BMC Anesthesiology

SYSTEMATIC REVIEW

Open Access

The safety and efficacy of remimazolam, ciprofol, and propofol anesthesia in endoscopy: a systematic review and network meta-analysis

Siqi Zhou[1†], Shangchen Yu[1†], Yuan Bi[1], Zhang Tian[1], Ruochen Pan[1], Tianqing Yan[1], Jianbo Deng[1] and Aijun Xu[1*]

Abstract

Background While propofol remains widely used for endoscopic sedation, its cardiovascular depression and injection pain limitations have prompted exploration of novel agents (remimazolam, ciprofol). This study aimed to compare their safety and efficacy profiles systematically.

Methods We conducted a network meta-analysis to evaluate remimazolam, ciprofol, and propofol for gastrointestinal endoscopy. Bayesian random-effects models were used to estimate relative risks (RR) and mean differences (MD) with 95% credible intervals(CrI).

Results Forty-two randomized controlled trials ($N = 10,540$ patients) were included. Remimazolam demonstrated superior cardiovascular safety (RR = 0.44, 95%CrI 0.35–0.54 vs propofol) and lowest respiratory depression risk (RR = 0.36, 0.28–0.46). Propofol showed faster recovery (MD -14.22 min, -2.35 to -30.83 vs remimazolam). Both remimazolam (RR = 0.045) and ciprofol (RR = 0.054) significantly reduced injection pain versus propofol.

Conclusion Remimazolam should be prioritized for high-risk patients (cardiovascular/respiratory comorbidities) despite slightly longer recovery times. Propofol remains suitable for low-risk procedures requiring rapid turnover, while ciprofol offers balanced efficacy for endoscopy.

Trial Registration The study was registered with the UK National Institute for Health Research's PROSPERO platform (CRD42024569405;https://www.crd.york.ac.uk/prospero/).

Keywords Anesthesia, Endoscopy, Propofol, Ciprofol, Remimazolam, Sedation

Introduction

Endoscopic procedures typically encompass non-invasive techniques such as gastrointestinal endoscopy, bronchoscopy, and hysteroscopy, among others [1]. The current standard practice involves performing endoscopic surgery with sedation [2]. Sedation is crucial for both patient comfort and the success of endoscopic procedures. This procedure is essential as patients undergoing endoscopy may experience anxiety, pain, fear, and gastrointestinal discomfort, which can reduce their cooperation and increase the risk of negative cardiovascular events. [3]. For procedural sedation and analgesia (PSA),

†Siqi Zhou and Shangchen Yu contributed equally to this work and share first authorship.

*Correspondence:
Aijun Xu
ajxu@tjh.tjmu.edu.cn
[1] Department of Anesthesiology, Hubei Key Laboratory of Geriatric Anaesthesiaand, Perioperative Brain Health, and Wuhan Clinical Research Center for Geriatric Anaesthesia, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

sedative agents need to strike a balance between providing enough sedation and maintaining hemodynamic stability, while also minimizing negative effects [4].

While sedation improves endoscopy and overall patient satisfaction, it poses a risk to patient safety if sedative medications are used inappropriately [5]. Among the various agents available, propofol has emerged as a popular choice due to its unique pharmacological profiles and sedative properties for sedation during endoscopic procedures [6]. As a long-standing sedative, propofol is renowned for its rapid induction and emergence characteristics [7, 8]. While effective, its use is associated with some limitations, such as cardiovascular depression and pain injection [9, 10].

Remimazolam is an ultra-short-acting benzodiazepine that has been noted for its rapid onset and offset of action, making it a contender for procedures requiring short-term sedation [11–13]. Its unique metabolism, largely through tissue esterases, allows for a predictable recovery profile, which can enhance patient satisfaction and operational efficiency in clinical settings. Ciprofol, a novel sedative agent developed with a pharmacokinetic profile tailored for short outpatient procedures, has gained attention for its potential to provide effective sedation with a reduced incidence of respiratory depression compared to traditional sedatives [14, 15]. Preliminary studies suggest that ciprofol may share some advantages over established agents in terms of safety and recovery time, although comprehensive evaluations are still needed [16]. Despite an increasing number of randomized controlled trials (RCTs) comparing these anesthetics, there remains a lack of consensus on the optimal choice for endoscopic procedures. Previous systematic reviews have primarily focused on direct comparisons between two agents [17, 18], leaving a gap in our understanding of the relative safety and efficacy of remimazolam, ciprofol, and propofol anesthesia in endoscopy. Given their widespread application, it is imperative to continually evaluate the effectiveness of remimazolam and ciprofol in comparison to propofol.

This systematic review and network meta-analysis aims to synthesize the existing literature and provide a comprehensive comparison of remimazolam, ciprofol, and propofol regarding their safety and efficacy in endoscopic procedures.

Methods

Data sources and strategy

This network meta-analysis evaluated the effectiveness and safety of three drugs, including ciprofol, propofol, and remimazolam. The study was conducted by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [19]. The study was registered with the UK National Institute for Health Research's PROSPERO platform (Date: 15 Jul 2024, CRD42024569405; https://www.crd.york.ac.uk/prospero/). No external funding was provided for this study.

A systematic search of the PubMed, Embase, and Web of Science databases was conducted up to December 11, 2024. To ensure the inclusion of as many relevant studies as possible, a combination of free and subject terms was used, including Ciprofol, Propofol, and Remimazolam. The search terms included Ciprofol, Propofol, Remimazolam, and endoscopy. The search strategy was adapted to the characteristics of each database (Supplementary Appendix 1).

Study selection

Titles and abstracts were independently screened by two researchers, with final inclusion determined at their discretion. Disagreements regarding the full text were resolved through discussion and consensus. If consensus could not be reached, advice was sought from independent experts. No language restrictions were applied for the inclusion of studies (Table S1).

Inclusion criteria

The study aimed to compare the effects of propofol, ciprofol, and remimazolam in pairs during endoscopic surgery. The RCTs included were required to have at least one outcome of interest. Only adults (age >18 years) were included.

Exclusion criteria

RCTs were excluded according to the following criteria: 1) studies comparing combinations of any two of propofol, ciprofol, and remimazolam with other drugs; 2) projects that had not yet begun; 3) studies that did not involve endoscopic surgery; and 4) studies that did not assess the safety and efficacy of the three drugs.

Outcomes

Primary outcomes were respiratory/cardiovascular adverse events. Additional outcomes were as follows: induction success rate, drug-related adverse effects(injection pain, postoperative nausea and vomiting), and patient anesthesia satisfaction time to induction, time to full consciousness. For the definitions of the above indicators, please refer to Supplementary Files.

Data extraction

Data were extracted by two investigators using a predesigned form, including the following: author names, type of procedure, study inclusion and exclusion criteria, number of patients enrolled and randomized, baseline demographic characteristics, ASA classification,

induction dose of each drug, and outcome data. Only trials with extractable data were included. No additional information was requested from the study authors.

Quality and risk of bias assessment

The risk of bias (RoB) in randomized controlled trials was assessed using the Cochrane Collaboration tool to evaluate the quality of the included trials [20]. Disagreements in the assessment were resolved through discussion and consensus. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess the certainty of evidence for each outcome [21].

Data synthesis and analysis

For continuous outcomes, including patient satisfaction, induction time, and time to full consciousness, the mean difference (MD) corresponding to 95% credible intervals (CrIs) were calculated for the outcomes. Since the patient satisfaction measurement scales were not identical, the linear transformation was applied to convert the measurements to outcomes within the range of 0–10, and MD was calculated to estimate the overall study outcomes. All eligible RCTs were primarily analyzed. For dichotomous outcomes, including hypotension, bradycardia, and injection pain, relative risks (RR) and corresponding 95% CrIs were calculated. Statistical heterogeneity between trials was assessed using visual inspection of forest plots and the I^2 statistic. For continuous outcomes reported as median and interquartile range, the method of Shi et al. [22] was used to assess whether they conformed to a normal distribution. If they did, they were transformed into means and standard deviations according to this method [23, 24]. Data that did not meet the transformation requirements were excluded. No interpolation was performed on the data.

