

Comparative efficacy and safety of remimazolam vs. dexmedetomidine: A systematic review and meta-analysis

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Received May 6, 2025; Accepted August 25, 2025

DOI: 10.3892/br.2026.2146

Abstract. Sedation is a critical component of modern anesthesia and procedural medicine, particularly outside the operating room. Dexmedetomidine and remimazolam have emerged as prominent sedatives due to their unique pharmacological profiles. However, the comparative efficacy and safety of these agents remain incompletely understood, especially regarding recovery times and adverse events. In the present study, a systematic review and meta-analysis as performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A comprehensive literature search was conducted across PubMed, Cochrane Library and Scopus from inception until March 2025. The eligible studies compared the sedation efficacy, safety and recovery time of the dexmedetomidine group with the remimazolam group. Data extraction was independently conducted by two reviewers using a standardized data collection form. The methodological quality of observational studies was assessed using the Risk of Bias in Non-randomized Studies-of Interventions (ROBINS-I) tool, while randomized controlled trials (RCTs) were evaluated using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool. Meta-analyses were conducted using random-effects models, and heterogeneity was evaluated through prediction interval analysis and sensitivity testing. A total of 9 studies were included, 4 of which were RCTs and judged to have low risk of bias across all domains. The remaining 5 observational studies, with most rated as having moderate risk of bias and 1 study rated as serious due to confounding and outcome measurement concerns. The forest plot analysis revealed that there was no statistically significant difference in the sedation efficacy between the dexmedetomidine group and the remimazolam group [standardized mean difference (SMD), 0.049; 95% confidence interval (CI), -0.101 to 0.198; $P=0.523$]. However, the remimazolam group consistently demonstrated

significantly shorter full alertness times compared with the dexmedetomidine group (SMDs ranging from -0.511 to -1.852, all $P<0.001$). There was no significant difference in the overall risk of adverse events between the two groups [odds ratio (OR), 1.509; 95% CI, 0.246-9.153; $P=0.654$]; however, the subgroup analysis showed that the risk of arrhythmia in the dexmedetomidine group was significantly higher than that in the remimazolam group (OR, 2.152; 95% CI, 1.158-3.999; $P=0.015$). In conclusion, both dexmedetomidine and remimazolam achieved similar sedation success rates, indicating no significant difference in procedural efficacy. However, remimazolam was associated with significantly faster recovery times and a lower risk of arrhythmia, making it particularly attractive for short-duration or outpatient procedures where rapid emergence and hemodynamic stability are prioritized.

Introduction

The use of sedatives in patients is a critical aspect of modern anesthesia and procedural medicine, particularly in non-operating room settings. Among the agents available, dexmedetomidine and remimazolam have emerged as prominent choices due to their unique pharmacological profiles and efficacy in achieving sedation with minimal adverse effects (1).

Dexmedetomidine, an α -2 adrenergic agonist, is known for its sedative and analgesic properties and is often utilized in various procedures including, orthopedic surgeries, cardiovascular surgeries and neurosurgery procedures (2). Dexmedetomidine offers advantages such as reduced opioid requirements and minimal respiratory depression, making it suitable for use in patients undergoing sedation outside the operating room (3,4). However, its use is not without challenges; higher doses can lead to bradycardia and hypotension, necessitating careful monitoring and dosage adjustments (5,6).

By contrast, remimazolam, a newer benzodiazepine, has gained attention for its rapid onset and short duration of action, which may be particularly beneficial when quick recovery from sedation is often desired (7). Studies have indicated that remimazolam provides comparable hemodynamic stability to dexmedetomidine, with a lower incidence of adverse cardiovascular events (8,9). This characteristic is crucial in patients who may be more susceptible to the hemodynamic fluctuations associated with sedation (8). Furthermore, remimazolam has been associated with a reduced incidence of postoperative delirium compared with traditional sedatives (9,10).

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Key words: remimazolam, dexmedetomidine, sedation, anesthesia, recovery time, adverse events, meta-analysis, systematic review

Despite the promising profiles of both agents, the existing literature reveals a gap in large-scale comparative studies. Most studies to date have been limited in scope, often involving small sample sizes and heterogeneous populations, which complicates the generalizability of their findings (8,9). A systematic review and meta-analysis focusing on the comparative efficacy of dexmedetomidine and remimazolam in sedation is warranted to synthesize the available evidence and provide clearer insights into their relative advantages and disadvantages. Moreover, the safety profiles of these agents must be carefully evaluated. While dexmedetomidine is generally well-tolerated, its potential for inducing bradycardia and hypotension raises concerns, particularly in vulnerable patients (5,6). Additionally, remimazolam, despite its rapid metabolism and favorable recovery profile, has been associated with rare but serious adverse events, including anaphylaxis (11). Understanding these risks is essential for clinicians when selecting the appropriate sedative for patients. In conclusion, the comparative efficacy of dexmedetomidine and remimazolam in sedation represents a critical area of inquiry. The present systematic review and meta-analysis aims to elucidate the relative safety and efficacy of these two agents, providing evidence-based guidance for clinicians involved in sedation practices. By addressing the existing gaps in the literature, the present study seeks to enhance the understanding of sedation strategies, ultimately improving patient outcomes and safety.

Materials and methods

Study design and reporting standards. The present systematic review and meta-analysis was conducted to compare the efficacy and safety of dexmedetomidine and remimazolam for sedation. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor and transparency in reporting (12). This review was not registered on PROSPERO or any other public platform.

Literature search. A comprehensive literature search was performed across multiple electronic databases, including PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Cochrane Library (<https://www.cochranelibrary.com/>), Scopus (<https://www.scopus.com/>), Web of Science (<https://clarivate.com/>), Embase (<https://www.embase.com/>) and trial registries (<https://clinicaltrials.gov/>) from their inception until March 2025. The search strategy included keywords such as 'dexmedetomidine', 'remimazolam' and 'sedation'. The search was limited to studies published in English and involving populations aged >18 years.

Inclusion and exclusion criteria. Studies were included if they met the following criteria: i) Randomized controlled trials (RCTs) or observational studies comparing the sedative effects of dexmedetomidine and remimazolam; ii) reported outcomes related to sedation efficacy, safety or adverse events; and iii) provided sufficient data for meta-analysis. Studies were excluded if they involved pediatric populations, were not peer-reviewed or if they lacked relevant outcome measures, defined as the absence of any data on sedation success rates, recovery times (such as time to full alertness or discharge) or adverse events (such as arrhythmia, hypotension or hypoxia).

Data extraction. In total, two independent reviewers extracted data from the included studies using a standardized data extraction form. The extracted data included study characteristics (including author, year and sample size), patient demographics (including age and sex), sedation protocols (including dosage and administration route) and outcomes (including sedation success rates, adverse events and recovery times). Sedation success was defined as the achievement of an adequate depth of sedation, as determined by the individual study protocols, without the need for rescue sedatives or conversion to general anesthesia. Most studies determined this using standardized sedation scales (such as Modified Observer's Assessment of Alertness/Sedation score of ≤ 3 Richmond Agitation-Sedation Scale of -2 to -3) with no major sedation-related complications (13,14). Sedation failure includes: i) Poor sedation effect; ii) the need for additional unplanned sedation measures; and iii) patient movement causing interruption of the operation or switching to other sedatives. Procedure success was defined as the uninterrupted and complete performance of the intended intervention (such as flexible bronchoscopy, gastrointestinal endoscopy or transcatheter aortic valve replacement) without escalation of sedation, patient intolerance or procedure abandonment. Consistent with Kim *et al* (15), surgery failure was defined as conversion to general anesthesia, need for sedation intensification beyond protocol or premature termination due to patient non-cooperation or sedation-related complications. There was a high agreement between the two reviewers regarding the extracted data ($\kappa=82\%$). Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.

Quality assessment. For quality assessment of non-randomized studies, the Risk of Bias in Non-randomized Studies-of Interventions (ROBINS-I) tool (version 2016; <https://www.riskofbias.info/welcome/home>) was employed. Each study was classified as having low, moderate, serious or critical risk of bias overall, according to the highest risk level obtained in any of the seven domains. Studies judged to have low or moderate risk of bias were considered of good quality, whereas those rated serious or critical were considered of poor quality. For RCTs, the revised Cochrane risk-of-bias tool for randomized trials (RoB 2.0; <https://www.riskofbias.info/welcome/rob-2-0-tool>) was applied. This evaluates bias arising from the randomization process, deviations from intended interventions, missing outcome data, outcome measurement and selective reporting. In total, two reviewers independently performed the assessments and any discrepancies were resolved by consensus.

