



Anesthetic efficacy with remimazolam compared with propofol: a systematic review and meta-analysis of randomized controlled trials

Yang Xing, PhD^{a,†}, Zekun Lang, BA^{a,†}, Xinrun Wang, PhD^a, Jie Liu, PhD^a, Xiaoxia Han, PhD^a, Jia Zhou, PhD^a, Yufang Leng, PhD^{b,*}

Background: Remimazolam is a novel, ultra-short-acting benzodiazepine. This systematic review and meta-analysis compared the anesthetic efficacy and safety of remimazolam versus propofol for procedural sedation and general anesthesia.

Method: A comprehensive search of PubMed, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials was conducted through 26 July 2024. Randomized controlled trials comparing remimazolam and propofol for procedural sedation or general anesthesia were included. The primary outcome was the success rate of sedation or general anesthesia. Data were analyzed using fixed and random-effects models to calculate pooled risk ratios (RRs), mean differences, 95% confidence intervals (CIs), and *P* values.

Results: Twenty-seven studies involving 7283 patients met the inclusion criteria. Sedation and general anesthesia success rates were comparable between remimazolam and propofol (RR: 0.99; 95% CI: 0.97–1.00; *P* = 0.10; *N* = 4858). While remimazolam had a longer time to awake, it was associated with significantly lower rates of hypotension and injection pain. Rates of nausea, vomiting, and discharge times were similar between the drugs. Subgroup analyses revealed that during procedural sedation, remimazolam resulted in longer awakening times and a reduced risk of hypoxemia. However, these effects were not observed in general anesthesia.

Conclusion: Remimazolam and propofol achieved comparable success rates for sedation and general anesthesia. Remimazolam reduced hypoxemia risk but prolonged awakening times during procedural sedation. It also lowered the incidence of hypotension and injection pain across both procedural sedation and general anesthesia. Additional studies are needed to further clarify its role, particularly in general anesthesia.

Keywords: general anesthesia, meta-analysis, propofol, remimazolam

Introduction

Remimazolam is a novel ultra-short-acting benzodiazepine^[1] known for its rapid onset and quicker neuropsychiatric recovery compared to midazolam^[2]. It exerts its effects through GABA receptor modulation and features organ-independent metabolism^[3]. Previous studies have highlighted its advantages over midazolam^[4]. However, its benefits and drawbacks relative to propofol – the most commonly used anesthetic – require further exploration to better define its clinical potential. While

HIGHLIGHTS

- Remimazolam reduces intraoperative hypoxia, hypotension, and enhances stability.
- It minimizes complications and improves patient comfort with less injection pain.
- Despite prolonged awakening times, its overall benefits support clinical use.

^aFirst Medical College of Lanzhou University, Lanzhou Gansu, China and

^bDepartment of Anesthesiology, First Hospital of Lanzhou University, Lanzhou Gansu, China

[†]Y.X. and Z.L. contributed equally to this paper.

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*Corresponding author. Address: Department of Anesthesiology, First Hospital of Lanzhou University, Donggangxi Rd. 1, 730000 Lanzhou Gansu, China. Tel.: +86 17793175611. E-mail: lengyf@lzu.edu.cn (Y. Leng).

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several studies have compared remimazolam and propofol for procedural sedation and general anesthesia, their findings have rarely been synthesized comprehensively. The only existing review that aggregated these results included just ten studies, limiting the reliability of its conclusions^[4]. A systematic review and meta-analysis was conducted to evaluate the efficacy and safety of remimazolam compared to propofol for procedural sedation and general anesthesia. The analysis focused on success rates, recovery times, and adverse events. This article adheres to the TITAN Guidelines 2025 for the declaration and use of

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Table 1
Overview of clinical trials participating in the meta-analysis

Study	Year	Gender	Age(yrs)	Country	Sample size	ASA ¹	Type of surgery/ intervention	Indication	Dose subgroup	Dose	Infusion/ bolus	Comparator
Chang Xu ^[28]	2022	Both	18–85	China	914	2	Painless Gastrosocopy	Sedation	No	0.2 mg/kg/2.5 mg	Bolus	Propofol bolus
Enci Ye ^[30]	2022	Both	≥65	China	129	1–2	Outpatient painless gastroscopy	Sedation	No	0.2 mg/kg/3 mg	Bolus	Propofol bolus
Fang Tang ^[26]	2021	Both	19–75	China	80	1–3	Cardiac surgery	Induction	No	0.3 mg/kg	Bolus	Propofol bolus
Guangrong Dai ^[11]	2021	Both	18–65	China	189	1–2	Elective surgery	Induction	Three doses	0.2/0.3/0.4 mg/kg	Bolus	Propofol bolus
Hongmeng Lan ^[17]	2024	Both	18–60	China	146	1–3	Elective urological surgery	Induction + maintenance	No	10 mg/kg/h for induction 0.2–2 mg/kg/h for maintenance	Infusion	Propofol infusion
Huichen Zhu ^[35]	2024	Both	18–60	China	1883	1–2	Gastroscopy	Sedation	Two doses	0.15/0.2 mg/kg	Bolus	Propofol bolus
Jian Guo ^[15]	2022	Both	≥65	China	77	1–2	Gastrointestinal endoscopy	Sedation	No	0.15 mg/kg/0.05 mg/kg	Bolus	Propofol bolus
Juan Li ^[20]	2021	Both	18–60	China	104	1–2	General anesthesia undergoing elective endotracheal intubation	Induction + maintenance	No	0.2 mg/kg for induction 0.2–0.6 mg/kg/h for maintenance	Infusion	Propofol infusion
Jungnam Lee ^[18]	2023	Both	>18	Korea	108	1–3	A diagnostic or therapeutic ERCP	Sedation	No	5.0 mg/2.5 mg	Bolus	Propofol bolus
Li Luo ^[22]	2023	Both	18–60	China	192	1–2	Short laparoscopic surgery	Induction + maintenance	Three doses	6.0 mg/kg/h for induction 1.0 mg/kg/h for maintenance 9.0 mg/kg/h for induction 2.0 mg/kg/h for maintenance 12.0 mg/kg/h for induction 3.0 mg/kg/h for maintenance	Infusion	Propofol infusion
Lu Yang ^[29]	2023	Both	20–69	China	80	1–2	Urological surgery	Induction + maintenance	No	3 mg/kg/h for induction 0.5–1.0 mg/kg/h for maintenance	Infusion	Propofol infusion
Matsuyuki Doi ^[12]	2020	Both	≥20	Japan	375	1–2	Elective surgery requiring tracheal intubation and hospitalization for ≥ 3 days	Induction + maintenance	Two doses	0.25 mg/kg for induction 1–2 mg/kg for maintenance 0.50 mg/kg for induction 1–2 mg/kg/h for maintenance	Infusion	Propofol infusion
Nan Zhao ^[33]	2022	Both	18–60	China	100	1–2	Third molar extraction	Induction + maintenance	No	80 µg/ kg for induction 0.3 mg/kg/h for maintenance	Infusion	Propofol infusion
Shaohui Chen ^[9]	2020	Both	18–65	China	384	1–2	Diagnostic or therapeutic colonoscopy	Sedation	No	5.0 mg/2.5 mg	Bolus	Propofol bolus
Shao-Hui Chen ^[10]	2020	Both	18–60	China	378	1–2	Upper GI endoscopy	Sedation	No	5.0 mg/2.5 mg	Bolus	Propofol bolus
Shu-An Dong ^[13]	2023	Both	≥18	China	505	1–3	Elective ERCP	Sedation	No	0.3 mg/kg for induction 0.2–1 mg/kg/h for maintenance	Infusion	Propofol infusion
Shunyi Fan ^[14]	2023	Female	20–60	China	83	1–2	Hysteroscopy	Sedation	No	0.25 mg/kg for induction 0.25 mg/kg/h for maintenance 0.48 mg/kg/h for induction 0.25 mg/kg for maintenance	Bolus	Propofol bolus
Shuoya Zhang ^[31]	2021	Female	18–55	China	90	1–2	Hysteroscopy	Sedation	Two doses	0.25 mg/kg for induction 0.48 mg/kg/h for maintenance 0.25 mg/kg for induction 0.6 mg/kg/h for maintenance	Infusion	Propofol infusion
Tae Young Lee ^[19]	2023	Both	20–80	Korea	101	1–3	Elective laparoscopic cholecystectomy	Induction + maintenance	No	0.2 mg/kg for induction 1–2 mg/kg/h for maintenance	Infusion	Propofol infusion
Tianxiao Liu ^[21]	2021	Both	35–65	China	60	3	Heart valve replacement	Induction	No	0.3 mg/kg	Infusion	Propofol infusion
Wenchen Luo ^[23]	2023	Both	18–75	China	76	1–2	Day surgery	Induction + maintenance	No	0.3 mg/kg for induction 1–3 mg/kg/h for maintenance	Infusion	Propofol infusion

(Continues)

Table 1
(Continued).