The feasibility of performing network meta-analyses for each outcome was assessed. When appropriate, Bayesian random-effects models were used to calculate direct effect estimates for different comparisons using the Markov Chain Monte Carlo (MCMC) method. The heterogeneity of the random-effects model was evaluated using the I^2 statistic. Convergence diagnostic plots, trajectory plots, and density plots were used to assess the stability and reliability of the MCMC simulation results. Cumulative probability ranking plots were generated, followed by the use of the Surface Under the Cumulative Ranking Curve (SUCRA) to explain the relative effectiveness of different interventions. Consistency assumptions were verified using node splitting [25].

A network diagram with nodes and lines was constructed to represent different interventions, where the size of the nodes represented the population size, and the thickness of the lines between the nodes indicated the number of studies.

The network structure was visualized using STATA software version 17.0. All analyses were performed using RStudio version 2024.04.2 +764, with the gemtc package version 1.0.2, which interfaces with the rjags package version 4.16 to execute MCMC simulations.

Results

Search results and study characteristics

A total of 83 records were identified, of which 56 were reviewed in full text. A total of 14 studies were excluded: six were excluded due to incompatibility with the study objectives [26–31], three were research protocols [32–34], four were registrations only, and one was unrelated to endoscopic surgery [35]. Finally, 42 RCTs were finally included, with a total sample size of n = 10,540. Among these, 31 studies compared propofol with remimazolam [36–66], 10 compared ciprofol with propofol [67–76], and one was a comparison of the three drugs (Fig. 1) [77]. The characteristics of the included trials were detailed in the table. Of these 42 studies, 31 were assessed as having a low RoB [36, 37, 39–41, 44–50, 69, 78], two as having a high RoB [51, 62], and the remainder as unclear RoB [38, 42, 43, 63, 65, 67, 68, 70, 73] (Fig. 2).

Primary outcomes

Respiratory adverse events

Respiratory adverse events, such as apnea, hypoxemia, and respiratory depression, were defined by the included studies. Figure 3A presents a forest plot of these findings. The forest plot showed that the RRs for respiratory adverse events for ciprofol and remimazolam, using propofol as the baseline, were 0.4800 (95% CrI [0.3200, 0.7000], moderate certainty) and 0.3600 (95% CrI [0.2800, 0.4600], high certainty), respectively. The p-value for the indirect comparison of remimazolam to ciprofol was greater than 0.05, indicating a high level of credibility in the network analysis results. The RR of remimazolam relative to ciprofol was 0.7600 (95% CrI [0.4800, 1.2000], moderate certainty), indicating no significant difference in respiratory adverse events. The probability ranking plot showed that remimazolam ranked first, with a probability of 0.8817 and an SUCRA value of 0.9408, whereas propofol ranked third, with a probability of 0.9995 and an SUCRA value of 0.0003 (Fig. 4).

Cardiac adverse events

Adverse reactions affecting the cardiovascular system included hypotension and bradycardia. The network diagram for this outcome is available in Fig. 5. The risk ratio (RR) for ciprofol relative to propofol was 0.7600 (95% CrI [0.5300, 1.1000], moderate certainty), whereas

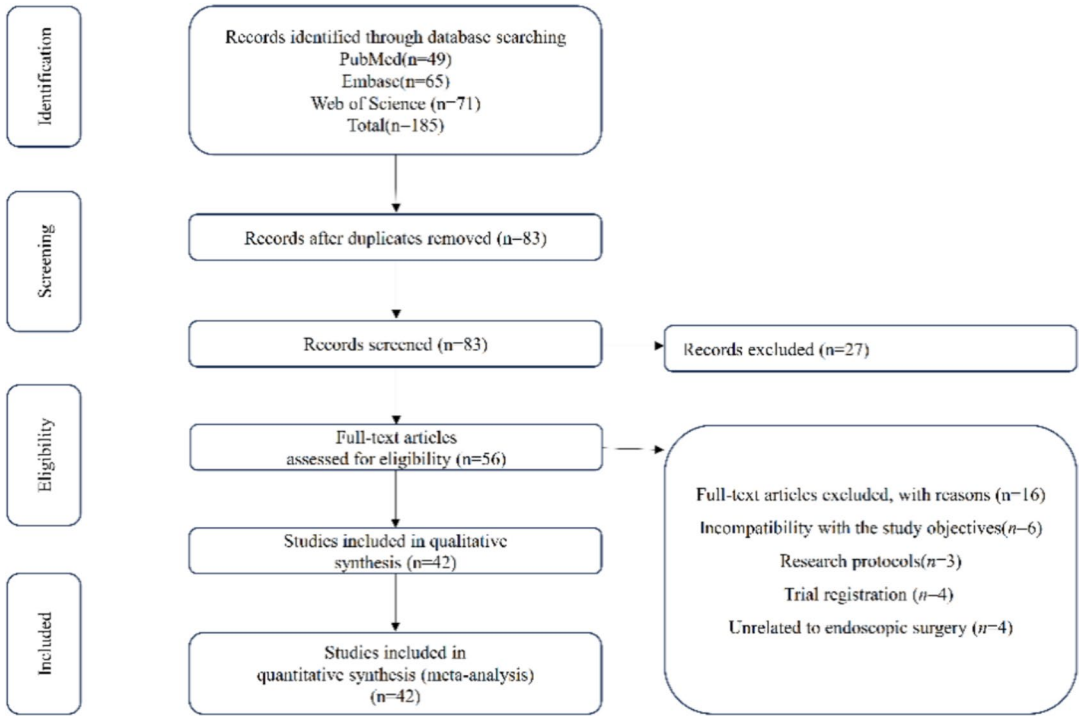

Fig. 1 Study Flow Chart

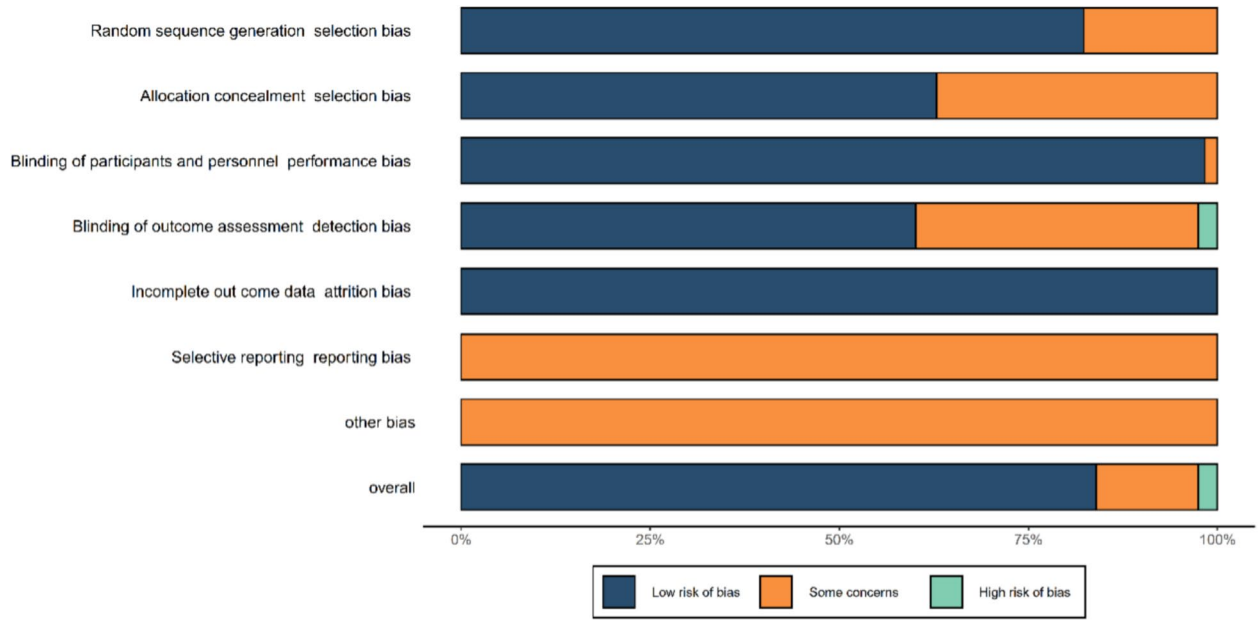

Fig. 2 Risk of Bias Summary Chart

that for remimazolam was 0.4400 (95% CrI [0.3500, 0.5500], moderate certainty). The network analysis indicated an RR of 0.5800 (95% CrI [0.3800, 0.8700], moderate certainty) for remimazolam compared with ciprofol, supported by higher-quality evidence (Fig. 3B). The probability that remimazolam would result in the fewest adverse events affecting the cardiovascular system was 0.9951. Propofol demonstrated a third-ranked probability

