings emphasize the pressing need for routine preoperative anxiety screening and the development of targeted interventions to mitigate its impact. By addressing pre-operative anxiety, healthcare providers may significantly improve patient experiences, optimize resource utilization, and ultimately enhance surgical outcomes. Future research addressing the identified priorities will further enhance our understanding of pre-operative anxiety and lead to the development of more effective strategies to mitigate its impact on surgical outcomes.

## **References:**

- 1. Nigussie S, Belachew T, Wolancho W. Predictors of preoperative anxiety among surgical patients in Jimma University specialized teaching hospital, South Western Ethiopia. *BMC Surg*. 2014;14:1-10.
- 2. Newman D. Surgical Recovery in the Elderly: Systematic Review of Patient-Centered Outcomes and Prospective Study of Post-Operative Delirium. McGill University (Canada); 2011.
- 3. Johnston M. Pre-operative emotional states and post-operative recovery. In: *Psychological Aspects of Surgery*. Vol 15. Karger Publishers; 1986:1-22.
- 4. Wallace LM. Pre-operative state anxiety as a mediator of psychological adjustment to and recovery from surgery. *Br J Med Psychol*. 1986;59(3):253-261.
- 5. Caumo W, Ferreira MBC. Perioperative anxiety: psychobiology and effects in postoperative recovery. *Pain Clin.* 2003;15(2):87-101.
- 6. Ni K, Zhu J, Ma Z. Preoperative anxiety and postoperative adverse events: a narrative overview. *Anesthesiol Perioper Sci.* 2023;1(3):23.
- 7. Caumo W, Schmidt AP, Schneider CN, et al. Risk factors for preoperative anxiety in adults. *Acta Anaesthesiol Scand*. 2001;45(3):298-307.
- 8. Yilmaz M, Sezer H, Gürler H, Bekar M. Predictors of preoperative anxiety in surgical inpatients. *J Clin Nurs*. 2012;21(7-8):956-964.
- 9. Chen YYK, Soens MA, Kovacheva VP. Less stress, better success: a scoping review on the effects of anxiety on anesthetic and analgesic consumption. *J Anesth.* 2022;36(4):532-553.

- 10. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603-605.
- 11. Brockwell SE, Gordon IR. A simple method for inference on an overall effect in meta-analysis. *Stat Med.* 2007;26(25):4531-4543.
- 12. DerSimonian R, Kacker R. Random-effects model for meta-analysis of clinical trials: an update. *Contemp Clin Trials*. 2007;28(2):105-114.
- 13. Jackson D, Bowden J, Baker R. How does the DerSimonian and Laird procedure for random effects meta-analysis compare with its more efficient but harder to compute counterparts? *J Stat Plan Inference*. 2010;140(4):961-970.
- 14. Ersoy A, Güven BB, Ertürk T, Caki AC, Aksoy NT, Eksi I. Evaluation of the effect of preoperative anxiety on intraoperative hemodynamic stability and drug consumption in patients who underwent BIS-guided total intravenous anesthesia (TIVA) for neurophysiological monitoring in spine surgery. *Signa Vitae*. 2023;19(1).
- 15. Şahin SH, Çopuroğlu E, Altınpulluk EY, et al. Effect of Preoperative Anxiety on Depth of Anaesthesia and In Vitro Fertilization Success. *Turk J Anaesthesiol Reanim*. 2023;51(5):414.
- 16. Prayunanto E, Widyastuti Y, Sari D. The association of modified Yale perioperative anxiety scale and pediatric anesthesia behavior on postoperative emergence delirium in children: A prospective cohort study. *Bali J Anesthesiol*. 2023;7(2):88-93.
- 17. Mou Q, Gao M, Liu X, et al. Preoperative anxiety as an independent predictor of postoperative delirium in older patients undergoing elective surgery for lumbar disc herniation. *Aging Clin Exp Res.* 2023;35(1):85-90.
- 18. Arunalatha P, Adilakshmi E, Devi GJ, Yadhu K. THE IMPACT OF PREOPERATIVE ANXIETY ON ANESTHETIC REQUIREMENTS AND RECOVERY TIMES: A PROSPECTIVE OBSERVATIONAL STUDY. *Int J Acad Med Pharm.* 2023;5(3):2535-2538.
- 19. Kashif M, Hamid M, Raza A. Influence of preoperative anxiety level on postoperative pain after cardiac surgery. *Cureus*. 2022;14(2).
- 20. Fukunaga H, Sugawara H, Koyama A, et al. Relationship between preoperative anxiety and onset of delirium after cardiovascular surgery in elderly patients: focus on personality and coping process. *Psychogeriatrics*. 2022;22(4):453-459.
- 21. Ali AB. Emergence delirium and its association with preoperative anxiety in paediatric patients undergoing infra umbilical surgery under combined general and caudal anaesthesia: an