Study	Year	Gender	Age(yrs)	Country	Sample size	ASA ¹	Type of surgery/ intervention	Indication	Dose subgroup	Dose	Infusion/ bolus	Comparator
Wenyan Shi ^[24]	2022	Both	18–60	China	161	1–2	Painless gastroscopy or treatment	Sedation	No	0.33 mg/kg/2.5 mg	Bolus	Propofol bolus
Xiaoqiang Zhang ^[32]	2021	Female	18–65	China	82	1–2	Elective hysterectomy	Sedation	No	0.2 mg/kg for induction 1 mg/kg/ h for maintenance	Infusion	Propofol infusion
Ximei Wang ^[27]	2022	Both	18–65	China	477	1–3	A diagnostic or therapeutic colonoscopy	Sedation	No	7 mg/2.5 mg	Bolus	Propofol bolus
Yingjie Tan ^[25]	2022	Both	>60	China	99	1–2	Upper gastrointestinal endoscopy	Sedation	Two doses	0.1/0.2 mg/kg	Bolus	Propofol bolus
Ying-Yong Zhou ^[34]	2022	Both	18–75	China	310	1–3	Bronchoscopy for diagnosis and/or treatment	Sedation	No	0.2 mg/kg/0.1 mg/kg	Bolus	Propofol bolus
Yunping Huang ^[16]	2024	Both	9–76	China	100	1–2	Elective facial plastic surgery	Sedation	No	0.1–0.12 mg/kg/0.05–0.06 mg/kg	Bolus	Propofol bolus

RCT: Randomized clinical trial.
¹ASA: American Society of Anesthesiologists physical status classification system.

artificial intelligence in scientific writing (<https://doi.org/10.70389/PJS.100082>)^[5].

Method

The work has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) prospective and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines^[6].

Data sources and search strategy

A comprehensive search of PubMed, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials was conducted on 26 July 2024, with no restrictions on language or publication status. Additionally, reference lists of the included studies and relevant systematic reviews were manually screened to identify any further eligible studies. The full search strategy is detailed in Supplementary Digital Material 1 (available at: <http://links.lww.com/JJS9/E379>).

Study selection

Prospective, randomized controlled trials (RCTs) comparing remimazolam and propofol for sedation or general anesthesia in patients undergoing surgical or procedural interventions were included. Studies were excluded if they met any of the following criteria: (i) insufficient or incomplete data for quantitative synthesis; or (ii) non-randomized designs, including observational studies, animal experiments, conference abstracts, letters to the editor, study protocols, case reports, duplicate publications, and other non-eligible formats.

Data collection and quality evaluation

Two authors independently performed data extraction, achieving excellent interobserver agreement. Extracted data included patient demographics (age, sex, ASA physical status), study characteristics (country, procedure type, sample size), intervention details (dosage, timing, comparators), and outcomes. The risk of bias for included studies was independently assessed by two authors, using the Cochrane risk-of-bias tool^[6]. The reviewers also assessed potential conflicts of interest and industry sponsorship. Any discrepancies in evaluation were resolved through discussion, achieving interobserver agreement ranging from $\kappa = 0.6$ to 1.0. When additional information on trial methodology or unreported outcomes was required, the corresponding study authors were contacted. Authors were deemed unresponsive if they did not reply after three attempts, consistent with established practices. The quality of evidence for each outcome was assessed using the GRADE approach to ensure reliability and transparency in the findings^[7].

Outcomes and definitions

The primary outcome was the success rate of sedation or general anesthesia, defined by the following criteria: completion of surgery or intervention, a BIS score ≤ 60 after drug administration, and no need to switch sedatives. Secondary outcomes included the incidence of hypotension (SBP < 90 mmHg, MAP < 60 mmHg, and MAP or SBP decreased by more than 20% of the basal value), hypoxemia (SpO₂ < 90%), postoperative

nausea and vomiting (PONV), injection pain, as well as awakening and discharge times.

Statistical analysis

For dichotomous outcomes, pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated, while continuous outcomes were analyzed using mean differences (MDs) and corresponding 95% CIs. Meta-analyses were performed using the Mantel–Haenszel method for binary outcomes and the inverse variance method for continuous data. Depending on the degree of heterogeneity, either fixed-effects or random-effects models were applied. Heterogeneity was evaluated using the χ^2 test (with a significance level of $P < 0.10$) and quantified by the I^2 statistic, with $I^2 > 50\%$ indicating substantial heterogeneity. When outcome data were reported as medians with interquartile ranges (IQRs), they were converted to means and standard deviations using validated estimation methods. In trials that assessed multiple doses of remimazolam, data from different dosing arms were pooled into a single group to avoid unit-of-analysis errors. For studies with zero events in one or more arms, a continuity correction of 0.5 was applied to all cells of the 2×2 contingency table to allow for computation. Subgroup analyses were pre-specified and conducted according to the type of sedation (procedural sedation vs. general anesthesia). Forest plots were used to display the effect estimates and

95% CIs^[8]. Publication bias was assessed using Egger’s regression asymmetry test for the primary outcomes, and funnel plots were visually inspected for asymmetry, particularly when at least ten studies were available and the risk of bias was considered low.

Results

Study selection

A total of 732 records were identified through database searches, including PubMed (n = 130), EMBASE (n = 121), Web of Science (n = 320), and the Cochrane Library (n = 161). After the removal of 215 duplicate entries and 456 records excluded based on title and abstract screening using EndNote reference manager, 61 full-text articles were assessed for eligibility. Following full-text review, 34 studies were excluded for the following reasons: non-randomized controlled trials, conference abstracts, or study protocols (n = 13); data could not be transformed into a usable form (n = 6); or comparators were not clearly defined (n = 15). Ultimately, 27 randomized controlled trials met the inclusion criteria and were included in the final qualitative and quantitative synthesis. Fig. 1 presents the PRISMA flow diagram outlining the process of study identification, screening, and inclusion.