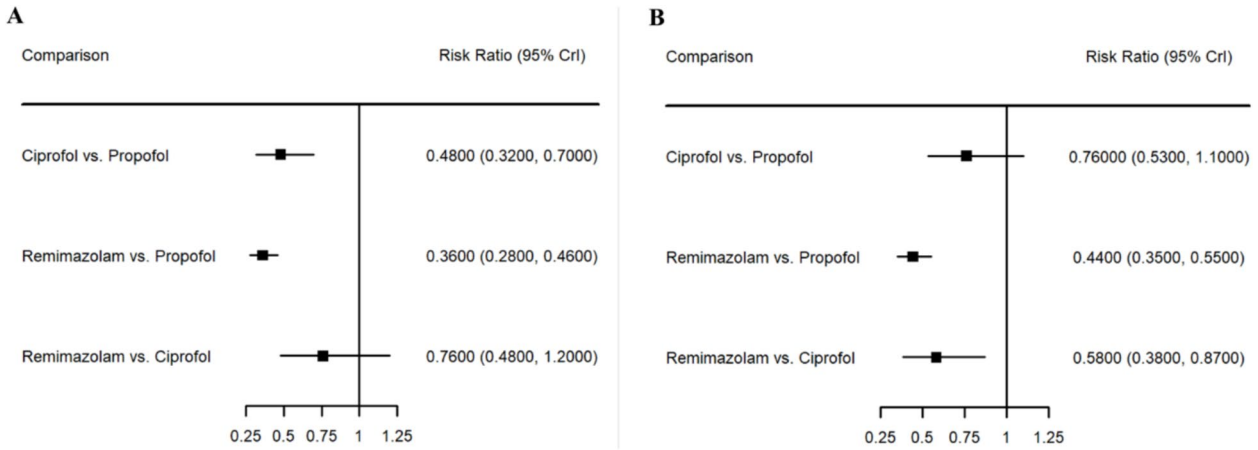

Fig. 3 **A** Forest Plot of Respiratory Adverse Events. **B** Forest Plot of Cardiac Adverse Events

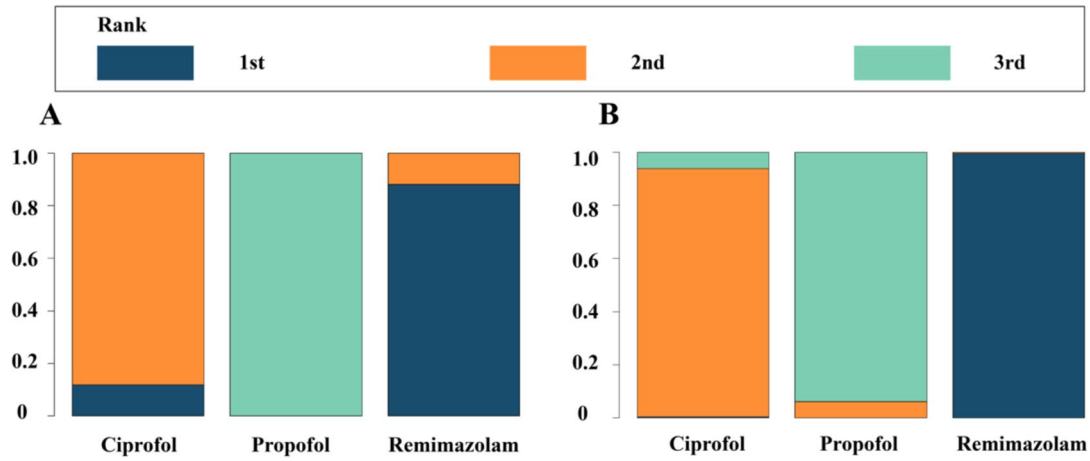

Fig. 4 **A** Cumulative Probability Distribution Diagram of Respiratory Adverse Events. **B** Cumulative Probability Distribution Diagram of Cardiac Adverse Events

of 0.9379 for inducing adverse events affecting the cardiovascular system, exceeding that for ciprofol and remimazolam (Fig. 4). The SUCRA values for remimazolam and ciprofol were 0.9976 and 0.4714, respectively.

Secondery outcomes

Induction time and sedation recovery time

Ciprofol demonstrated a relatively longer induction time than propofol (mean difference [MD] 0.2039 min longer, 95% CrI [−0.2177, 0.6284], low certainty). Similarly, remimazolam had a longer induction time compared to propofol (MD 0.1596 min longer, 95% CrI [−0.1428, 0.4576], high certainty). The mean difference (MD) for remimazolam was −0.0450 (95% CrI [−0.5700, 0.4700], low certainty) when compared to ciprofol, indicating a lower effect size in the indirect comparison of remimazolam with ciprofol (Fig. 3A). The probability that propofol had the fastest induction time was 0.7251, which was greater than 0.1509 for ciprofol and 0.1240 for remimazolam. The probability of ciprofol having the longest induction time among the three drugs was 0.5606, and the cumulative probability ranking plot is shown in Fig. 4. The SUCRA values for ciprofol, propofol, and remimazolam were 0.2951, 0.8504, and 0.3545, respectively, further supporting the cumulative probability results.

When comparing sedation recovery time, propofol had a significantly shorter time to full consciousness than ciprofol and remimazolam (MD reduction of 1.0271 min, 95% CrI [−0.5486, 2.6190], low certainty; MD reduction of 0.2382 min, 95% CrI [−0.8651, 1.3340], very low certainty). The indirect mean difference (MD) between remimazolam and ciprofol was 0.7900, with a 95% CrI of [−1.1000, 2.7000], with very low certainty (Fig. 3B). Propofol had the highest

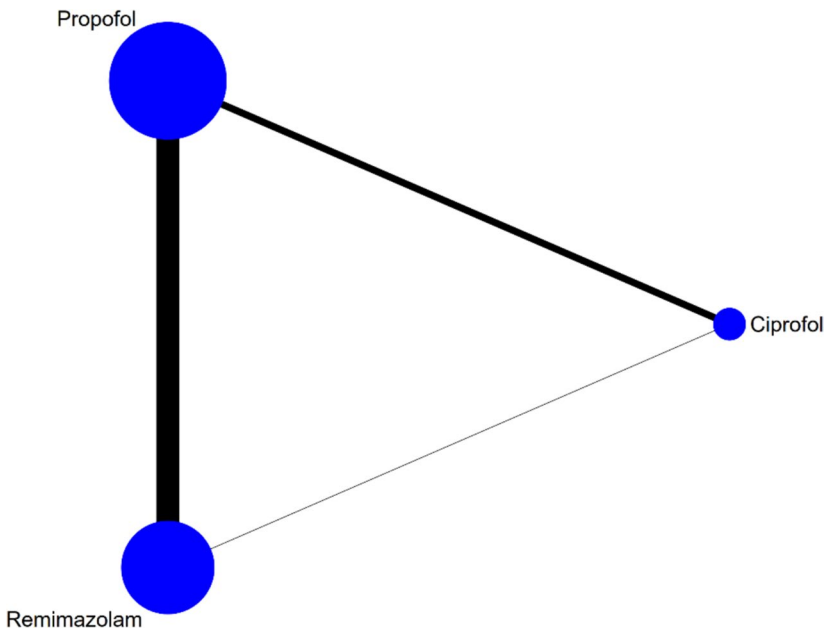

Fig. 5 Network map for Cardiac adverse events for x-node analysis. The size of the node corresponds to the number of patients randomised to that intervention. The thickness of the line and the associated numbers correspond to the number of studies comparing the two linked interventions

probability of the shortest awakening time among the three drugs, at 0.6088. The probability of ciprofol having the shortest awakening time was 0.0795, and remimazolam ranked first with a probability of 0.3117. Additionally, ciprofol had a higher probability of ranking third compared to both ciprofol and propofol, with a probability of 0.7834 (Fig. 4). The SUCRA values for the three drugs were 0.7885, 0.5634, and 0.1481, in descending order, indicating that propofol ranked first for the shortest time to full consciousness, while ciprofol ranked last.