- observational study from a tertiary care centre in a South Asian country. *Turk J Anaesthesiol Reanim*. 2022;50(2):129.
- 22. Ren A, Zhang N, Zhu H, Zhou K, Cao Y, Liu J. Effects of preoperative anxiety on postoperative delirium in elderly patients undergoing elective orthopedic surgery: a prospective observational cohort study. *Clin Interv Aging*. Published online 2021:549-557.
- 23. Ma J, Li C, Zhang W, et al. Preoperative anxiety predicted the incidence of postoperative delirium in patients undergoing total hip arthroplasty: a prospective cohort study. *BMC Anesthesiol*. 2021;21:1-8.
- 24. Yilmaz Inal F, Yilmaz Camgoz Y, Daskaya H, Kocoglu H. The effect of preoperative anxiety and pain sensitivity on preoperative hemodynamics, propofol consumption, and postoperative recovery and pain in endoscopic ultrasonography. *Pain Ther.* 2021;10:1283-1293.
- 25. Cheng HW, Liu CY, Chen YS, Shih CC, Chen WY, Chiou AF. Assessment of preoperative frailty and identification of patients at risk for postoperative delirium in cardiac intensive care units: a prospective observational study. *Eur J Cardiovasc Nurs*. 2021;20(8):745-751.
- 26. Uysal Aİ, Altıparmak B, Korkmaz Toker M, Dede G, Sezgin Ç, Gümüş Demirbilek S. The effect of preoperative anxiety level on mean platelet volume and propofol consumption. *BMC Anesthesiol*. 2020;20:1-6.
- 27. Jooma Z, Perrie H, Scribante J, Kleyenstuber T. Emergence delirium in children undergoing dental surgery under general anesthesia. *Pediatr Anesth.* 2020;30(9):1020-1026.
- 28. Milisen K, Van Grootven B, Hermans W, et al. Is preoperative anxiety associated with postoperative delirium in older persons undergoing cardiac surgery? Secondary data analysis of a randomized controlled trial. *BMC Geriatr*. 2020;20:1-9.
- 29. Wada S, Inoguchi H, Sadahiro R, et al. Preoperative anxiety as a predictor of delirium in cancer patients: a prospective observational cohort study. *World J Surg.* 2019;43:134-142.
- 30. Masri SNNS, Rahman RA, Masdar A, Mat WRW, Nor NM, Izaham A. Does anxious patients require more propofol at induction? *Anaesth Pain Intensive Care*. 2018;22(4).
- 31. Barreto ACTP, Paschoal ACR da R, Farias CB, Borges PSGN, Andrade RGA da C, de Orange FA. Risk factors associated with anesthesia emergence delirium in children undergoing outpatient surgery. *Rev Bras Anestesiol*. 2018;68:162-167.