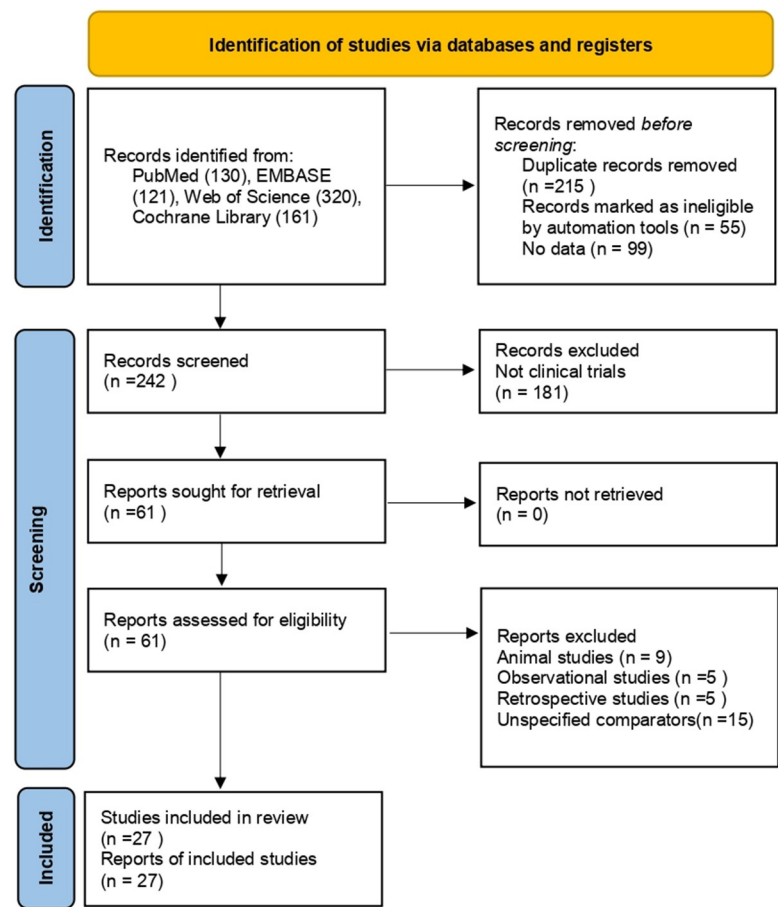


Figure 1. PRISMA flowchart depicting the systematic review process.

Baseline characteristics and study assessment

A total of 27 randomized controlled trials enrolling 8315 participants were included in the meta-analysis. The studies spanned from 2020 to 2024, with the majority conducted in China (24 studies), and the remainder in Korea (2 studies) and Japan (1 study). Participants were predominantly adults aged 18 to 85 years, with three trials focusing on elderly patients aged ≥65 years and one study involving a wide age range of 9 to 76 years. Both male and female patients were included in most trials, though three studies enrolled female participants exclusively, primarily in the context of hysteroscopic procedures. The American Society of Anesthesiologists (ASA) physical status classification of enrolled subjects ranged mostly from I to II, with a few studies including ASA III patients. Remimazolam was administered either via bolus injection or continuous infusion, tailored to procedural requirements such as sedation, induction, or maintenance of general anesthesia. Comparator groups uniformly received propofol through analogous routes. Surgical and diagnostic interventions varied widely, encompassing gastrointestinal endoscopy, cardiac surgery, laparoscopic procedures, urological operations, bronchoscopy, and outpatient plastic surgeries, reflecting a broad clinical applicability of remimazolam across diverse perioperative settings. Table 1 shows the baseline data.^[9-35]

The methodological quality of the included studies was generally moderate to high. Among the 28 included randomized

controlled trials, the majority demonstrated a low risk of bias for random sequence generation (24/28, 85.7%) and allocation concealment (22/28, 78.6%). Blinding of participants and personnel was adequately reported in 75% of studies, while blinding of outcome assessment was clearly described in 82.1%. Incomplete outcome data and selective reporting were well controlled in most trials. However, two studies showed high or unclear risk in several domains, particularly for performance and detection bias. A small number of studies had unclear risk due to insufficient reporting of allocation or blinding procedures. Despite this, no study was excluded due to critical methodological flaws (Supplementary Digital Material 2, available at: <http://links.lww.com/JS9/E380>). The overall certainty of evidence, as evaluated using the GRADE approach, was rated as high for the primary outcome, and moderate for most secondary outcomes. The downgrading was mainly due to inconsistency or imprecision across studies. These results suggest a generally reliable body of evidence with some variation in methodological rigor (Supplementary Digital Material 3, available at: <http://links.lww.com/JS9/E381>).

Primary endpoint

Sedation success rates were reported in 15 studies involving 4858 participants. High-quality evidence indicated no significant difference between remimazolam and propofol in terms of success rates (RR: 0.99; 95% CI: 0.97–1.00; $P = 0.10$; $df = 14$; $I^2 = 77\%$;

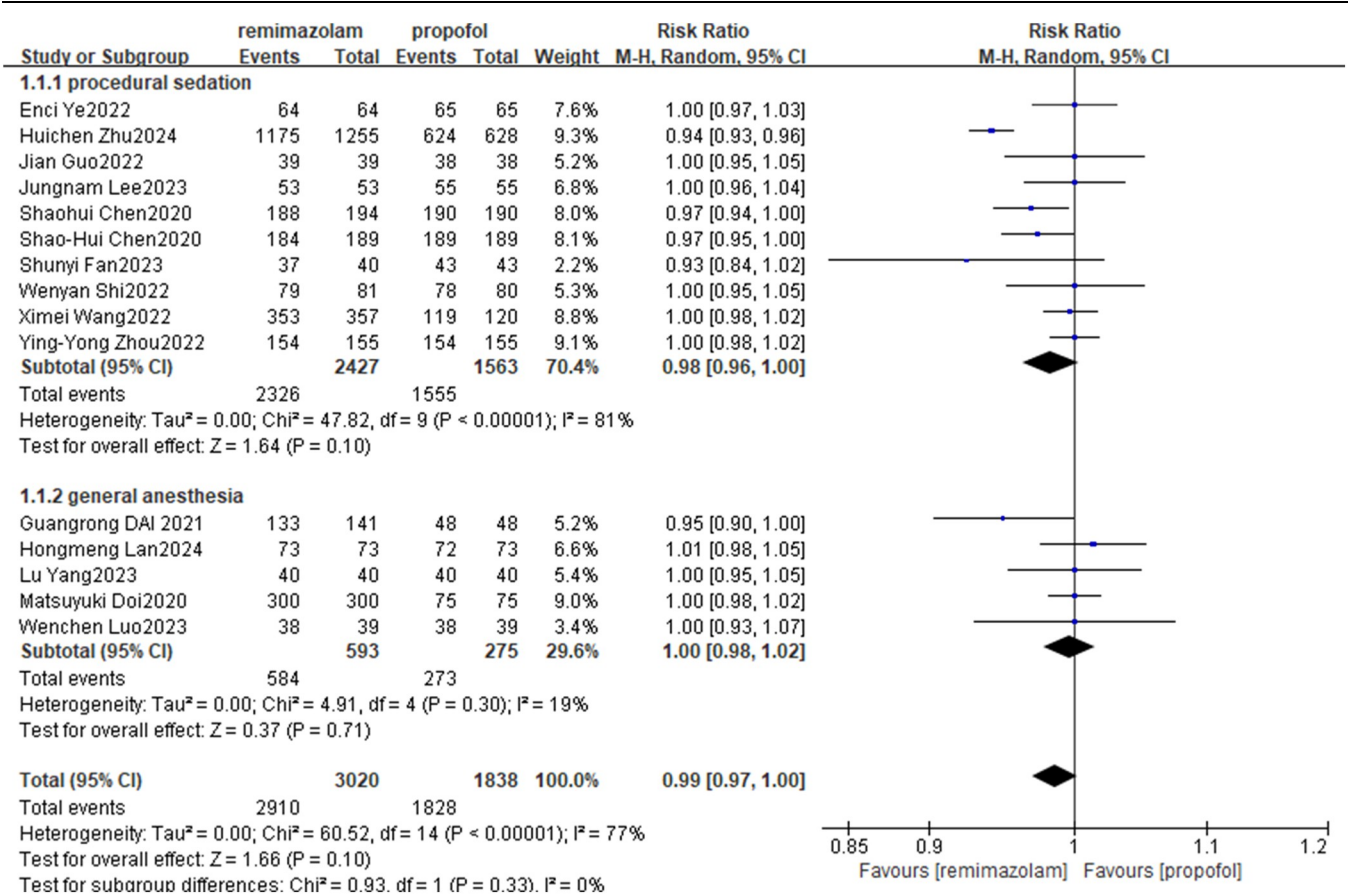


Figure 2. Forest plot for the success rate of procedural sedation or general anesthesia. Subgroup analysis was done based on procedural sedation/ general anesthesia. The overall effect shows that remimazolam and propofol were not different on the success rate. Odds ratios for random effects were determined using the Mantel-Haenszel method. The error bars indicate a 95% confidence interval. RR: Risk ratio.