Injection pain

Injection pain is a common adverse event associated with propofol. The probabilities of the three drugs, ciprofol, propofol, and remimazolam, causing the least injection pain were ranked as follows: remimazolam first at 0.5046, ciprofol second at 0.4955, and propofol third at 0. (Supplementary file). The SUCRA values of ciprofol, propofol, and remimazolam were 0.747725, 0.000000, and 0.752275, respectively. The RR for ciprofol versus propofol was 0.0550 (95% CrI [0.0130, 0.1600], low certainty). The RR for remimazolam versus propofol was 0.0540 (95% CrI [0.0190, 0.1200], high certainty). The RR for remimazolam versus ciprofol was 0.9900 (95% CrI [0.2400, 4.300], low certainty) (Supplementary file).

Gastrointestinal adverse events

The included studies defined gastrointestinal adverse events as nausea and vomiting. Ciprofol ranked first with the highest probability of causing the fewest nausea and vomiting events (0.8281) and a SUCRA value of 0.8668. Remimazolam ranked third with the greatest probability of 0.4940 and a SUCRA value of 0.3058 (Supplementary file). Using propofol as the reference, the RRs and 95% CrI for ciprofol and remimazolam were 0.7300 (95% CrI [0.4000, 1.3000], moderate certainty) and 1.0000 (95% CrI [0.7800, 1.5000], moderate certainty), respectively. The indirect RR for remimazolam relative to ciprofol was 1.400 (95% CrI [0.7700, 3.0000], moderate certainty) (Supplementary file).

Patient satisfaction

In a comparison of patient satisfaction, the MD for ciprofol versus propofol was 0.3610 (95% CrI [−0.4363, 1.1810], low certainty). The MD for remimazolam versus propofol was 0.3984 (95% CrI [−0.2070, 1.0240], very low certainty), whereas the indirect MD for remimazolam versus ciprofol was 0.0370 (95% CrI [−0.9800, 1.1000]), very low certainty (Supplementary file). The rank order of cumulative probability for patient satisfaction is shown in Supplementary file, with remimazolam having the greatest probability of ranking first at 0.5230. Propofol ranked third with a probability of 0.7648, which was higher than that for ciprofol (0.1609)

and remimazolam (0.0743). Remimazolam ranked second with a probability of 0.4027, exceeding the second-ranking probabilities of both ciprofol and propofol (Supplementary file). The SUCRA values for propofol, ciprofol, and remimazolam were 0.1258, 0.6498, and 0.7243, respectively.

Other adverse events

Other common adverse reactions include body movements, dizziness, and cough. The three drugs, ciprofol, propofol, and remimazolam, had the highest safety-ranked probabilities of 0.7541, 0.1343, and 0.1116, respectively. The third-ranked probability for remimazolam was the highest at 0.6115, indicating a higher probability of body movements compared to the other two (Fig. 4). Compared with propofol, ciprofol and remimazolam had relative risks (RRs) of 0.7000 (95% CrI: 0.3000–1.600) and 1.100 (95% CrI: 0.7100–1.9000), respectively, with moderate certainty for ciprofol and very low certainty for remimazolam. The indirect relative risk (RR) of body movement for remimazolam compared with ciprofol was 1.6000, with a 95% CrI of 0.5700–4.7000, and the evidence was rated as very low certainty (Supplementary file).

According to the probability plot, the probability of remimazolam being safer than the other two drugs in causing dizziness is the highest, at 0.7900. The probability of propofol causing postoperative dizziness is 0.6677, indicating that compared to the other two drugs, propofol is more likely to cause dizziness (Supplementary file). The indirect comparison p-value for remimazolam versus ciprofol is 0.9031, suggesting that the result obtained through network analysis is reliable. The specific value was RR 0.6800 with a 95% CrI of [0.2400, 1.800], which is rated as low certainty (Supplementary file).

When comparing the adverse effects of cough, ciprofol demonstrated the highest safety probability of 0.6091, which was greater than those of propofol at 0.2621 and remimazolam at 0.1289. Remimazolam was ranked third, indicating that it was more likely to induce cough compared to both ciprofol and propofol, with a probability value of 0.6339 (Supplementary file). Compared with propofol, the relative risks (RRs) of ciprofol and remimazolam were 0.7000 (95% CrI: 0.0910–5.4000) and 1.6000 (95% CrI: 0.4500–7.6000), respectively, with the evidence graded as high certainty for ciprofol and very low certainty for remimazolam. The figure showed that remimazolam had an RR of 2.2000 for the occurrence of cough compared to ciprofol, with a 95% CrI ranging from 0.2200 to 31.00. The certainty of the evidence was rated as very low (Supplementary file).

Discussion

This systematic review and network meta-analysis summarized the strengths and weaknesses of the three sedative drugs. Specifically, propofol was found to have the shortest induction and awakening times, although it was associated with a higher incidence of cardiovascular and respiratory adverse effects and was linked to postoperative dizziness, gastrointestinal adverse effects, and lower patient satisfaction. Both remimazolam and ciprofol exhibited a higher safety profile than propofol. They significantly reduced the incidence of propofol injection pain and were associated with a lower incidence of cardiovascular and respiratory adverse effects. Remimazolam was associated with fewer cardiovascular and respiratory events than ciprofol and significantly reduced the incidence of bradycardia. However, remimazolam was linked to an increased incidence of cough and body movements.

The duration of patient recovery from PSA is significant from a resource utilization perspective, as close monitoring is required until full recovery is achieved. According to the results of the network meta-analysis, propofol demonstrated superior performance in induction and postoperative awakening times, having the shortest induction time and enabling a faster awakening process. However, these differences were not statistically significant, with minimal differences observed between groups. Therefore, selecting propofol solely based on time and resource considerations may not be advisable. The results of this study indicate that remimazolam has the longest induction time. A longer induction time may require extra time for patient preparation and monitoring. In clinical practice, it is essential to continuously assess the level of consciousness in patients undergoing PSA. This ongoing evaluation is important for monitoring the patient's physiological status and ensuring that anesthesia is adequate [79].

Based on safety considerations during patient examinations, remimazolam may be the preferred choice for patients with compromised airway conditions, those undergoing respiratory endoscopy, and patients requiring sedation with cardiovascular disorders (e.g., critically ill patients). The current meta-analysis also concluded that propofol has a higher risk of respiratory depression compared to remimazolam [18]. Propofol, being strongly linked to respiratory and cardiovascular events, should be avoided in patients with respiratory or cardiovascular complications [80, 81]. These observations may be due to cardiorespiratory inhibition caused by the effect of propofol on central chemoreceptor sensitivity [82]. Although benzodiazepines may cause hypotension, combining sedative drugs has been shown to reduce single-drug doses, thereby potentially mitigating adverse effects [1].

In terms of gastrointestinal adverse reactions, ciprofol demonstrated the lowest incidence, followed by remimazolam, while propofol exhibited the highest rate. Based on this analysis, propofol may be considered more suitable for PSA in patients undergoing gastrointestinal endoscopy or those with pre-existing gastrointestinal conditions. However, it is important to note that this comparison did not reach statistical significance, underscoring the necessity for further research to identify the optimal sedative for gastrointestinal endoscopic procedures.

The findings also revealed that both remimazolam and ciprofol significantly reduced the incidence of injection pain. In particular, our results indicated that remimazolam had a significantly lower incidence of injection pain compared to propofol with high certainty. This may be due to the short metabolic half-life of remimazolam, reduced local and in vivo accumulation, and decreased release of active metabolites [83]. Propofol injection pain (PIP) is a long-standing issue [84, 85]. It can cause discomfort, heightened tension, anxiety, and other unpleasant experiences, as well as induce body movements and symptoms that hinder the successful completion of endoscopy [86]. No significant differences were found between remimazolam and propofol in indirect comparisons. Therefore, both drugs may be suitable options for minimizing injection pain. It is important to acknowledge that the decrease in injection pain can significantly enhance the patient experience during anesthesia induction. However, it should be noted that this advantage was not seen at higher doses of ciprofol, suggesting that the effect is dose-dependent [79].

However, remimazolam may lead to higher rates of cough and body movements. Our research indicated that when comparing the adverse effects of cough, the RR of ciprofol was 0.70 (95% CrI: 0.091–5.4) compared with propofol, with the evidence graded as high certainty. Our study was the first meta-analysis to observe that ciprofol had a lower incidence of cough compared to propofol. Due to the gastroscopy or bronchoscopy will be performed in the throat area, sudden unexpected cough may cause damage to unwanted tissues or nerves, which may be difficult to predict[87], it is crucial to constantly monitor any reactions of the patient during the PSA. However, propofol exhibited the highest incidence of neurological adverse effects, such as post-examination dizziness. These differences were not statistically significant, and no studies have reported serious neurological complications associated with any of the three drugs. As a benzodiazepine, greater consideration should be given to the possibility that remimazolam may induce paradoxical reactions [88]. A study on dream induction reported that two patients experienced unpleasant dreams with remimazolam use[77]. While this result does not significantly affect the overall comparison, attention should still be given to patient experience and neurological symptoms, particularly in patients with pre-existing conditions. Reducing benzodiazepine use may improve sedation comfort in such cases.