Statistical analysis. Meta-analyses were conducted using Comprehensive Meta-analysis Software (version 2; <https://meta-analysis.com/pages/v2download>). The primary outcomes assessed were sedation success rates and the incidence of adverse events. Continuous outcomes, such as recovery times, were analyzed using mean differences, while dichotomous and continuous outcomes were analyzed using odds ratios (ORs) and standardized mean differences (SMDs), respectively. A random-effects model was employed to account for variability between studies. Heterogeneity was assessed using prediction interval analysis. Sensitivity analyses were performed to evaluate the robustness of the findings. $P < 0.05$ was considered to indicate a statistically significant difference.

Publication bias and small-study effects. To assess the robustness of the pooled estimate against publication bias two complementary analyses were conducted. First, the classic Fail-safe N (Rosenthal method) was calculated to determine how many additional 'null' studies (mean OR=1.00) would be required to render the overall result non-significant at $P=0.05$. A threshold of $5k + 10$ (where k is the number of included studies) was used to judge whether the Fail-safe N was sufficiently large. Second, Duval & Tweedie's trim-and-fill procedure was applied to estimate potentially missing studies and to provide an adjusted pooled effect size. Both analyses were performed using the 'metafor' package (version 4.4-0) in R 4.3.1 (<https://www.r-project.org/>). $P<0.05$ was considered to indicate a statistically significant difference.

Ethical considerations. As the present study involved a systematic review of previously published data, ethical approval was not required. However, all included studies were required to have obtained appropriate ethical approvals from their respective institutional review boards.

Results

General study characteristics. A total of 9 studies were included in the final analysis (Fig. 1), comprising 4 RCTs and 5 observational studies, as detailed in Table I. The 4 RCTs included were conducted by Chen *et al* (16), Chen *et al* (17), Lee *et al* (18) and Xu *et al* (19). These trials primarily compared the procedural sedation of remimazolam with dexmedetomidine in a controlled clinical setting, such as awake tracheal intubation and fiberoptic bronchoscopy. Most trials used standardized sedation protocols, enabling robust head-to-head comparisons. The 5 observational studies included were by Kitaura *et al* (7), Hong *et al* (20), Deng *et al* (21), Zhou *et al* (22) and Kim *et al* (1). These studies employed retrospective or prospective cohort designs to evaluate remimazolam and dexmedetomidine in real-world clinical practice, including transcatheter aortic valve replacement (TAVR), gastrointestinal surgery in obese patients and scoliosis procedures. Sample sizes ranged from 60 to 464.

Across all studies, remimazolam was administered intravenously (IV) at doses between 0.05 and 12 mg/kg/h, while dexmedetomidine was administered at doses of 0.5 to 1 $\mu\text{g}/\text{kg}$ IV. Sedation success rates were consistently high for both agents: 70.9 to 96.2% for remimazolam and 65.1 to 92.8% for dexmedetomidine. Notably, remimazolam was consistently associated with faster recovery time, underscoring its clinical advantage in time-sensitive procedural environments.

Main study outcomes. Overall, the six outcomes analyzed showed mixed findings (Fig. 2), with most pooled estimates crossing the line of no effect (the CIs pass through 0). For the discharge time, SMDs ranged from -2.423 to 0.653 [for example, Chen *et al* (16): SMD=-0.796, $P<0.001$; Lee *et al* (18): SMD=0.653, $P=0.005$], reflecting inconsistency across studies. Expert satisfaction (SMDs ranging -0.729 to 0.660) and procedure success (SMDs ranging -0.901 to 0.423) similarly showed no clear direction of benefit. By contrast, patient satisfaction was predominantly positive (SMDs ranging from 0.238 to 0.533), with a few estimates achieving

significance at $P<0.05$. Procedure time ranged close to zero (for example, -1.990 to 0.465, with P -values from <0.001 to 0.781), suggesting no robust advantage for either agent. The one consistently favoring result emerged in the time to fully alert outcome, where nearly all studies reported significantly shorter times (SMDs ranging -0.511 to -1.852, all $P<0.001$) in the remimazolam group. Notably, when all outcomes were pooled (bottom diamond), the effect size was SMD=0.049 [standard error, 0.076; 95% confidence interval (CI), -0.101 to 0.198; $P=0.523$], indicating no overall statistically significant difference in the efficacy between dexmedetomidine and remimazolam across the included studies. While the pooled SMD for overall efficacy was non-significant, recovery-related endpoints such as time to full alertness consistently favored remimazolam, indicating potential procedural advantages in select clinical contexts.

Meta-regression and moderator analysis. The moderator analysis assessed the influence of patient age and drug dose on the comparative efficacy of remimazolam vs. dexmedetomidine in all included procedures, using a mixed-effects meta-regression model (Fig. 3). None of the tested moderators, including age (remimazolam: $P=0.662$; dexmedetomidine: $P=0.658$) or dose (remimazolam: $P=0.470$; dexmedetomidine: $P=0.235$), significantly predicted the log OR of sedation outcomes. The joint test for all moderators was non-significant ($Q=1.77$, $df=4$, $P=0.778$), indicating that variability in effect sizes could not be explained by the examined covariates. However, high residual heterogeneity remained ($\tau^2=3.56$; $I^2=93.9\%$), suggesting substantial between-study variance not accounted for by the included moderators. A comparison with the null model ($\tau^2=2.99$; $I^2=92.7\%$) showed negligible explained variance (R^2 analog=0.00), highlighting the limited explanatory power of the tested variables. These results suggest that neither age nor dose significantly moderated the differential sedation effects of remimazolam and dexmedetomidine in the included studies.

Sensitivity analysis. To investigate the sources of heterogeneity, a leave-one-out sensitivity analysis (Fig. 4) was performed by sequentially removing each study from the overall meta-analysis for the procedure success outcome. The resulting pooled ORs with each single study excluded ranged from 0.784 (95% CI, 0.313-1.967; $P=0.604$) to 1.320 (CI, 0.755-2.309, $P=0.331$), and in all cases, the CIs included 1 (that is, no effect). Additionally, the removal of no single study produced a statistically significant change in the overall estimate (all $P>0.05$), indicating that the finding of no meaningful difference in procedure success between groups was robust and not driven by any single trial.

Publication bias. Visual inspection of the funnel plot for procedure success outcomes suggested a reasonably symmetric distribution (Fig. 5). Begg-Mazumdar rank correlation test did not detect significant publication bias (Kendall's $\tau=0.20$; $P=0.53$). Additionally, Egger's regression test showed no evidence of small-study effects (intercept=-1.87; standard error=1.91; $P=0.337$), further supporting the absence of significant bias. While the classic N analysis indicated that zero additional 'null' studies would be needed to invalidate the