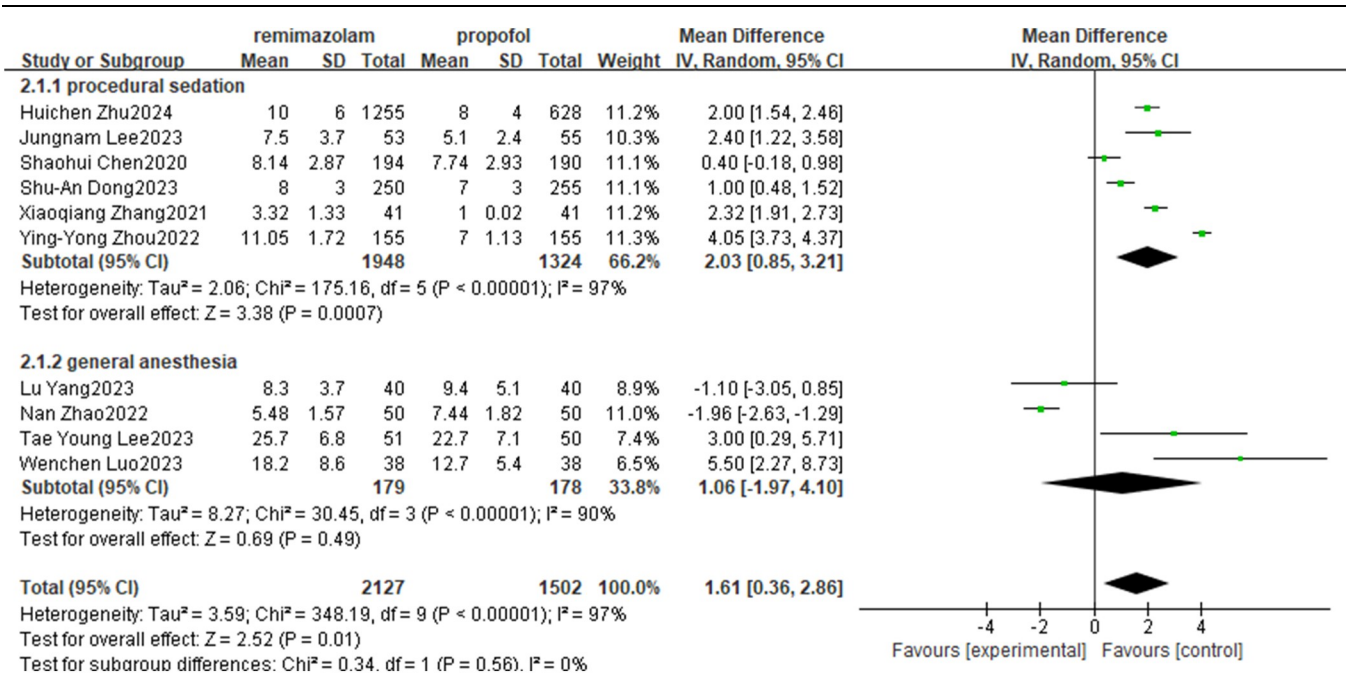


Figure 3. Forest plot for the time to awake. The plot shows that time to awake was shorter for propofol than remimazolam. Subgroup analysis showed that time to awake was not different between remimazolam and propofol for general anesthesia, but was different for procedural sedation. Mean differences (MD) are calculated.

Fig. 2 and Supplementary Digital Material 3, available at: <http://links.lww.com/J9/E381>).^[9-12,14,15,17,18,23,24,27,29,30,34,35]

The analysis revealed significant heterogeneity among the studies regarding sedation success rates. As shown in Fig. 2, the study by Huichen Zhu reported results that deviated substantially from the others, likely accounting for much of the observed heterogeneity^[35]. The analysis revealed significant heterogeneity among the studies regarding sedation success rates. As shown in Fig. 2, the study by Huichen Zhu produced results

that were notably different from the others, likely contributing to the observed heterogeneity.

Time to awake and to discharge

Ten trials involving 3629 participants assessed the time to awake. The results indicated that time to awake was shorter with propofol compared to remimazolam (MD, 1.61; 95% CI: 0.36–2.86; $P = 0.01$; $df = 9$; $I^2 = 97\%$; Fig. 3).^[9,13,18,19,23,29,32-35]

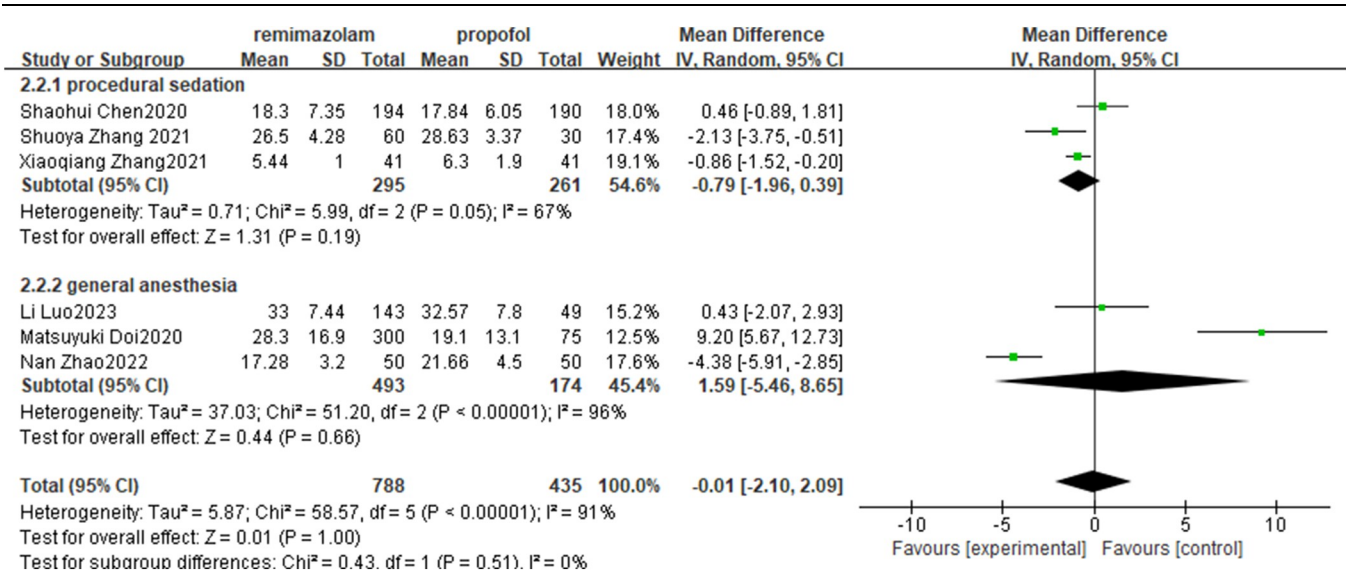


Figure 4. Forest plot for the time to discharge. The plot shows time to discharge during both procedural sedation and general anesthesia were not different between the two drugs. Mean differences (MD) are calculated.