In terms of patient satisfaction, propofol achieved the lowest scores. Although these differences did not reach statistical significance, they may be related to the higher incidence of propofol-induced adverse reactions, such as injection pain, gastrointestinal discomfort, and dizziness, potentially contributing to lower patient satisfaction and a less favorable sedation experience.

All in all, based on our findings, we propose the following clinical recommendations: For high-risk respiratory patients (e.g., COPD, OSA), remimazolam is preferred due to its significantly lower risk of respiratory depression (RR = 0.36 vs propofol; Fig. 6B), This result aligns with current European guidelines[89], which emphasize the need for careful evaluation of cardiovascular and respiratory risk factors before elective procedures. Similarly, for cardiovascular-compromised patients (e.g., heart failure, hypotension), remimazolam demonstrates superior safety with a 56% reduction in bradycardia risk (RR = 0.44). Therefore, perhaps in staffing models where an anesthesiologist is not available, remimazolam might be the safest option. In gastrointestinal endoscopic procedures, ciprofol emerges as the optimal choice given its favorable gastrointestinal tolerance profile (SUCRA = 0.8475). For injection pain-sensitive patients, either remimazolam or ciprofol is recommended, both showing dramatically reduced incidence compared to propofol (RR = 0.045). These evidence-based selections should be tailored to individual patient characteristics and procedural requirements. Based on patient-specific characteristics, we recommend the following medication protocols: For elderly patients (> 65 years), remimazolam (0.1–0.2 mg/kg) is recommended with titrated administration to avoid drug accumulation[56]. Obese patients (BMI $\geq$30) should receive ciprofol (0.4 mg/kg) with halved initial doses and close monitoring for respiratory depression[69]. For patients with hepatic impairment, remimazolam requires no dose adjustment due to its metabolism by tissue esterases.

However, the interpretation of our findings must consider several key factors: 1) Protocol heterogeneity: Variability in sedation protocols (e.g., adjuvant opioids, monitoring standards) may explain the wide CrIs for recovery times (Fig. 3B). 2) Dose–response ambiguity: While remimazolam reduced injection pain (RR = 0.045), dose-dependent effects were rarely analyzed—higher doses may attenuate this benefit. 3) Population generalizability: Exclusion of high-risk subgroups (e.g., ASA

III-IV) limits applicability to real-world endoscopic settings. 4) Indirect comparison limitations: The single direct trial comparing remimazolam and ciprofol necessitates cautious interpretation of their relative rankings. Future research directions should include: RCTs directly comparing remimazolam and ciprofol (currently only 1 study [78]); Dose optimization studies for special populations (particularly pediatric, obese patients); Comprehensive evaluation of long-term cognitive impacts.

Limitations of this study include the low incidence of adverse reactions and the difficulty in including special groups, such as underage and obese patients, due to an insufficient sample size. This limits generalizability to these populations. Future studies should prioritize inclusion of diverse cohorts to validate our findings. Secondly, although sedation protocols standardized MOAA/S ≤ 3 as the target depth, variability in drug dosing and monitoring practices across studies may have influenced complication rates. While stratified analyses showed no significant interaction between sedation depth and adverse events ($p > 0.05$), residual confounding cannot be entirely excluded. The use of different criteria for defining adverse reactions may result in biased statistical outcomes. Therefore, more case reports and scoping reviews are needed to explore and standardize the criteria for defining adverse reactions. Thirdly, while indirect comparisons of remimazolam and ciprofol could reduce heterogeneity, further studies are necessary to directly compare the sedative effects of both drugs in endoscopy. Forthly, our protocol excluded studies comparing combination regimens (e.g., remimazolam + opioids). Consequently, we could not evaluate synergistic effects or safety profiles of polypharmacy, which is common in clinical practice. This gap underscores the need for future RCTs to assess combination strategies. Fively, variations in dosing regimens (e.g., remimazolam 0.1–0.4 mg/kg) across trials may have introduced heterogeneity. We attempted to mitigate this by pooling standardized mean doses, but residual variability in pharmacokinetic responses remains a concern. Last but not least, the safety and efficacy of sedatives are sometimes dose-dependent, and future research requires larger sample sizes and more dose subgroup analyses.

Conclusion

In summary, this network meta-analysis demonstrates that remimazolam significantly reduces cardiovascular risk by 56% compared to propofol while maintaining comparable recovery times, making it a safer alternative for high-risk patients. Furthermore, ciprofol exhibits superior gastrointestinal safety, positioning it as the optimal choice for prolonged endoscopic procedures requiring extended sedation. Importantly, these findings underscore that drug selection should be guided by individualized patient risk profiles—prioritizing remimazolam for cardiovascular/respiratory compromise, ciprofol for gastrointestinal-focused interventions, and propofol for rapid-turnover settings in low-risk populations.

Abbreviations

AE	Adverse Event
ASA	American Society of Anesthesiologists
CrI	Credible Interval
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
MCMC	Markov Chain Monte Carlo
MD	Mean Difference
MOAA/S	Modified Observer's Assessment of Alertness/Sedation Scale
PIP	Propofol Injection Pain
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Procedural Sedation and Analgesia
RCT	Randomized Controlled Trial
RoB	The Risk of Bias
RR	Relative Risks
STATA	Statistical Analysis System
SUCRA	Surface Under the Cumulative Ranking Curve

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-03108-9.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Acknowledgements
Not applicable.

Authors' contributions
Conceptualization and methodology: A-JX, S-QZ, S-CY Investigation and project administration: S-QZ, S-CY, YB, R-CP, TQ-Y, J-BD Supervision: A-JX Formal analysis and data curation: S-QZ, S-CY, YB, R-CP, TQ-Y, J-BD Writing-original draft: S-QZ, S-CY Writing—Review & Editing: A-JX, S-CY All authors reviewed the final manuscript. Zhou and Yu contributed equally.

Funding
The study did not receive any funding.

Data availability
All data generated during this study are included in this published article. Available upon request from the corresponding author at ajxu@tjh.tjmu.edu.cn.

Declarations

Ethics approval and consent to participate
The study was registered with the UK National Institute for Health Research's PROSPERO platform (CRD42024569405;https://www.crd.york.ac.uk/prospero/).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 6 January 2025 Accepted: 30 April 2025
Published online: 08 May 2025