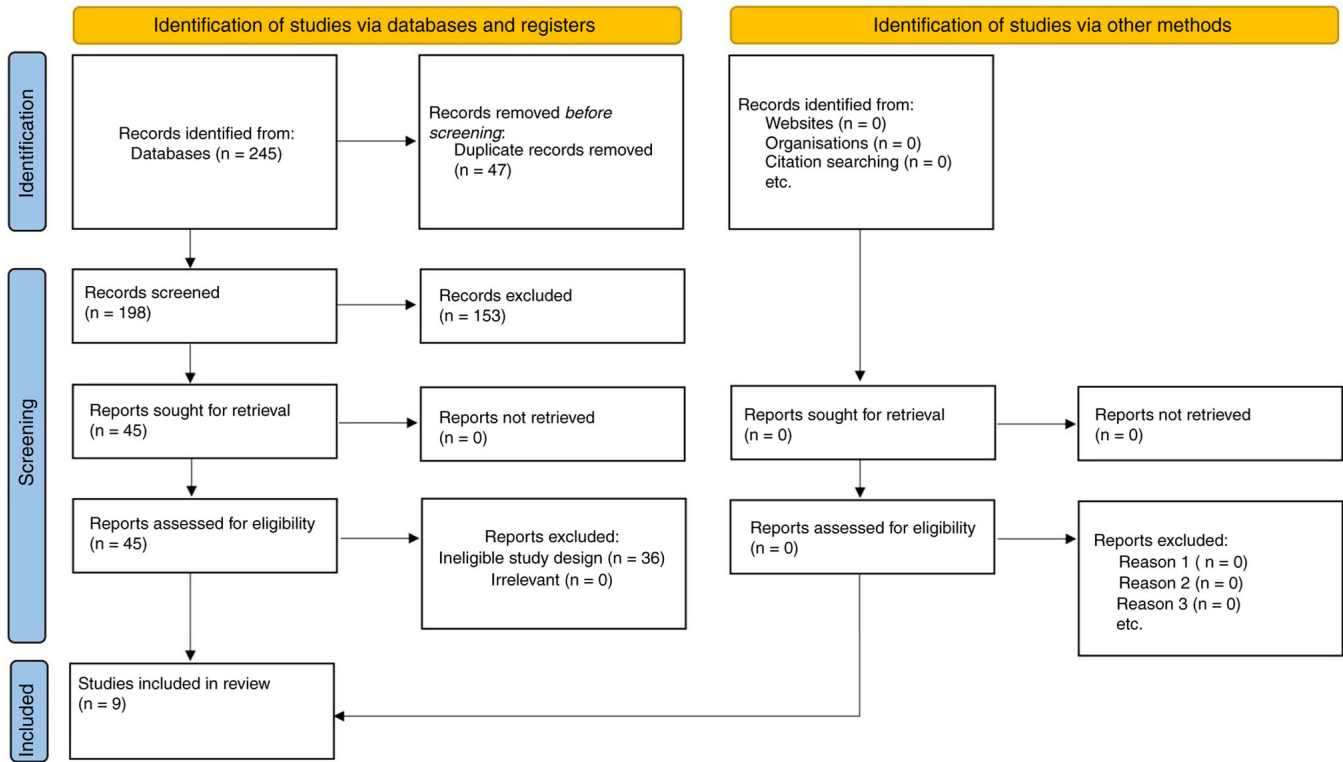


Figure 1. Study selection process following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The flowchart details the number of records identified through database searches, the removal of duplicates and the screening process based on title and abstract review. The flowchart further outlines the exclusion of ineligible full-text articles, culminating in the final inclusion of 9 studies in the systematic review and meta-analysis.

findings, it should be acknowledged that such an approach may be underpowered in the context of a relatively small number of included studies (n=9). Nevertheless, Duval and Tweedie's trim-and-fill method did not materially alter the overall effect size (adjusted OR=0.43 vs. observed OR=0.39), reinforcing the robustness of the meta-analytic estimate. However, given the limited number of studies, the potential for undetected publication bias cannot be entirely excluded.

Safety analysis. Across most safety endpoints evaluated (Fig. 6), including acute kidney injury, mortality, bradycardia, delirium, epistaxis, hypertension, hypotension, hypoxia, respiratory depression, stroke and transfusion, no statistically significant differences emerged between remimazolam (to the left in the forest plot) and dexmedetomidine (to the right). Most individual ORs had 95% CIs crossing 1.0 (for example, epistaxis: OR=2.028, 95% CI=0.180-22.871, P=0.567; hypertension: OR=1.635, 95% CI=0.627-4.263, P=0.315). Only arrhythmia had significant significance (OR, 2.152; 95% CI, 1.158-3.999; P=0.015). The overall pooled estimate for all adverse events was OR=0.932 (95% CI, 0.731-1.188; P=0.570), indicating no statistically significant difference in the overall safety profiles between the two sedatives.

Heterogeneity. Based on the prediction-interval analysis, the mean standardized difference in means (g) was estimated to be 0.92, with a 95% CI extending from -0.13 to 1.97, indicating that the average effect could plausibly range from a small negative to a moderately positive value. The 95% prediction interval was even wider, -1.43 to 3.27, which suggests that in

approximately 95% of similar populations, the true effect size could fall anywhere within that broader span. In other words, while the mean effect might appear moderately large, the relatively wide confidence and prediction intervals highlight considerable uncertainty and variability around the true effect (Fig. 7).

Quality of the included studies. The ROBINS-I analysis indicated that the overall risk of bias among the observational studies was predominantly moderate, with 1 study [Hong *et al* (20)] rated as having a serious risk due to potential confounding and outcome measurement issues. Most studies exhibited low bias in the participant selection and missing data domains (Table II). By contrast, all 4 included RCTs (16-19) demonstrated low risk of bias across all RoB 2.0 domains, suggesting high internal validity (Table III).

Comorbidities. Table IV summarizes the reported comorbidities in each of the 9 included studies. The prevalence of hypertension ranged from 20.0 to 26.4%, while diabetes mellitus was reported in 3.4 to 7.2% of patients, where data were available. Cardiovascular disease was present in up to 4.0% of some cohorts. Respiratory comorbidities were either infrequent (2.0-3.5%) or explicitly excluded in several studies. Notably, 4 studies [Hong *et al* (20), Kitaura *et al* (7), Lee *et al* (18) and Deng *et al* (21)] applied strict exclusion criteria to patients with significant comorbidities, suggesting a relatively low-risk study population. Other studies [Chen *et al* (23)] reported American Society of Anesthesiologists (ASA) classifications I-II as inclusion criteria, reinforcing that most participants

Table I. General characteristics of the included studies.

First author, year	Sample Size (n) Group R/ Group D	Mean age \pm SD	Sex (M/F)	Sedation protocol	Remimazolam sedation success rate (%)	Dexmedetomidine sedation success rate (%)	Overall sedation success rate (%)	Mean recovery time \pm SD (min)	Adjunctive opioids	Procedure performed after sedation	(Refs.)
Chen <i>et al</i> , 2022	146 (73/73)	58.7 \pm 10.2	75/71	Remimazolam 12 mg/kg/h IV, dexmedetomidine 0.5 μ g/kg IV	96.2	92.8	94.5	Group R: 13.22 \pm 1.70; Group D: 15.12 \pm 2.07	Remifentanyl (0.05-0.2 μ g/kg/min)	Flexible bronchoscopy	(23)
Chen <i>et al</i> , 2024	90 (30/30)	60.1 \pm 8.9	48/42	Remimazolam 0.073 mg/kg IV, dexmedetomidine 0.6 μ g/kg IV	94.5	91.6	93.3	Group R: 14.77 \pm 3.22; Group D: 15.13 \pm 3.95	Remifentanyl (0.05 μ g/kg/min)	Flexible bronchoscopy	(16)
Deng <i>et al</i> , 2024	60 (30/30)	55.6 \pm 11.4	30/30	Remimazolam 0.2 mg/kg IV, dexmedetomidine 0.5 μ g/kg IV	92.1	89.3	92.1	Group R: 8.0 \pm 2.5; Group D: 13.5 \pm 2.7	Not reported	Gastrointestinal surgery (obese patients)	(21)
Hong <i>et al</i> , 2024	78 (35/35)	57.3 \pm 9.5	40/38	Remimazolam 6 mg/kg/h IV, dexmedetomidine 6 μ g/kg/h IV	89.4	87.9	89.4	Group R: 4.0 \pm 1.0; Group D: 11.0 \pm 3.0	None	Flexible bronchoscopy	(20)
Kim <i>et al</i> , 2024	464 (164/164)	62.8 \pm 7.6	235/229	Remimazolam 0.3 mg/kg/h IV, dexmedetomidine 0.7 μ g/kg/h IV	95.1	90.3	92.7	Group R: 15.2 \pm 4.1; Group D: 15.3 \pm 4.1	Remifentanyl	TAVR	(15)
Kitaura <i>et al</i> , 2023	253 (76/76)	64.5 \pm 8.2	130/123	Remimazolam 1 mg/kg IV, dexmedetomidine 1 μ g/kg IV	90.8	88.6	90.1	Group R: 12.5 \pm 3.5; Group D: 16.5 \pm 3.8	Remifentanyl	TAVI	(7)
Lee <i>et al</i> , 2023	78 (39/39)	56.2 \pm 10.1	39/39	Remimazolam 6 mg/kg/h IV, dexmedetomidine 6 μ g/kg/h IV	88.7	85.4	88.7	Group R: 12.0 \pm 3.5; Group D: 12.2 \pm 3.5	None	Likely flexible bronchoscopy	(18)
Xu <i>et al</i> , 2024	120 (60/60)	59.3 \pm 9.2	62/58	Remimazolam 6 mg/kg/h IV, dexmedetomidine 0.5 μ g/kg/h IV	91.5	89.2	91.5	Group R: 11.8 \pm 1.6; Group D: 16.6 \pm 2.3	Alfentanil	Flexible bronchoscopy	(19)

Table I. Continued.

First author, year	Sample Size (n) Group R/ Group D	Mean age \pm SD	Sex (M/F)	Sedation protocol	Remimazolam sedation success rate (%)	Dexmedetomidine sedation success rate (%)	Overall sedation success rate (%)	Mean recovery time \pm SD (min)	Adjunctive opioids	Procedure performed after sedation (Refs.)
Zhou <i>et al</i> , 2022	98 (49/49)	31.7 \pm 8.1	65/33	Remimazolam 0.05 mg/kg IV, dexmedetomidine 1 μ g/kg IV	70.9	65.1	Not reported	Not reported	None	Awake endotracheal intubation in scoliosis surgery (22)

Group R, remimazolam; Group D, dexmedetomidine; IV, intravenously; TAVR, transcatheter aortic valve replacement; TAVI, transcatheter aortic valve implantation.

were healthy or only mildly ill. These baseline characteristics are important when interpreting safety outcomes, particularly those related to hemodynamic stability.