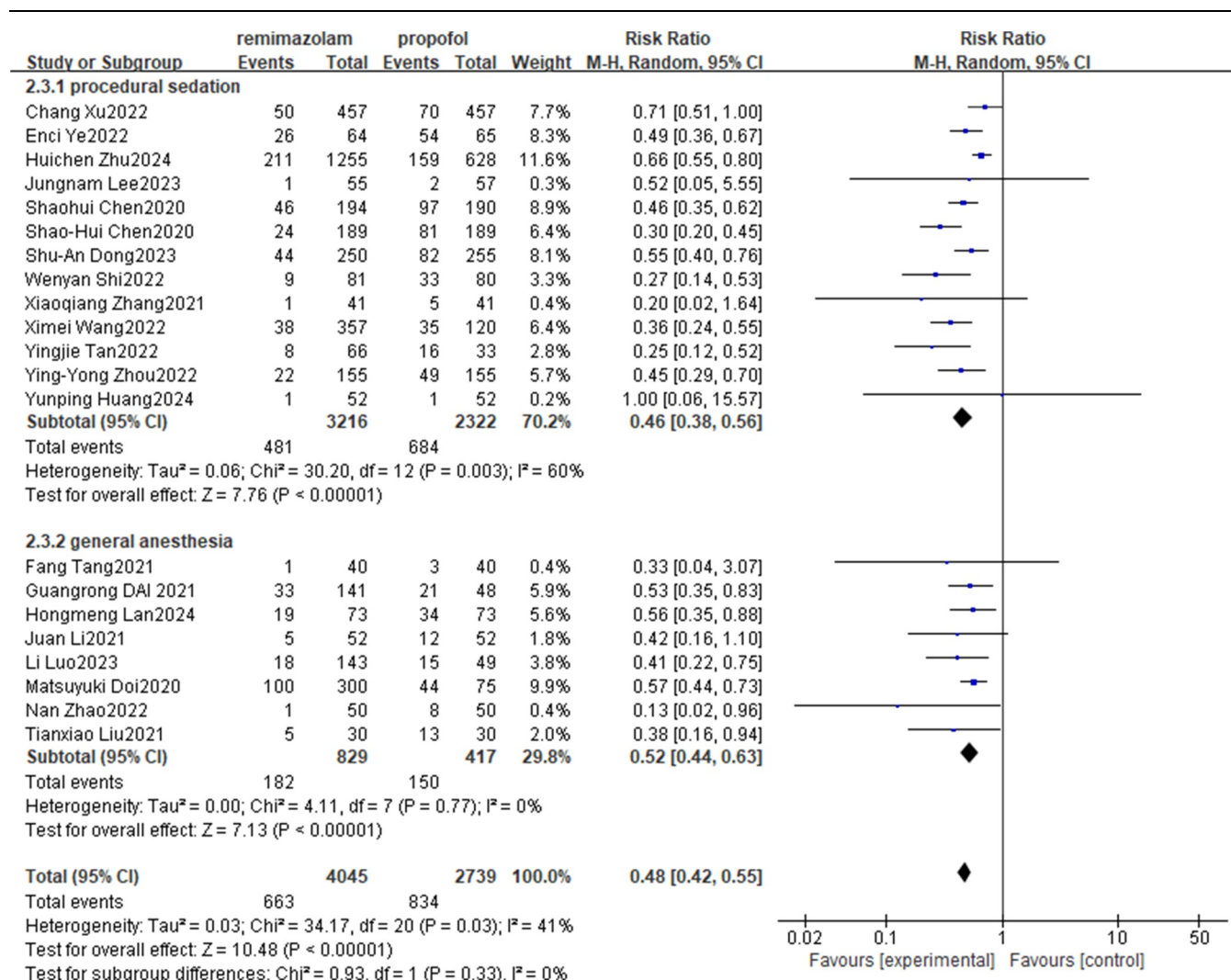


Figure 5. Forest plot for the incidence of hypotension. The plot shows that incidences of hypotension during both procedural sedation and general anesthesia were lower in patients receiving remimazolam. The error bars indicate a 95% confidence interval. RR: Risk ratio.

Subgroup analysis revealed no significant difference in time to awake between remimazolam and propofol for general anesthesia (MD, 1.06; 95% CI: -1.97 to 4.10; $P = 0.49$; $df = 3$; $I^2 = 90\%$; Fig. 3). However, propofol led to a shorter time to awake than remimazolam in procedural sedation (MD, 2.03; 95% CI: 0.85–3.21; $P = 0.0007$; $df = 5$; $I^2 = 97\%$; Fig. 3).

Six trials with 1223 participants examined the time to discharge. There was no significant difference between the two drugs in time to discharge (MD, -0.01; 95% CI: -5.46 to 8.65; $P = 1.00$; $df = 5$; $I^2 = 91\%$; Fig. 4).^[9,12,22,31–33] Subgroup analysis showed no difference in discharge times between the drugs for either procedural sedation or general anesthesia (Fig. 4).

Incidence of hypotension and hypoxemia

Twenty-one trials involving 6784 participants compared the incidence of hypotension between propofol and remimazolam. Remimazolam was associated with a significantly lower incidence of hypotension compared to propofol (RR, 0.48; 95% CI: 0.42–0.55; $P < 0.00001$; $df = 20$; $I^2 = 41\%$; Fig. 5).^[9–13,16–18,20–22,24–28,30,32–35] Subgroup analysis showed that remimazolam

reduced the incidence of hypotension in both procedural sedation and general anesthesia (Fig. 5).

Ten trials with 4043 participants compared hypoxemia rates between propofol and remimazolam. Remimazolam resulted in a lower incidence of hypoxemia than propofol (RR, 0.36; 95% CI: 0.23–0.55; $P < 0.00001$; $df = 9$; $I^2 = 31\%$; Fig. 6)^[9,11,13,16,18,24,25,27,30,35]. Subgroup analysis revealed that remimazolam significantly reduced the incidence of hypoxemia during procedural sedation (RR, 0.35; 95% CI: 0.22–0.55; $P < 0.00001$; $df = 8$; $I^2 = 39\%$; Fig. 6). However, there was no significant difference in hypoxemia rates between the two drugs during general anesthesia (RR, 0.35; 95% CI: 0.02–5.49; $P = 0.45$; Fig. 6). It is important to note that only one trial recorded hypoxemia incidents after general anesthesia.

Incidence of PONV and injection pain

Eight trials involving 996 participants compared the incidence of postoperative nausea and vomiting (PONV) between remimazolam and propofol. No significant difference was found in the