- 32. Manjunatha S, Hazra R, Das A, et al. Effect of pre-anesthetic anxiety and heart rate on propofol dose requirement for induction: A correlation study. *Asian J Med Sci.* 2017;8(2):64-68.
- 33. Van Grootven B, Detroyer E, Devriendt E, et al. Is preoperative state anxiety a risk factor for postoperative delirium among elderly hip fracture patients? *Geriatr Gerontol Int.* 2016;16(8):948-955.
- 34. Ali A, Altun D, Oguz BH, Ilhan M, Demircan F, Koltka K. The effect of preoperative anxiety on postoperative analgesia and anesthesia recovery in patients undergoing laparascopic cholecystectomy. *J Anesth.* 2014;28:222-227.
- 35. Gras S, Servin F, Bedairia E, et al. The effect of preoperative heart rate and anxiety on the propofol dose required for loss of consciousness. *Anesth Analg.* 2010;110(1):89-93.
- 36. Osborn TM, Sandler NA. The effects of preoperative anxiety on intravenous sedation. *Anesth Prog.* 2004;51(2):46.
- 37. Maranets I, Kain ZN. Preoperative anxiety and intraoperative anesthetic requirements. *Anesth Analg.* 1999;89(6):1346.
- 38. Dudeney J, Aaron RV, Hathway T, et al. Anxiety and Depression in Youth With Chronic Pain: A Systematic Review and Meta-Analysis. *JAMA Pediatr*.
- 39. Ganenco A, Lozovanu S, Arnaut O, Grabovschi I, Moldovanu I. The role of depression and anxiety in pain perception. *Mold Med J.* 2023;66(1):24-30.
- 40. Konstandi M, Johnson EO, Lang MA. Consequences of psychophysiological stress on cytochrome P450-catalyzed drug metabolism. *Neurosci Biobehav Rev.* 2014;45:149-167.
- 41. Ploghaus A, Narain C, Beckmann CF, et al. Exacerbation of pain by anxiety is associated with activity in a hippocampal network. *J Neurosci*. 2001;21(24):9896-9903.
- 42. Schonberger RB, Dai F, Michel G, et al. Association of propofol induction dose and severe pre-incision hypotension among surgical patients over age 65. *J Clin Anesth*. 2022;80:110846.
- 43. Kakazu C, Lippmann M. Playing with fire: debate about propofol-induced hypotension. *Br J Anaesth*. 2015;114(1):164-165.
- 44. Kotani Y, Pruna A, Turi S, et al. Propofol and survival: an updated meta-analysis of randomized clinical trials. *Crit Care*. 2023;27(1):139.
- 45. Jin H jung, Shin MH, Myung E. Factors affecting recovery time after sedation for upper gastrointestinal endoscopy. *Chonnam Med J.* 2020;56(3):191.

- 46. Sneyd JR, Absalom AR, Barends CRM, Jones JB. Hypotension during propofol sedation for colonoscopy: a retrospective exploratory analysis and meta-analysis. *Br J Anaesth*. 2022;128(4):610-622. doi:10.1016/j.bja.2021.10.044
- 47. Saugel B, Bebert EJ, Briesenick L, et al. Mechanisms contributing to hypotension after anesthetic induction with sufentanil, propofol, and rocuronium: a prospective observational study. *J Clin Monit Comput.* Published online 2022:1-7.
- 48. Krajčová A, Waldauf P, Anděl M, Duška F. Propofol infusion syndrome: a structured review of experimental studies and 153 published case reports. *Crit Care*. 2015;19:1-9.
- 49. Mirrakhimov AE, Voore P, Halytskyy O, Khan M, Ali AM. Propofol infusion syndrome in adults: a clinical update. *Crit Care Res Pract*. 2015;2015(1):260385.
- 50. Wappler F, Horn J. Propofol infusion syndrome: is there any more information? *Anesthesiology*. 2007;107(1):175-176.
- 51. Cremer OL. The propofol infusion syndrome: more puzzling evidence on a complex and poorly characterized disorder. *Crit Care*. 2009;13:1-2.
- 52. Ludbrook GL. The hidden pandemic: the cost of postoperative complications. *Curr Anesthesiol Rep.* Published online 2022:1-9.
- 53. Mahajan A, Esper SA, Cole DJ, Fleisher LA. Anesthesiologists' role in value-based perioperative care and healthcare transformation. *Anesthesiology*. 2021;134(4):526-540.
- 54. Anis AH, Wang X hua, Leon H, Hall R, Propofol Study Group. Economic evaluation of propofol for sedation of patients admitted to intensive care units. *J Am Soc Anesthesiol*. 2002;96(1):196-201.
- 55. Tang J, Chen L, White PF, et al. Recovery profile, costs, and patient satisfaction with propofol and sevoflurane for fast-track office-based anesthesia. *J Am Soc Anesthesiol*. 1999;91(1):253-261.
- 56. Andrade TR, Salluh JIF, Garcia R, et al. A cost-effectiveness analysis of propofol versus midazolam for the sedation of adult patients admitted to the intensive care unit. *Rev Bras Ter Intensiva*. 2021;33:428-433.
- 57. Mccann WD, Hou XY, Stolic S, Ireland MJ. Predictors of psychological distress among post-operative cardiac patients: A narrative review. In: Vol 11. MDPI; 2023:2721.