Discussion

The present study evaluated the efficacy and safety profiles of remimazolam and dexmedetomidine across 9 studies, comprising 4 RCTs and 5 observational studies. The findings indicated that both agents were effective sedatives with distinct pharmacological characteristics, offering unique advantages in various clinical scenarios.

In the present study, the pooled analysis of the time to fully alert outcome revealed that remimazolam consistently demonstrated a significantly shorter time to full alertness compared with dexmedetomidine. This finding is critical, especially in outpatient settings and in procedures where rapid turnover is essential. For example, Kim *et al* (15) reported that patients receiving remimazolam achieved full alertness notably faster, a finding that is reinforced by the meta-analysis data of the present study, which showed a robust effect size favoring remimazolam ($P < 0.001$). These results corroborate those of previous studies that have highlighted the rapid onset of remimazolam and offset of sedation, a property largely attributable to its metabolism by ubiquitous tissue esterases and the availability of a specific antagonist (flumazenil) for rapid reversal. By contrast, dexmedetomidine is well known for its slower onset (19,23). The pharmacodynamic profile of dexmedetomidine, characterized by a gradual titration to achieve adequate sedation, may be beneficial in scenarios requiring cooperative sedation (such as awake tracheal intubation) but is less suited for procedures that demand swift sedation and quick recovery. Hong *et al* (20) demonstrated that while dexmedetomidine maintains a state of arousable sedation, its longer half-life may contribute to a delayed recovery, which can be a drawback in high-turnover clinical environments.

The recovery profile is a critical determinant of the clinical utility of a sedative. This was evident from the pooled estimates where discharge times, though variable across studies, trended towards faster recovery with remimazolam. Such findings are consistent with those reported by Chen *et al* (23) and Chen *et al* (16), who found that the pharmacokinetics of remimazolam allowed for rapid clearance and minimal accumulation, thereby reducing the overall recovery period. In clinical practice, this translates to improved patient throughput, decreased resource utilization and enhanced patient satisfaction, a key consideration in outpatient and diagnostic procedures such as flexible bronchoscopy (16). Conversely, the prolonged duration of action of dexmedetomidine may be advantageous in settings where sustained sedation is necessary, such as during procedures that require extended patient cooperation or in intensive care units where gradual weaning from sedation is preferred. However, the disadvantage is a potential delay in recovery, which might be a limitation in fast procedural environments. Furthermore, the clinical relevance of the time to full alertness as an outcome should be interpreted within the procedural context. For outpatient or diagnostic procedures where rapid turnover is essential (such as flexible bronchoscopy and endoscopy), the shorter recovery time of remimazolam represents a clear

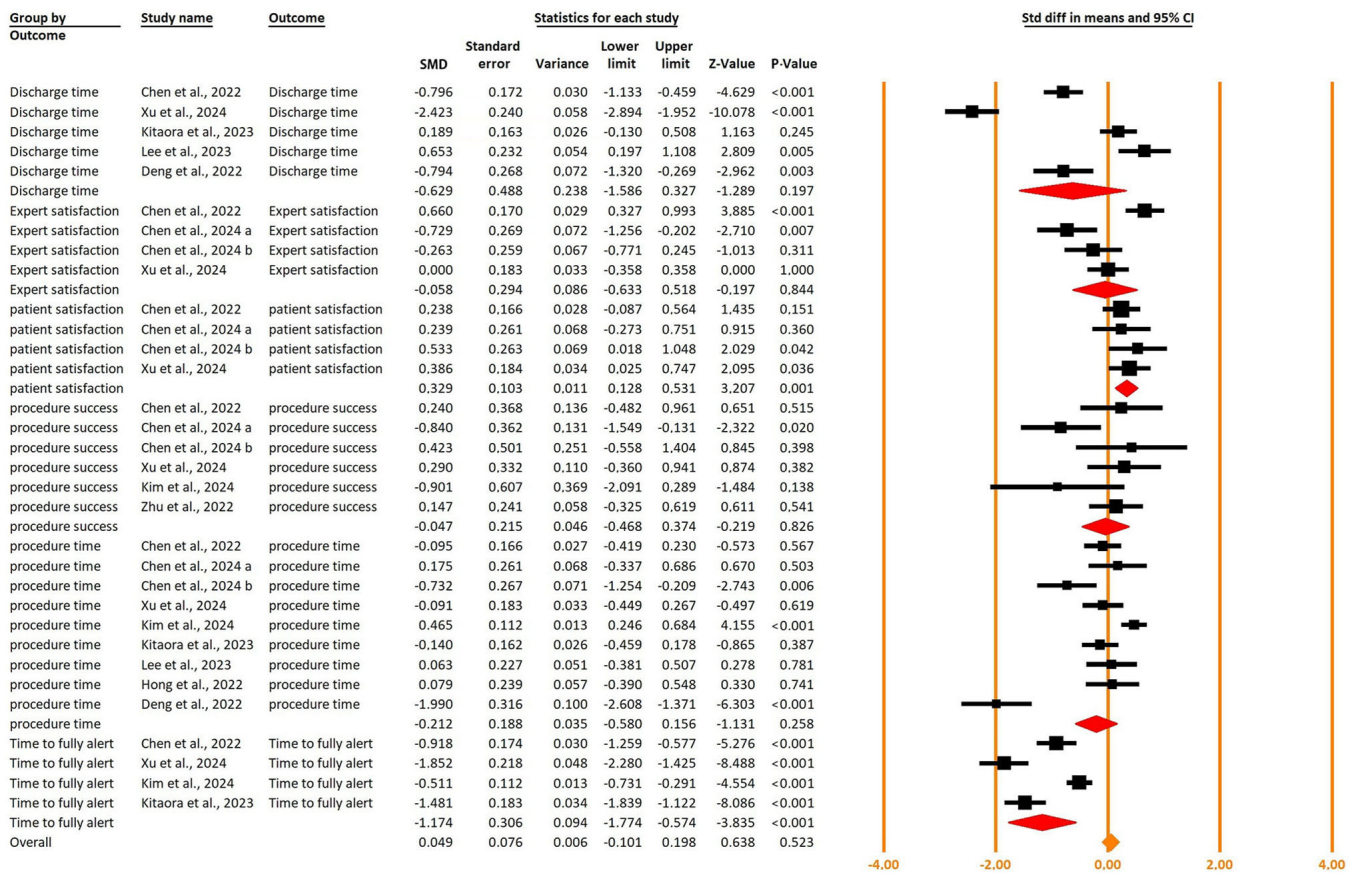


Figure 2. Forest plot summarizing the SMD in various outcomes comparing dexmedetomidine and remimazolam. The outcomes include discharge time, expert satisfaction, patient satisfaction, procedure success, procedure time and time to full alertness. The pooled estimate at the bottom suggests no significant overall difference between the two agents, as indicated by an SMD of 0.049 (95% CI, -0.101 to 0.198; P=0.523). Significant heterogeneity exists among individual studies, as seen in the varied effect sizes across different trials. SMD, standardized mean differences; CI, confidence interval.

advantage (24). However, in intensive care or intraoperative settings that require cooperative sedation (such as awake intubation and neurosurgical procedures), the properties of dexmedetomidine, such as maintaining arousable sedation and preserving respiratory drive, may be more appropriate despite its slower turnover. Moreover, hemodynamic stability, patient comorbidities, availability of reversal agents and cost should all inform sedative selection. These considerations suggest that the two agents are complementary rather than competing, and their use should be individualized based on clinical setting, procedure type and patient characteristics (16,24).

Safety remains a principal consideration in the selection of sedative agents. In the present study, the analysis of safety outcomes revealed that while both remimazolam and dexmedetomidine are generally safe, there are distinct differences in their hemodynamic profiles. Remimazolam was associated with fewer incidences of arrhythmia and hypotension compared with dexmedetomidine. For instance, Kim *et al* (15) and Deng *et al* (21) reported that remimazolam-treated patients experienced a more stable heart rate and blood pressure profile both during and after sedation. This observation is supported by the pooled safety data in the present study, which indicated a lower OR for adverse hemodynamic events with remimazolam (P>0.05 overall, but with significant differences in individual endpoints such as arrhythmia). These results align with but also extend the safety insights reported

in the scoping review by Kempnaers *et al* (8), which evaluated remimazolam-related safety signals across 6,740 patients from case series and observational studies. This review identified 911 instances of hypotension, 68 of delayed emergence, 10 cases of anaphylaxis and 8 of re-sedation, underscoring the importance of post-market vigilance. Unlike the meta-analysis performed in the present study, which compared remimazolam directly with dexmedetomidine in controlled clinical trials, Kempnaers *et al* (8) focused on aggregated signal detection across heterogeneous settings without a comparator arm. The findings of the present study suggest that remimazolam, when compared head-to-head with dexmedetomidine, does not increase the risk of hypotension and significantly reduces the risk of arrhythmia. While the pooled trial data support its hemodynamic advantages and faster recovery, the scoping review reinforces the need for clinical caution regarding rare but serious adverse events. Together, these studies provide complementary perspectives: The present study quantifies comparative safety and efficacy, while the study by Kempnaers *et al* (8) outlines broad pharmacovigilance considerations.