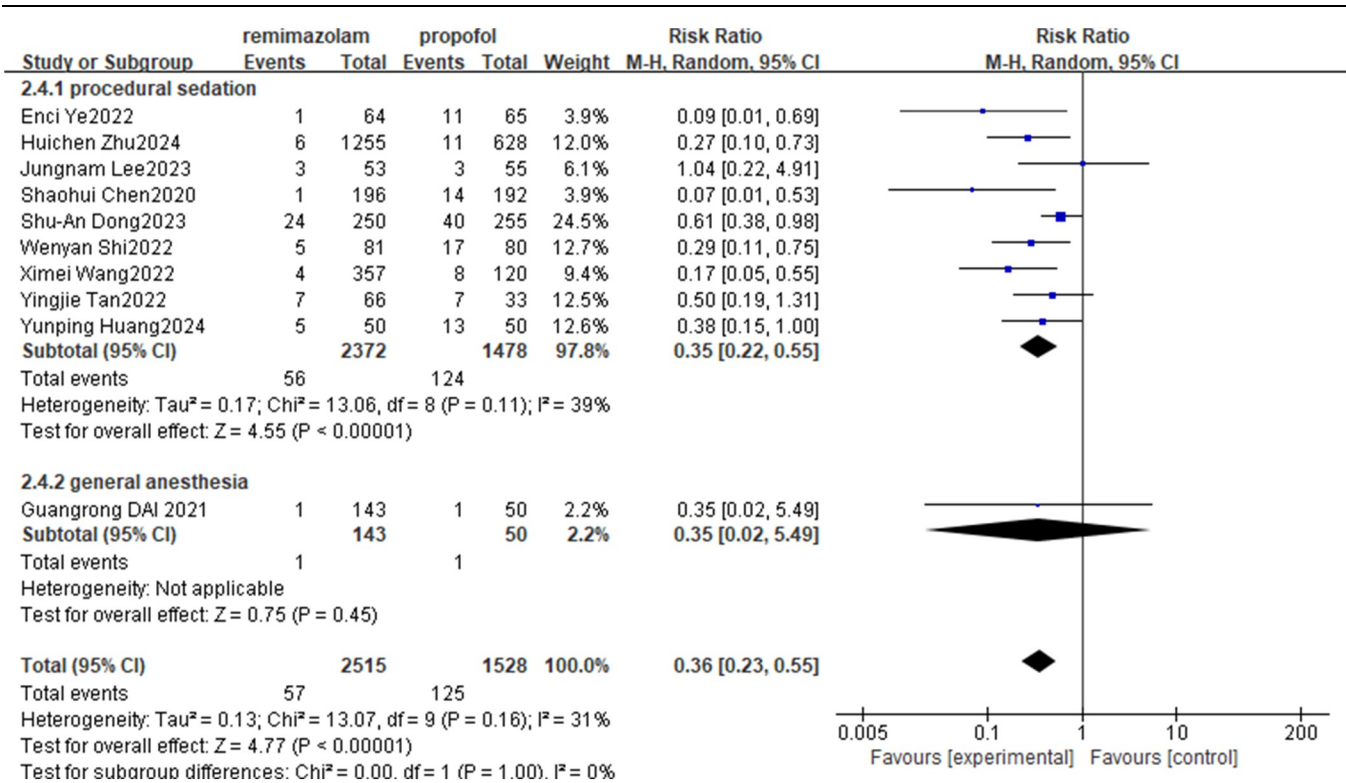


Figure 6. Forest plot for the incidence of hypoxemia. The plot shows that remimazolam had less hypoxemia than propofol. Subgroup analysis indicated that patients receiving remimazolam during procedural sedation experienced a lower incidence of hypoxemia. In contrast, no significant difference was observed in hypoxemia rates between remimazolam and propofol during general anesthesia. Error bars represent 95% CI. RR: Risk ratio.

overall analysis (RR, 0.92; 95% CI: 0.58–1.48; $P = 0.74$; $df = 7$; $I^2 = 0\%$; Fig. 7) nor in subgroup analyses for procedural sedation and general anesthesia^[11,15,17,20,22,23,29,31].

Nineteen trials with 5691 participants compared the incidence of injection pain between the two drugs. Remimazolam was associated with significantly less injection pain than propofol, both in the overall analysis (RR, 0.06; 95% CI: 0.03–0.11; $P < 0.00001$; $df = 18$; $I^2 = 68\%$; Fig. 8) and in subgroup analyses for procedural sedation and general anesthesia.^[9–13,15–17,20,23,24,27,29–35]

Meta-regression, publication bias, and sensitivity analysis

To further explore the potential sources of heterogeneity, meta-regression analyses were performed for four key outcomes: time to awake, incidence of hypotension, incidence of hypoxemia, and incidence of injection pain. The covariates included in the meta-regression were mean age, proportion of male participants, ASA classification, and sample size. The results indicated that none of these factors significantly contributed to between-study heterogeneity (all $P > 0.05$). For detailed results, see Supplementary Digital Material 4 (available at: <http://links.lww.com/JS9/E382>).

Publication bias was assessed for outcomes with eight or more included studies. Visual inspection of funnel plots, along with Begg’s and Egger’s tests, revealed no significant evidence of publication bias for the examined outcomes (all $P > 0.05$). For detailed results, see Supplementary Digital Material 5 (available at: <http://links.lww.com/JS9/E383>).

Sensitivity analyses, conducted by sequentially omitting each study, demonstrated that the overall pooled estimates remained consistent, indicating that the results were robust and not unduly influenced by any single study (Supplementary Digital Material 4, available at: <http://links.lww.com/JS9/E382>).

Discussion

High-quality evidence suggests no significant difference between remimazolam and propofol in terms of the success rate of sedation or general anesthesia. However, remimazolam was associated with a longer time to awake after procedural sedation and a lower incidence of hypoxemia, hypotension, and injection pain during both procedural sedation and general anesthesia compared to propofol.

The results of the risk of bias assessment revealed that the majority of studies demonstrated low risk of bias in random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential sources of bias. However, a small number of studies had unclear risk, and only one study was rated as high risk. The GRADE evaluation indicated that the quality of evidence for the primary outcomes was rated as high, demonstrating strong confidence in these findings. These results suggest that the overall quality of the included studies is robust, and the findings are highly reliable.

The pooled analysis of success rates showed no difference between the two drugs. Additionally, the analysis revealed that

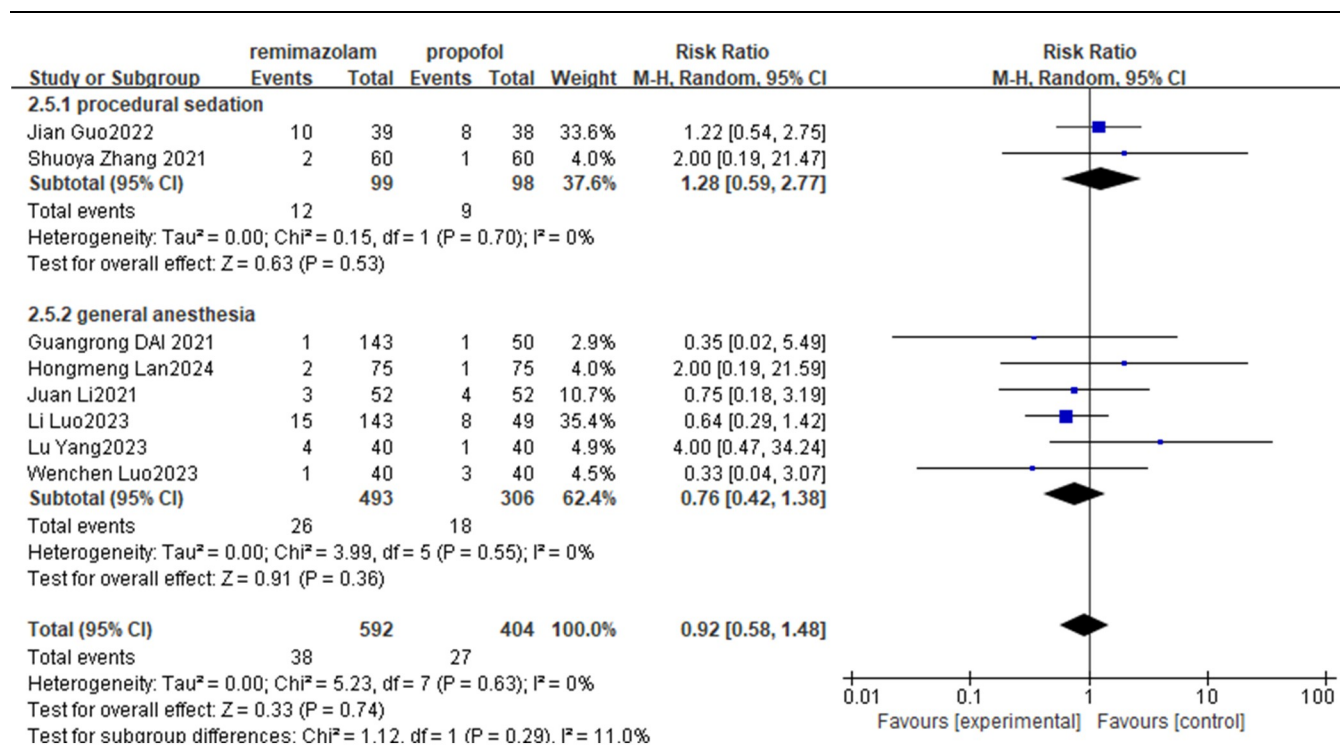


Figure 7. Forest plot for the incidence of PONV. The plot shows incidences of PONV during both procedural sedation and general anesthesia were not different between patients receiving remimazolam and propofol. Error bars represent 95% CI.