- 58. Pinto A, Faiz O, Davis R, Almoudaris A, Vincent C. Surgical complications and their impact on patients' psychosocial well-being: a systematic review and meta-analysis. *BMJ Open*. 2016;6(2):e007224.
- 59. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. *Psychiatr Clin.* 2009;32(3):483-524.
- 60. Turksal E, Alper I, Sergin D, Yüksel EA, Ulukaya S. The effects of preoperative anxiety on anesthetic recovery and postoperative pain in donor nephrectomy. *Transplantation*. 2017;101:S116-S117.
- 61. Eberhart L, Aust H, Schuster M, et al. Preoperative anxiety in adults-a cross-sectional study on specific fears and risk factors. *BMC Psychiatry*. 2020;20:1-14.
- 62. Wang E, Belley-Cote EP, Young J, et al. Effect of perioperative benzodiazepine use on intraoperative awareness and postoperative delirium: a systematic review and meta-analysis of randomised controlled trials and observational studies. *Br J Anaesth*. 2023;131(2):302-313.
- 63. Bilotta F, Russo G, Verrengia M, et al. Systematic review of clinical evidence on postoperative delirium: literature search of original studies based on validated diagnostic scales. *J Anesth Analg Crit Care*. 2021;1:1-18.
- 64. Sadeghirad B, Dodsworth BT, Gelsomino NS, et al. Perioperative factors associated with postoperative delirium in patients undergoing noncardiac surgery: An individual patient data meta-analysis. *JAMA Netw Open.* 2023;6(10):e2337239-e2337239.
- 65. Yousaf F, Seet E, Venkatraghavan L, Abrishami A, Chung F, Warner DS. Efficacy and safety of melatonin as an anxiolytic and analgesic in the perioperative period: a qualitative systematic review of randomized trials. *J Am Soc Anesthesiol*. 2010;113(4):968-976.
- 66. Baagil H, Baagil H, Gerbershagen MU. Preoperative Anxiety Impact on Anesthetic and Analgesic Use. *Medicina (Mex)*. 2023;59(12):2069.

Table 1. Baseline

Study	Surgery	Sample Size	Age (Mean ± SD)	Male n(%)	Anxiety Group, n(%)
Ersoy 2024	Spinal surgery	80	-	38 (47.5%)	-
Sahin 2023	Oocyte retrieval	131	34.15±5.39	0(0%)	60
Prayunato 2023	Elective surgery	100	6.6±3.4	59(59%)	-
Mou 2023	lumbar disc herniation	863	$68.2 \pm 8.3$	604(70%)	225
Arunalatha 2023	Elective surgery	100	45.31±2.34	52(52%)	50
Kashif 2022	Cardiac surgery	100	58.24±10.03	68(68%)	64
Fukunaga 2022	cardiovascular surgery	168	$74.9 \pm 6.1$	93(55.4%)	-
Ali 2022	Multiple infra-umbilical surgeries	250	-	230(92%)	-
Ren 2021	Elective Orthopedic Surgery	263	74.2±7.3	74 (28.1%)	40 (15.2%)
Ma 2021	Hip arthroplasty	325	52.1±13.8	60(63.2%)	95
Inal 2021	Endoscopic Ultrasound	80	53.79±9.99	37 (46.3%)	-
Cheng 2021	Cardiac Surgery	152	63.07±11.17	104 (68.42%)	-
Uysal 2020	laparoscopic	79	40.34±14.40	43(54.4%)	42

	cholecystectomy				
Jooma 2020	Dental surgery	91	3.9±0.9	58(63.7%)	63
Milisen 2020	Cardiac surgery	190	75.7±5.9	99(52.1%)	59(31.1%)
Wada 2019	tumor resections	91	66.0±10.0	62 (68.1%)	14
Masri 2018	Multiple surgeries	52	-	23 (44.2%)	-
Barreto 2018	Multiple surgeries	100	-	66(66%)	41(41%)
Manjunatha 2017	elective surgery under general anesthesia	42	-	13 (30.9%)	-
Van Grootven B 2016	Traumatic hip fracture surgery	86	80.1 ± 6.8	21 (24.4%)	-
Ali 2014	laparoscopic cholecystectomy	80	46.42±10.96	33(41.25%)	31
Gras 2010	Gynecological surgery	45	-	-	-
Osborn 2004	Dental surgery	25	-	-	9
Maranets 1999	bilateral laparoscopic tubal ligation	57	30.74±5.19	-	-