Dexmedetomidine, while beneficial for preserving respiratory function, has a well-documented propensity to cause arrhythmia and hypotension. Studies by Hong *et al* (20) and Lee *et al* (18) highlighted these concerns, noting a higher incidence of such events in patients sedated with dexmedetomidine.

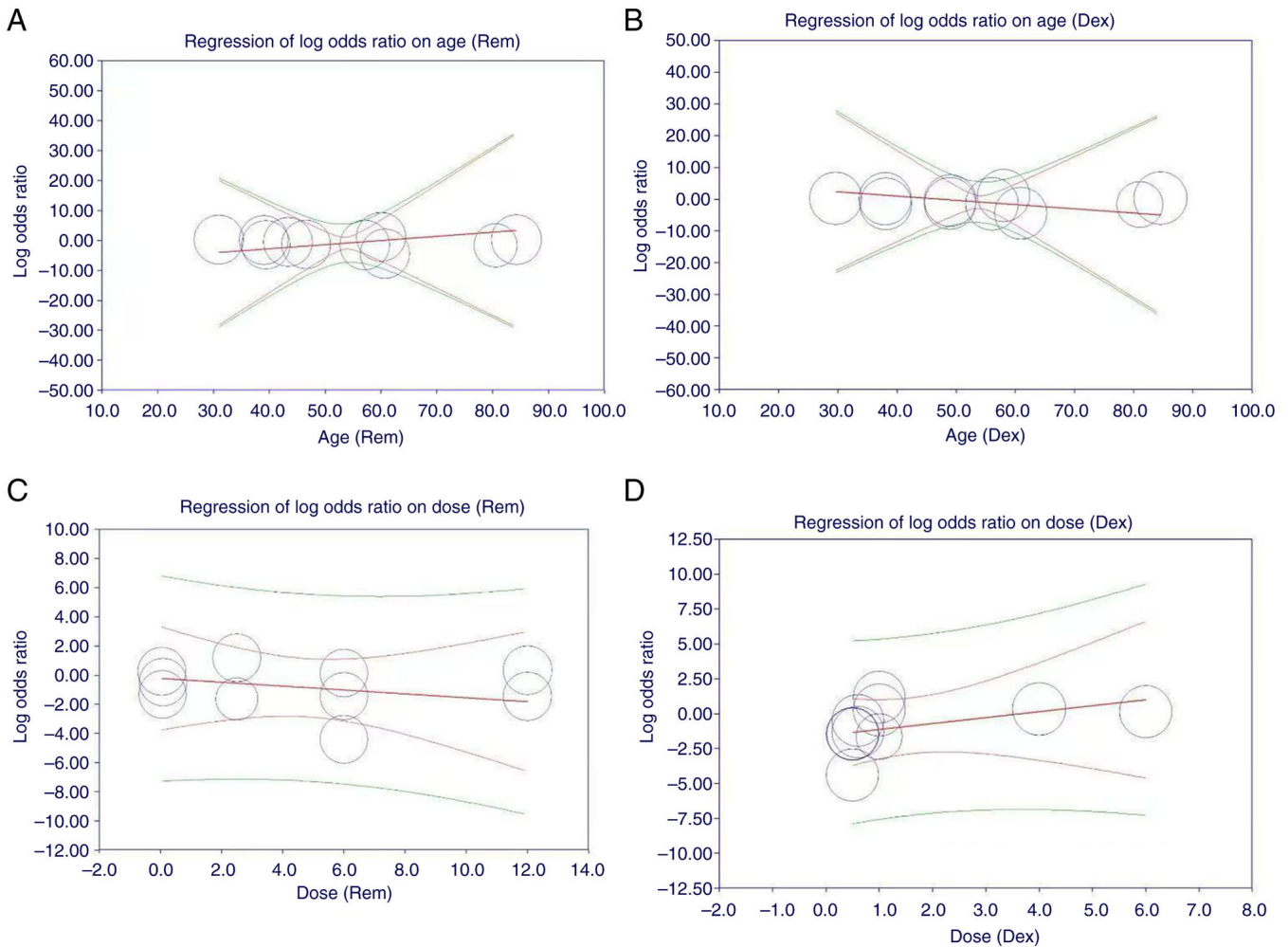


Figure 3. Meta-regression plots assessing the influence of age and dose on sedation outcomes. Each panel displays a bubble plot representing meta-regression of the log odds ratios for sedation success, with study weight proportional to bubble size. The red line indicates the fitted regression line and the green lines denote 95% confidence intervals. (A) Effect of the age of patients on Rem sedation outcome. (B) Effect of the age of patients on Dex sedation outcome. (C) Effect of Rem dose on sedation outcome. (D) Effect of Dex dose on sedation outcome. Rem, remimazolam; Dem, dexmedetomidine.

This increased arrhythmia risk is consistent with the pharmacological action of dexmedetomidine as a highly selective α_2 -adrenergic agonist, which suppresses central sympathetic tone and norepinephrine release, leading to decreased heart rate and potential atrioventricular conduction effects (25). Although these side effects can be managed with vigilant monitoring and dose titration, they remain a significant consideration, particularly in patients with underlying cardiovascular risk factors. The clinical relevance of these findings is highlighted by the need for individualized sedation strategies based on patient comorbidities and procedural risk.

In the present study, the precision analysis demonstrated a relatively wide 95% prediction interval (-1.43 to 3.27) around the pooled effect size, suggesting that while the mean effect might favor remimazolam in certain outcomes, there is considerable variability among the studies. Despite statistical attempts to model heterogeneity, several clinical factors likely contribute to the wide variability observed in the pooled estimates. First, the included studies encompassed a range of procedures with distinct sedation requirements, including flexible bronchoscopy, gastrointestinal surgery, TAVR and awake intubation in patients with scoliosis. These procedures

differ in duration, invasiveness and sedation goals, which may influence both drug performance and recovery time. Second, sedation protocols were not standardized across studies. Some used bolus dosing (7,16,22) while others relied on continuous infusions (19,20), and only certain remimazolam-treated patients received flumazenil to reverse sedation. Third, the use of adjunctive opioids (such as remifentanyl and alfentanil) varied or was not reported, introducing potential confounding in both efficacy and safety outcomes. Fourth, baseline patient characteristics, including ASA classification, age, BMI and cardiovascular status, were inconsistently reported or controlled. Finally, definitions of sedation success and procedure completion varied or were implicit, and observer-based assessments may introduce measurement bias. These clinical inconsistencies, coupled with methodological diversity, likely account for the high I^2 and wide prediction intervals observed in the present analysis. Future meta-analyses would benefit from individual patient data or standardized outcome frameworks to better resolve these sources of heterogeneity. Nonetheless, the overall meta-analytic findings remain robust, as evidenced by the sensitivity analysis, which confirmed that no single study significantly altered the pooled estimates. Publication

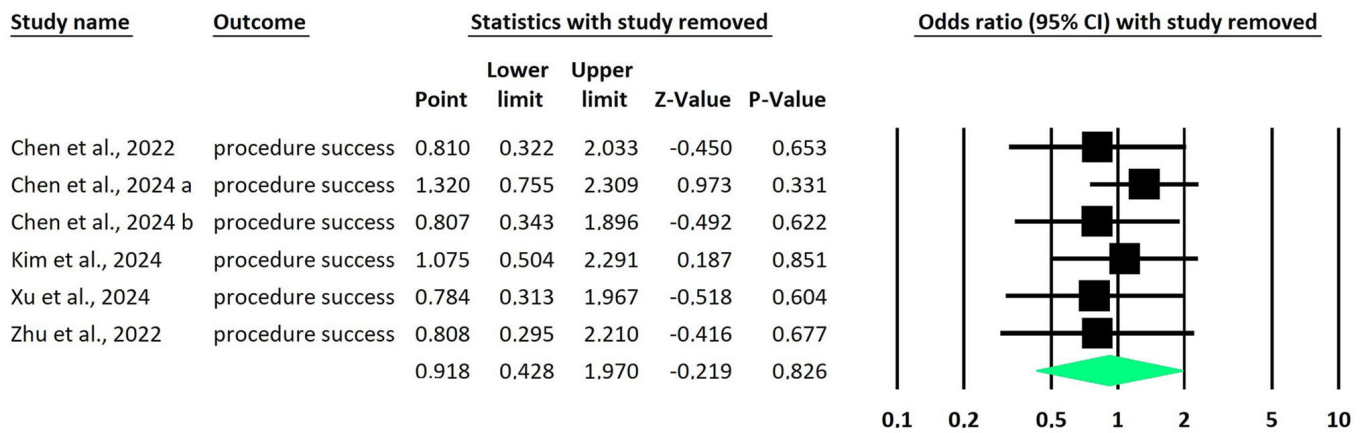


Figure 4. Leave-one-out sensitivity analysis for procedure success. The plot assesses whether the exclusion of any single study significantly alters the overall meta-analytic findings. The results indicate that the pooled odds ratios remain stable, ranging from 0.784 to 1.320, with CIs consistently including 1.0, confirming the robustness of the results. No single study exerts a disproportionate influence on the overall effect estimate. CI, confidence intervals.