References

1. Sharif S, et al. "Pharmacological agents for procedural sedation and analgesia in the emergency department and intensive care unit: a systematic review and network meta-analysis of randomised trials," (in eng). Br J Anaesth. 2024;132(3):491–506. https://doi.org/10.1016/j.bja.2023.11.050.
2. Stogiannou D, Protopapas A, Protopapas A, Tziomalos K. "Is propofol the optimal sedative in gastrointestinal endoscopy?," (in eng). Acta Gastroenterol Belg. 2018;81(4):520–4.
3. Zhang F, Sun HR, Zheng ZB, Liao R, Liu J. "Dexmedetomidine versus midazolam for sedation during endoscopy: A meta-analysis," (in eng). Exp Ther Med. 2016;11(6):2519–24. https://doi.org/10.3892/etm.2016.3186.
4. Kalsotra S, Khan S, McKee C, Tobias JD. "Remimazolam as the Primary Agent for Sedation During Cardiac Catheterization in Three Patients With Comorbid Cardiac Conduction Abnormalities," (in eng). Cardiol Res. 2023;14(1):86–90. https://doi.org/10.14740/cr1477.
5. Kothari D, et al. "An open-access endoscopy screen correctly and safely identifies patients for conscious sedation," (in eng). Gastroenterol Rep (Oxf). 2016;4(4):281–6. https://doi.org/10.1093/gastro/gow020.
6. Ootaki C, et al. "Does general anesthesia increase the diagnostic yield of endoscopic ultrasound-guided fine needle aspiration of pancreatic masses?," (in eng). Anesthesiology. 2012;117(5):1044–50. https://doi.org/10.1097/ALN.0b013e31826e0590.
7. Gepts E, Camu F, Cockshott ID, Douglas EJ. "Disposition of propofol administered as constant rate intravenous infusions in humans," (in eng). Anesth Analg. 1987;66(12):1256–63.
8. Vree TB, Lagerwerf AJ, Bleeker CP, de Grood PM. "Direct high-performance liquid chromatography determination of propofol and its metabolite quinol with their glucuronide conjugates and preliminary pharmacokinetics in plasma and urine of man," (in eng). J Chromatogr B Biomed Sci Appl. 1999;721(2):217–28. https://doi.org/10.1016/s0378-4347(98)00466-6.
9. Dong H, et al. "Evaluating Propofol Concentration in Blood From Exhaled Gas Using a Breathing-Related Partition Coefficient," (in eng). Anesth Analg. 2020;130(4):958–66. https://doi.org/10.1213/ane.0000000000004225.
10. X. Zhu et al., "Efficacy and Safety of Remimazolam in Endoscopic Sedation-A Systematic Review and Meta-Analysis," (in eng), Front Med (Lausanne), vol. 8, p. 655042, 2021, https://doi.org/10.3389/fmed.2021.655042.
11. Wang X, et al. "Safety and efficacy of remimazolam besylate in patients undergoing colonoscopy: A multicentre, single-blind, randomized, controlled, phase III trial," (in eng). Front Pharmacol. 2022;13: 900723. https://doi.org/10.3389/fphar.2022.900723.
12. Huang L, Liu H, Zou X, Ding J, Tao S. "Adverse Drug Events Observed with the Newly Approved Remimazolam in Comparison to Propofol for General Anesthesia in Patients Undergoing Surgery: A Meta-analysis," (in eng). Adv Ther. 2024;41(5):1896–910. https://doi.org/10.1007/s12325-024-02820-1.
13. Zhu H, et al. "Remimazolam Dosing for Gastroscopy: A Randomized Noninferiority Trial," (in eng). Anesthesiology. 2024;140(3):409–16. https://doi.org/10.1097/aln.0000000000004851.
14. Bian Y, et al. "Mass balance, pharmacokinetics and pharmacodynamics of intravenous HSK3486, a novel anaesthetic, administered to healthy subjects," (in eng). Br J Clin Pharmacol. 2021;87(1):93–105. https://doi.org/10.1111/bcp.14363.
15. Chen X, Guo P, Yang L, Liu Z, Yu D. "Comparison and Clinical Value of Ciprofol and Propofol in Intraoperative Adverse Reactions, Operation, Resuscitation, and Satisfaction of Patients under Painless Gastroenteroscopy Anesthesia," (in eng). Contrast Media Mol Imaging. 2022;2022:9541060. https://doi.org/10.1155/2022/9541060.
16. Li J, et al. "Comparison of ciprofol (HSK3486) versus propofol for the induction of deep sedation during gastroscopy and colonoscopy procedures: A multi-centre, non-inferiority, randomized, controlled phase 3 clinical trial," (in eng). Basic Clin Pharmacol Toxicol. 2022;131(2):138–48. https://doi.org/10.1111/bcpt.13761.
17. J. Liu, A. Hong, J. Zeng, and X. Liang, "The efficacy of ciprofol versus propofol on anesthesia in patients undergoing endoscopy: a systematic review and meta-analysis of randomized controlled trials," (in eng), BMC Anesthesiol, vol. 24, no. 1, p. 359, Oct 8 2024, https://doi.org/10.1186/s12871-024-02721-4.
18. Zhao MJ, Hu HF, Li XL, Li XM, Wang DC, Kuang MJ. "The safety and efficacy between remimazolam and propofol in intravenous anesthesia of endoscopy operation: a systematic review and meta-analysis," (in eng). Int J Surg. 2023;109(11):3566–77. https://doi.org/10.1097/js9.0000000000000638.
19. Hutton B, et al. "The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations," (in eng). Ann Intern Med. 2015;162(11):777–84. https://doi.org/10.7326/m14-2385.
20. J. P. Higgins et al., "The Cochrane Collaboration's tool for assessing risk of bias in randomised trials," (in eng), Bmj, vol. 343, p. d5928, Oct 18 2011, https://doi.org/10.1136/bmj.d5928.
21. Brignardello-Petersen R, et al. "Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis," (in eng). J Clin Epidemiol. 2018;93:36–44. https://doi.org/10.1016/j.jclinepi.2017.10.005.
22. Shi J, et al. "Detecting the skewness of data from the five-number summary and its application in meta-analysis," (in eng). Stat Methods Med Res. 2023;32(7):1338–60. https://doi.org/10.1177/09622802231172043.
23. Luo D, Wan X, Liu J, Tong T. "Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range," (in eng). Stat Methods Med Res. 2018;27(6):1785–805. https://doi.org/10.1177/0962280216669183.
24. X. Wan, W. Wang, J. Liu, and T. Tong, "Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range," (in eng), BMC Med Res Methodol, vol. 14, p. 135, Dec 19 2014, https://doi.org/10.1186/1471-2288-14-135.
25. Dias S, Welton NJ, Caldwell DM, Ades AE. "Checking consistency in mixed treatment comparison meta-analysis," (in eng). Stat Med. 2010;29(7–8):932–44. https://doi.org/10.1002/sim.3767.
26. Rex DK, Bhandari R, Lorch DG, Meyers M, Schippers F, Bernstein D. Safety and efficacy of remimazolam in high risk colonoscopy: A randomized trial. Digestive and Liver Disease, Article. 2021;53(1):94–101. https://doi.org/10.1016/j.dld.2020.10.039.
27. Xiao X, Xiao N, Zeng F, Chen H, Zhang L, He X. "Gastroscopy sedation: clinical trial comparing propofol and sufentanil with or without remimazolam," (in eng). Minerva Anestesiol. 2022;88(4):223–9. https://doi.org/10.23736/s0375-9393.21.15917-6.
28. J. Hu et al., "Comparison of anesthetic effects of different doses of alfentanil combined with ciprofol in elderly patients undergoing ERCP: a randomized controlled trial," (in eng), BMC Anesthesiol, vol. 23, no. 1, p. 353, Oct 31 2023, https://doi.org/10.1186/s12871-023-02325-4.
29. Lyu S, Deng Q, Lin W, Wu X. "Randomized controlled trial for anesthesia during gastroscopy: interactions between remimazolam and propofol in combination with sufentanil," (in eng). Int J Clin Pharm. 2023;45(4):857–63. https://doi.org/10.1007/s11096-023-01568-y.
30. X. Wu, L. Zeng, T. Zhang, W. Wu, Y. Tian, and S. Dong, "The study of different dosages of remazolam combined with sufentanil and propofol on painless gastroscopy: A randomized controlled trial," Medicine, Article vol. 102, no. 34, Aug 25 2023, Art no. e34731, https://doi.org/10.1097/md.0000000000034731.
31. R. Yuan et al., "Efficacy of pretreatment with remimazolam on prevention of propofol-induced injection pain in patients undergoing gastroscopy," (in eng), Sci Rep, vol. 13, no. 1, p. 19683, Nov 11 2023, https://doi.org/10.1038/s41598-023-47151-3.
32. Long YQ, et al. Esketamine as an Adjuvant to Ciprofol or Propofol Sedation for Same-Day Bidirectional Endoscopy: Protocol for a Randomized, Double-Blind, Controlled Trial With Factorial Design. Front Pharmacol. 2022;13: 821691. https://doi.org/10.3389/fphar.2022.821691.
33. L. Yan, X. Wang, Z. Chen, N. Wu, H. Li, and B. Yang, "Safety and efficacy of remimazolam tosilate combined with low-dose fentanyl for procedural sedation in obese patients undergoing gastroscopy: study protocol for a single-centre, double-blind, randomised controlled trial," Bmj Open, Article vol. 13, no. 12, Dec 2023, Art no. e079095, https://doi.org/10.1136/bmjopen-2023-079095.
34. Z. Li et al., "Effect of remimazolam vs propofol in high-risk patients undergoing upper gastrointestinal endoscopy: a non-inferiority randomized controlled trial," (in eng), Trials, vol. 25, no. 1, p. 92, Jan 27 2024, https://doi.org/10.1186/s13063-024-07934-z.