**Table 2.** Anxiety scales and odds of delirium.

Scale	OR	CI (95%)	Reference
STAI-S	0.98	0.89-1.08	(20)
STAI-T	1.01	0.93-1.11	(20)
mYPAS	1.23	1.16-1.30	(21)
APAIS-A	0.97	0.88-1.07	(28)
STAI-6	1.18	0.89-1.56	(33)
HADS-A	1.10	1.01-1.21	(23)

**Abbreviations:** STAI: State-Trait Anxiety Inventory, STAI-S: STAI-state subsystem, STAI-T: STAI-trait subsystem, STAI-6: State-Trait Anxiety Inventory - six items (shortened state subsystem), BAI: Beck's Anxiety Inventory, mYPAS: modified Yale Pediatric Anxiety Scale, MAS: Modified Aldrete Score, APIAS-A: Amsterdam Preoperative Anxiety and Information Scale - Anxiety, HADS-A: Hospital Anxiety and Depression Scale - Anxiety subsystem.

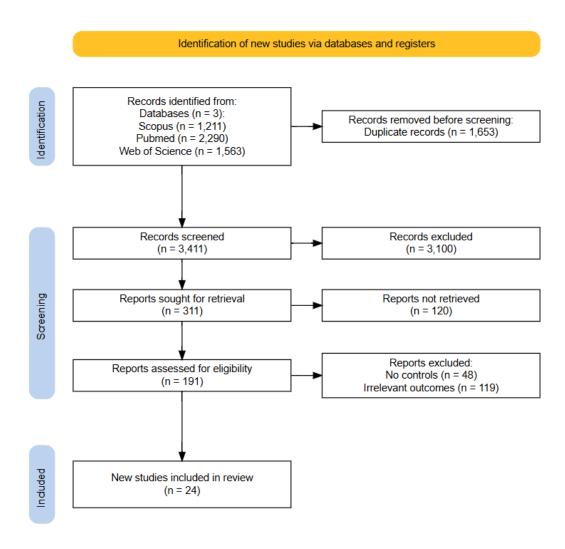
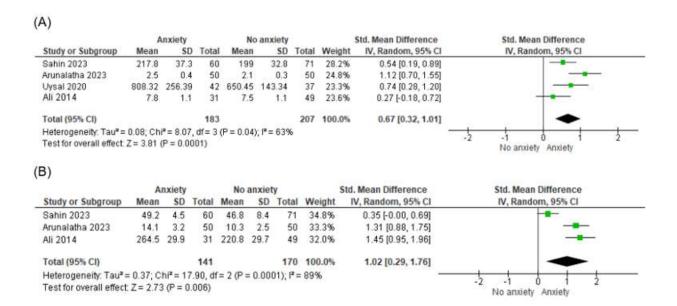
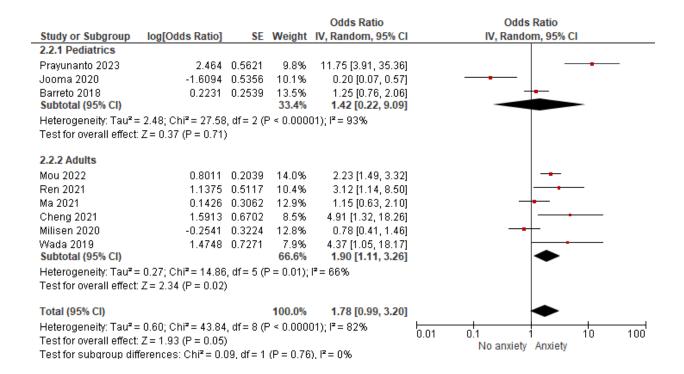


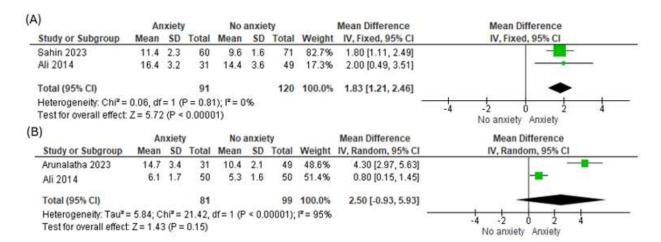
Figure 1. PRISMA flow chart of study screening and inclusion.