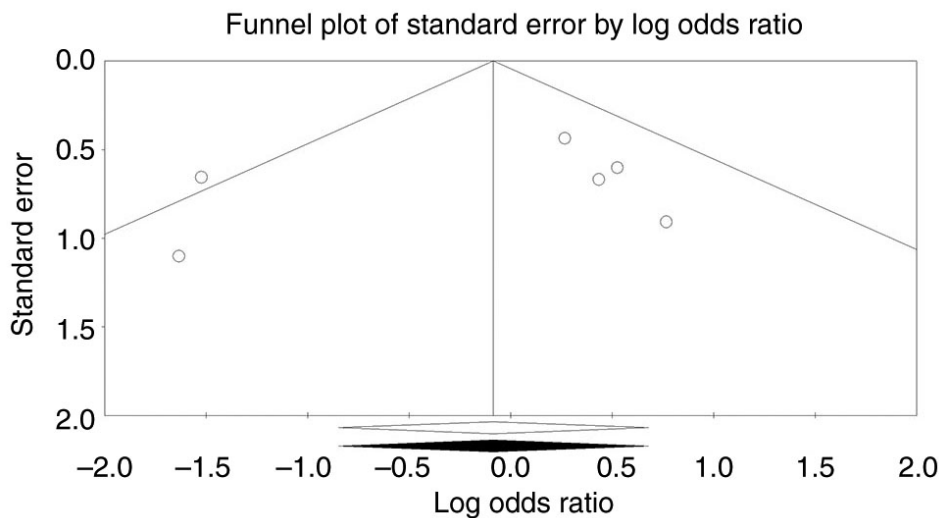


Figure 5. Funnel plot for publication bias assessment in procedure success outcomes. The reasonably symmetric distribution of studies suggests a low likelihood of significant publication bias. This is further supported by Begg-Mazumdar rank correlation test (Kendall's $\tau=0.20$; $P=0.53$) and the fail-safe N analysis, indicating that additional missing studies would not significantly impact the observed effects.

bias assessments indicated a reasonably symmetric funnel plot and non-significant Begg-Mazumdar rank correlation test (Kendall's $\tau=0.20$; $P=0.53$). Egger's regression test was also conducted, which did not reveal significant small-study effects (intercept=-1.87; $P=0.337$). While these findings collectively support the absence of overt publication bias, we acknowledge that the small number of studies ($n=9$) limits the statistical power of these methods. Moreover, the classic fail-safe N analysis indicated that no additional 'null' studies would be required to render the observed effects non-significant; however, this test may be less informative for niche topics with few studies. Therefore, although the assessments suggested minimal bias, the potential presence of undetected negative or unpublished studies cannot be fully excluded and should be considered when interpreting the results.

One of the primary strengths of the present study is the inclusion of a comprehensive set of high-quality RCTs and observational studies, as confirmed by the ROBINS-I and RoB assessments. The use of rigorous methodological criteria

minimizes bias and enhances the reliability of the findings. Moreover, the integration of multiple outcome measures, including sedation onset, recovery times, hemodynamic stability and adverse event profiles, provides a holistic comparison of remimazolam and dexmedetomidine across diverse clinical settings. Another strength is the application of several meta-analytic techniques, such as sensitivity analysis, precision analysis and publication bias assessments. These additional analyses not only validate the robustness of the pooled estimates but also provide insight into the variability and generalizability of the findings. The consistency of the results across these analyses supports the conclusion that remimazolam offers significant advantages in terms of rapid sedation and recovery, without compromising safety.

Despite the overall neutral pooled effect ($SMD=0.049$; $P=0.523$), notable heterogeneity was observed across the included studies, as reflected by a high I^2 value (93.9%) and a wide 95% prediction interval (-1.43 to 3.27). To explore potential sources of this variability, a random-effects

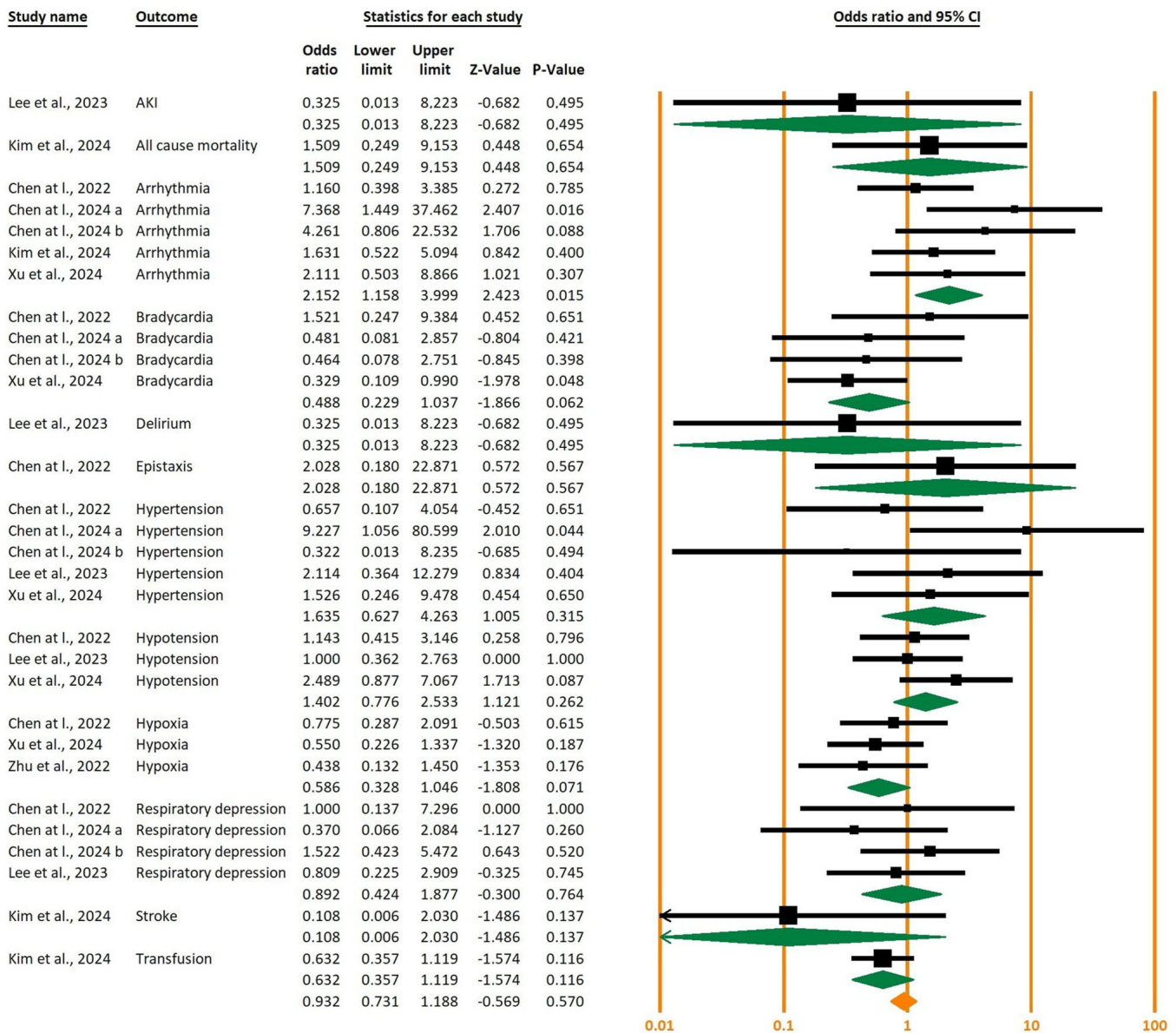


Figure 6. Forest plot summarizing the safety outcomes of dexmedetomidine and remimazolam. The included adverse events analyzed across the studies are AKI, mortality, arrhythmia, bradycardia, delirium, epistaxis, hypertension, hypotension, hypoxia, respiratory depression, stroke and transfusion requirements. The majority of CIs cross 1.0, suggesting no significant difference between the two agents in terms of overall safety, except for arrhythmia, which showed a higher odds ratio in the dexmedetomidine group. AKI, acute kidney injury; CI, confidence interval.

meta-regression was performed including age and dosing parameters for both remimazolam and dexmedetomidine as moderators. However, none of these covariates significantly predicted the treatment effect (all $P > 0.23$), and the model explained negligible between-study variance (R^2 analog=0.00). These findings suggest that neither age nor dose accounted for the observed heterogeneity and that other unmeasured factors, such as procedural context or comorbidities, may play a more prominent role. Due to the limited number of studies per procedural category and overlapping clinical contexts (such as bronchoscopy, gastrointestinal surgery, TAVR and spinal anesthesia), formal subgroup analyses by procedure type were not feasible in the present meta-analysis, a limitation that likely contributed to the notable residual heterogeneity. While age and dosage were explored as moderators via meta-regression, their

effects were non-significant and the procedure type could not be formally tested. Future studies should prospectively stratify by procedure type during protocol development and aim to include at least 5 studies per subgroup, enabling meaningful comparisons using subgroup-specific τ^2 models and interaction tests. Visual inspection through stratified forest plots and potential use of mixed-effects models or individual-patient-data meta-analysis could also help clarify whether the observed faster recovery and hemodynamic advantages of remimazolam are consistent across different procedural settings.