35. Yue L, et al. Remimazolam versus propofol in combination with esketamine for surgical abortion: A double-blind randomized controlled trial. Cts-Clinical and Translational Science, Article. 2023;16(9):1606–16. https://doi.org/10.1111/cts.13572.
36. Chen S-H, et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. Journal of Gastroenterology and Hepatology, Article. 2021;36(2):474–81. https://doi.org/10.1111/jgh.15188.
37. Liu X, et al. "The Efficacy and Safety of Remimazolam Tosilate versus Etomidate-Propofol in Elderly Outpatients Undergoing Colonoscopy: A Prospective, Randomized, Single-Blind, Non-Inferiority Trial," (in eng). Drug Des Devel Ther. 2021;15:4675–85. https://doi.org/10.2147/dddt.S339535.
38. X. Zhang, S. Li, and J. Liu, "Efficacy and safety of remimazolam besylate versus propofol during hysteroscopy: single-centre randomized controlled trial," (in eng), BMC Anesthesiol, vol. 21, no. 1, p. 156, May 20 2021, https://doi.org/10.1186/s12871-021-01373-y.
39. Cao Y, Chi P, Zhou C, Lv W, Quan Z, Xue FS. Remimazolam Tosilate Sedation with Adjuvant Sufentanil in Chinese Patients with Liver Cirrhosis Undergoing Gastroscopy: a Randomized Controlled Study. Medical science monitor, Journal article. 2022;28: e936580. https://doi.org/10.12659/MSM.936580.
40. Guo L, Liu T, Zhang Y, Qi D. Effect of remimazolam versus propofol sedation on the quality of recovery after colonoscopy A randomised, controlled, noninferiority trial. European Journal of Anaesthesiology, Letter. 2022;39(12):953–5. https://doi.org/10.1097/eja.0000000000001701.
41. Hu B, et al. "Effect of Remimazolam Tosilate on Respiratory Depression in Elderly Patients Undergoing Gastroscopy: A Multicentered, Prospective, and Randomized Study," (in eng). Drug Des Devel Ther. 2022;16:4151–9. https://doi.org/10.2147/dddt.S391147.
42. Lu K, et al. Remimazolam versus propofol for deep sedation/anaesthesia in upper gastrointestinal endoscopy in elderly patients: a multicenter, randomized controlled trial. Journal of clinical pharmacy and therapeutics, Journal article. 2022;47(12):2230–6. https://doi.org/10.1111/jcpt.13797.
43. Shi W, et al. Efficacy and Safety of the Remimazolam-Alfentanil Combination for Sedation During Gastroscopy: a Randomized, Double-Blind, Single-Center Controlled Trial. Clinical therapeutics, Journal article. 2022;44(11):1506–18. https://doi.org/10.1016/j.clinthera.2022.09.014.
44. Tan Y, Ouyang W, Tang Y, Fang N, Fang C, Quan C. "Effect of remimazolam tosilate on early cognitive function in elderly patients undergoing upper gastrointestinal endoscopy," (in eng). J Gastroenterol Hepatol. 2022;37(3):576–83. https://doi.org/10.1111/jgh.15761.
45. Xu C, et al. "Efficacy and Safety of Remimazolam Besylate Combined with Alfentanil in Painless Gastroscopy: A Randomized, Single-Blind, Parallel Controlled Study," (in eng). Contrast Media Mol Imaging. 2022;2022:7102293. https://doi.org/10.1155/2022/7102293.
46. Yao Y, Guan J, Liu L, Fu B, Chen L, Zheng X. "Discharge readiness after remimazolam versus propofol for colonoscopy: A randomised, double-blind trial," (in eng). Eur J Anaesthesiol. 2022;39(12):911–7. https://doi.org/10.1097/eja.0000000000001715.
47. Zhang F, Chang H, Qing W, Yu R, Liao Q, Tong J. "Remimazolam Tosylate Combined with Low-Dose Propofol Improves Sedation and Safety in Hysteroscopy," (in eng). Drug Des Devel Ther. 2022;16:4101–8. https://doi.org/10.2147/dddt.S390403.
48. Zhang S, Wang J, Ran R, Peng Y, Xiao Y. "Efficacy and safety of remimazolam tosylate in hysteroscopy: A randomized, single-blind, parallel controlled trial," (in eng). J Clin Pharm Ther. 2022;47(1):55–60. https://doi.org/10.1111/jcpt.13525.
49. X. Cui et al., "Efficacy and Safety of Different Doses of Remimazolam Tosilate Applied in Upper Gastrointestinal Endoscopy: A Prospective Randomized Controlled Double-Blind Trial," Drug Design Development and Therapy, Article vol. 17, pp. 2889–2896, 2023 2023, https://doi.org/10.2147/dddt.S422531.
50. Dong SA, et al. A randomized, controlled clinical trial comparing remimazolam to propofol when combined with alfentanil for sedation during ERCP procedures. Journal of clinical anesthesia, Journal article. 2023;86: 111077. https://doi.org/10.1016/j.jclinane.2023.111077.
51. Gao S, Wang T, Cao L, Li L, Yang S. Clinical effects of remimazolam alone or in combination with dexmedetomidine in patients receiving bronchoscopy and influences on postoperative cognitive function: a randomized-controlled trial. International Journal of Clinical Pharmacy, Article. 2023;45(1):137–45. https://doi.org/10.1007/s11096-022-01487-4.
52. Lee J, Jeong S, Lee DH, Park JS. "Finding the ideal sedative: a non-inferiority study of remimazolam vs propofol in endoscopic retrograde cholangiopancreatography," (in eng). J Gastroenterol Hepatol. 2023;38(12):2160–6. https://doi.org/10.1111/jgh.16354.
53. Li W, et al. "The Efficacy and Safety of Remimazolam Besylate Combined with Esketamine for Outpatient Colonoscopy: A Prospective, Randomized, Controlled Clinical Trial," (in eng). Drug Des Devel Ther. 2023;17:2875–87. https://doi.org/10.2147/dddt.S425860.
54. L. Wang et al., "Cardiopulmonary Adverse Events of Remimazolam versus Propofol During Cervical Conization: A Randomized Controlled Trial," Drug Design Development and Therapy, Article vol. 17, pp. 1233–1243, 2023 2023, https://doi.org/10.2147/dddt.S405057.
55. Wei A, et al. "The safety and efficacy of remimazolam tosylate combined with propofol in upper gastrointestinal endoscopy: A multicenter, randomized clinical trial," (in eng). PLoS ONE. 2023;18(8): e0282930. https://doi.org/10.1371/journal.pone.0282930.
56. Ye E, et al. "Comparison of 95% effective dose of remimazolam besylate and propofol for gastroscopy sedation on older patients: A single-centre randomized controlled trial," (in eng). Br J Clin Pharmacol. 2023;89(11):3401–10. https://doi.org/10.1111/bcp.15839.
57. Zhang J, et al. "Comparison of Remimazolam and Propofol for Drug-Induced Sleep Endoscopy: A Randomized Clinical Trial," (in eng). Otolaryngol Head Neck Surg. 2023;169(5):1356–65. https://doi.org/10.1002/ohn.387.
58. Zhang L, Yu L, Xu L, Wang JF, Li JY, Chen ZJ. "Effectiveness of remimazolam besylate combined with alfentanil for fiberoptic bronchoscopy with preserved spontaneous breathing: a prospective, randomized, controlled clinical trial," (in eng). Eur Rev Med Pharmacol Sci. 2023;27(13):6071–80. https://doi.org/10.26355/eurrev_202307_32961.
59. D. Chen, M. Liao, X.-r. Wu, T.-y.-m. Zhao, and H. Sun, "Comparison of efficacy and safety of equivalent doses of remimazolam versus propofol for gastroscopy anesthesia in elderly patients," Scientific Reports, Article vol. 14, no. 1, Apr 1 2024, Art no. 7645, https://doi.org/10.1038/s41598-024-58294-2.
60. H.-y. Chen et al., "Comparison of the recovery time of remimazolam besylate and propofol for gastrointestinal endoscopy sedation in elderly patients," International Journal of Medical Sciences, Article vol. 21, no. 7, pp. 1250–1256, 2024 2024, https://doi.org/10.7150/ijms.93045.
61. J. W. Choe et al., "Safety and efficacy of remimazolam versus propofol during EUS: a multicenter randomized controlled study," Gastrointestinal Endoscopy, Article vol. 100, no. 2, pp. 183-+, Aug 2024, https://doi.org/10.1016/j.gie.2024.04.001.
62. B. Huang, N.-P. Li, G.-K. Tan, and N. Liang, "Effectiveness and safety of remimazolam combined with alfentanil in hysteroscopic examination: A prospective, randomized, single-blind trial," Medicine, Article vol. 103, no. 15, Apr 12 2024, Art no. e37627, https://doi.org/10.1097/md.0000000000037627.
63. Q. Sun, J. Cheng, W. Lei, X. Lu, Y. Huang, and J. Sun, "The effects of remimazolam combined with sufentanil on respiration, circulation and sedation level in patients undergoing colonoscopy," BMC anesthesiology, ; Randomized Controlled Trial vol. 24, no. 1, pp. 252–252, 2024 Jul 2024, https://doi.org/10.1186/s12871-024-02644-0.
64. Yang C, Jiao J, Nie Y, Shao W, Zhang H, Huang S. "Comparison of the bispectral indices of patients receiving remimazolam and propofol for general anesthesia: a randomized crossover trial," (in eng). Anaesth Crit Care Pain Med. 2024;43(3): 101377. https://doi.org/10.1016/j.accpm.2024.101377.
65. Zhang Q, Zhao R, Wu Y, Zhang L, Feng Y. "Etomidate Combined with Propofol versus Remimazolam for Sedation in Elderly Patients During Gastrointestinal Endoscopy: A Randomized Prospective Clinical Trial," (in eng). Drug Des Devel Ther. 2024;18:2681–02692. https://doi.org/10.2147/dddt.S454314.
66. Zhu H, et al. Remimazolam dosing for gastroscopy: a randomized noninferiority trial. Anesthesiology, Journal article. 2024;140(3):409–16. https://doi.org/10.1097/ALN.0000000000004851.
67. Y. Teng et al., "Efficacy and safety of ciprofol for the sedation/anesthesia in patients undergoing colonoscopy: Phase IIa and IIb multi-center clinical trials," Eur J Pharm Sci, vol. 164, p. 105904, Sep 1 2021, https://doi.org/10.1016/j.ejps.2021.105904.