the incidence of hypotension and injection pain was lower in patients who received either general anesthesia or procedural sedation with remimazolam. In the sensitivity analysis, significant heterogeneity remained; however, excluding the study by Huichen Zhu led to a notable reduction in heterogeneity. Two factors may explain this heterogeneity: (1) a higher dose of remimazolam (0.20 mg/kg) might be more effective for sedation than the lower dose (0.15 mg/kg) used in some studies, and (2) the intensity of pain varied across different procedures, which may have required different levels of sedation. The incidence of hypoxemia was lower in patients receiving procedural sedation with remimazolam, consistent with previous reports^[36]. Only one included study reported the incidence of hypoxemia during general anesthesia^[28]. This limited evidence precludes drawing definitive conclusions about differences between remimazolam and propofol in respiratory outcomes. Although remimazolam was associated with a lower incidence of hypoxemia overall, this conclusion is primarily driven by studies conducted in procedural sedation settings. Only one included study (Tang *et al*) reported hypoxemia incidence during general anesthesia. Therefore, the current evidence is insufficient to determine whether remimazolam confers respiratory advantages during general anesthesia. This limitation should be taken into account when applying the findings to clinical practice, and further studies specifically focused on respiratory outcomes in general anesthesia are needed to validate this effect. Therefore, further well-designed, large-scale randomized controlled trials are needed to more comprehensively evaluate the impact of remimazolam on respiratory function during general anesthesia. Clinicians should consider this limitation when interpreting current evidence and making treatment decisions. The overall

heterogeneity of the studies was moderate, supporting the advantage of remimazolam in terms of hemodynamic stability, respiratory events, and injection pain.

The findings also indicated that time to awakening was shorter with propofol during procedural sedation, while discharge times were similar for both drugs. This may be due to remimazolam having a longer half-life than propofol, which causes it to remain in the body for an extended period.^[37,38] Recovery time in the remimazolam group was on average prolonged by 1.61 minutes compared to propofol. Although statistically significant, the clinical significance of this difference remains uncertain. The use of remimazolam was associated with a statistically significant prolongation in time to awake (mean difference: 1.61 minutes), the clinical significance of this delay is likely to be modest. In most routine anesthesia settings, such a short delay may not substantially impact patient throughput or recovery room efficiency. However, in fast-track or high-volume ambulatory surgical units, even minimal delays could accumulate and influence scheduling. Furthermore, there is currently limited evidence to determine whether this slight prolongation affects patient experience, including risks of emergence agitation or dissatisfaction. Further research is warranted to evaluate the clinical relevance of recovery profiles in different procedural contexts. This slight delay may have implications for surgical workflow efficiency, especially in high-turnover settings such as day surgery units. Moreover, the potential impact on patient experience, including risks related to emergence agitation or delayed discharge readiness, warrants further investigation. Future studies should explore these clinical outcomes to better inform anesthetic choice. During general anesthesia, the pharmacokinetic differences between remimazolam and

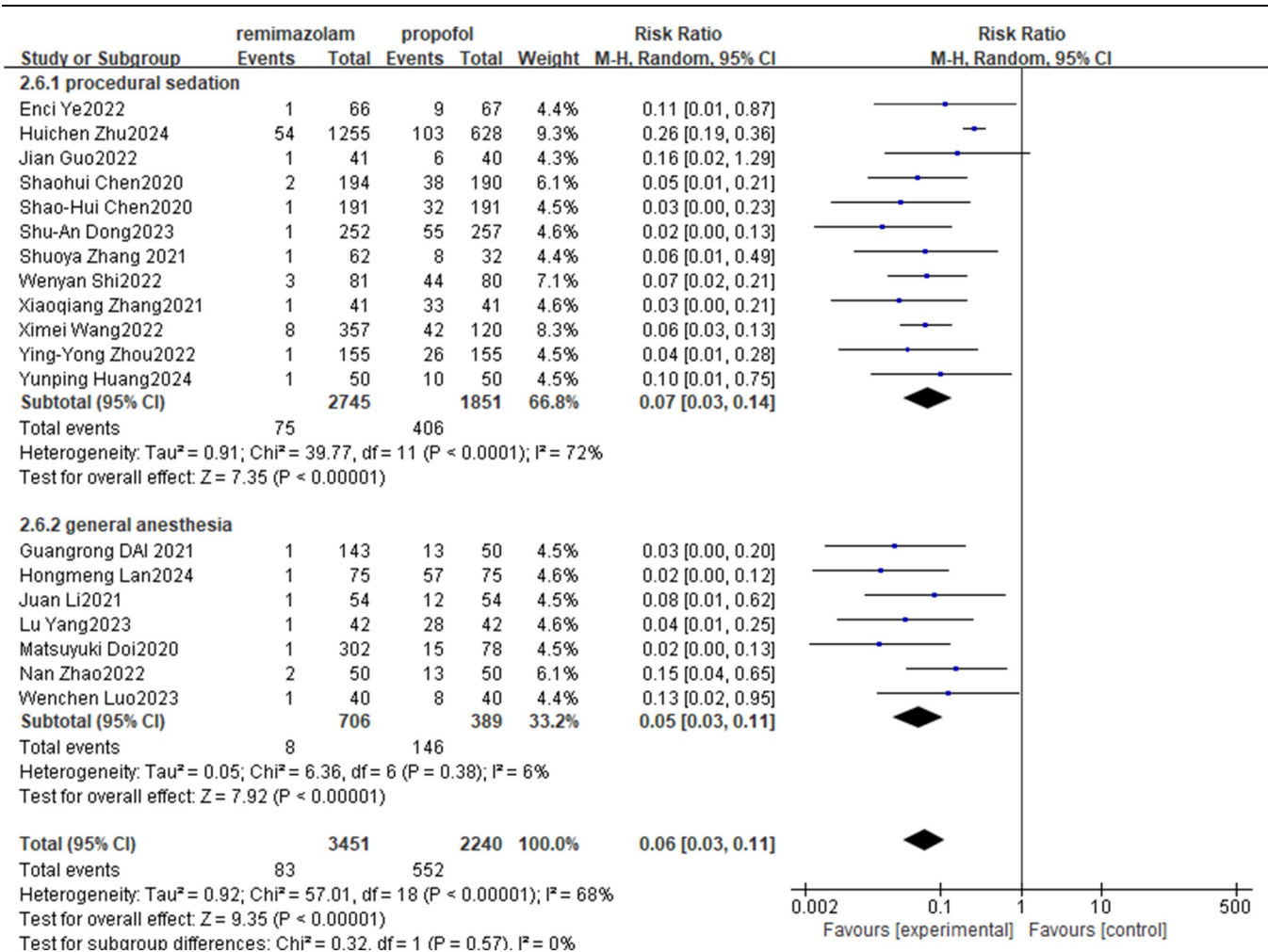


Figure 8. Forest plot for the incidence of injection pain. The plot shows that incidences of injection pain were lower in patients receiving remimazolam. Error bars represent 95% CI. RR: Risk ratio.

propofol may be minimized due to the co-administration of other drugs, resulting in similar time to awake, which is consistent with previous research findings^[39]. The discharge time is not only determined by drug metabolism but also influenced by the patient's overall recovery condition, such as pain control, nausea and vomiting, hemodynamic stability, and other factors^[7,40]. In the sensitivity analysis, significant heterogeneity persisted, but the leave-one-out approach showed that no single study had an undue influence on the effect estimate or contributed substantially to the heterogeneity. Three factors may explain this variation: (1) differing definitions of time to awake and time to discharge across studies, (2) the varying intensity of pain and sedation requirements for different procedures, and (3) differences in post-anesthesia patient management protocols.