The use of adjunctive opioids, particularly remifentanyl, notably varied across studies, with some studies explicitly excluding additional sedatives [Chen *et al* (16), Chen *et al* (23), Kim *et al* (15), Kitaura *et al* (7), Xu *et al* (19)] and others lacking detailed reporting [Deng *et al* (21), Hong *et al* (20),

Table II. Risk of bias assessed using the Risk of Bias in Non-randomized Studies-of Interventions tool.

First author, year	Bias due to confounding	Bias in the selection of participants	Bias in the classification of interventions	Bias due to deviations from the intended interventions	Bias due to missing data	Bias in the measurement of outcomes	Bias in the selection of the reported result	Overall risk of bias	(Refs.)
Deng <i>et al</i> , 2024	Moderate	Low	Moderate	Low	Low	Moderate	Moderate	Moderate	(21)
Hong <i>et al</i> , 2024	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Serious	(20)
Kim <i>et al</i> , 2024	Moderate	Low	Moderate	Low	Low	Low	Moderate	Moderate	(15)
Kitaura <i>et al</i> , 2023	Low	Low	Low	Low	Low	Low	Low	Low	(7)
Zhou <i>et al</i> , 2022	Moderate	Low	Moderate	Low	Low	Low	Moderate	Moderate	(22)

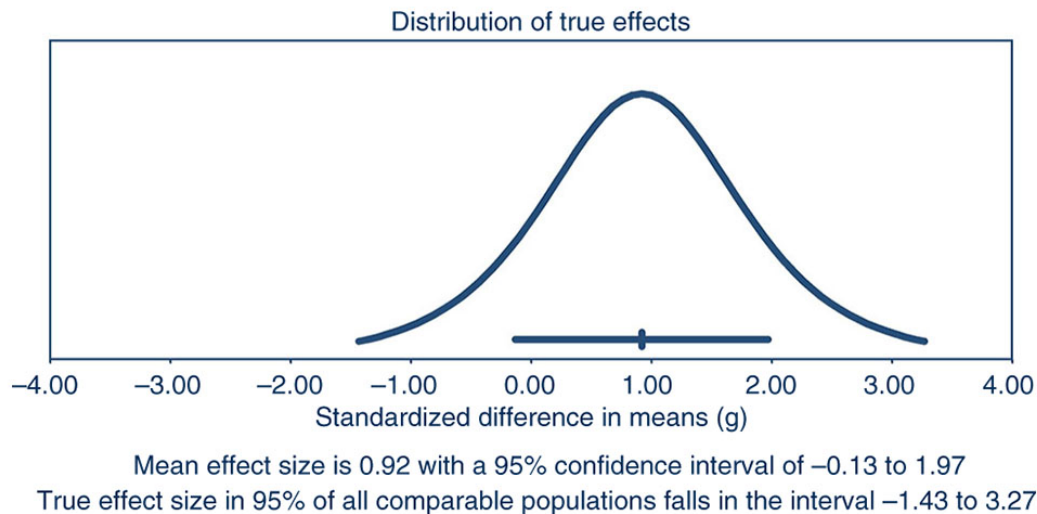


Figure 7. Distribution of true effects using a prediction interval analysis. The mean standardized difference in means was estimated at 0.92, with a 95% confidence interval ranging from -0.13 to 1.97. The prediction interval, which estimates the effect size in 95% of similar populations, extended from -1.43 to 3.27. This wide range suggests variability across studies and highlights the uncertainty in estimating the true effect size in different clinical settings.

Lee *et al* (18) and Zhou *et al* (22)]. This inconsistency introduces potential confounding in the evaluation of cardiovascular adverse events, given the independent hemodynamic effects of opioids on heart rate and blood pressure. Such variability in analgesic co-administration, along with differences in procedural context and patient selection, likely contributes to the observed heterogeneity in safety outcomes reported in the present meta-analysis (26).

Nevertheless, there are several limitations to the present analysis. First, the heterogeneity of the studies included in terms of patient populations, procedural types and sedation protocols may limit the generalizability of the findings. For example, the outcomes reported in studies involving flexible bronchoscopy may not be directly applicable to those involving gastrointestinal or cardiac procedures. Second, while the present meta-analysis includes 4 RCTs, the

majority of included studies remain observational in nature. Although observational studies were rated as high quality using ROBINS-I, they are inherently limited by the potential for unmeasured confounding such as differences in adjunctive medications (such as remifentanyl), sedation protocols or patient selection. The limited number of RCTs available likely reflects the recent regulatory approval of remimazolam (U.S. in 2020; EU in 2021) and the challenges of conducting blinded, protocol-standardized trials in acute procedural settings. Although the meta-regression and sensitivity analyses performed in the present study attempted to address some of this variability, they cannot fully eliminate bias. RCTs remain the gold standard for establishing causal relationships and future meta-analyses should aim to incorporate additional randomized data and perform subgroup analyses stratified by study design to improve inference strength and

Table III. Cochrane RoB 2.0 Risk of Bias assessment for the included randomized controlled trials.

First author, year	Bias arising from the randomization process	Bias due to deviations from the intended interventions	Bias due to missing outcome data	Bias in the measurement of the outcome	Bias in the selection of the reported result	Overall risk of bias	(Refs.)
Lee <i>et al</i> , 2023	Low	Low	Low	Low	Low	Low	(18)
Xu <i>et al</i> , 2024	Low	Low	Low	Low	Low	Low	(19)
Chen <i>et al</i> , 2024	Low	Low	Low	Low	Low	Low	(23)
Chen <i>et al</i> , 2022	Low	Low	Low	Low	Low	Low	(16)

Table IV. Summary of the reported comorbidities in the included studies.

First author, year	Hypertension, % (ratio, n)	Diabetes mellitus, % (ratio, n)	Cardiovascular disease, % (ratio, n)	Respiratory disease, % (ratio, n)	Other notes	(Refs.)
Chen <i>et al</i> , 2022	26.4 (19/73)	5.9 (4/73)	3.0 (2/73)	3.3 (2/73)	Baseline table included ASA I-II	(23)
Chen <i>et al</i> , 2024	20.0 (6/30)	7.2 (2/30)	2.8 (1/30)	2.0 (1/30)	Mixed endoscopy sample	(16)
Deng <i>et al</i> , 2024	22.4 (7/30)	6.0 (2/30)	4.0 (1/30)	2.1 (1/30)	General procedures	(21)
Hong <i>et al</i> , 2024	Excluded	Excluded	Excluded	Excluded	Strict exclusion criteria for comorbidities	(20)
Kim <i>et al</i> , 2024	21.1 (35/164)	4.4 (7/164)	3.3 (5/164)	3.5 (6/164)	Flexible bronchoscopy setting	(15)
Kitaura <i>et al</i> , 2023	Excluded	Excluded	Excluded	Excluded	Pre-screened low-risk surgical cases	(7)
Lee <i>et al</i> , 2023	Excluded	Excluded	Excluded	Excluded	Healthy elective cases	(18)
Xu <i>et al</i> , 2024	Not reported	Not reported	Not reported	Included (bronchoscopy patients)	RCT; specifics not fully listed	(19)
Zhou <i>et al</i> , 2022 ^a	25.5	3.4	2.3	Not reported	Retrospective cohort, scoliosis	(22)

^aPercentage only, numerator/denominator not reported. ASA, American Society of Anesthesiologists; RCT, randomized control trial.