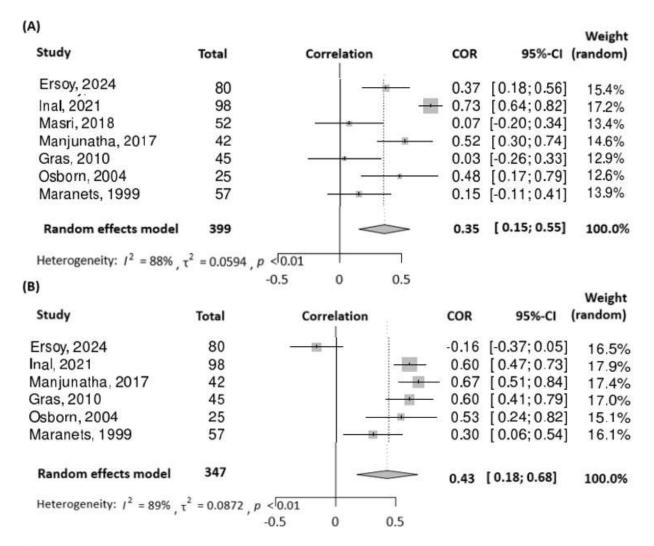
**Figure 2. Anesthesia-related outcomes.** (A) Forest plot of anesthetic drug dose requirements. The x-axis represents the standardized mean difference (SMD) in anesthetic drug dose between anxious and non-anxious patients. (B) Forest plot of analgesic drug dose requirements. The x-axis represents the SMD in analgesic drug dose between anxious and non-anxious patients. For both plots, squares represent individual studies, with size proportional to study weight. Diamond represents the pooled effect size. Horizontal lines represent 95% confidence intervals.



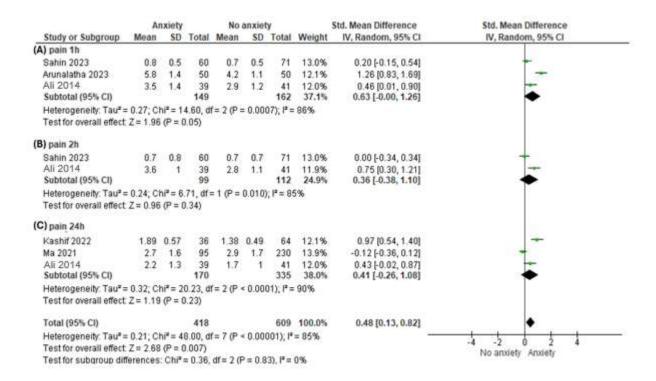
**Figure 3. Post-operative delirium and anxiety scales.** Forest plot of post-operative delirium occurrence. The x-axis represents the odds ratio (OR) of delirium occurrence in anxious versus non-anxious patients. Squares represent individual studies, with size proportional to study weight. Diamond represents the pooled effect size. Horizontal lines represent 95% confidence intervals.



**Figure 4. Recovery times.** (A) Forest plot of time to reach Modified Aldrete Score of 9. (B) Forest plot of extubation time. The x-axis represents the mean difference in minutes between anxious and non-anxious patients. For both plots, squares represent individual studies, with size proportional to study weight. Diamond represents the pooled effect size. Horizontal lines represent 95% confidence intervals.



**Figure 5.** (A) Forest plot and meta-analysis of correlation coefficients testing the relationship between pre-op state anxiety (STAI-S scale) and Propofol consumption (B) Forest plot and meta-analysis of correlation coefficients testing the relationship between pre-op trait anxiety (STAI-T scale) and propofol consumption. For both plots, squares represent individual studies, with size proportional to study weight. Diamond represents the pooled effect size. Horizontal lines represent 95% confidence intervals



**Figure 6. Pain** (A) Forest plot of pain 1h post-operatively (B) Forest plot of pain 2h post-operatively (C) Forest plot of pain 24h post-operatively. For all plots, squares represent individual studies, with size proportional to study weight. Diamond represents the pooled effect size. Horizontal lines represent 95% confidence intervals