68. X. Chen, P. Guo, L. Yang, Z. Liu, and D. Yu, "Comparison and Clinical Value of Ciprofol and Propofol in Intraoperative Adverse Reactions, Operation, Resuscitation, and Satisfaction of Patients under Painless Gastroenteroscopy Anesthesia," Contrast Media & Molecular Imaging, Article vol. 2022, Jul 18 2022, Art no. 9541060, https://doi.org/10.1155/2022/9541060.
69. Li J, et al. Comparison of ciprofol (HSK3486) versus propofol for the induction of deep sedation during gastroscopy and colonoscopy procedures: a multi-centre, non-inferiority, randomized, controlled phase 3 clinical trial. Basic & clinical pharmacology & toxicology, Journal article. 2022;131(2):138–48. https://doi.org/10.1111/bcpt.13761.
70. L. Chen et al., "The Effect of Different Doses of Ciprofol in Patients with Painless Gastrointestinal Endoscopy," Drug Design Development and Therapy, Article vol. 17, pp. 1733–1740, 2023 2023, https://doi.org/10.2147/dddt.S414166.
71. Lan H, et al. "Efficacy and Safety of Ciprofol for Sedation/Anesthesia in Patients Undergoing Hysteroscopy: A Randomized, Parallel-Group, Controlled Trial," (in eng). Drug Des Devel Ther. 2023;17:1707–17. https://doi.org/10.2147/dddt.S414243.
72. J. Liao et al., "Effect of ciprofol on swallowing function in patients undergoing painless gastrointestinal endoscopy," (in eng), Medicine (Baltimore), vol. 102, no. 35, p. e34422, Sep 1 2023, https://doi.org/10.1097/md.0000000000034422.
73. Zhong J, et al. Efficacy and safety of Ciprofol for procedural sedation and anesthesia in non-operating room settings. J Clin Anesth. 2023;85:111047. https://doi.org/10.1016/j.jclinane.2022.111047.
74. S.-H. Gao et al., "The efficacy and safety of ciprofol and propofol in patients undergoing colonoscopy: A double-blind, randomized, controlled trial," Journal of Clinical Anesthesia, Article vol. 95, Aug 2024, Art no. 111474, https://doi.org/10.1016/j.jclinane.2024.111474.
75. T. Li et al., "Effect of propofol and ciprofol on the euphoric reaction in patients with painless gastroscopy: A prospective randomized controlled trial," Heliyon, vol. 10, no. 9, p. e30378, May 15 2024, https://doi.org/10.1016/j.heliyon.2024.e30378.
76. Zhang J, et al. Comparison of ciprofol-alfentanil and propofol-alfentanil sedation during bidirectional endoscopy: A prospective, double-blind, randomised, controlled trial. Dig Liver Dis. 2024;56(4):663–71. https://doi.org/10.1016/j.dld.2023.09.016.
77. Zhou R, et al. Influences of Propofol, Ciprofol and Remimazolam on Dreaming During Anesthesia for Gastrointestinal Endoscopy: A Randomized Double-Blind Parallel-Design Trial. Drug Des Devel Ther. 2024;18:1907–15. https://doi.org/10.2147/DDDT.S455915.
78. !!! INVALID CITATION !!! .
79. Akhtar SMM, et al. "Efficacy and safety of Ciprofol compared with Propofol during general anesthesia induction: A systematic review and meta-analysis of randomized controlled trials (RCT)," (in eng). J Clin Anesth. 2024;94: 111425. https://doi.org/10.1016/j.jclinane.2024.111425.
80. Sidhu R, et al. "British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy," (in eng). Gut. 2024;73(2):219–45. https://doi.org/10.1136/gutjnl-2023-330396.
81. Schick A, Driver B, Moore JC, Fagerstrom E, Miner JR. "Randomized Clinical Trial Comparing Procedural Amnesia and Respiratory Depression Between Moderate and Deep Sedation With Propofol in the Emergency Department," (in eng). Acad Emerg Med. 2019;26(4):364–74. https://doi.org/10.1111/acem.13548.
82. Oka S, et al. "Sedation outcomes for remimazolam, a new benzodiazepine," (in eng). J Oral Sci. 2021;63(3):209–11. https://doi.org/10.2334/josnusd.21-0051.
83. Wesolowski AM, Zaccagnino MP, Malapero RJ, Kaye AD, Urman RD. "Remimazolam: Pharmacologic Considerations and Clinical Role in Anesthesiology," (in eng). Pharmacotherapy. 2016;36(9):1021–7. https://doi.org/10.1002/phar.1806.
84. K. A. Desousa, "Pain on propofol injection: Causes and remedies," (in eng), Indian J Pharmacol, vol. 48, no. 6, pp. 617–623, Nov-Dec 2016, https://doi.org/10.4103/0253-7613.194845.
85. P. J. Leff, B. A. Dinner, K. Y. Chuang, and D. B. Leff, "Characteristics that increase the risk for pain on propofol injection," (in eng), BMC Anesthesiol, vol. 24, no. 1, p. 190, May 28 2024, https://doi.org/10.1186/s12871-024-02573-y.
86. Miniksar OH, Yuksek A. "Effects of preoperative anxiety levels and the D-type personality on propolol injection pain," (in eng). North Clin Istanb. 2022;9(1):1–7. https://doi.org/10.14744/nci.2020.61214.
87. Togawa E, Hanamoto H, Maegawa H, Yokoe C, Niwa H. "Dexmedetomidine and Midazolam Sedation Reduces Unexpected Patient Movement During Dental Surgery Compared With Propofol and Midazolam Sedation," (in eng). J Oral Maxillofac Surg. 2019;77(1):29–41. https://doi.org/10.1016/j.joms.2018.07.002.
88. Jin EH, Song JH, Lee J, Bae JH, Chung SJ. "Midazolam dose is associated with recurrence of paradoxical reactions during endoscopy," (in eng). World J Clin Cases. 2021;9(29):8763–72. https://doi.org/10.12998/wjcc.v9.i29.8763.
89. M. Lamperti et al., "Preoperative assessment of adults undergoing elective noncardiac surgery: Updated guidelines from the European Society of Anaesthesiology and Intensive Care," (in eng), European Journal of Anaesthesiology, vol. 42, no. 1, 2025, https://doi.org/10.1097/EJA.0000000000002069.

Publisher's Note