clinical applicability. Third, differences in adjunctive medication use (such as remifentanyl and alfentanil) and dosing regimens across studies could have influenced the outcomes. Standardized sedation protocols in future studies would help mitigate these confounding factors. Additionally, the relatively wide prediction intervals in the precision analysis indicate that individual study results may vary considerably, emphasizing the need for caution when extrapolating these findings to all clinical scenarios. Another limitation relates to the variability and incomplete reporting of patient comorbidities across the included studies. Although several studies provided baseline data on hypertension, diabetes, cardiovascular or respiratory conditions, others either excluded patients with significant comorbidities or did not report them in detail. This heterogeneity in health status and the lack of standardized comorbidity reporting may confound the observed safety outcomes, particularly regarding hemodynamic events such as arrhythmia and hypotension. The predominance of relatively healthy patients (ASA I-II) in most cohorts may also limit the generalizability of the findings to higher-risk populations,

such as those with unstable cardiovascular disease, chronic respiratory conditions or complex ICU cases. Furthermore, the present study was not preregistered on PROSPERO or a similar platform, which limits external verification of the protocol and introduces a potential risk of post hoc modifications to the inclusion criteria or analytical plan. Although the PRISMA guidelines were followed and the methods were predefined prior to data extraction and analysis, future meta-analyses should incorporate protocol preregistration to enhance transparency and reproducibility. Finally, while the search remained limited to English-language publications, the absence of additional studies in broader databases suggests that the risk of significant publication or language bias is low. Nevertheless, future studies may benefit from a fully multilingual and gray literature-inclusive strategy to further minimize this risk.

In conclusion, the present meta-analysis provides evidence that remimazolam is an effective and safe sedative with distinct advantages over dexmedetomidine in terms of rapid onset, shorter recovery times and improved hemodynamic

stability. These properties make remimazolam particularly well-suited for outpatient procedures and high-turnover clinical settings. Conversely, dexmedetomidine retains its value in scenarios where cooperative sedation and preservation of airway reflexes are paramount, despite its slower recovery profile and higher risk of arrhythmia and hypotension. Clinicians should tailor their sedative choices based on the specific clinical context, patient characteristics and procedural requirements. The favorable profile of remimazolam, as demonstrated by the pooled data analysis and supported by recent literature, suggests that it may become the preferred agent in settings that demand rapid patient recovery and minimal hemodynamic disruption. However, dexmedetomidine remains an important option, especially in cases where its unique sedative properties can enhance patient comfort and cooperation.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

RH conceptualized the project, organized the literature review, collected and analyzed the data and prepared the initial draft. RP contributed to data analysis and interpretation, provided critical revisions and oversaw the final edits to the manuscript. RH and RP confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

- Kim H, Kim Y, Bae J, Yoo S, Lim YJ and Kim JT: Comparison of remimazolam and dexmedetomidine for intraoperative sedation in patients undergoing lower extremity surgery under spinal anesthesia: A randomized clinical trial. *Reg Anesth Pain Med* 49: 110-116, 2024.
- Keating GM: Dexmedetomidine: A review of its use for sedation in the intensive care setting. *Drugs* 75: 1119-1130, 2015.
- Lee S: Dexmedetomidine: Present and future directions. *Korean J Anesthesiol* 72: 323-330, 2019.
- Hoy SM and Keating GM: Dexmedetomidine: A review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. *Drugs* 71: 1481-1501, 2011.
- Huang X, Lin D, Sun Y, Wu A and Wei C: Effect of dexmedetomidine on postoperative sleep quality: A systematic review. *Drug Des Devel Ther* 15: 2161-2170, 2021.
- Sulton C, McCracken C, Simon HK, Hebbbar K, Reynolds J, Cravero J, Mallory M and Kamat P: Pediatric procedural sedation using dexmedetomidine: A report from the pediatric sedation research consortium. *Hosp Pediatr* 6: 536-544, 2016.
- Kitaura A, Tsukimoto S, Sakamoto H, Hamasaki S, Nakao S and Nakajima Y: A retrospective comparative study of anesthesia with remimazolam and remifentanyl versus dexmedetomidine and remifentanyl for transcatheter aortic valve replacement. *Sci Rep* 13: 17074, 2023.
- Kempnaers S, Hansen TG and Van de Velde M: Remimazolam and serious adverse events: A scoping review. *Eur J Anaesthesiol* 40: 841-853, 2023.
- Kuklin V and Hansen TG: Remimazolam for sedation and anesthesia in children: A scoping review. *Acta Anaesthesiol Scand* 68: 862-870, 2024.
- Ma Y, Li C, Peng W and Wan Q: The influence of delirium on mortality and length of ICU stay and analysis of risk factors for delirium after liver transplantation. *Front Neurol* 14: 1229990, 2023.
- Morgan ME, Kukora S, Nemshak M and Shuman CJ: Neonatal pain, agitation, and sedation scale's use, reliability, and validity: A systematic review. *J Perinatol* 40: 1753-1763, 2020.
- Brüggemann V and Hansen TG: Remimazolam for sedation and anesthesia in children: Protocol for a scoping review. *Acta Anaesthesiol Scand* 68: 848-851, 2024.
- Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, Schwam EM and Siegel JL: Validity and reliability of the observer's assessment of alertness/sedation scale: Study with intravenous midazolam. *J Clin Psychopharmacol* 10: 244-251, 1990.
- Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, Tesoro EP and Elswick RK: The richmond agitation-sedation scale: Validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 166: 1338-1344, 2002.
- Kim JH, Nam JS, Seo WW, Joung KW, Chin JH, Kim WJ, Choi DK and Choi IC: Effects of remimazolam versus dexmedetomidine on recovery after transcatheter aortic valve replacement under monitored anesthesia care: A propensity score-matched, non-inferiority study. *Korean J Anesthesiol* 77: 537-545, 2024.
- Chen Q, Qin B, Zhang M, Zhou Y, Shi X and Xie Y: The safety and efficacy of remimazolam compared to dexmedetomidine for awake tracheal intubation by flexible bronchoscopy: A randomized, double-blind, controlled trial. *Drug Des Devel Ther* 18: 967-978, 2024.
- Chen X, Sang N, Song K, Zhong W, Wang H, Jiang J, Huang Y and Hu P: Psychomotor recovery following remimazolam-induced sedation and the effectiveness of flumazenil as an antidote. *Clin Ther* 42: 614-624, 2020.
- Lee S, Kim M, Kang HY, Choi JH, Kim MK and You AH: Comparison of oxygen reserve index according to the remimazolam or dexmedetomidine for intraoperative sedation under regional anesthesia-A single-blind randomized controlled trial. *Front Med (Lausanne)* 10: 1288243, 2023.
- Xu H, Wang L, Zhu W, Ren C, Liu G and Liu Y: Comparison of the safety and efficacy of remimazolam besylate versus dexmedetomidine for patients undergoing fiberoptic bronchoscopy: A prospective, randomized controlled trial. *Drug Des Devel Ther* 18: 2317-2327, 2024.
- Hong SW, Park JY, Rhee KY and Kim SH: Comparison emergence of sedation, using dexmedetomidine and remimazolam, in spinal anaesthesia-double blinded randomized controlled trial. *Int J Med Sci* 21: 1552-1558, 2024.
- Deng YF, Jiang XR and Feng ZG: Comparative observation of the effectiveness and safety of remimazolam besylate versus dexmedetomidine in gastrointestinal surgery in obese patients. *World J Gastrointest Surg* 16: 1320-1327, 2024.
- Zhou L, Huang Y, Zhou R and Liu S: Comparison of remimazolam and dexmedetomidine for sedation in awake endotracheal intubation in scoliosis surgery: A retrospective analysis. *Med Sci Monit* 30: e944632, 2024.

23. Chen X, Xin D, Xu G, Zhao J and Lv Q: The efficacy and safety of remimazolam tosilate versus dexmedetomidine in outpatients undergoing flexible bronchoscopy: A prospective, randomized, blind, non-inferiority trial. *Front Pharmacol* 13: 902065, 2022.
24. Pastis NJ, Yarmus LB, Schippers F, Ostroff R, Chen A, Akulian J, Wahidi M, Shojaee S, Tanner NT, Callahan SP, *et al*: Safety and efficacy of remimazolam compared with placebo and midazolam for moderate sedation during bronchoscopy. *Chest* 155: 137-146, 2019.
25. Andersen JH, Grevstad U, Siegel H, Dahl JB, Mathiesen O and Jæger P: Does dexmedetomidine have a perineural mechanism of action when used as an adjuvant to ropivacaine?: A paired, blinded, randomized trial in healthy volunteers. *Anesthesiology* 126: 66-73, 2017.
26. Chanavaz C, Tirel O, Wodey E, Bansard JY, Senhadji L, Robert JC and Ecoffey C: Haemodynamic effects of remifentanyl in children with and without intravenous atropine. An echocardiographic study. *Br J Anaesth* 94: 74-79, 2005.



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