The strengths of our study include a comprehensive literature review that identified 27 relevant publications, enabling robust subgroup analyses. The research rigorously followed Cochrane methodology, and efforts were made to contact authors to assess the risk of bias and obtain any unpublished data that could inform the analysis. Compared to the previous study^[4], the literature our research included is more comprehensive, making our conclusions more reliable. Additionally, some conclusions of this study differ from those of prior research. The earlier study

indicated that remimazolam had a higher success rate for procedural sedation and a lower incidence of hypoxemia during general anesthesia compared to propofol, and that there was no difference in the wake-up time between remimazolam and propofol. However, through a more extensive review of the literature, it was demonstrated that there is no difference in the success rate of procedural sedation and the incidence of hypoxemia during general anesthesia between remimazolam and propofol. Moreover, remimazolam was found to result in a longer wake-up time during procedural sedation.

This review has several limitations. One important limitation of this meta-analysis is the geographic and demographic concentration of the included studies. Among the 27 randomized controlled trials analyzed, 24 were conducted in China and 3 in South Korea, with no studies originating from Western populations such as those in Europe or North America (Fig. 9). This regional concentration may limit the generalizability of our findings to other ethnic groups and healthcare systems. While this reflects the current state of available evidence, it underscores the need for future high-quality randomized trials in more diverse populations to validate the efficacy and safety of remimazolam compared to propofol across broader clinical settings. The second limitation is the lack of standardized definitions for certain clinical outcomes

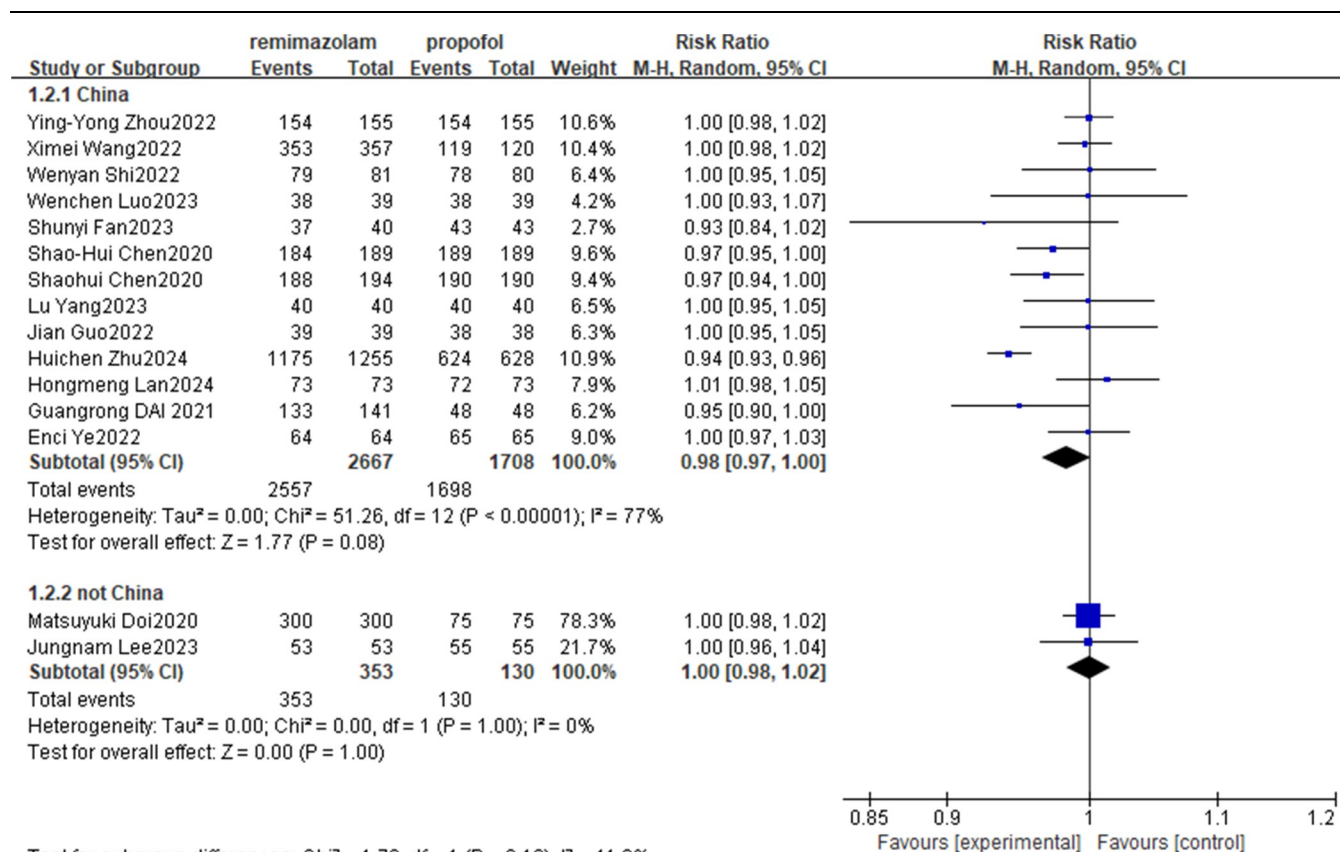


Figure 9. Forest plot for the success rate in China or not China. Subgroup analysis revealed no significant differences between trials conducted in China and those conducted outside China. Odds ratios for random effects were determined using the Mantel–Haenszel method. The error bars indicate a 95% confidence interval. RR: Risk ratio.

across the included trials. For example, “success rate” and “hypotension” were variably defined depending on local clinical protocols and study-specific thresholds. Similarly, although remimazolam was consistently associated with a lower incidence of injection pain, most studies did not specify the assessment tools or time points used to evaluate pain. These inconsistencies may have introduced measurement bias and reduced the comparability between studies. Future trials should aim to adopt unified, validated outcome definitions and assessment methods to improve the robustness of evidence synthesis. Another limitation is the variability in dosing regimens of remimazolam and propofol across the included studies. The recommended doses for these agents are typically expressed as a range in official prescribing information, and their use is influenced by institutional protocols, regional practice differences, and manufacturer-specific formulations. Moreover, some studies did not provide detailed dosing information, precluding further dose-based subgroup analysis. As such, although all included doses fell within clinically accepted ranges, potential differences in pharmacodynamic response cannot be entirely excluded.

Conclusions

This meta-analysis found no significant difference between remimazolam and propofol in terms of sedation or general anesthesia success rates. Remimazolam was associated with a lower incidence of hypoxemia, although it resulted in a longer time to

awake during procedural sedation. Additionally, it was linked to a reduced occurrence of hypotension and injection pain in both procedural sedation and general anesthesia. However, the limitations of the studies included in this analysis prevent us from drawing definitive conclusions regarding remimazolam’s role in general anesthesia. In addition, the dosage of the drug should be determined according to the patient’s condition and the type of surgery, and should not be generalized, so as to achieve more precise treatment and benefit the patient. In the future, large-scale, well-designed randomized controlled trials (RCTs) are anticipated to help validate and expand on these findings.

Ethical approval

This study did not require ethical approval as it involved no human or animal subjects.

Consent

This study did not involve human participants, and therefore informed consent was not required.

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Author contributions

Y.X.: conceptualization, data curation, writing – original draft; Z.L.: conceptualization, data curation, formal analysis; X.W.: conceptualization, writing – original draft; X.H.: formal analysis; J.Z.: formal analysis; Jie Liu: data curation, writing – review & editing; Y.L.: conceptualization, data curation, formal analysis, funding acquisition, writing – review & editing.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

Research registration unique identifying number (UIN)

The protocol was registered at PROSPERO (CRD42024509305).

Guarantor

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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